

2023 Traumatic Brain Injury Center of Excellence Publications Catalog

The purpose of this document is to (1) summarize key findings and potential clinical implications of calendar year 2023 TBICoE publications, (2) increase awareness of TBICoE research and surveillance initiatives, and (3) assist in the planning of future brain health efforts. This document contains figures that visually categorize the publications, as well as publication citations, abstracts, and summaries, organized by category or primary topic as shown in the table of contents. Accompanying the abstracts are summaries of the potential clinical impact of the work and the associated lead and collaborative TBICoE Network sites (including HQ Research and Clinical Affairs).

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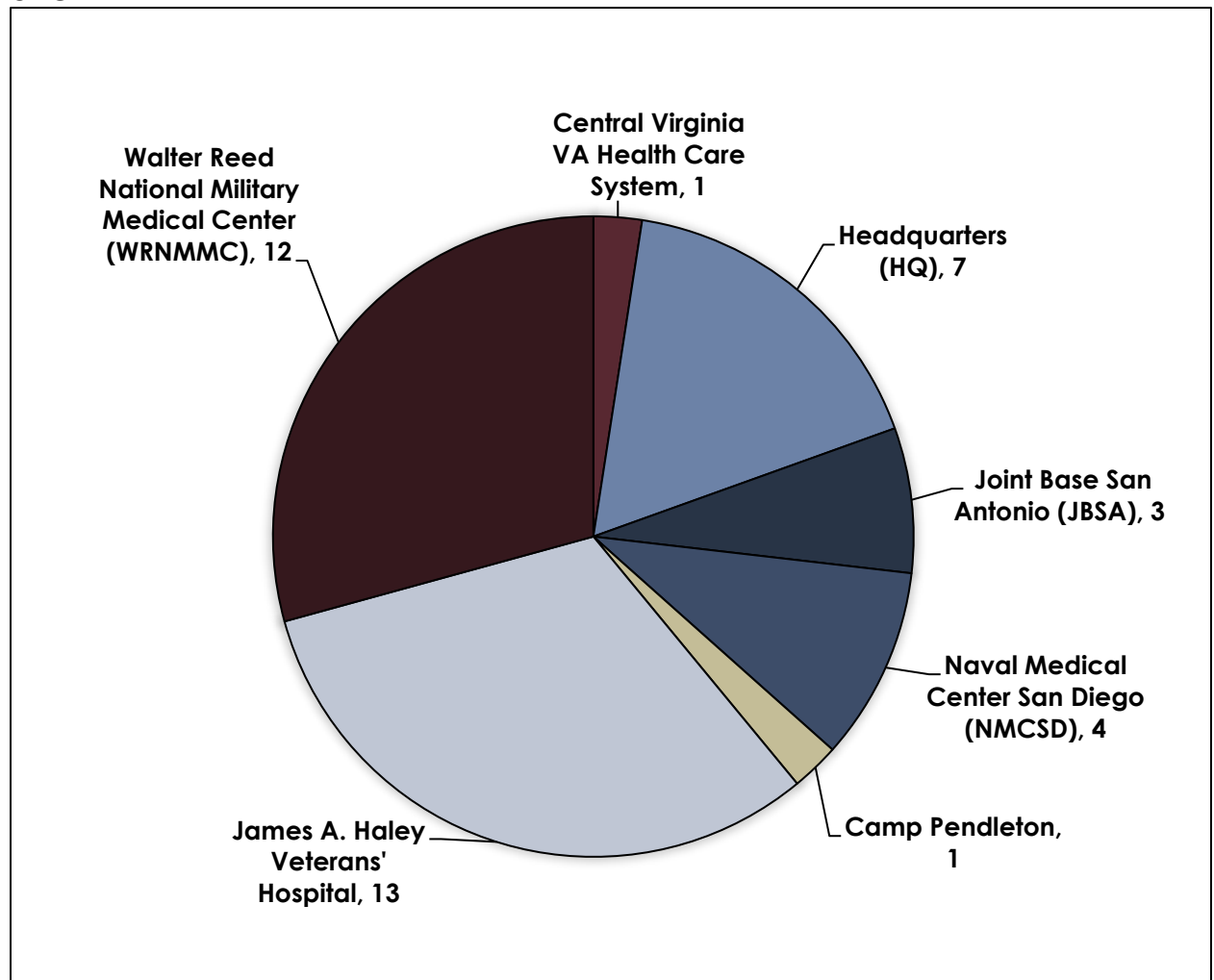
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PUBLICATION METRICS OVERVIEW

The metrics below reflect the 42 articles published by TBICoE in calendar year 2023, which highlight the distribution of articles by the publication month, TBI related categories/topics, research methods, and the annual number of TBICoE articles published over the past five years. Articles were also characterized by network site, TBICoE research portfolio study, the journals published in, and journal impact factor.

Figure 1: Number of TBICoE Articles Published in 2023 per Network Site



Notes: This metric exclusively considers lead network sites and incorporates publications involving multiple lead sites. The Central Virginia VA Health Care System, a site in Richmond, Virginia, is no longer part of the TBICoE research network.

Figure 2: Number of TBICoE Articles Published in 2023 per TBI-Related Topic

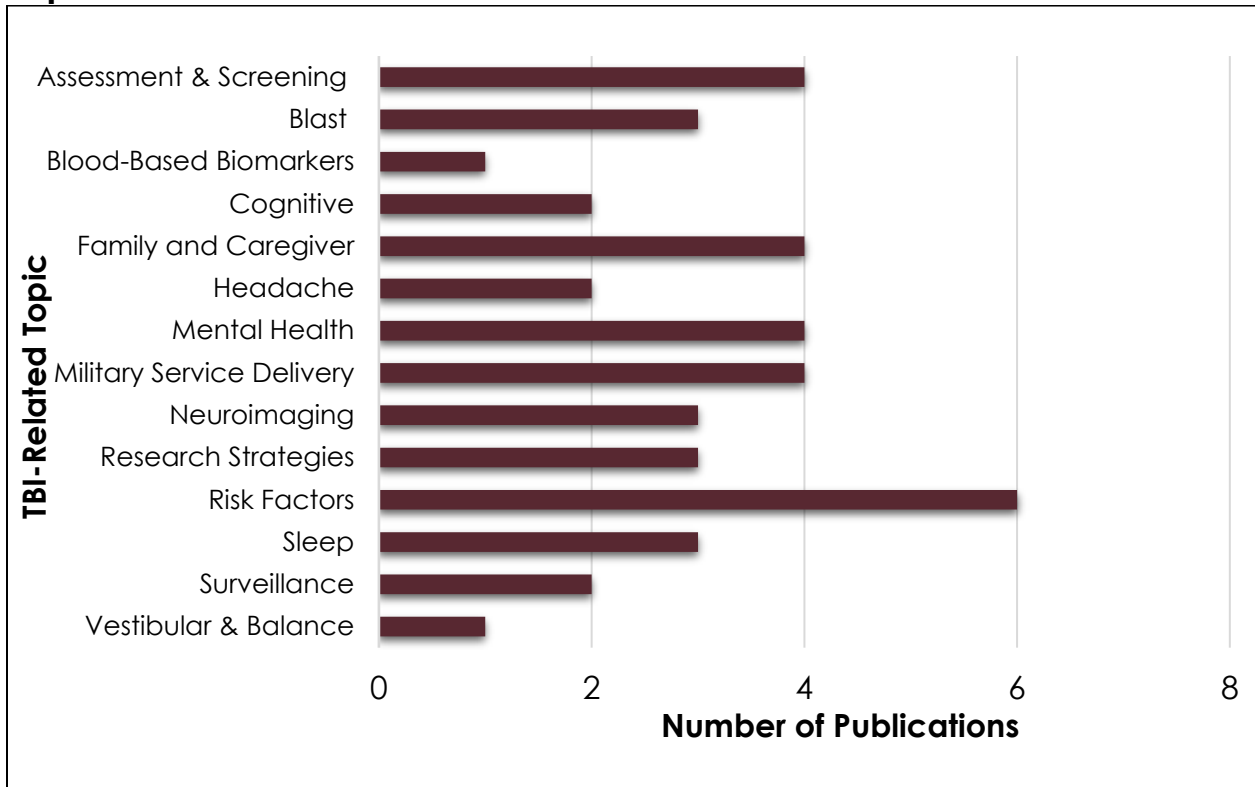


Figure 3: Number of TBICoE Articles Published in 2023 per Month

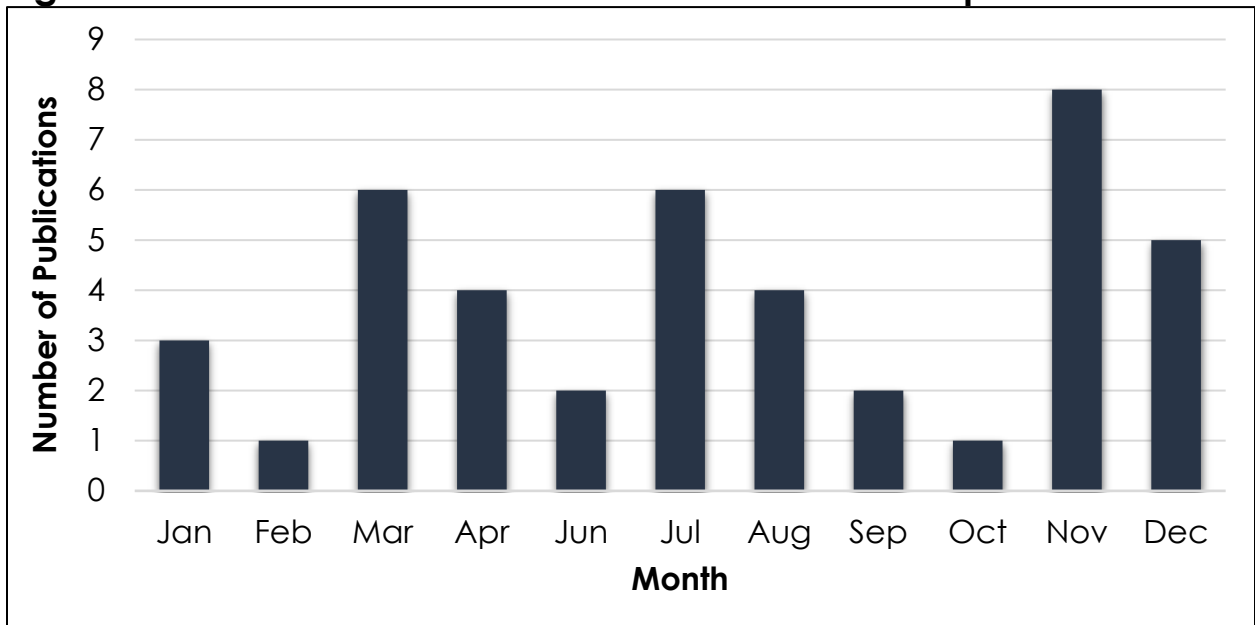
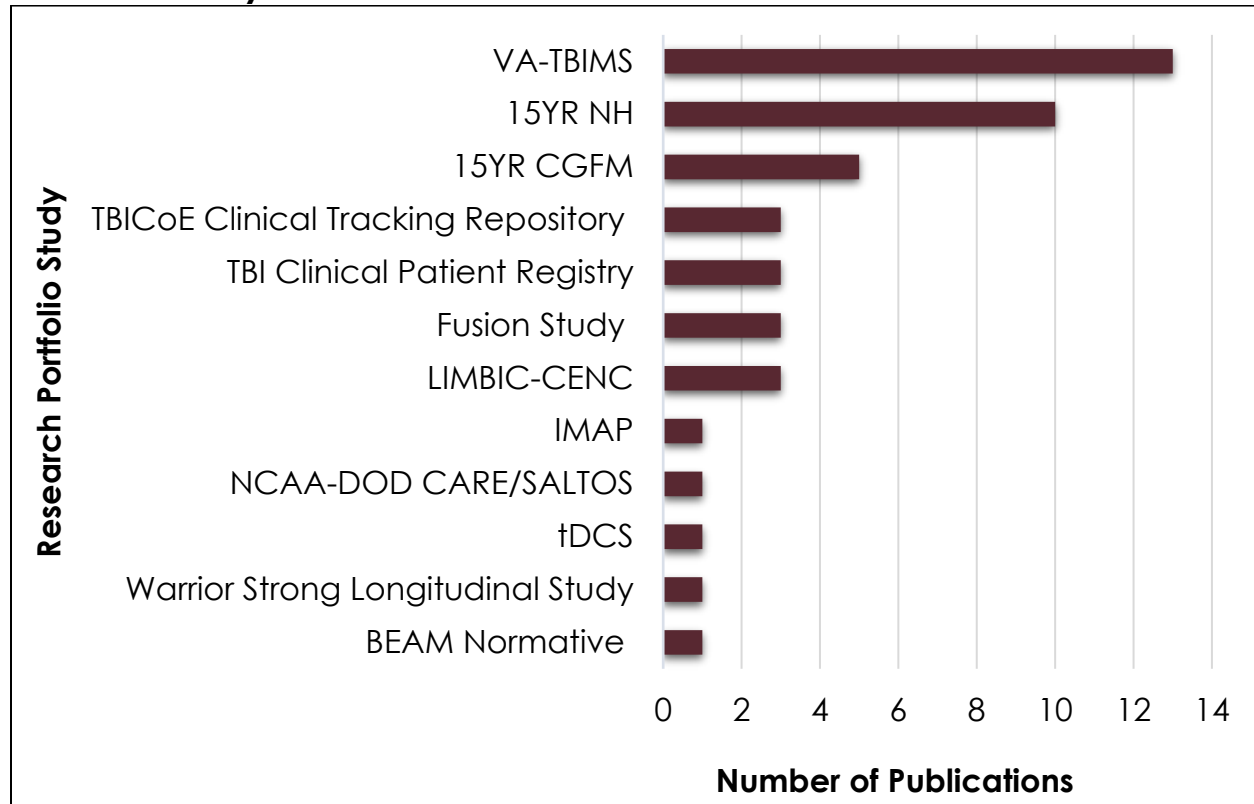


Figure 4: Number of TBICoE Articles Published in 2023 per Research Portfolio Study



Note: This metric includes the number of publications from different TBICoE research portfolio studies. Full study names are provided below.

- Veterans Affairs TBI Model Systems (VA-TBIMS)
- Defense and Veterans Brain Injury Center - Traumatic Brain Injury Center of Excellence (DVBIC-TBICoE) 15-Year Natural History Study (15YR NH)
- DVBIC-TBICoE 15-Year Caregiver and Family Member Study (15YR CGFM)
- Long-Term Impact of Military-Relevant Brain Injury Consortium Chronic Effects of Neurotrauma Consortium (LIMBIC-CENC)
- Improved Understanding of Medical and Psychological Needs (IMAP) in Veterans and Service Members with Chronic TBI
- National Collegiate Athletic Association (NCAA)–DOD Concussion Assessment, Research and Education Consortium inclusive of the Service Academy Longitudinal mTBI Outcomes Study (CARE/SALTOS)
- Transcranial Direct Current Stimulation (tDCS)
- Bethesda Eye & Attention Measure (BEAM) Normative Study

