

2022 Traumatic Brain Injury Center of Excellence Publication Catalog

The purpose of this document is to (1) summarize key findings and potential clinical implications of calendar year 2022 TBICoE publications, (2) increase awareness, and (3) assist in planning of future efforts. This document contains figures that help visually categorize the publications, as well as citations and abstracts of each (abbreviations in abstracts may be modified for consistency throughout this document). Accompanying the abstracts are the potential clinical impact summaries of the work and the associated Research Network site (including Research HQ).

TBICoE publication citations and summaries are organized by category, or overarching research topic, as shown in the table of contents below.

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Publication Metrics Overview

Metrics for the articles published by the TBICoE research network in 2022 are included below. A total of 44 articles were published between January – December 2022. Articles were classified by TBI related topic. Articles were further characterized by lead research network site, if it was a part of the TBICoE research portfolio, the annual average number of publications per site, the journal an article was published in, and the journal impact factor.

Figure 1: Distribution of 2022 Publications in Each TBI Related Category