Figure 5: Number of TBICoE Articles Published in 2023 per Research Method

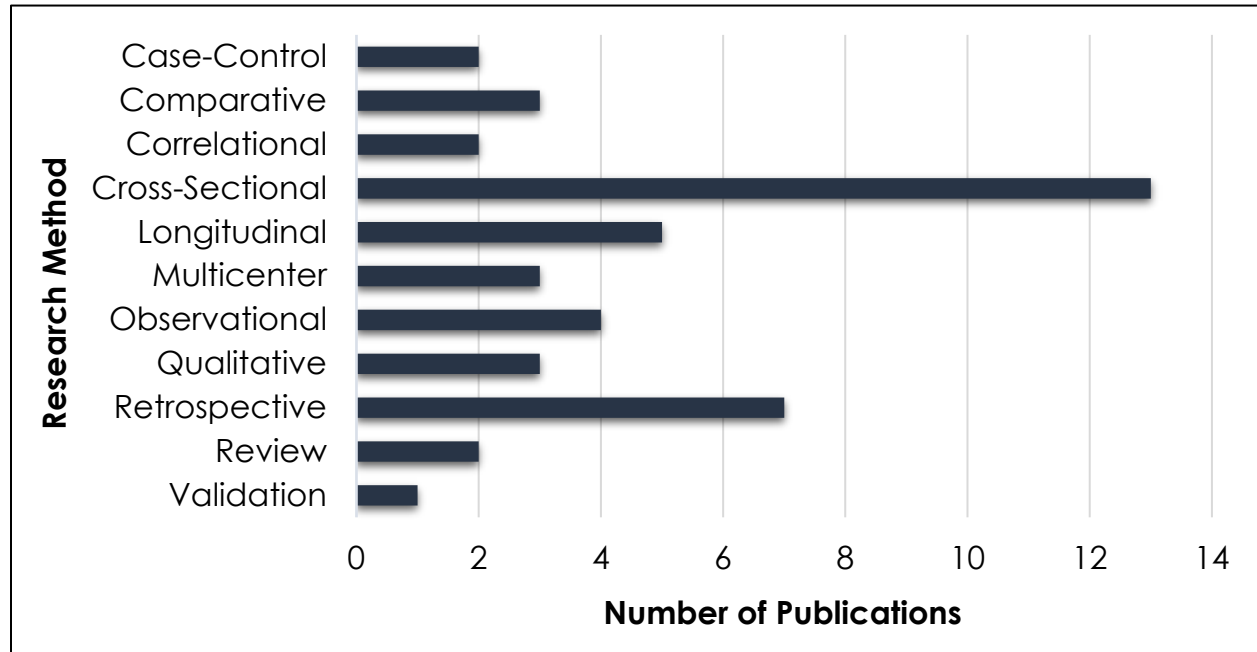


Figure 6: Number of TBICoE Articles Published in 2023 per Journal

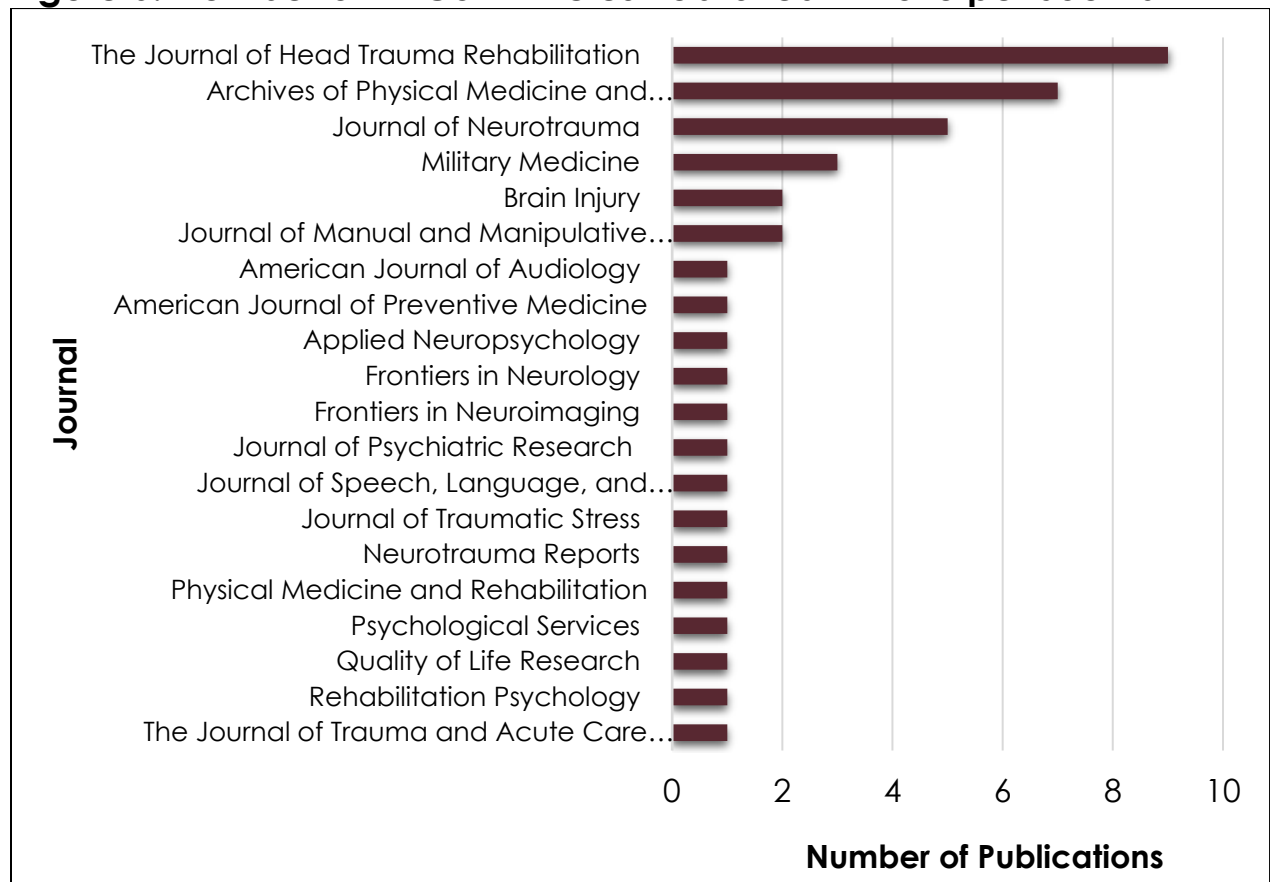
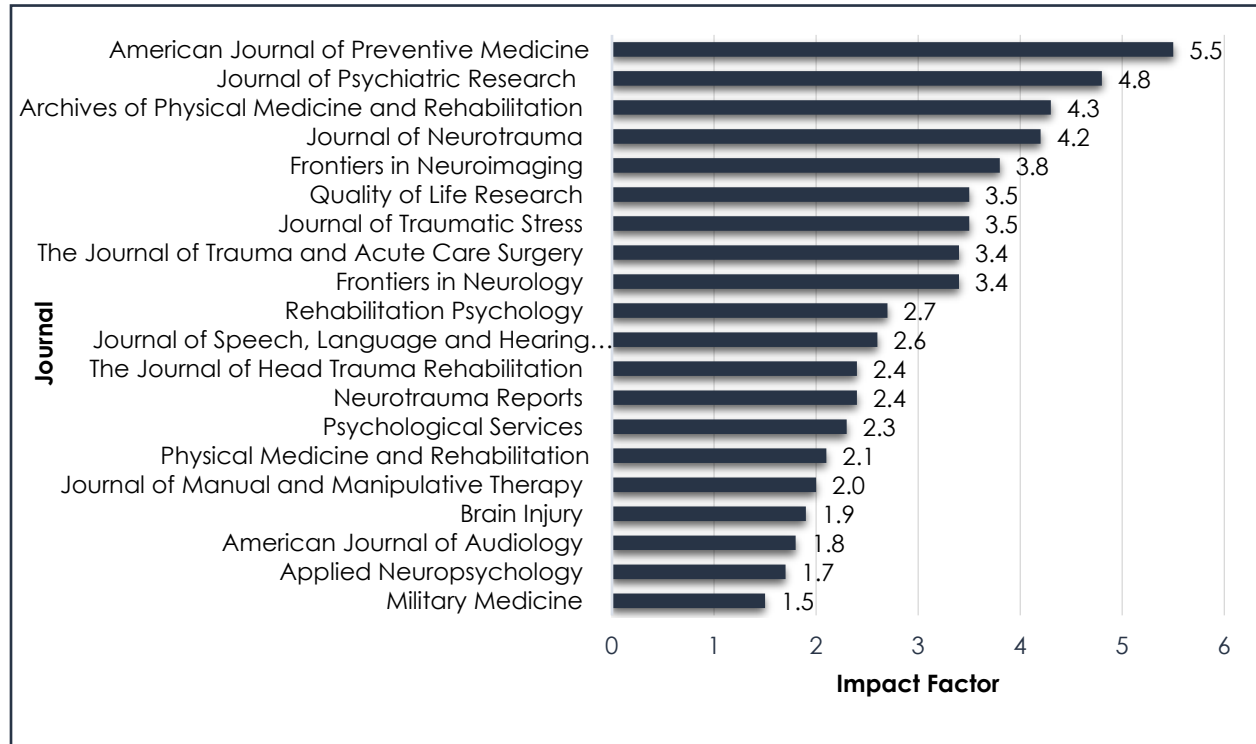
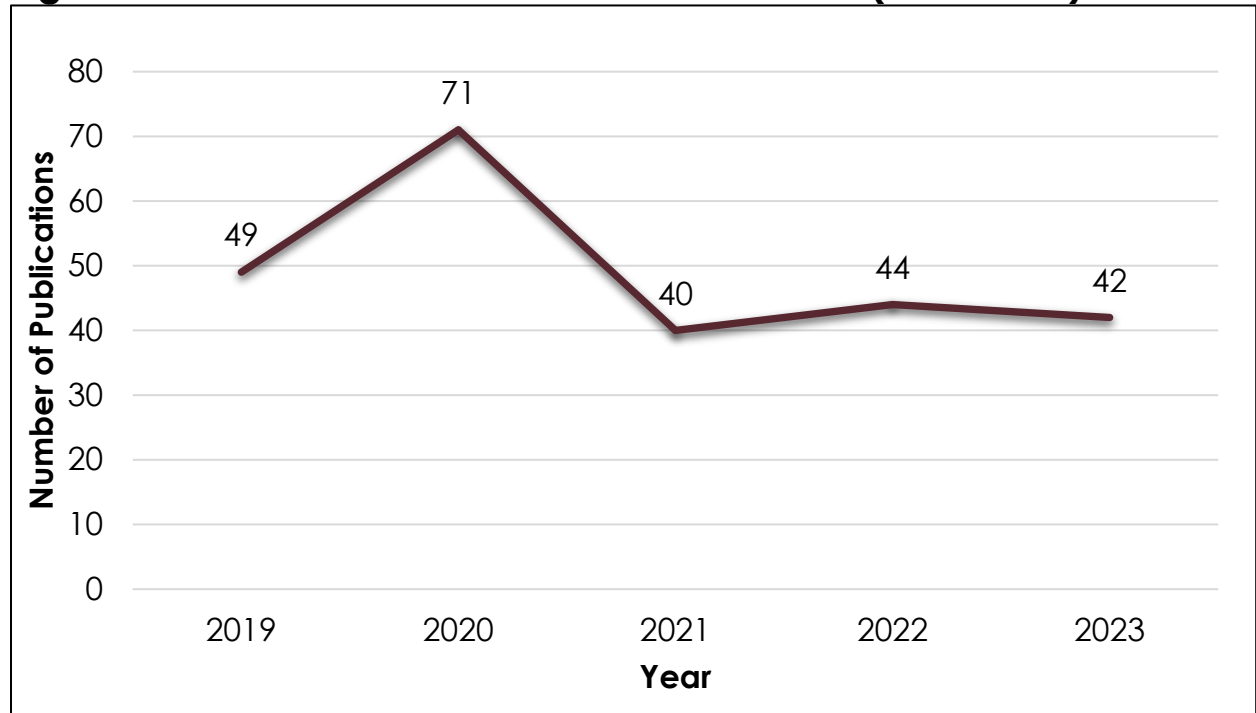


Figure 7: Impact Factor of Journals that Published TBICoE Articles in 2023



Note: Impact factors for 2023 are not available for all journals. The impact factors reported here are based on 2022 journal metrics.

Figure 8: Annual Number of TBICoE Publications (2019-2023)



ARTICLE ABSTRACTS AND SUMMARIES OF POTENTIAL TBI CLINICAL IMPACT

ASSESSMENT & SCREENING

1. Davidson A, Eitel M, Lange RT, et al. Efficient Estimation of the Binaural Masking Level Difference Using a Technique Based on Manual Audiometry. *J Speech Lang Hear Res.* 2023;66(4):1378-1393. doi:10.1044/2022_JSLHR-22-00519

Lead Site: Walter Reed National Military Medical Center (WRNMMC)

Collaborative Site(s): N/A

Abstract

Purpose: The masking level difference (MLD) has been used for decades to evaluate the binaural listening advantage. Although originally measured using Bekesy audiometry, the most common clinical use of the MLD is the CD-based Wilson 500-Hz technique with interleaved NOS0 and NOS π components. Here, we propose an alternative technique based on manual audiometry as a faster way of measuring the MLD. The article describes the advantages to this administration technique and evaluates if it is a viable alternative for the Wilson technique. **Method:** Data were retrospectively analyzed on 264 service members. All service members completed both the Wilson and Manual MLDs. Descriptive and correlational statistics were applied to evaluate the comparisons between the two techniques and highlight the differences. Equivalence measures were also completed to compare the tests using a standardized cutoff score. Analyses were also made to compare both techniques to subjective and objective measures of hearing performance.

Results: Moderate to high positive correlations were determined between Wilson and Manual measures of each threshold (NOS π and NOS0). Although the Manual and Wilson MLD techniques produced significantly different thresholds, simple linear transformations can be used to obtain approximately equivalent scores on the two tests, and agreement was high for using these transformed scores to identify individuals with substantial MLD deficits. Both techniques had moderate test-retest reliability. The Manual MLD and components had stronger correlations to the subjective and objective hearing measures than the Wilson.

Conclusions: The Manual technique is a faster method for obtaining MLD scores that is just as reliable as the CD-based Wilson test. With the significant reduction in assessment time and comparable results, the Manual MLD is a viable alternative for direct use in the clinic.

Potential Clinical Impact: In support of the 15-Year TBI Longitudinal Study, WRNMMC investigators retrospectively analyzed 264 service members with TBI to examine the difference between two techniques for measuring the MLD, an audiological test of signal detection in a noisy background. The two techniques had similar reliability, but the Manual MLD technique had stronger correlations to subjective and objective hearing measures and a shorter administration time, indicating it may be a more efficient tool for use in audiology clinics.

2. **Agtarap S, Hungerford LD, Ethenhofer ML. Identifying Unique Symptom Groups Following Mild Traumatic Brain Injury Using the Neurobehavioral Symptom Inventory and PTSD Checklist-5 in Military Personnel: A Bifactor Analysis. *J Head Trauma Rehabil.* 2023;38(6):E371-E383. doi:10.1097/HTR.0000000000000854**

Lead Site: Naval Medical Center San Diego (NMCSD)

Collaborative Site(s): N/A

Abstract

Objective: To identify both shared and unique groups of posttraumatic stress and post-concussive symptoms using bifactor analysis. **Setting:** Two large military outpatient TBI rehabilitation clinics in the Southwestern United States.

Participants: A sample of 1476 active-duty service members seeking treatment for a mild TBI sustained more than 30 days previously, without history of moderate or severe TBI, who completed measures of post-concussive and posttraumatic stress symptoms assessed at clinic intake. **Design:** Observational, correlational study with data taken from an institutional review board-approved clinical registry study. **Main measures:** Neurobehavioral Symptom Inventory (NSI) and Posttraumatic Stress Disorder (PTSD) Checklist for Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition) (DSM-V) (PCL-5). Concurrent measures were Patient Health Questionnaire (PHQ-8), Pittsburgh Sleep Quality Index (PSQI), and Headache Impact Test (HIT-6). **Results:** Results identified a bifactor model demonstrating unique posttraumatic stress, depressive, cognitive, and neurological/somatic symptom groups that were still evident after accounting for a universal factor representing general distress. These symptom groups were differentially related to concurrently measured clinical outcomes.

Conclusion: Use of a bifactor structure may help derive clinically useful signals from self-reported symptoms among active-duty service members seeking outpatient treatment for mild TBI.

Potential Clinical Impact: PTSD and PCS are often studied together in active-duty service members with mTBI, and “general distress” has been suggested to influence the self-reporting of symptoms by patients with these conditions. Thus, TBICoE researchers at NMCSD analyzed data from common symptom inventory measures for PTSD and PCS to determine whether accounting for the effect of

“general distress” would result in differential associations between symptoms and the injury characteristics and clinical outcomes scores. The results showed that accounting for “general distress” led to different associations between the PTS, cognitive, depressive, and neurologic/somatic symptom domains and the injury characteristics and clinical outcome measures. While these results need to be replicated, this type of analysis may increase the interpretability of findings involving the symptom domains assessed within the clinical symptom inventories commonly used in mTBI rehabilitation settings.

- 3. Silva MA, Miles SR, O'Neil-Pirozzi TM, et al. Alternative Structure Models of the Traumatic Brain Injury Rehabilitation Needs Survey: A Veterans Affairs TBI Model Systems Study. *Arch Phys Med Rehabil.* 2023;104(7):1062-1071. doi:10.1016/j.apmr.2023.01.004**

Lead Site: James A. Haley Veterans' Hospital

Collaborative Site(s): N/A

Abstract

Objective: To explore the factor structure of the Rehabilitation Needs Survey (RNS). **Design:** Secondary analysis of observational cohort study who were 5-years post-TBI. **Setting:** Five Inpatient Rehabilitation Facilities.

Participants: Veterans enrolled in the TBI Model Systems longitudinal study who completed the RNS at 5-year follow-up ($N=378$). **Main outcome measure(s):** RNS.

Results: RNS factor structure was examined with exploratory factor analysis (EFA) with oblique rotation. Analyses returned 2- and 3-factor solutions with Cronbach alphas ranging from 0.715 to 0.905 and corrected item-total correlations that ranged from 0.279 to 0.732. The 2-factor solution accounted for 61.7% of the variance with ≥ 3 exclusively loading items on each factor with acceptable internal consistency metrics and was selected as the most parsimonious and clinically applicable model. Ad hoc analysis found the RNS structure per the EFA corresponded with elements of the International Classification of Functioning, Disability and Health (ICF) conceptual framework. All factors had adequate internal consistency ($\alpha \geq 0.70$) and 20 of the 21 demonstrated good discrimination (corrected item-total correlations ≥ 0.40). **Conclusions:** The 2-factor solution of the RNS appears to be a useful model for enhancing its clinical interpretability.

Although there were cross-loading items, they refer to complex rehabilitation needs that are likely influenced by multiple factors. Alternatively, there are items that may require alteration and redundant items that should be considered for elimination.

Potential Clinical Impact: The RNS was designed by the TBIMS team to identify the post-discharge care needs of service members and veterans during the chronic stage of TBI recovery. In this study, TBIMS researchers at the James A. Haley Veterans' Hospital conducted an exploratory factor analysis of the

structure of the RNS items by comparing a 3-factor model to a 2-factor model. Researchers found the 2-factor model was better at categorizing RNS survey items for interpreting TBI rehabilitation needs of service member and veterans. These findings should be validated, but the results show promise for standardizing and improving the RNS for clinical use to measure the needs of service members and veterans during TBI recovery and rehabilitation.

- 4. Silverberg ND, Iverson GL, et al. ACRM Brain Injury Special Interest Group Mild TBI Task Force members: The American Congress of Rehabilitation Medicine Diagnostic Criteria for Mild Traumatic Brain Injury. *Arch Phys Med Rehabil.* 2023;104(8):1343-1355. doi:10.1016/j.apmr.2023.03.036**

Lead Site: Headquarters (HQ)

Collaborative Site(s): N/A

Abstract

Objective: To develop new diagnostic criteria for mild traumatic brain injury (mTBI) that are appropriate for use across the lifespan and in sports, civilian trauma, and military settings. **Design:** Rapid evidence reviews on 12 clinical questions and Delphi method for expert consensus. **Participants:** The Mild Traumatic Brain Injury Task Force of the American Congress of Rehabilitation Medicine Brain Injury Special Interest Group convened a Working Group of 17 members and an external interdisciplinary expert panel of 32 clinician-scientists. Public stakeholder feedback was analyzed from 68 individuals and 23 organizations. **Results:** The first two Delphi votes asked the expert panel to rate their agreement with both the diagnostic criteria for mild TBI and the supporting evidence statements. In the first round, 10 of 12 evidence statements reached consensus agreement. Revised evidence statements underwent a second round of expert panel voting, where consensus was achieved for all. For the diagnostic criteria, the final agreement rate, after the third vote, was 90.7%. Public stakeholder feedback was incorporated into the diagnostic criteria revision prior to the third expert panel vote. A terminology question was added to the third round of Delphi voting, where 30 of 32 (93.8%) expert panel members agreed that the diagnostic label “concussion” may be used interchangeably with “mild TBI” when neuroimaging is normal or not clinically indicated. **Conclusions:** New diagnostic criteria for mild TBI were developed through an evidence review and expert consensus process. Having unified diagnostic criteria for mild TBI can improve the quality and consistency of mild TBI research and clinical care.

Potential Clinical Impact: As a member of the American Congress of Rehabilitation Medicine (ACRM) Brain Injury Mild TBI Task Force, TBICoE's Dr. Gary McKinney contributed his military TBI expertise to assist in the development of new diagnostic criteria for mTBI, which had not been updated since 1993. The

task force used the Delphi consensus process to develop new mTBI diagnostic criteria (i.e., mechanism of injury, clinical signs, acute symptoms, clinical examination and laboratory findings, neuroimaging, and confounding factors) to promote standardization in clinical and research practice for civilian, sport, and military communities.

BLAST

1. Lange RT, French LM, Lippa SM, et al. High Lifetime Blast Exposure Using the Blast Exposure Threshold Survey Is Associated with Worse Warfighter Brain Health Following Mild Traumatic Brain Injury. *J Neurotrauma*. 2024;41(1-2):186-198. doi:10.1089/neu.2023.0133

Lead Site: WRNMMC

Collaborative Site(s): Camp Pendleton & NMCS D

Abstract

Objective: The purpose of this study was to extend previous research by examining the relationship between lifetime blast exposure (LBE) and neurobehavioral functioning after mTBI by (a) using a comprehensive measure of lifetime blast exposure, and (b) controlling for the influence of PTSD. **Design:** Participants were 103 United States service members and veterans with a medically documented diagnosis of mTBI, recruited from three military treatment facilities (74.8%) and community-based recruitment initiatives (25.2%, e.g., social media, flyers). Participants completed a battery of neurobehavioral measures 12 or more months post-injury (Neurobehavioral Symptom Inventory, PTSD-Checklist PCLC, TBI-Quality of Life), including the Blast Exposure Threshold Survey (BETS). The sample was classified into two LBE groups: High ($n = 57$) and Low ($n = 46$) LBE. In addition, the sample was classified into four LBE/PTSD subgroups: High PTSD/High LBE ($n = 38$); High PTSD/Low LBE ($n = 19$); Low PTSD/High LBE ($n = 19$); and Low PTSD/Low LBE ($n = 27$). **Results:** The High LBE group had consistently worse scores on all neurobehavioral measures compared with the Low LBE group. When controlling for the influence of PTSD (using ANCOVA), however, only a handful of group differences remained. When comparing measures across the four LBE/PTSD subgroups, in the absence of clinically meaningful PTSD symptoms (i.e., Low PTSD), participants with High LBE had worse scores on the majority of neurobehavioral measures (e.g., post-concussion symptoms, sleep, fatigue). When examining the total number of clinically elevated measures, the High LBE subgroup consistently had a greater number of clinically elevated scores compared with the Low LBE subgroup for the majority of comparisons (i.e., 4 to 15 or more elevated symptoms). In contrast, in the presence of clinically meaningful PTSD symptoms (i.e., High PTSD), there were no differences between High versus Low LBE subgroups for all measures. When examining the total number of clinically elevated measures, however, there were meaningful

differences between High versus Low LBE subgroups for those comparisons that included a high number of clinically elevated scores (i.e., 6 to 10 or more), but not for a low number of clinically elevated scores (i.e., 1 to 5 or more). High LBE, as quantified using a more comprehensive measure than utilized in past research (i.e., BETS), was associated with worse overall neurobehavioral functioning after mTBI. **Conclusion:** This study extends existing literature showing that lifetime blast exposure that is largely subconcussive may negatively impact warfighter brain health and readiness beyond diagnosable brain injury.

Potential Clinical Impact: In support of the NDAA FY07 final Sec 721 report to Congress, DVBIC-TBICoE 15-Year Longitudinal Study researchers sought to explore the relationship between lifetime blast exposure and neurobehavioral functioning in service members and veterans with mTBI using the BETS. The authors concluded that high lifetime blast exposure is associated with worse neurobehavioral functioning after mTBI and that this relationship is influenced by PTSD. These results highlight the importance of considering the negative impact of lifetime blast exposure and PTSD on service members' and veterans' outcomes, including those related to brain health and readiness.

- 2. Lippa SM, Yeh PH, Kennedy JE, et al. Lifetime Blast Exposure Is Not Related to White Matter Integrity in Service Members and Veterans with and Without Uncomplicated Mild Traumatic Brain Injury. *Neurotrauma Rep.* 2023;4(1):827-837. Published 2023 Dec 14. doi:10.1089/neur.2023.0043**

Lead Site: WRNMMC

Collaborative Site(s): Camp Pendleton & Joint Base San Antonio (JBSA)

Abstract

Objective: This study examines the impact of lifetime blast exposure on white matter integrity in service members and veterans. **Design:** Participants were 227 service member and veterans, including those with a history of mTBI (n = 124), orthopedic injury controls (n = 58), and non-injured controls (n = 45), prospectively enrolled in a DVBIC-TBICoE study. Participants were divided into three groups based on number of self-reported lifetime blast exposures: none (n = 53); low (i.e., 1-9 blasts; n = 81); and high (i.e., ≥ 10 blasts; n = 93). All participants underwent diffusion tensor imaging (DTI) at least 11 months post-injury. Tract-of-interest analysis was applied to investigate fractional anisotropy and mean, radial, and axial diffusivity (AD) in left and right total cerebral white matter as well as 24 tracts. Benjamini-Hochberg false discovery rate (FDR) correction was used. **Results:** Regressions investigating blast exposure and mTBI on white matter integrity, controlling for age, revealed that the presence of mTBI history was associated with lower AD in the bilateral superior longitudinal fasciculus and arcuate fasciculus and left cingulum (β s = -0.255 to -0.174; ps < 0.01); however, when non-injured controls were removed from the sample (but

orthopedic injury controls remained), these relationships were attenuated and did not survive FDR correction. Regression models were rerun with modified PTSD diagnosis added as a predictor. After FDR correction, PTSD was not significantly associated with white matter integrity in any of the models. **Conclusion:** Overall, there was no relationship between white matter integrity and self-reported lifetime blast exposure or PTSD.

Potential Clinical Impact: TBICoE researchers examined the impact of self-reported lifetime blast exposure on white matter integrity in service members and veterans with and without an uncomplicated mTBI who were enrolled in the DVBIC-TBICoE 15-Year Longitudinal Study. Investigators also explored the relationship between blast exposure and white matter integrity, as well as the association between PTSD and white matter integrity. The results did not demonstrate conclusive evidence to support a relationship between lifetime blast exposure and white matter integrity; similarly, a relationship between PTSD and white matter integrity was not observed. In brief, further longitudinal research with refined blast exposure metrics is necessary to fully assess the relationship between blast exposure and white matter integrity.

- 3. Lange RT, French LM, Lippa SM, et al. Convergent and Discriminant Validity of the Blast Exposure Threshold Survey in United States Military Service Members and Veterans. *J Neurotrauma*. Published online December 20, 2023. doi:10.1089/neu.2023.0379**

Lead site: WRNMMC

Collaborative Site(s): Camp Pendleton, HQ, & NMCS D

Abstract

Background: The BETS is a recently developed and promising new self-report measure of lifetime blast exposure (LBE). However, no studies have examined the psychometric properties of the BETS, which currently limits its clinical utility.

Objective: The purpose of this study was to examine the convergent and discriminant validity of the BETS by comparing the BETS Generalized Blast Exposure Value (GBEV) to five variables hypothesized to be associated with LBE (i.e., single-item LBE, combat exposure, years in the military, number of combat deployments, and military occupation specialty [MOS]) and three variables hypothesized not to be associated with LBE (i.e., age at the time of injury, estimated pre-morbid Full-Scale Intelligence Quotient [FSIQ], and resilience).

Design: Participants were 202 United States service members and veterans prospectively enrolled from three military medical treatment facilities (68.7%) and via community recruitment initiatives (31.3%). Participants completed the BETS, Combat Exposure Scale (CES), Deployment Risk and Resiliency Inventory-2 Combat Experiences (DRRI-2 CE), Traumatic Brain Injury-Quality of Life Resilience scale, and a brief structured interview. For some analyses, participants were

classified into two blast-risk MOS groups: high ($n = 89$) and low ($n = 94$). **Results:** The BETS GBEV was not significantly correlated with all three non-blast related variables ($r_s = 0.01$ to $r_s = -0.12$). In contrast, GBEV was significantly ($p < 0.001$) associated with all blast-related variables; single-item LBE ($r_s = 0.76$), CES ($r_s = 0.58$), number of combat deployments ($r_s = 0.53$), DRRI-2 CE ($r_s = 0.48$), and high blast risk MOS ($r = 0.36$, medium effect size). However, a stronger relationship was found between the blast-related variables and three modified GBEV scores when excluding some small weapons categories; single-item LBE ($r_s = 0.80-0.82$), CES ($r_s = 0.64-0.67$), number of combat deployments ($r_s = 0.56$), DRRI-2 CE ($r_s = 0.51-0.53$), and high blast risk MOS ($r = 0.42-0.49$, medium-large effect size).

Conclusion: This is the first study to examine the psychometric properties of the BETS. Overall, these results offer support for the convergent and discriminant validity of the BETS. In order to ensure that the BETS can be confidently used as a valid and reliable measure of LBE, more research is needed to further examine the psychometric properties of the test, particularly with regard to the establishment of test-retest reliability.

Potential Clinical Impact: Using DVBIC-TBICoE 15YR NH data, TBICoE and National Intrepid Center of Excellence (NICoE) researchers aimed to examine the convergent and discriminant validity of the BETS, a recently developed tool aimed to measure lifetime blast exposure (LBE). This aim was achieved by comparing the general blast exposure value (GBEV) scores of the BETS with variables that were and were not associated with LBE. The results indicated that three non-blast variables (including age at time of injury, resilience, and intelligence) were not significantly associated with GBEV scores; however, GBEV scores were significantly associated with all five blast-related variables (e.g., combat exposure and deployments). This study supports the convergent and discriminant validity of the BETS; however, continued research on the psychometric properties of the BETS is necessary to confirm its ability to measure LBE.

BLOOD-BASED BIOMARKERS

1. Lange RT, Gill JM, Lippa SM, et al. Elevated Serum Tau and UCHL-1 Concentrations Within 12 Months of Injury Predict Neurobehavioral Functioning 2 or More Years Following Traumatic Brain Injury: A Longitudinal Study. *J Head Trauma Rehabil*. Published online June 19, 2023. doi:10.1097/HTR.0000000000000877

Lead Site: WRNMMC

Collaborative Site(s): NMCSD

Abstract

Objective: Blood-based biomarkers have received considerable attention for

their diagnostic and prognostic value in the acute and post-acute period following TBI. The purpose of this study was to examine whether blood-based biomarker concentrations within the first 12 months of TBI can predict neurobehavioral outcome in the chronic phase of the recovery trajectory.

Setting: Inpatient and outpatient wards from 3 military medical treatment facilities. **Participants:** A total of 161 service members and veterans classified into 3 groups: (a) uncomplicated mild TBI (mTBI; n = 37), (b) complicated mild, moderate, severe, penetrating TBI combined (STBI; n = 46), and (c) controls (CTRL; n = 78). **Design:** Prospective longitudinal. **Main measures:** Participants completed 6 scales from the Traumatic Brain Injury Quality of Life (i.e., Anger, Anxiety, Depression, Fatigue, Headaches, and Cognitive Concerns) within 12 months (baseline) and at 2 or more years (follow-up) post-injury. Serum concentrations of tau, neurofilament light, glial fibrillary acidic protein, and UCHL-1 at baseline were measured using SIMOA. **Results:** Baseline tau was associated with worse anger, anxiety, and depression in the STBI group at follow-up ($R^2 = 0.101-0.127$), and worse anxiety in the mTBI group ($R^2 = 0.210$). Baseline ubiquitin carboxyl-terminal hydrolase L1 (UCHL-1) was associated with worse anxiety and depression at follow-up in both the mTBI and STBI groups ($R^2\Delta = 0.143-0.207$), and worse cognitive concerns in the mTBI group ($R^2\Delta = 0.223$). **Conclusions:** A blood-based panel including these biomarkers could be a useful tool for identifying individuals at risk of poor outcome following TBI.

Potential Clinical Impact: In support of the NDAA FY07 final Sec 721 report to Congress, TBICoE researchers and collaborators sought to assess the association between the levels of blood-based biomarkers (i.e., serum tau, NFL, GFAP and UCHL-1) measured within a year of TBI and neurobehavioral outcomes evaluated in service members and veterans at two or more years post-injury. Participants included in this study were enrolled in the DVBIC-TBICoE 15YR NH on TBI. The results indicated that elevated serum tau and UCHL-1 levels were associated with mood and cognitive concerns at two or more years post-injury. Further research is necessary to confirm the utility of serum tau and UCHL-1 levels for predicting TBI outcomes and their potential use in enabling targeted intervention.

COGNITIVE

1. Jinkerson JD, Lu LH, Kennedy J, Armistead-Jehle P, Nelson JT, Seegmiller RA. Grooved Pegboard Adds Incremental Value Over Memory-Apparent Performance Validity Tests in Predicting Psychiatric Symptom Report. *Appl Neuropsychol Adult*. Published online April 24, 2023. doi:10.1080/23279095.2023.2192409

Lead Site: JBSA

Collaborative Site(s): N/A

Abstract

Objective: The present study evaluated whether Grooved Pegboard (GPB), when used as a performance validity test (PVT), can incrementally predict psychiatric symptom report elevations beyond memory apparent PVTs. **Design:** Participants ($N = 111$) were military personnel and were predominantly White (84%), male (76%), with a mean age of 43 ($SD = 12$) and having on average 16 years of education ($SD = 2$). Individuals with disorders potentially compromising motor dexterity were excluded. Participants were administered GPB, three memory apparent PVTs (Medical Symptom Validity Test, Non-Verbal Medical Symptom Validity Test, Reliable Digit Span), and a symptom validity test (Personality Assessment Inventory Negative Impression Management [NIM]). Results from the three-memory apparent PVTs were entered into a model for predicting NIM, where failure of two or more PVTs was categorized as evidence of non-credible responding. **Results:** Hierarchical regression revealed that non-dominant hand GPB T-score incrementally predicted NIM beyond memory-apparent PVTs ($F(2,108) = 16.30, p < .001; R^2$ change = .05, $\beta = -0.24, p < .01$). In a second hierarchical regression, GPB performance was dichotomized into pass or fail, using T-score cutoffs (≤ 29 for either hand, ≤ 31 for both). Non-dominant hand GPB again predicted NIM beyond memory apparent PVTs ($F(2,108) = 18.75, p < .001; R^2$ change = .08, $\beta = -0.28, p < .001$). **Conclusion:** Results indicated that noncredible/failing GPB performance adds incremental value over memory apparent PVTs in predicting psychiatric symptom report.

Potential Clinical Impact: The Grooved Pegboard Test (GPB) is commonly used to measure motor speed and dexterity. In this study, TBICoE researchers at JBSA collaborated with the Hearing Center of Excellence and Brooke Army Medical Center to determine whether administering the GPB along with standard performance validity tests (PVTs) would add clinical value in predicting symptom exaggeration among service members. The GPB explained a small but statistically significant amount of variance in psychiatric symptom reporting. PVTs judge the credibility of obtained neurocognitive scores; in this study, the GPB added incremental value over standard memory PVTs, improving the ability to assess the credibility of psychiatric symptom reporting in a military setting.

- 2. Ivins B, Risling M, Wisén N, Schwab K, Rostami E. Mild Traumatic Brain Injury in the Maturing Brain: An Investigation of Symptoms and Cognitive Performance in Soldiers Returning from Afghanistan and Iraq. *J Head Trauma Rehabil.* Published online December 7, 2023. doi:10.1097/HTR.0000000000000919**

Lead Site: HQ

Collaborative Site(s): N/A

Abstract. Objective: The majority of TBIs are classified as mild and occur in young individuals. The course of recovery varies but can result in chronic or troubling

outcomes. The impact of age on TBI outcomes in young adults before complete brain maturation is not well studied. **Methods:** In this study, we compared the effects of mild TBI on cognitive performance and self-reported TBI symptoms and PTSD in 903 soldiers in three age groups: 24 years or younger, 25 to 27 years, and 28 to 40 years. The soldiers had returned from war zones in Iraq and were screened for TBI within a few days of return. Cognitive performance was measured with the Automated Neuropsychological Assessment Metrics of Military TBI Version 4 (ANAM4). Symptoms associated with mild TBI were self-reported on the Neurobehavioral Symptom Inventory, and the PTSD Checklist-Civilian Version (PCL-C). **Results:** Soldiers with TBI in every age group had significantly higher prevalence of most symptoms than those with no TBI. Soldiers with TBI also reported more chronic pain sites, regardless of age. Soldiers aged 28 to 40 years with TBI had the lowest cognitive performance scores (ANAM) across several subtests, both unadjusted and adjusted. The Global Deficit Score was significantly higher for soldiers aged 28 to 40 years and 25 to 27 years with TBI than for soldiers younger than 24 years with no TBI. After adjusting for PTSD symptoms, education, and number of lifetime TBIs, the overall test battery mean for soldiers aged 28 to 40 years with TBI was significantly lower than for soldiers younger than 24 years with no TBI. **Conclusion:** Soldiers with mild TBI in the younger age group show more symptoms associated to frontal lobe function while soldiers in the older group suffer more cognitive impairment. This may warrant further study as it may indicate a propensity to later cognitive decline among soldiers who were older at the time of injury.

Potential Clinical Impact: TBICoE researchers and collaborators conducted a study to evaluate the impact of mild TBI on cognitive outcomes in three age groups of soldiers (< 24 years, 25 to 27 years, and 28 to 40 years). The results indicated that service members with mTBI had a higher prevalence of chronic pain, PTSD symptoms, and worse symptoms on the NSI regardless of age than service members without TBI. The results also showed that cognitive symptoms were age specific; younger soldiers exhibited altered frontal lobe function, whereas older soldiers were more vulnerable to cognitive decline. This study stresses the importance of monitoring cognitive performance across the lifespan.

FAMILY & CAREGIVER

1. **Carlozzi NE, Graves C, Troost JP, et al. Initial Evidence for Reliable and Valid Use of Scores on the 8-Item Econ-QOL Short Form to Measure Economic Quality of Life in Caregivers of Persons with Traumatic Brain Injury. *Arch Phys Med Rehabil.* 2023;104(3):430-437. doi:10.1016/j.apmr.2022.07.015**

Lead Site: James A. Haley Veterans' Hospital

Collaborative Site(s): WRNMMC

Abstract

Objective: To provide reliability and validity data to support the clinical utility of Economic Quality of Life Measure (Econ-QOL) scores in caregivers of civilians and service members/veterans with TBI. **Design:** Cross-sectional survey study.

Setting: Three academic medical centers and a VA treatment facility.

Participants: 376 caregivers of civilians ($n=213$) and service members/veterans ($n=163$) with TBI ($N=376$). **Interventions:** N/A. **Main outcome measures:** Econ-QOL and several patient-reported outcome measures (Traumatic Brain Injury Caregiver Quality of Life Caregiver-Specific Anxiety and Caregiver Strain, Patient-Reported Outcomes Measurement Information System sleep-related impairment, Neurological Quality of Life Measurement System positive affect and well-being) and measures of financial status (self-reported income).

Results: Internal consistency reliability of the Econ-QOL Short Form scores were excellent (all Cronbach's alphas $\geq .92$). There were no floor or ceiling effects for scores. There was evidence of convergent and discriminant validity, with the Econ-QOL scores having the strongest relationships with self-reported income (convergent validity evidence) and weak relationships with the other measures (discriminant validity evidence). Individuals with scores that were "below or possibly below" the poverty line (according to 2016 federal government poverty level thresholds) reported worse economic quality of life relative to those individuals who were definitely above the poverty line, supporting known-groups validity. **Conclusions:** This article establishes the clinical utility of scores on the Econ-QOL Short Form in caregivers of persons with TBI and provides evidence that it is valid and appropriate to use such scores not only in a variety of different disability populations (e.g., spinal cord injury, stroke) but also in caregivers.

Potential Clinical Impact: TBICoE participated in a project in 2013 that led to the development of the first TBI assessment to measure health-related quality of life (HRQOL) in caregivers of civilians, service members, and veterans with TBI. Collaborators continue to investigate the reliability and validity of item banks, including the Economic Quality of Life (Econ-QOL), which intends to measure the effect of perceived economic factors on HRQOL in caregivers of civilians, service members, and veterans with TBI. The Econ-QOL was found to accurately identify individuals with greater economic hardship/need, and worse Econ-QOL was observed in individuals below the federal poverty level than in those above it. The results of this study indicate the reliability and clinical utility of the Econ-QOL for assessing caregivers of civilians, service members, and veterans with TBI.

- 2. Brickell TA, Wright MM, Sullivan JK, et al. Health Outcomes Before and During the COVID-19 Pandemic in Caregivers of Service Members and Veterans with Traumatic Brain Injury. *Qual Life Res.* 2023;32(12):3463-3474. doi:10.1007/s11136-023-03491-1**

Lead Site: WRNMMC

Collaborative Site(s): NMCS D

Abstract

Purpose: To examine change in HRQOL during the COVID-19 pandemic in caregivers of service members and veterans with TBI, by comparing HRQOL during the first year of the pandemic to HRQOL 12 months pre-pandemic.

Methods: Caregivers (N = 246) were classified into three COVID-19 Pandemic Impact groups based on impact ratings of the pandemic on HRQOL: No Impact (n = 50), Mild Impact (n = 117), and Moderate-Severe Impact (n = 79).

Caregivers completed 19 measures across physical, social, caregiving, and economic HRQOL domains, and a measure of service member and veterans Adjustment. T-scores were used to determine individual symptom trajectories for each measure as follows: Asymptomatic (pre + during < 60 T); Developed (pre < 60 + during ≥ 60 T); Improved (pre ≥ 60 T + during < 60 T); and Persistent (pre + during ≥ 60 T). **Results:** Using ANOVA, during the pandemic, the Moderate-Severe Impact group reported worse scores on 19 measures (d = 0.41-0.89) compared to the No Impact group and 18 measures (d = 0.31-0.62) compared to the Mild Impact group (d = 0.31-0.38). The Mild Impact group reported worse scores on two measures compared to the No Impact group (d = 0.42-0.43). Using the entire sample, the majority of HRQOL measures were classified as Asymptomatic (47.2-94.7%), followed by Persistent (2.4-27.2%). Few were classified as Developed (0.4-12.6%) or Improved (2.4-13.8%). Using repeated measures ANOVA, no meaningful effects sizes were found for mean scores on all measures completed pre-pandemic compared to during the pandemic (d ≤ 0.17). **Conclusion:** The vast majority of caregivers reported stability in HRQOL pre-pandemic compared to during the pandemic. The COVID-19 pandemic was not associated with a high prevalence of decline in caregiver HRQOL.

Potential Clinical Impact: To evaluate the impact of the COVID-19 pandemic on participants in the 15-Year Longitudinal Study on TBI, TBICoE Caregiver & Familiar Member (CGFM) study researchers at WRNMMC assessed changes in TBI caregiver HRQOL before and during the first year of the pandemic. Close to one-third of caregivers of service members and veterans with TBI reported that the COVID-19 pandemic had a moderate-to-severe impact on their HRQOL, and close to half of caregivers reported a mild impact. The Moderate-to-Severe COVID-19 Impact group reported worse scores on HRQOL measures than the Mild and No Impact groups. However, across the sample, the majority of caregivers reported HRQOL stability both before and during the pandemic. The absence of a decline in caregivers' HRQOL during the pandemic could be attributed to demographic factors, established DOD and VA caregiver support programs, and support from community-based organizations.

3. **Brickell TA, Wright MM, Sullivan JK, et al. Health Outcomes in Caregivers of Service Members and Veterans with Traumatic Brain Injury Enrolled in the U.S. Veterans Affairs Caregiver Support Program. *Psychol Serv.* Published online October 12, 2023. doi:10.1037/ser0000771**

Lead Site: WRNMMC

Collaborative Site(s): N/A

Abstract

Objective: To explore health outcomes in caregivers of service members and veterans with TBI enrolled in General and Comprehensive programs with the U.S. Department of Veterans Affairs Caregiver Support Program (VA CSP), and those not enrolled. **Design:** Participants were 290 caregivers classified into three groups: (a) General Program ($n = 34$); (b) Comprehensive Program ($n = 104$); and (c) Not Enrolled ($n = 152$). **Results:** Main outcome measures assessed caregiver HRQOL, service member and veterans' functional ability, and caregiver needs. Compared to the Not Enrolled group, the General, and Comprehensive Program groups reported worse scores on 5 of 25 caregiver HRQOL measures and had a higher proportion of elevated scores on two measures. The Comprehensive Program group reported worse scores on an additional seven HRQOL measures and a higher proportion of elevated scores on three measures compared to the Not Enrolled group. Over 20% of caregivers in each group reported clinically elevated scores on eight HRQOL measures. Few differences between caregiver groups were identified for unmet needs. In the total sample, eight HRQOL measures consistently emerged that were more strongly associated with caregiver needs. Caregivers enrolled in the VA CSP tended to report worse HRQOL and caring for a service member and veterans with worse functional ability compared to those not enrolled. **Conclusion:** A better understanding of health care utilization for those not enrolled in the CSP and in need of help is required.

Potential Clinical Impact: In support of the NDAA FY07 final Sec 721 report to Congress, DVBIC-TBICoE 15YR CGFM researchers sought to compare outcomes in caregivers of service members and veterans with TBI enrolled in two programs within the VA CSP with outcomes in individuals who were not enrolled in the program. The results indicated that caregivers enrolled in the VA CSP had worse HRQOL and that they cared for service members and veterans who had worse overall functional ability measures; however, all caregivers, including those who were not enrolled, in the program had clinically significant HRQOL concerns. The study emphasizes the need for clinical services that will support military caregivers and address the challenges they face.

4. Brickell TA, Wright MM, Sullivan JK, et al. Longitudinal Health-Related Quality of Life in Military Caregivers No Longer Providing Care. *Rehabil Psychol.* 2023;68(4):396-406. doi:10.1037/rep0000489

Lead Site: WRNMMC

Collaborative Site(s): N/A

Abstract

Objective: To examine HRQOL in caregivers when providing care and no longer providing care to service members/veterans with traumatic brain injury. **Design:** Participants included 466 caregivers enrolled in a 15-Year Longitudinal Study. During an annual follow-up evaluation, a subsample of caregivers self-identified as no longer providing care and were retained in the study as a No Longer Caregiving group (n = 48). Scores on HRQOL measures when providing care (baseline) and no longer providing care (follow-up) were examined. Scores on HRQOL measures were also compared with the remaining 418 caregivers (Caregiving group). **Results:** The most frequent reasons for no longer caregiving were no longer being in a relationship with the service member and veterans and service member and veterans that had recovered/no longer required care. The No Longer Caregiving group at follow-up reported better scores on five measures compared to baseline, and three measures compared to the Caregiving group. There were no differences in the proportion of clinically elevated scores on HRQOL measures for the No Longer Caregiving group between baseline and follow-up. Compared to the Caregiving group, the No Longer Caregiving group reported a higher prevalence of clinical elevated scores on General Life Satisfaction at baseline and follow-up, and worse scores on Caregiving Relationship Satisfaction and the Couples Satisfaction Index at baseline. **Conclusions:** While some improvement in HRQOL was noted when caregivers were no longer providing care, many continued to report elevated scores. Services and supports are required for caregivers when providing care, but also when transitioning out of a caregiving role.

Potential Clinical Impact: In support of the NDAA FY07 final Sec 721 report to Congress, the DVBIC-TBICoE 15-Year CGFM Study researchers assessed the change in caregiver HRQOL after the participants transitioned from caregiving to non-caregiving roles for service members and veterans with TBI. The study determined that there was an improvement to HRQOL measures such as resilience, emotional support, and sleep-related impairment. However, despite improvements, many caregivers reported clinically elevated HRQOL scores, suggesting that providing care can have a lasting impact. Overall, this study emphasizes the importance of addressing the unmet needs and challenges of caregivers through resources and services during their transition from caregiving to non-caregiving roles.

HEADACHE

1. Hammerle MH, Thomas LC, Swan AA, Lu LH, Treleaven JM. Sub-Occipital Muscle Pressure Pain Thresholds Correlate to Direction of Symptomatic Active Comfortable Sustained Neck Rotation Testing in Post-Concussive Headache: A Retrospective Observational Cross-Sectional Study. *J Man Manip Ther.* 2023;31(2):124-129. doi:10.1080/10669817.2022.2122370

Lead Site: JBSA

Collaborative Site(s): N/A

Abstract

Objectives: To compare sub-occipital muscle pressure pain thresholds (PPTs) in individuals with persistent post-traumatic headache (PPTH) in relation to the presence or not of cranial nerve and/or autonomic symptoms reported during sustained neck rotation (SNR). **Background:** Previously 81% of military service members with PPTH demonstrated symptoms with SNR up to 60 seconds. Of these, 54% reported symptoms in one (Uni-Symp) and 46% in both directions of rotation (Bi-Symp). Sub-occipital PPTs, in relation to SNR direction, were of interest. **Methods:** Retrospective review of records of 77 individuals, with PPTH with both SNR and PPTs. Average sub-occipital and scalene PPTs were compared between Asymptomatic (n = 13), upon SNR testing, or Symptomatic (Uni-Symp, n = 32, Bi-Symp, n = 32), groups. **Results:** The Bi-Symp group had significantly reduced sub-occipital PPTs relative to the Asymptomatic group on both sides [p < 0.009] with no side-to-side differences in either group. The Uni-Symp group had significantly lower sub-occipital PPTs on the symptomatic SNR test direction compared to the asymptomatic side [t(31) = 3.37, p = 0.002]. There were no differences within or between groups in the scalene PPTs (p's > 0.08). **Conclusions:** An upper cervical mechanical trigger of symptoms during SNR tests in some individuals with PPTH is possible. The direction of symptomatic SNR tests may indicate direction of guarded hypermobile dysfunction and direct treatment.

Potential Clinical Impact: A TBICoE researcher at JBSA supported a study that PPTs in the sub-occipital and scalene muscles during SNR in service members with PPTH after TBI. Patients who experienced symptoms during the SNR test had significantly reduced PPT only in the sub-occipital muscle relative to the direction the rotation occurred. These results, though speculative, provide insight on a potential mechanism for PPTH and suggest a direction for future treatment methods.

2. **Hammerle MH, Lu LH, Thomas LC, et al. Possible Autonomic or Cranial Nerve Symptoms Triggered During Sustained Neck Rotation in Persistent Headache Post-Concussion: A Retrospective Observational Cross-Sectional Study. *J Man Manip Ther.* 2023;31(2):113-123. Doi:10.1080/10669817.2022.2085850**

Lead Site: JBSA

Collaborative Site(s): N/A

Abstract

Objectives: To examine and categorize symptoms occurring within 60 seconds of vertebrobasilar-insufficiency (VBI) testing (left- and right-neck rotation) in individuals with persistent post-traumatic headache. **Background:** As part of routine clinical cervical screening in our patients, we found extended VBI testing often triggered additional symptoms. Therefore, we aimed to document the prevalence and precise symptoms occurring during each movement direction of this test and determine any demographic or baseline signs or symptoms associated with a positive test. **Methods:** A retrospective medical record review on military personnel receiving treatment for persistent post-traumatic headache was performed. Participants were grouped according to presence of non-headache related symptoms triggered during the tests. Frequency, onset, and symptom characteristics reported were categorized as potentially vascular and/or possible autonomic or cranial nerve in nature. **Results:** At least one symptom was reported by 81.3% of 123 patients. Of these, 54% reported symptoms in one and 46% in both directions of rotation, yielding 146 abnormal tests. Most reported symptoms were tear disruption (41%), altered ocular-motor-control (25%), and blepharospasm (16%). Enlisted individuals and those with altered baseline facial sensation were more likely to have a positive test. **Conclusions:** The majority reported symptoms not typical of VBI within 60 seconds of sustained neck rotation. Further study is needed to better understand the mechanisms and clinical relevance.

Potential Clinical Impact: A retrospective medical record review of active-duty service members evaluated for PPTH was performed at JBSA to detect the incidence of symptoms during a 60 second sustained vertebrobasilar insufficiency (VBI) test. Of the 123 records reviewed, 81.3% had at least one symptom during the SNR test, and the majority of symptoms reported were not typical of VBI. Prospective research is needed to determine the causes of PPTH and whether extending the VBI test to 60 seconds has clinical utility.

MENTAL HEALTH

1. Hungerford L, Agtarap S, Ettenhofer M. Impact of Depression and Post-Traumatic Stress on Manual and Oculomotor Performance in Service Members with A History of Mild TBI. *Brain Inj.* 2023;37(8):680-688. doi:10.1080/02699052.2023.2210293

Lead Site: NMCS D

Collaborative Site(s): N/A

Abstract

Objective: To determine the impact of depression and post-traumatic stress on an automated oculomotor and manual measure of visual attention, compared to conventional neuropsychological assessment. **Setting:** Military TBI rehabilitation program. **Participants:** 188 active-duty service members with a history of mild TBI. **Design:** A cross-sectional and correlational study with data obtained through an IRB-approved data registry study. Main measures: BEAM; brief neuropsychological battery; self-reported symptom surveys including NSI, Patient Health Questionnaire-8 (PHQ-8), and PTSD Checklist-5 (PCL-5).

Results: Small effect sizes were found for partial correlations between both depression and post-traumatic stress and key BEAM metrics. In contrast, small-to-medium effects sizes were found across all traditional neuropsychological test measures. **Conclusion:** This study illustrates the profile of impairments associated with depression and post-traumatic stress on saccadic eye movements and manual responses to BEAM relative to conventional neuropsychological tests. Results demonstrated that among active-duty service members seen for mTBI, depression and PTS exert a significant negative impact on measures of processing speed, attention, executive function, and memory across saccadic, manual, and conventional neuropsychological tests. However, the unique psychometric features of each of these assessment approaches may assist in distinguishing the effects of psychiatric comorbidities within this population.

Potential Clinical Impact: Comorbid depression and post-traumatic stress (PTS) can predict poor neurocognitive outcomes in individuals with mTBI, while also having a synergistic influence on persistent mTBI symptoms. During this TBI Registry study, TBICoE researchers at NMCS D evaluated the impact of depression and PTS on oculomotor and manual performance in active-duty service members with mTBI by comparing outcomes from conventional neuropsychological tests to those from the BEAM. Across both methods, depression and PTS had significant negative effects on test outcomes; the unique properties of each assessment may assist with differential diagnosis and enable enhanced, targeted treatment.

- 2. Klyce DW, Perrin PB, Ketchum JM, et al. Suicide Attempts and Ideation Among Veterans/Service Members and Non-Veterans Over 5 Years Following Traumatic Brain Injury: A Combined NIDILRR and VA TBI Model Systems Study. *J Head Trauma Rehabil*. Published online September 29, 2023. doi:10.1097/HTR.0000000000000902**

Lead Site: Central Virginia VA Health Care System

Collaborative Site(s): James A. Haley Veterans' Hospital

Abstract

Objective: This study compared rates of suicide attempt (SA) and suicidal ideation (SI) during the first 5 years after TBI among veterans and service members in the VA and the National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR) Model Systems National Databases to each other and to non-veterans in the NIDILRR database. **Setting:** Twenty-one NIDILRR and five VA TBIMS inpatient rehabilitation facilities in the United States. **Participants:** Participants with TBI were discharged from rehabilitation alive, had a known military status recorded (either non-veteran or history of military service), and successful 1-, 2-, and/or 5-year follow-up interviews completed between 2009 and 2021. The year 1 cohort included 8737 unique participants (8347 with SA data and 3987 with SI data); the year 2 (7628 participants) and year 5 (4837 participants) cohorts both had similar demographic characteristics to the year 1 cohort. **Design:** Longitudinal design with data collected across TBIMS centers at 1-, 2-, and 5-years post-injury. **Main outcomes and measures:** History of SA in past year and SI in past 2 weeks assessed by the Patient Health Questionnaire-9 (PHQ-9). Patient demographics, injury characteristics, and rehabilitation outcomes were also assessed. **Results:** Full sample rates of SA were 1.9%, 1.5%, and 1.6%, and rates of SI were 9.6%, 10.1%, and 8.7% (respectively at years 1, 2, and 5). There were significant differences among groups based on demographic, injury-related, mental/behavioral health, and functional outcome variables. Characteristics predicting SA/SI related to mental health history, substance use, younger age, lower functional independence, and greater levels of disability. **Conclusions:** Compared with participants with TBI in the NIDILRR system, higher rates of SI among service members and veterans with TBI in the VA system appear associated with risk factors observed within this group, including mental/behavioral health characteristics and overall levels of disability.

Potential Clinical Impact: In support of the NDAA FY07 final Sec 721 report to Congress, IMAP and TBIMS researchers performed a comparison of suicide ideation (SI) and suicide attempt (SA) rates during the first five years post-TBI among service members and veterans and non-veterans enrolled in the TBIMS database of the VA Polytrauma Rehabilitation Centers (PRCs) and the NIDILRR. The results indicated that service members and veterans with TBI in the VA PRC

system had higher rates of SI and SA than non-veterans. Factors such as mental health history, age, and disability served as predictors for SI and SA. The findings highlight the importance of mental health history screening among service members and veterans diagnosed with TBI throughout rehabilitation.

- 3. Remigio-Baker RA, Hungerford LD, Ettenhofer ML, et al. Presenting Symptoms as Prognostic Measures of Mental Health Recovery Among Service Members with Concussion. *Front Neurol.* 2023;13:1070676. Published 2023 Jan 13. doi:10.3389/fneur.2022.1070676**

Lead Site: HQ

Collaborative Site(s): Camp Pendleton & NMCS D

Abstract

Background: Comorbid mental illness may negatively impact recovery from concussion. This study evaluated whether the level of symptom clusters at clinic intake contribute to poor mental health recovery in concussed patients during treatment, which may in turn serve as a target intervention. **Objective:** The objective of this study is to examine the association between the level of initial symptoms and mental health symptoms among service members with concussion. **Methods:** Data were obtained from 483 active-duty service members treated in interdisciplinary treatment programs for traumatic brain injury, all of which were concussions. Pre-treatment symptom clusters included self-reported hyperarousal, dissociation/depression, cognitive dysfunction/headache, and neurological symptoms. The outcomes, clinically relevant decreases in depressive symptoms (assessed by the 8-item Patient Health Questionnaire, PHQ-8) and PTSD symptoms (assessed by the PTSD Checklist for DSM-5, PCL-5), were defined as a decrease in PHQ-8 > 5 and PCL-5 > 7, respectively. Poisson regression with robust error variance was used to evaluate the relationship between the level of each symptom cluster and clinically relevant decrease in outcomes. **Results:** Participants with higher (vs. lower) levels of pre-treatment hyperarousal and dissociation/depression symptom cluster were less likely to improve in depressive and PTSD symptoms during treatment. The level of cognitive/headache and neurological symptom clusters were not significantly associated with any symptom changes. **Conclusion:** These findings support the need for individualized treatment for symptoms identified and treated after determining concussion history, with particular attention to high levels of hyperarousal and dissociation/depression prior to treatment.

Potential Clinical Impact: TBICoE researchers at HQ, NMCS D, and Camp Pendleton examined clinically relevant changes in depressive and PTSD symptoms after concussion treatment among active-duty service members to determine whether symptom clusters were predictive of mental health recovery.

Active-duty service members with higher levels of pre-treatment hyperarousal and depression/dissociation were less likely to have clinically relevant decreases in depressive and PTSD symptoms during treatment than individuals with lower pre-treatment levels. Clinicians may need to provide early, targeted mental health treatment to patients upon initial evaluation to optimize positive outcomes.

- 4. Remigio-Baker RA, Bailie JM, Ettenhofer ML, Cordero E, Hungerford LD. The Impact of Lifetime Traumatic Brain Injury (TBI) On Mental Health Symptoms Among Service Members in Interdisciplinary TBI Programs. *Mil Med.* 2023;188(Suppl 6):199-207. doi:10.1093/milmed/usad085**

Lead Site: HQ

Collaborative Site(s): Camp Pendleton & NMCS D

Abstract

Introduction: TBI is highly prevalent among active-duty service members and imposes a significant health burden, particularly on mental health (e.g., PTSD and depressive symptoms). Little is known about how TBI setting characteristics impact PTSD and depressive symptom expression in service members undergoing interdisciplinary TBI care. **Materials and methods:** The study included 455 patients enrolled in interdisciplinary, outpatient TBI programs within the military health system. Using Poisson regression with robust error variance, TBI injury setting characteristics (i.e., before military service, during military training, and during noncombat/combat deployment) were evaluated against clinically elevated PTSD (PTSD Checklist, DSM-5 score ≥ 33) and depressive (Patient Health Questionnaire-8 score ≥ 15) symptoms. **Results:** In adjusted models, TBI sustained before military service was associated with less likelihood for clinically elevated PTSD symptoms at pretreatment (prevalence ratio [PR] = 0.76, confidence interval [CI] = 0.60-0.96) and post-treatment (PR = 0.67, CI = 0.52-0.87). TBI sustained during combat deployment, however, resulted in the greatest impact on clinically elevated pretreatment PTSD (PR = 1.49, CI = 1.16-1.91) and depressive (PR = 1.47, CI = 1.06-2.03) symptoms. Null results were found between military training/noncombat deployment and mental health symptoms. Regardless of the TBI setting, following TBI treatment, there remained 37.5% (n = 180) and 24.8% (n = 108) with clinically elevated PTSD and depressive symptoms, respectively. **Conclusions:** There was a differential impact of TBI settings, particularly between TBI sustained before military service and that from combat deployment among active-duty service members enrolled in outpatient TBI programs. This may be indicative of differences in the characteristics of these environments (e.g., injury severity) or the impact of such an event during recovery from current TBIs. The large percentage of active-duty service members who present with clinically elevated mental health symptoms after

treatment may suggest the need for additional resources to address mental health needs before, during, and after treatment in TBI programs.

Potential Clinical Impact: TBICoE HQ and Camp Pendleton researchers sought to better understand how TBI setting characteristics (i.e., where and when the TBI was sustained) impact active-duty service members' mental health symptoms, such as PTSD and depression, after treatment. TBIs sustained prior to military service were associated with better PTSD symptoms at pre- and posttreatment timepoints, while TBIs sustained during military involvement were associated with more neurobehavioral, PTSD, and depressive symptoms after treatment. Interestingly, those who sustained TBIs during combat deployment were more likely to have clinically relevant decreases in the number of cognitive and physical symptoms following interdisciplinary TBI treatment programs, indicating good program fit for combat related TBI. These findings emphasize the importance of considering the context and timing of TBI and the nature of symptom presentation when developing treatment strategies and suggest the need for additional mental health resources in TBI programs.

MILITARY SERVICE DELIVERY

1. Cotner BA, Nakase-Richardson R, O'Connor DR, et al. **Barriers and Facilitators to Accessing Rehabilitation Health Care: A Veterans Affairs Traumatic Brain Injury Model Systems Qualitative Study.** *Arch Phys Med Rehabil.* 2023;104(3):380-389. doi:10.1016/j.apmr.2022.09.020

Lead Site: James A. Haley Veterans' Hospital

Collaborative Site(s): N/A

Abstract

Objective: To compare barriers and facilitators to accessing health care services among service members and veterans by TBI severity groups. **Design:** Qualitative descriptive study guided by an access to health care services conceptual framework. **Setting:** Five VA PRCs. **Participants:** Service member and veterans (N=55, including 10 caregivers as proxies) ≥ 2 years post-TBI recruited from the VA TBIMS and grouped by TBI severity (mild/moderate, severe). **Main outcome measures:** Barriers and facilitators accessing care. **Results:** The main facilitators included ease of communicating with providers to help service member and veterans identify and utilize appropriate health care, family advocates who promoted engagement in health care, ability to use government and community facilities, and online resources or equipment. Distance to services was uniformly identified as a main barrier for both patient groups. However, facilitators and barriers to health care access differed by TBI severity. Service member and veterans with severe TBI highlighted the role of nonprofit organizations in promoting health care engagement and the availability of VA

specialty residential programs in meeting health care needs. Having unrecognized health care needs in chronic stages and communication difficulties with providers were more commonplace for those with greater TBI severity and affected quality of care. Those with mild/moderate TBI highlighted challenges associated with paying for services in the community and scheduling of services. **Conclusions:** Barriers and facilitators exist across multiple dimensions of a health care access framework and vary by TBI severity. Results suggest possible mechanistic links between health care access and service member and veterans' health outcomes. Findings support current policy and practice efforts to facilitate health care access for service members and veterans with TBI but highlight the need for tailored approaches for those with greater disability.

Potential Clinical Impact: In support of the 15-Year Longitudinal Study (NDAA 2007, Sec 721), IMAP/ TBIMS researchers used qualitative methods to investigate barriers and facilitators to accessing health care services 2 years post-TBI among 55 service members and veterans. Overall, facilitators and barriers varied by TBI severity, with severe TBI patients noting unrecognized health care needs and a desire for more/new care, whereas this barrier was rarely mentioned by mTBI patients. These findings support the need to improve policies by considering TBI severity to address service members' and veterans' health care needs and access to care.

2. Dismuke-Greer CE, Almeida EJ, Silva MA, et al. Effect of Post-traumatic Amnesia Duration on Traumatic Brain Injury (TBI) First Year Hospital Costs: A Veterans Affairs Traumatic Brain Injury Model Systems Study. *Arch Phys Med Rehabil.* 2023;104(7):1007-1015. doi:10.1016/j.apmr.2023.03.023

Lead Site: James A. Haley Veterans' Hospital

Collaborative Site(s): N/A

Abstract

Objective: To examine the association between severity of TBI as measured by duration of post-traumatic amnesia (PTA) and first year hospitalization costs for service members and veterans treated for TBI at PRCs within the Veterans Health Administration (VHA). **Design:** Multivariable models of merged datasets from the VA TBIMS national database containing TBI clinical characterization including PTA with VHA hospital cost data. **Setting:** Five VA PRCs. **Participants:** VA TBIMS participants with known PTA who received inpatient rehabilitation within one year of their TBI at any of five PRCs between 2010 and 2020 (N=717).

Interventions: N/A. **Main outcome measures:** Total, acute care, rehabilitation, intensive care unit (ICU), and surgery costs across all VA hospitals. **Results:** A total of 717 service member and veterans (mean age 36.9 years, 94.1% men, 76.8% non-Hispanic White, 7.8% active duty) met inclusion criteria for the unadjusted analyses. Unadjusted mean total hospital costs in the first-year post TBI were

approximately \$201,214 higher for those with PTA duration ≥ 24 hours (\$351,157) than PTA < 24 hours (\$149,943). In adjusted models ($n=583$), each additional day of PTA duration incrementally increased total (\$1453), rehabilitation (\$1324), ICU (\$78), and surgery (\$39) costs. Other significant covariates included age, acute care length of stay, Disability Rating Scale on rehabilitation admission, penetrating violent cause of injury, and drug abuse. **Conclusions:** This study demonstrates that PTA as a quantitative measure of TBI severity significantly affects first-year hospitalization costs of service member and veterans treated at PRCs. Each additional day of PTA was associated with higher total, rehabilitation, ICU, and surgery costs. Mean first year hospital costs were also found to exceed the highest budget allocation to VHA facilities for a veteran treated at a PRC. These findings have possible implications for hospital care provision for those receiving inpatient rehabilitation in VHA settings.

Potential Clinical Impact: Post-traumatic amnesia (PTA) is a component of the DOD criteria for classifying TBI severity. Civilian research has demonstrated that PTA is a stronger predictor of hospitalization after TBI and its associated costs than ICD codes. To understand how PTA, when used as a proxy measurement for TBI severity, may predict the cost of hospitalization related services, VA TBIMS and TBICoE researchers conducted health economics research in support of the Sec 721 15-Year Longitudinal Studies on TBI. Investigators merged VHA and TBIMS administrative data from 717 service members and veterans who received inpatient rehabilitation at a PRC within one year of TBI. A longer duration of PTA significantly predicted higher rehabilitation, surgery, and ICU costs. Mechanism of injury had the greatest impact on cost; patients with penetrating TBIs sustained through violent causes had a notably higher rehabilitation cost than those who sustained TBIs through other mechanisms of injury. This study is an important first step in advancing our understanding of factors that drive TBI hospitalization time and rehabilitation costs and our ability to predict health care resourcing needs after TBI. Researchers are currently working with DOD administrative and cost databases to understand factors relevant to MHS TBI care.

3. Cogan AM, Bailie JM. Therapeutic Relationship in mTBI Rehabilitation: The Disparity Between the Illness Experience and Clinical Definitions. *Mil Med.* 2023;188(9-10):e3010-e3016. doi:10.1093/milmed/usad143

Lead Site: Camp Pendleton

Collaborative Site(s): N/A

Abstract

Introduction: A positive therapeutic relationship is characterized by trust and mutually perceived genuineness. It is positively associated with patients' adherence to treatment, satisfaction, and health outcomes. When service

members with a history of mTBI present to rehabilitation clinics with nonspecific symptoms, a disparity between their experience of disability and clinical expectations of mTBI may disrupt the establishment of a positive therapeutic relationship between patients and providers. The objectives of this study are to (1) explore disparities between military service members and rehabilitation clinicians about the clinical diagnosis and illness experience of mTBI and (2) identify barriers to the establishment of a positive therapeutic relationship.

Materials and methods: This is a qualitative descriptive study of military service members with prior mTBI (n = 18) and clinicians (n = 16) who participated in interviews and focus groups. Data were analyzed thematically using Kleinman's framing of illness experience and clinical diagnosis. **Results:** Three themes reflected the potential breakdowns in the therapeutic relationship. The first theme, clinical expectations for post-injury recovery versus patients' experience of ongoing disability, reflects the inconsistency between clinicians' expectations of symptom resolution within 90 days following mTBI and service members' experiences of symptoms that worsened over several months or years. The second theme, symptom attribution to mental health conditions versus tissue injury, describes the difficulty in attributing symptoms to the physical impact of the mTBI or mental health diagnoses that may also stem from the injury event. The third theme, suspected malingering versus valid disability, describes clinicians' reports of frustration with cases in which they suspected malingering for secondary gains in contrast with service members' feelings that their problems were not taken seriously by clinicians. **Conclusions:** This study extended previous research on therapeutic relationships by examining the situation of mTBI rehabilitation services for military service members. The findings reinforce the best practice recommendations of acknowledging patients' experiences, addressing the presenting symptoms and problems, and encouraging progressive return to activity following mTBI. Acknowledgment of and attention to patients' illness experience by rehabilitation clinicians is necessary and important for supporting a positive therapeutic relationship and ultimately to optimize patients' health outcomes and reduce disability.

Potential Clinical Impact: To better understand barriers in establishing positive therapeutic clinician-patient relationships, TBICoE NMCSO researchers teamed up with VA researchers at the Center for the Study of Healthcare Innovation, Implementation and Policy to interview and conduct focus groups with active-duty service members with a history of mTBI and their care providers. Thematic analysis identified three conflicting trends that inhibit the establishment of positive clinician-patient relationships: (1) "Clinical expectations for post-injury recovery versus patients' experience of ongoing disability," (2) "Symptom attribution to mental health conditions versus tissue injury," and (3) "Suspected malingering versus valid disability." Clinician use of objective assessments to supplement patient self-report may alleviate some concerns about malingering. Additionally, approaching treatment by using an "ethnographic attitude" to

understand patient experiences and promoting patient education may help eliminate these barriers.

4. **Gurney JM, Tadlock MD, Dengler BA, et al. Committee on Surgical Combat Casualty Care Position Statement: Neurosurgical Capability for The Optimal Management of Traumatic Brain Injury During Deployed Operations. *J Trauma Acute Care Surg.* 2023;95(2S Suppl 1):S7-S12. doi:10.1097/TA.0000000000004058**

Lead Site: JBSA (not TBICoE affiliated)

Collaborative Site(s): HQ

Abstract

Background: Experiences over the last 3 decades of war have demonstrated a high incidence of TBI resulting in a persistent need for a neurosurgical capability within the deployed theatre of operations. Despite this, no doctrinal requirement for a deployed neurosurgical capability exists. Through an iterative process, the Joint Trauma System Committee on Surgical Combat Casualty Care (CoSCCC) developed a Position Statement to inform medical and non-medical military leaders about the risks of the lack of a specialized neurosurgical capability.

Methods: The need for deployed neurosurgical capability Position Statement was identified during the spring 2021 CoSCCC meeting. A tri-service working group of experienced forward-deployed caregivers developed a preliminary statement. An extensive iterative review process was then conducted to ensure that the intended messaging was clear to senior medical leaders and operational commanders. To provide additional context and a civilian perspective, statement commentaries were solicited from civilian clinical experts including a recently retired military trauma surgeon boarded in Neurocritical Care, a trauma surgeon instrumental in developing the Brain Injury Guidelines (BIG), a practicing neurosurgeon with world-renowned expertise in TBI, and the Chair of the Committee on Trauma (COT). **Results:** After multiple revisions, Position Statement was finalized it was approved by the CoSCCC membership in February 2023. Challenges identified include: 1) military neurosurgeon attrition; 2) the lack of a doctrinal neurosurgical capabilities requirement during deployed combat operations; 3) the need for neurosurgical telemedicine capability and in-theatre CT scans to triage TBI casualties requiring neurosurgical care. **Conclusion:** Challenges identified regarding neurosurgical capabilities within the deployed trauma system include military neurosurgeon attrition and the lack of a doctrinal requirement for neurosurgical capability during deployed combat operations. To mitigate risk to the force in a future peer-peer conflict several evidence-based recommendations are made. The solicited civilian commentaries strengthen these recommendations by putting them into the context of civilian TBI management. These neurosurgical capabilities position

statement is intended to be a forcing function and a communication tool to inform operational commanders and military medical leaders on the use of these teams on current and future battlefields.

Potential Clinical Impact: Joint Trauma System Committee of Surgical Combat Casualty Care (CoSCCC) providers issued a Position Statement concerning the critical need for neurosurgeons at Role 3 MTFs. CoSCCC providers noted the risks associated with the lack of neurosurgical care providers in theater, including delayed care and increased morbidity and mortality for service members with a TBI. They issued six recommendations to mitigate the risk to the Joint Force from TBI, such as increased neurosurgical telemedicine capability and in-theater CT scans for triage.

NEUROIMAGING

1. Lippa SM, Yeh PH, Ollinger J, Brickell TA, French LM, Lange RT. **White Matter Integrity Relates to Cognition in Service Members and Veterans After Complicated Mild, Moderate, and Severe Traumatic Brain Injury, But Not Uncomplicated Mild Traumatic Brain Injury.** *J Neurotrauma*. 2023;40(3-4):260-273. doi:10.1089/neu.2022.0276

Lead Site: WRNNMC

Collaborative Site(s): N/A

Abstract

Background: The extant literature investigating the relationship between diffusion tensor imaging (DTI) and cognition following TBI is limited by small sample sizes and inappropriate control groups. **Objective:** The present study examined DTI metric differences between service members and veterans with bodily injury (Trauma Control; TC), uncomplicated mTBI, complicated mild TBI (compTBI), and severe-moderate TBI combined (smTBI), and how DTI metrics related to cognition within each group. **Design:** Participants were 226 service member and veterans (56 TC, 112 mTBI, 29 compTBI, 29 smTBI) with valid neuropsychological testing and DTI at least 11 months post-injury. **Results:** The smTBI group demonstrated decreased fractional anisotropy (FA) and increased axial diffusivity (AD), mean diffusivity (MD), and radial diffusivity (RD) of the cerebral white matter (CWM) and several individual white matter tracts compared with the TC, mTBI, and compTBI groups (all $p < 0.05$; $r_s = 0.17$ to 0.49). The TC, mTBI, and compTBI groups did not differ in terms of any DTI metrics. Within the smTBI group, FA, AD, MD, and RD of the total CWM and several white matter tracts were related to Processing Speed ($|r_s| : 0.43$ to 0.66 ; $p_s < 0.05$), and/or Delayed Memory ($|r_s| : 0.41$ to 0.67 ; $p_s < 0.05$). In the compTBI group, Processing Speed was related to left arcuate fasciculus and superior longitudinal fasciculus (SLF) FA, MD, and RD, as well as left uncinatus fasciculus MD and RD. In

contrast, there were no significant relationships between DTI metrics and cognition/emotional functioning within the mTBI or TC groups. **Conclusion:** Overall, findings suggest a dose-response relationship between TBI severity and the strength of the relationship between white matter integrity and cognitive performance, with essentially no relationship in mTBI, some findings in compTBI, and several strongly significant relationships in smTBI. In contrast to previously reported findings, there were no differences in DTI metrics between controls, mTBI, and compTBI, and DTI metrics were unrelated to cognition in our relatively large mTBI group.

Potential Clinical Impact: In this study, 15-Year Longitudinal Study researchers, collaborating with NICoE, explored the differences in diffuse tensor imaging (DTI) metrics among service members and veterans with uncomplicated mTBI, complicated mTBI, severe-moderate TBI, and controls without TBI to determine whether DTI metrics that vary among groups relate to cognition. Only individuals with severe-moderate TBI had DTI metrics that differed significantly from those in all other groups. In addition, some DTI measures in the severe-moderate and complicated mTBI groups were associated with decreased processing speed and delayed memory. Utilization of DTI protocols may eventually provide data on areas of the brain associated with cognitive deficits observed after TBI.

- 2. Gimbel SI, Wang CC, Hungerford L, Twamley EW, Ettenhofer ML. Associations of mTBI And Post-Traumatic Stress to Amygdala Structure and Functional Connectivity in Military Service Members. *Front Neuroimaging*. 2023;2:1129446. Published 2023 Mar 8. doi:10.3389/fnimg.2023.1129446**

Lead Site: NMCSD

Collaborative Site(s): N/A

Abstract

Introduction: TBI is one of the highest public health priorities, especially among military personnel where comorbidity with post-traumatic stress symptoms and resulting consequences is high. Brain injury and post-traumatic stress symptoms are both characterized by dysfunctional brain networks, with the amygdala specifically implicated as a region with both structural and functional abnormalities. **Methods:** This study examined the structural volumetrics and resting state functional connectivity of 68 active-duty service members with or without chronic mild TBI (mTBI) and comorbid symptoms of Post-Traumatic Stress (PTS). **Results and discussion:** Structural analysis of the amygdala revealed no significant differences in volume between mTBI and healthy comparison participants with and without post-traumatic stress symptoms. Resting state functional connectivity with bilateral amygdala revealed decreased anterior network connectivity and increased posterior network connectivity in the mTBI group compared to the healthy comparison group. Within the mTBI group, there

were significant regions of correlation with amygdala that were modulated by PTS severity, including networks implicated in emotional processing and executive functioning. An examination of a priori regions of amygdala connectivity in the default mode network, task positive network, and subcortical structures showed interacting influences of TBI and PTS, only between right amygdala and right putamen. These results suggest that mTBI and PTS are associated with hypo-frontal and hyper-posterior amygdala connectivity. Additionally, comorbidity of these conditions appears to compound these neural activity patterns. PTS in mTBI may change neural resource recruitment for information processing between the amygdala and other brain regions and networks, not only during emotional processing, but also at rest.

Potential Clinical Impact: Due to the high prevalence of comorbid TBI and PTSD among service members and veterans, TBICoE researchers at NMCSD analyzed the connectivity and volumetric changes of the amygdala, which has been implicated in both conditions. Among those diagnosed with mTBI, researchers found no changes in amygdala volume but observed greater amygdala resting state functional connectivity to the posterior brain and lower amygdala connectivity to the frontal brain in those with mTBI and PTS symptoms. Overall, these findings suggest that the amygdala may play a role in information processing with other brain regions when at rest and during emotional processing; further research is required to better understand the mechanism underlying these processes.

- 3. Gimbel SI, Hungerford LD, Twamley EW, Ettenhofer ML. White Matter Organization and Cortical Thickness Differ Among Active-Duty Service Members with Chronic Mild, Moderate, and Severe Traumatic Brain Injury. *J Neurotrauma*. Published online November 15, 2023. doi:10.1089/neu.2023.0336**

Lead Site: NMCSD

Collaborative Site(s): N/A

Abstract

Objective: This study compared findings from whole-brain diffusion tensor imaging (DTI) and volumetric magnetic resonance imaging (MRI) among 90 active-duty service members with chronic mild traumatic brain injury (TBI; n = 52), chronic moderate-to-severe TBI (n = 17), and TBI-negative controls (n = 21).

Methods: Data were collected on a Philips Ingenia 3T MRI with DTI in 32 directions. **Main outcomes and measures:** Results demonstrated that history of TBI was associated with differences in white matter microstructure, white matter volume, and cortical thickness in both mild TBI and moderate-to-severe TBI groups relative to controls. However, the presence, pattern, and distribution of these findings varied substantially depending on the injury severity. Spatially

defined forms of DTI fractional anisotropy (FA) analyses identified altered white matter organization within the chronic moderate-to-severe TBI group, but they did not provide clear evidence of abnormalities within the chronic mild TBI group. In contrast, DTI FA “pothole” analyses identified widely distributed areas of decreased FA throughout the white matter in both the chronic mild TBI and chronic moderate-to-severe TBI groups. Additionally, decreased white matter volume was found in several brain regions for the chronic moderate-to-severe TBI group compared with the other groups. Greater number of DTI FA potholes and reduced cortical thickness were also related to greater severity of self-reported symptoms. **Conclusion:** In sum, this study expands upon a growing body of literature using advanced imaging techniques to identify potential effects of brain injury in military Service Members. These findings may differ from work in other TBI populations due to varying mechanisms and frequency of injury, as well as a potentially higher level of functioning in the current sample related to the ability to maintain continued Active-Duty status after injury. In conclusion, this study provides DTI and volumetric MRI findings across the spectrum of TBI severity. These results provide support for the use of DTI and volumetric MRI to identify differences in white matter microstructure and volume related to TBI. In particular, DTI FA pothole analysis may provide greater sensitivity for detecting subtle forms of white matter injury than conventional DTI FA analyses.

Potential Clinical Impact: TBICoE NMCSD researchers conducted a study to compare white and grey matter integrity in active-duty service members with a history of chronic/symptomatic TBI with that in a control group of uninjured service members. After comparing whole brain Diffuse Tensor Imaging (DTI) and volumetric MRI findings, the results indicated that a history of TBI is associated with differences in white matter microstructure, white matter volume, and cortical thickness. DTI analysis indicated decreased fractional anisotropy (FA) and a greater number and distribution of potholes (i.e., white matter with abnormally low FA values) in the TBI groups, which was associated with more neurobehavioral symptoms. Overall, this study provides insights into how TBI impacts the brain and underscores the importance of considering injury severity in research settings.

RESEARCH STRATEGIES

1. Turner SM, Kiser SA, Gipson BJ, Martin EMM, Smith JM. Surveying the Landscape: A Review of Longitudinal Traumatic Brain Injury Studies in Service Member and Veteran Populations. *J Neurotrauma*. 2023;40(11-12):1060-1074. doi:10.1089/neu.2022.0237

Lead Site: HQ

Collaborative Site(s): N/A

Abstract

Background: TBI is known to be a signature wound of the post-9/11 conflicts. In response, the U.S. Department of Defense (DOD) and other federal organizations have directed significant investments toward TBI research on characterizing injury populations and understanding long-term outcomes. To address legislative requirements and research gaps, several observational, longitudinal TBI studies were initiated as an effective means of investigating TBI clinical management, outcomes, and recovery. **Objective:** This review synthesizes the landscape (i.e., requirements and gaps, infrastructure, geography, timelines, TBI severity definitions, military and injury populations of interest, and measures) of DOD-funded longitudinal TBI studies being conducted in service member and veteran populations. **Conclusion:** Based on the landscape described here, we present recommended actions and solutions that would allow a consolidated and cooperative future state of longitudinal TBI research, optimized continued investments, and advances in the state of the science without redundancy.

Potential Clinical Impact: The TBICoE HQ staff synthesized the landscape of DOD-funded longitudinal studies being conducted in service members and veterans to facilitate the visibility and coordination of existing research efforts. Recommendations are also outlined to inform targeted research strategies to meet the evolving needs of the DOD and maximize return on investment.

2. Pickett TC, Walker WC, Lippa SM, et al. Crosswalk Comparison of the DVBIC-TBICoE and LIMBIC-CENC Combat-Related Concussion Prospective Longitudinal Study Datasets. Arch Phys Med Rehabil. 2023;104(7):1072-1080.e1. doi:10.1016/j.apmr.2023.02.003.

Lead Site: WRNMMC

Collaborative Site(s): HQ

Abstract

Objective: To describe and compare cohorts between 2 large, longitudinal, federally funded TBI studies of Service members and veterans across demographic, self-report, and neuropsychological variables. **Design:** Analysis of data from the DVBIC-TBICoE and LIMBIC-CENC prospective longitudinal studies (PLS). **Setting:** Recruitment locations spanning Department of Defense and Veterans Affairs hospitals across the U.S. **Participants:** 1463 participants ($N=1463$) enrolled in the DVBIC-TBICoE study and divided among non-injured (NIC) ($n=191$), injured control (IC) ($n=349$), mTBI) ($n=682$), and (severe, moderate, penetrating, and complicated mild traumatic brain injury (smcTBI) ($n=241$) subgroups. 1550 participants enrolled in the LIMBIC-CENC study and divided

between IC ($n=285$) and mTBI ($n=1265$) subgroups. IC and mTBI study groups were compared across demographic and military characteristics, self-reported symptoms, and neuropsychological test scores. **Interventions:** None. **Main outcome measures:** Neurobehavioral Symptom Inventory, PTSD Checklist-Military Version, TBI quality of life, Test of Premorbid Functioning, Wechsler Adult Intelligence Scale-IV Visual Puzzles, Symbol Search, Coding, Letter-Number Sequencing, and Digit Span, Trail Making Test, Delis-Kaplan Executive Functioning System Verbal Fluency, Letter Fluency, and Category Fluency, California Verbal Learning Test-II, and Grooved Pegboard. **Results:** Compared with DVBIC-TBICoE, LIMBIC-CENC participants have higher enrollment age, education level, proportion of Black race, and time from injury as well as less combat deployments and are less likely to be married. The distribution of military service branches also differed. Further, symptom profiles differed between cohorts. LIMBIC-CENC participants endorsed higher posttraumatic stress disorder symptomatology. DVBIC-TBICoE study IC participants endorsed higher somatosensory and vestibular symptoms (medium effect sizes). Other symptom measure differences had very small effect sizes (≤ 0.2). Differences were found on many cognitive test results, but are difficult to interpret given the demographic differences and generally very small effect sizes. **Conclusions:** The heavy use of National Institutes of Health common data elements in both studies and collaboration with the DVBIC-TBICoE study team on development of the LIMBIC-CENC assessment battery enabled this comparative analysis. Results highlight unique differences in study cohorts and add perspective and interpretability for assimilating past and future findings.

Potential Clinical Impact: The DVBIC-TBICoE 15-Year Longitudinal Study on TBI researchers worked with LIMBIC-CENC study investigators to conduct a crosswalk comparison of their datasets to evaluate the feasibility of combining their data to better understand the long-term impact of military TBI. The crosswalk indicated some differences in demographics, symptoms, and neuropsychological outcomes across their more than 3,000 total participants. Overall, each study adds unique insights into the landscape of TBI outcomes. Study teams accomplished this comparison mainly by their intentional use of NIH common data elements and collaboration in study development.

- 3. Hamilton JA, Ketchum JM, Hammond FM, et al. Comparison of Veterans' Affairs and NIDILRR Traumatic Brain Injury Model Systems Participants with Disorders of Consciousness. *Brain Inj.* 2023;37(4):282-292. doi:10.1080/02699052.2022.2158226**

Lead Site: James A. Haley Veterans' Hospital

Collaborative Site(s): N/A

Abstract

Objective: To characterize demographic, pre-injury, and outcome data within the NIDILRR and VA TBIMS cohorts with severe TBI with no command-following ability at time of admission to acute rehabilitation. **Design:** Retrospective cohort. **Setting:** NIDILRR and VA TBIMS centers. **Participants:** 396 NIDILRR and 72 VA participants without command-following ability who experienced TBI with subsequent Disorder of Consciousness (DoC). **Main outcome measure:** Pre-injury and injury characteristics, rehabilitation outcomes, and 1-year self-reported outcomes. **Results:** VA TBIMS cohort included individuals who were active duty or had military service before their injury. The VA cohort were more likely to be re-hospitalized at 1-year follow-up or residing in a long-term care or rehab setting. The NIDILRR TBIMS cohort had higher FIM and DRS scores at rehabilitation discharge, while the VA participants saw longer lengths of stay and higher numbers of “violent” injury types. **Conclusions:** This study allows for a better understanding of the comparability between VA and NIDILRR DoC cohorts providing guidance on how veteran and civilian samples might be merged in future TBIMS studies to explore predictors of recovery from a DoC.

Potential Clinical Impact: The TBIMS team at the James A. Haley Veterans' Hospital collaborated on a study to compare injury and rehabilitation outcome data from patients treated for severe TBI and DoC at a VA PRC with that obtained from individuals in a civilian setting. Patient data in the NIDILRR TBIMS and VA TBIMS data sets were compared. The civilian and military data sets differed in a variety of injury characteristics, rehabilitation outcomes, and 1-year post-injury outcomes. Findings of this study support the future use of merged TBIMS data sets to compare heterogeneous populations across rehabilitation settings to guide evidence-based treatment, rehabilitation, and management after TBI.

RISK FACTORS

1. Lange RT, French LM, Lippa S, et al. Risk Factors for The Presence and Persistence of Posttraumatic Stress Symptoms Following Traumatic Brain Injury in U.S. Service Members and Veterans. *J Trauma Stress*. 2023;36(1):144-156. doi:10.1002/jts.22892

Lead Site: WRNMMC

Collaborative Site(s): Camp Pendleton & NMCS D

Abstract

Objective: This study aimed to identify risk factors predictive of the presence and persistence of PTSD symptom reporting following TBI. **Design:** Participants were 1,301 U.S. service members and veterans divided into four groups:

uncomplicated mTBI (n = 543); complicated mild, moderate, severe, and penetrating TBI (n = 230); injured controls (n = 340); and noninjured controls (n = 188). We examined 25 factors related to demographic, injury-related, military-specific, treatment/health care need, and mental health/social support variables. Seven factors were statistically associated with the presence of DSM-IV-TR symptom criteria for PTSD: premorbid IQ, combat exposure, depression, social participation, history of mTBI, need for managing mood and stress, and need for improving memory and attention, $p < .001$ (51.3% variance). **Results:** When comparing the prevalence of these risk factors in a longitudinal cohort (n = 742) across four PTSD trajectory groups (i.e., asymptomatic, improved, developed, persistent), a higher proportion of participants in the persistent PTSD group reported worse depression, a lack of social participation, and history of mTBI. Additionally, a higher proportion of participants in the persistent and developed PTSD groups reported the need for managing mood/stress and improving memory/attention. When considered simultaneously, the presence of ≥ 1 or ≥ 2 risk factors was associated with a higher proportion of participants in the developed and persistent PTSD groups, $ps < .001$. **Conclusion:** These risk factors may be useful in identifying service member and veterans at risk for the development and/or persistence of PTSD symptoms who may need intervention.

Potential Clinical Impact: In this study, 15-Year Longitudinal TBI Study researchers sought to identify risk factors predictive of PTSD symptoms in service members and veterans with and without a history of TBI. The investigators reviewed the persistence of symptoms over time in 1,301 service member and veterans. Seven of the total twenty-five risk factors evaluated were associated with PTSD symptoms, including low premorbid IQ, high combat exposure, severe depressive symptoms, lack of social participation, history of mTBI, service needs for managing mood or stress, and service needs for improving memory and attention. Additionally, the presence of four (4) or more of these risk factors was strongly associated with the persistence of PTSD symptom reporting over time. Clinicians should screen service members and veterans for these seven risk factors upon return from deployment and during treatment to identify risk and provide early clinical intervention to optimize outcomes.

- 2. Sander AM, Williams M, Loyo K, et al. Disparities in Chronic Pain Experience and Treatment History Among Persons with Traumatic Brain Injury: A Traumatic Brain Injury Model Systems Study. *J Head Trauma Rehabil.* 2023;38(2):125-136. doi:10.1097/HTR.0000000000000870**

Lead Site: James A. Haley Veterans' Hospital

Collaborative Site(s): N/A

Abstract

Objective: To determine disparities in pain severity, pain interference, and history of pain treatment for non-Hispanic Whites, non-Hispanic Blacks, and Hispanics with TBI and chronic pain. **Setting:** Community following discharge from inpatient rehabilitation. **Participants:** A total of 621 individuals with medically documented moderate to severe TBI who had received acute trauma care and inpatient rehabilitation (440 non-Hispanic Whites, 111 non-Hispanic Blacks, and 70 Hispanics). **Design:** A multicenter, cross-sectional, survey study. **Main Measures:** Brief Pain Inventory; receipt of opioid prescription; receipt of nonpharmacologic pain treatments; and receipt of comprehensive interdisciplinary pain rehabilitation. **Results:** After controlling for relevant sociodemographic variables, non-Hispanic Blacks reported greater pain severity and greater pain interference relative to non-Hispanic Whites. Race/ethnicity interacted with age, such that the differences between Whites and Blacks were greater for older participants (for severity and interference) and for those with less than a high school education (for interference). There were no differences found between the racial/ethnic groups in the odds of having ever received pain treatment. **Conclusions:** Among individuals with TBI who report chronic pain, non-Hispanic Blacks may be more vulnerable to difficulties managing pain severity and to interference of pain in activities and mood. Systemic biases experienced by many Black individuals with regard to social determinants of health must be considered in a holistic approach to assessing and treating chronic pain in individuals with TBI.

Potential Clinical Impact: TBIMS researchers at James A. Haley Veterans' Hospital explored racial/ethnic disparities in the experience and treatment of chronic pain after TBI among 621 individuals previously treated at a TBIMS inpatient rehabilitation facility. In this study, non-Hispanic Blacks self-reported greater pain severity and pain interference than non-Hispanic Whites. Additionally, this interaction further increased with older age and lower educational attainment. However, race/ethnicity was not a predictor of having received treatment for pain. Clinicians should consider social determinants of health and how they might influence a patient's response to treatment to provide equitable treatment for TBI.

- 3. Sander AM, Christensen K, Loyo K, et al. Coping with Chronic Pain After Traumatic Brain Injury: Role of Race/Ethnicity and Effect on Participation Outcomes in a TBI Model Systems Sample. *Arch Phys Med Rehabil.* 2023;104(7):1099-1106. doi:10.1016/j.apmr.2023.03.003**

Lead Site: James A. Haley Veterans' Hospital

Collaborative Site(s): N/A

Abstract

Objective: To investigate catastrophizing and self-efficacy for managing pain among Non-Hispanic Whites, Non-Hispanic Blacks, and Hispanics with chronic pain after TBI, and whether coping interacts with race/ethnicity to predict participation outcomes. **Setting:** Community after discharge from inpatient rehabilitation. **Participants:** 621 individuals with moderate to severe TBI and chronic pain, who completed follow-up as part of a national longitudinal study of TBI and also participated in a collaborative study on chronic pain.

Design: Multicenter, cross-sectional, survey study. **Main measures:** Catastrophizing subscale from the Coping with Pain Scale; Pain Self-Efficacy Questionnaire; Participation Assessment with Recombined Tools-Objective. **Results:** After controlling for relevant sociodemographic variables, a significant interaction was observed between race/ethnicity and insurance status, such that Blacks who had public health insurance reported greater catastrophizing in response to pain compared with Whites. Race/ethnicity and self-efficacy for managing pain were unrelated. Greater catastrophizing was associated with lower participation but did not interact with race/ethnicity. Blacks reported lower participation relative to Whites, independent of catastrophizing. **Conclusions:** Black individuals who have TBI and chronic pain, and who have public insurance, may be vulnerable to difficulties managing pain. They are more likely to cope by catastrophizing, and catastrophizing is related to worse participation outcomes. The results suggest that access to care may affect response to chronic pain after TBI.

Potential Clinical Impact: In support of the NDAA FY07 final Sec 721 report to Congress, TBICoE supported a study aimed to examine racial/ethnic differences related to coping with chronic pain after TBI and how these coping strategies can predict participation outcomes. Participants of the study were enrolled in the TBI Model Systems longitudinal national database. The results showed greater catastrophizing in Blacks who had public health insurance and socioeconomic disadvantages; additionally, both Blacks and Hispanics with greater catastrophizing had lower participation than whites. Overall, this study highlights the importance of considering socioeconomic factors and their relation to race/ethnicity when treating TBI.

- 4. Hoffman JM, Ketchum JM, Agtarap S, et al. Characterizing Extreme Phenotypes for Perceived Improvement from Treatment in Persons with Chronic Pain Following Traumatic Brain Injury: A NIDILRR and VA TBI Model Systems Collaborative Project. *J Head Trauma Rehabil.* 2024;39(1):43-55. doi:10.1097/HTR.0000000000000905.**

Lead Site: James A. Haley Veterans' Hospital

Collaborative Site(s): N/A

Abstract

Objective: To define and characterize extreme phenotypes based on perceived improvement in pain for persons with chronic pain following TBI.

Setting: Eighteen Traumatic Brain Injury Model System (TBIMS) Centers.

Participants: A total of 1762 TBIMS participants 1 to 30 years post-injury reporting chronic pain at their most recent follow-up interview. **Primary measures:** The Patient's Global Impression of Change (PGIC) related to pain treatment.

Sociodemographic, injury, functional outcome, pain, and pain treatment characteristics. **Results:** Participants were mostly male (73%), White (75%), middle-aged (mean 46 years), injured in motor vehicle accidents (53%), or falls (20%). Extreme phenotypes were created for an extreme improvement phenotype (n = 512, 29.8%) defined as "moderately better" or above on the PGIC and an extreme no-change group (n = 290, 16.9%) defined as no change or worse. Least absolute shrinkage and selection operator (LASSO) regression combined with logistic regression identified multivariable predictors of improvement versus no-change extreme phenotypes. Higher odds of extreme improvement phenotype were significantly associated with being female (odds ratio [OR] = 1.85), married versus single (OR = 2.02), better motor function (OR = 1.03), lower pain intensity (OR = 0.78), and less frequent pain, especially chest pain (OR = 0.36). Several pain treatments were associated with higher odds of being in the extreme improvement versus no-change phenotypes including pain medication (OR = 1.85), physical therapy (OR = 1.51), yoga (OR = 1.61), home exercise program (OR = 1.07), and massage (OR = 1.69).

Conclusion: Investigation of extreme phenotypes based on perceived improvement with pain treatment highlights the ability to identify characteristics of individuals based on pain treatment responsiveness. A better understanding of the biopsychosocial characteristics of those who respond and do not respond to pain treatments received may help inform better surveillance, monitoring, and treatment. With further research, the identification of risk factors (such as pain intensity and frequency) for treatment response/nonresponse may provide indicators to prompt changes in care for individuals with chronic pain after TBI.

Potential Clinical Impact: James A. Haley Veterans' Hospital TBIMS researchers collaborated with their NIDILRR counterparts to identify and characterize extreme phenotypes of pain based on perceived improvement in those who experienced chronic pain following TBI. To characterize these phenotypes, authors examined sociodemographic, injury, treatment, pain characteristics and functional outcomes. The results showed that the extreme improvement phenotype was associated with being White, married, employed, and college educated; this phenotype was also associated with greater independence, lower pain intensity scores, and higher treatment/rehabilitation utilization rates. Overall, of the characteristics assessed, the authors concluded that pain intensity was the strongest predictor of the perceived improvement phenotype.

5. Hoffman JM, Ketchum JM, Agtarap S, et al. **Characterizing Extreme Phenotypes for Pain Interference in Persons with Chronic Pain Following Traumatic Brain Injury: A NIDILRR and VA TBI Model Systems Collaborative Project.** *J Head Trauma Rehabil.* 2024;39(1):31-42.
doi:10.1097/HTR.0000000000000909

Lead Site: James A. Haley Veterans' Hospital

Collaborative Site(s): N/A

Abstract

Objective: To define and characterize extreme phenotypes based on pain interference for persons with chronic pain following TBI. **Setting:** Eighteen Traumatic Brain Injury Model System (TBIMS) Centers. **Participants:** A total of 1762 TBIMS participants 1 to 30 years post-injury reporting chronic pain at their most recent follow-up interview. **Primary measures:** The Brief Pain Inventory (BPI) interference scale, sociodemographic, injury, functional outcome, pain, and treatment characteristics. **Results:** Participants were predominantly male (73%), White (75%), middle-aged (mean 46 years), and who were injured in motor vehicle accidents (53%) or falls (20%). Extreme phenotypes were identified based on upper and lower 25th percentiles to create low-interference (n = 441) and high-interference (n = 431) extreme phenotypes. Bivariate comparisons found several sociodemographic, injury, function, pain, and treatment differences between extreme phenotype groups, including significant differences (P < .001) on all measures of concurrent function with those in the low-interference extreme phenotype experiencing better function than those in the high-interference extreme phenotype. Lasso regression combined with logistic regression identified multivariable predictors of low- versus high-interference extreme phenotypes. Reductions in the odds of low- versus high-interference phenotypes were significantly associated with higher pain intensity (odds ratio [OR] = 0.33), having neuropathic pain (OR = 0.40), migraine headache (OR = 0.41), leg/feet pain (OR = 0.34), or hip pain (OR = 0.46), and more pain catastrophizing (OR = 0.81). **Conclusion:** Results suggest that for those who experience current chronic pain, there is high variability in the experience and impact of pain. Future research is needed to better understand how pain experience impacts individuals with chronic pain and TBI given that pain characteristics were the primary distinguishing factors between phenotypes. The use of extreme phenotypes for pain interference may be useful to better stratify samples to determine efficacy of pain treatment for individuals with TBI.

Potential Clinical Impact: James A. Haley Veterans' Hospital TBIMS researchers collaborated with their NIDILRR counterparts to identify and characterize extreme phenotypes of pain based on pain interference in those who experienced chronic pain following TBI. To characterize these phenotypes, the authors examined sociodemographic, injury, treatment, and pain characteristics

and functional outcomes. The results showed that individuals with the low-interference phenotype had lower pain intensity scores, treatment utilization rates, and utilization of rehabilitation programs; this phenotype was also commonly found in White, married, and college educated individuals. Overall, of the characteristics assessed, the authors concluded that pain characteristics were the key determinates of extreme pain interference phenotypes.

6. **Ketchum JM, Hoffman JM, Agtarap S, et al. Relationship Between Extreme Pain Phenotypes and Psychosocial Outcomes in Persons with Chronic Pain Following Traumatic Brain Injury: A NIDILRR and VA TBI Model Systems Collaborative Project. *J Head Trauma Rehabil.* 2024;39(1):56-67. doi:10.1097/HTR.0000000000000908**

Lead Site: James A. Haley Veterans' Hospital

Collaborative Site(s): N/A

Abstract

Objective: To examine the relationship between extreme pain phenotypes (interference and improvement) and psychosocial outcomes among those with chronic pain after TBI. **Setting:** Community. **Participants:** In total, 1762 TBI Model Systems (TBIMS) participants 1 to 30 years postinjury reporting chronic pain.

Design: Multisite, cross-sectional, observational cohort study. **Primary measures:** Life satisfaction, posttraumatic stress, depression and anxiety symptoms, sleep and participation, the Brief Pain Inventory (BPI) interference scale, and the Patient's Global Impression of Change (PGIC). **Results:** Persons in the extreme high interference phenotype (vs extreme low interference phenotype) and/or extreme no change phenotype (vs extreme improvement phenotype) had poorer psychosocial outcomes, with extreme pain interference phenotypes having a larger effect on outcomes than extreme perceived improvement phenotypes. After controlling for covariates, large effect sizes (ES) related to pain interference were observed for posttraumatic stress symptoms (ES = -1.14), sleep quality (ES = -1.10), depression (ES = -1.08), anxiety (ES = -0.82), and life satisfaction (ES = 0.76); effect sizes for participation outcomes, although significant, were relatively small (ES = 0.21-0.36). Effect sizes related to perceived improvement were small for life satisfaction (ES = 0.20) and participation (ES = 0.16-0.21) outcomes. Pain intensity was identified as a meaningful confounding factor of the relationships between extreme phenotypes and posttraumatic stress, depression, anxiety, and sleep quality. **Conclusions:** Examination of extreme phenotypes provides important insights into the experience of individuals living with chronic pain and TBI. Results suggest that the relationships among a variety of characteristics of the person, their experience with pain, and treatment of pain are complex. Further research is needed to better understand these complex relationships and how differences in pain interference and

perceived improvement from treatment can assist in assessment and treatment of chronic pain after TBI.

Potential Clinical Impact: James A. Haley Veterans' Hospital TBIMS researchers collaborated with their NIDILRR counterparts to explore the relationship among extreme phenotypes of pain (pain interference and perceived improvement) and psychosocial outcomes in those who experienced chronic pain following a TBI. The results showed that the extreme low interference phenotype and extreme improvement phenotype were associated with improved psychosocial outcomes, with extreme interference phenotypes having a larger effect on outcomes. In an adjusted analysis for pain interference and perceived improvement, pain intensity was found to be a significant covariate for both phenotypes, indicating its importance in the relationship between extreme phenotype response and psychosocial outcomes. Overall, this study highlights the importance of routine screening for pain, pain phenotypes, and psychosocial function to improve the assessment and treatment of chronic pain after TBI.

SLEEP

1. Miles SR, Martindale SL, Flanagan JC, et al. Putting the Pieces Together to Understand Anger in Combat Veterans and Service Members: Psychological and Physical Contributors. *J Psychiatr Res.* 2023;159:57-65. doi:10.1016/j.jpsychires.2023.01.013

Lead Site: James A. Haley Veterans' Hospital

Collaborative Site(s): N/A

Abstract

Background: Dysregulated anger can result in devastating health and interpersonal consequences for individuals, families, and communities. Compared to civilians, combat veterans and service members report higher levels of anger and often have risk factors for anger including PTSD, TBI, pain, alcohol use, and impaired sleep. **Objective:** The current study examined the relative contributions of established variables associated with anger (e.g., combat exposure, current PTSD symptoms, history of TBI, pain interference, and hazardous alcohol use) in 1263 combat veterans and service members. Sleep impairments, represented by poor sleep quality and obstructive sleep apnea (OSA) risk, were also evaluated as potential mediators of the relationships between established risk factors and anger, and therefore potential modifiable treatment targets. **Results:** Multiple regression model results revealed that PTSD symptoms ($\beta = 0.517, p < .001$), OSA risk ($\beta = 0.057, p = .016$), pain interference ($\beta = 0.214, p < .001$), and hazardous alcohol use ($\beta = 0.054, p = .009$) were significantly associated with anger. Results of the mediation models revealed

that OSA risk accounted for the association between PTSD and anger, in addition to the association between pain interference and anger. **Conclusion:** The current study extends previous literature by simultaneously examining factors associated with anger using a multivariable model in a large sample of combat veterans and service members. Additionally, treating OSA may be a novel way to reduce anger in combat veterans and service members who have PTSD and/or pain interference.

Potential Clinical Impact: A TBICoE researcher at James A. Haley Veterans' Hospital contributed to a LIMBIC-CENC study examining how PTSD, obstructive sleep apnea (OSA) risk, pain interference, and alcohol misuse contribute to anger in combat veterans and service members with a history of mTBI. Researchers additionally investigated whether sleep quality and OSA mediate the relationship between the risk factors of interest and anger. OSA risk moderated both the relationship between PTSD and anger and the relationship between pain and anger, indicating that treatment for OSA may be beneficial for service members and combat veterans who report these symptoms. Sleep quality and OSA did not mediate the effect between alcohol misuse and anger, suggesting that treatments other than those that target sleep are needed for these individuals.

- 2. Silva MA, Gonzalez AV, Tang X, et al. Examining the Relationship Between Sleep Apnea Diagnosis and Suicide Risk in Veterans with Traumatic Brain Injury: A VA TBI Model Systems Study. *J Head Trauma Rehabil.* 2023;38(5):359-367. Doi:10.1097/HTR.0000000000000856**

Lead site: James A. Haley Veterans' Hospital

Collaborative Site(s): N/A

Abstract

Objective: Obstructive sleep apnea (OSA) is a common sleep disorder in people with TBI. Although sleep disturbances have been associated with an increased risk of suicide compared with the general population, the relationship between OSA and suicide risk after TBI is not well documented. In this study, we hypothesized that OSA diagnosis would predict suicide risk in veterans with TBI.

Setting: Five VA PRCs. **Participants:** Participants were drawn from the VA TBI Model Systems study, with follow-up interviews at year 1 (n = 392), year 2 (n = 444), year 5 (n = 498), or year 10 (n = 252) post-TBI (7.8%-14.5% follow-up attrition).

Design: This was a retrospective analysis from observational data using logistic regression with repeated measurements. Suicide ideation and suicide attempts were examined as outcomes at each follow-up to evaluate the relationship between OSA and suicide risk after adjusting for other risk factors determined a priori via literature review. **Main measures:** Suicidal ideation (Patient Health

Questionnaire-9 item 9), suicide attempt during the past year (self-reported), and OSA diagnosis (self-reported). **Results:** Contrary to study hypotheses, OSA diagnosis had no statistically significant association with suicide ideation or attempt after accounting for known predictors. However, greater depression symptoms, headache severity, and pre-TBI suicidal ideation and attempts predicted suicide risk at follow-up after accounting for other predictors.

Conclusions: Results of this study did not support a relationship between OSA and suicide risk, possibly due to methodological limitations of OSA measurement. Future research on this topic should include objective measures of OSA severity and OSA treatment including adherence. Although suicide is a low base rate occurrence, the impact is disastrous and further research is needed to mitigate suicide risk.

Potential Clinical Impact: TBICoE researchers contributed to a VA TBI Model Systems study examining the risk of suicidal ideation (SI) and suicide attempts (SA) among veterans with a history of TBI and obstructive sleep apnea (OSA). The results showed that SI was predicted by pre-TBI SAs, depression, headache, fatigue, insomnia, thwarted belongingness, and perceived symptom improvement. SA was predicted by younger age, pre-TBI SAs, depression, headache, and SI. OSA was not associated with SI or SAs. Overall, this study provided information on risk factors of SI/SA that clinicians need to be aware of and assess when screening their patients.

3. Skop KM, Bajor L, Sevigny M, et al. Exploring the Relationship Between Sleep Apnea and Vestibular Symptoms Following Traumatic Brain Injury. *PM R.* 2023;15(12):1524-1535. doi:10.1002/pmrj.13044

Lead Site: James A. Haley Veterans' Hospital

Collaborative Site(s): N/A

Abstract

Background: TBI is a complex health problem in military veterans and service members that often involves comorbid vestibular impairment. Sleep apnea is another comorbidity that may exacerbate, and/or be exacerbated by, vestibular dysfunction. **Objective:** To examine the relationship between sleep apnea and vestibular symptoms in service member and veterans diagnosed with TBI of any severity. **Design:** Multicenter cohort study; cross-sectional sample. **Setting:** In-patient TBI rehabilitation units within five VA PRCs. **Participants:** service member and veterans with a diagnosis of TBI (N = 630) enrolled in the VA TBI Model Systems study. **Intervention:** Not applicable. **Methods:** A multivariable regression model was used to evaluate the association between sleep apnea and vestibular symptom severity while controlling for relevant covariates, for example, PTSD. **Main outcome measures:** Lifetime history of sleep apnea was determined via best source reporting. Vestibular disturbances were measured

with the 3-item Vestibular subscale of the NSI. **Results:** One third (30.6%) of the sample had a self-reported sleep apnea diagnosis. Initial analysis showed that participants who had sleep apnea had more severe vestibular symptoms ($M = 3.84$, $SD = 2.86$) than those without sleep apnea ($M = 2.88$, $SD = 2.67$, $p < .001$). However, when the data was analyzed via a multiple regression model, sleep apnea no longer reached the threshold of significance as a factor associated with vestibular symptoms. PTSD severity was shown to be significantly associated with vestibular symptoms within this sample ($p < .001$). **Conclusion:** Analysis of these data revealed a relationship between sleep apnea and vestibular symptoms in with TBI. The significance of this relationship was affected when PTSD symptoms were factored into a multivariable regression model. However, given that the mechanisms and directionality of these relationships are not yet well understood, we assert that in terms of clinical relevance, providers should emphasize screening for each of the three studied comorbidities (sleep apnea, vestibular symptoms, and PTSD).

Potential Clinical Impact: Researchers at the James A. Haley Veterans' Hospital in Tampa, Florida, aimed to assess the relationship between sleep apnea and vestibular symptoms in participants enrolled in the VA TBI Model Systems (TBIMS) with varying severities of TBI. The results initially indicated a positive relationship between sleep apnea and vestibular symptoms; however, when PTSD or other covariates were considered, the relationship weakened. Overall, examination of all factors (i.e., sleep apnea, PTSD, vestibular symptoms) is key to address patient distress and improve quality of life.

SURVEILLANCE

1. Le TD, Gurney JM, Singh KP, et al. Trends in Traumatic Brain Injury Among U.S. Service Members Deployed in Iraq and Afghanistan, 2002-2016. *Am J Prev Med.* 2023;65(2):230-238. doi:10.1016/j.amepre.2023.01.043

Lead Site: HQ

Collaborative Site(s): N/A

Abstract

Introduction: TBI is a major health issue for service members deployed and is more common in recent conflicts; however, a thorough understanding of risk factors and trends is not well described. This study aims to characterize the epidemiology of TBI in U.S. service members and the potential impacts of changes in policy, care, equipment, and tactics over the 15 years studied.

Methods: Retrospective analysis of U.S. Department of Defense Trauma Registry data (2002–2016) was performed on service members treated for TBI at Role 3 medical treatment facilities in Iraq and Afghanistan. Risk factors and trends in TBI were examined in 2021 using Joinpoint regression and logistic regression. **Results:**

Nearly one third of 29,735 injured service members (32.4%) reaching Role 3 medical treatment facilities had TBI. The majority sustained mild (75.8%), followed by moderate (11.6%) and severe (10.6%) TBI. TBI proportion was higher in males than in females (32.6% vs 25.3%; $p < 0.001$), in Afghanistan than in Iraq (43.8% vs 25.5%; $p < 0.001$), and in battle than in nonbattle (38.6% vs 21.9%; $p < 0.001$). Patients with moderate or severe TBI were more likely to have polytrauma ($p < 0.001$). TBI proportion increased over time, primarily in mild TBI ($p = 0.02$), slightly in moderate TBI ($p = 0.04$), and most rapidly between 2005 and 2011, with a 2.48% annual increase. **Conclusions:** One third of injured service members at Role 3 medical treatment facilities experienced TBI. Findings suggest that additional preventive measures may decrease TBI frequency and severity. Clinical guidelines for field management of mild TBI may reduce the burden on evacuation and hospital systems. Additional capabilities may be needed for military field hospitals.

Potential Clinical Impact: TBICoE Surveillance HQ staff supported an analysis of 29,735 service members treated at a Role 3 medical treatment facility or combat hospital in Iraq and Afghanistan between 2002-2016 to characterize the epidemiology of TBIs in service members and investigate the impact of policy, medical care, equipment, and tactics during OIF and OEF on TBIs reported. Nearly one-third of the sample population sustained a TBI, with the most common severity being mild. The most common mechanism of injury was blast (68.9%). The odds of TBI were higher among service members who were younger, male, non-White/non-Black/or non-Hispanic (i.e., "other" including American Indian, Alaskan Native and Asian/Pacific Islander), and deployed in Afghanistan, and in those who experienced combat and had a higher injury severity score. Overall, there was an increasing proportion of TBIs treated annually from 2003-2011, with stabilization of cases thereafter. The authors suggest that the rise in TBI incidence may have been a result of increased awareness and enforcement of TBI related policies. While there was improved engineering of protective equipment, the authors suggest that the future threat of more lethal combat warrants improved capabilities to prevent, diagnose, and treat TBIs in theater.

2. Hai T, Agimi Y, Stout K. Prevalence of Comorbidities in Active and Reserve Service Members Pre and Post Traumatic Brain Injury, 2017-2019. *Mil Med.* 2023;188(1-2):e270-e277. doi:10.1093/milmed/usab342

Lead Site: HQ

Collaborative Site(s): N/A

Abstract

Objective: To understand the prevalence of comorbidities associated with TBI patients among active and reserve service members in the U.S. Military.

Methods: Active and reserve service members diagnosed with an incident TBI from January 2017 to October 2019 were selected. Nineteen comorbidities associated with TBI as identified in the literature and by clinical subject matter experts were described in this article. Each patient's medical encounters were evaluated from 6 months before to 2 years following the initial TBI diagnoses date in the Military Data Repository, if data were available. Time-to-event analyses were conducted to assess the cumulative prevalence over time of each comorbidity to the incident TBI diagnosis. **Results:** We identified 47,299 TBI patients, of which most were mild (88.8%), followed by moderate (10.5%), severe (0.5%), and of penetrating (0.2%) TBI severity. Two years from the initial TBI diagnoses, the top five comorbidities within our cohort were cognitive disorders (51.9%), sleep disorders (45.0%), PTSD; 36.0%), emotional disorders (22.7%), and anxiety disorders (22.6%) across severity groups. Cognitive, sleep, PTSD, and emotional disorders were the top comorbidities seen within each TBI severity group. Comorbidities increased pre-TBI to post-TBI; the more severe the TBI, the greater the prevalence of associated comorbidities. **Conclusion:** A large proportion of our TBI patients are afflicted with comorbidities, particularly post-TBI, indicating many have a complex profile. The military health system should continue tracking comorbidities associated with TBI within the U.S. Military and devise clinical practices that acknowledge the complexity of the TBI patient.

Potential Clinical Impact: TBICoE HQ staff evaluated the prevalence of comorbidities associated with TBI among active duty and reserve service members. Using ICD-10-CM codes, 47,299 TBI patients were identified from the Armed Forces Health Surveillance Division (AFHSD) and Military Health System Data Repository (MDR). PTSD, sleep, and cognitive, emotional, and anxiety disorders were the top 5 comorbidities among all TBI patients. Additionally, researchers found the number of comorbid diagnoses increased both post-TBI and with increasing TBI severity. Given the complex profile of symptoms in military TBI patients, clinicians should adapt treatment plans to the individual to address specific conditions.

VESTIBULAR & BALANCE

1. Talian DS, Eitel MM, Zion DJ, et al. Normative Ranges for, and Interrater Reliability of, Rotational Vestibular and Balance Tests in U.S. Military Service Members and Veterans. *Am J Audiol.* 2023;32(3S):694-705. doi:10.1044/2022_AJA-22-00128

Lead Site: WRNMMC

Collaborative Site(s): N/A

Abstract

Purpose: The objectives of this study were to (a) describe normative ranges-

expressed as reference intervals (RIs)-for vestibular and balance function tests in a cohort of service members and veterans and (b) to describe the interrater reliability of these tests. **Method:** As part of the DVBIC-TBICoE 15-Year Longitudinal Traumatic Brain Injury Study, participants completed the following: vestibulo-ocular reflex suppression, visual-vestibular enhancement, subjective visual vertical, subjective visual horizontal, sinusoidal harmonic acceleration, the computerized rotational head impulse test (crHIT), and the sensory organization test. RIs were calculated using nonparametric methods and interrater reliability was assessed using intraclass correlation coefficients between three audiologists who independently reviewed and cleaned the data. **Results:** Reference populations for each outcome measure comprised 40 to 72 individuals, 19 to 61 years of age, who served either as noninjured controls (NIC) or injured controls (IC) in the 15-Year Longitudinal Study; none had a history of TBI or blast exposure. A subset of 15 service member and veterans from the NIC, IC, and TBI groups were included in the interrater reliability calculations. RIs are reported for 27 outcome measures from the seven rotational vestibular and balance tests. Interrater reliability was considered excellent for all tests except the crHIT, which was found to have good interrater reliability. **Conclusion:** This study provides clinicians and scientists with important information regarding normative ranges and interrater reliability for rotational vestibular and balance tests in service member and veterans.

Potential Clinical Impact: WRNMMC and NICOE researchers evaluated data from common vestibular and balance function tests completed during the TBICoE 15-Year Longitudinal TBI Study to provide estimated reference intervals (RI) and expected interrater reliability with similar methodology. Clinicians and researchers should follow similar RI calculation guidelines in the future to compare clinical and research results across studies.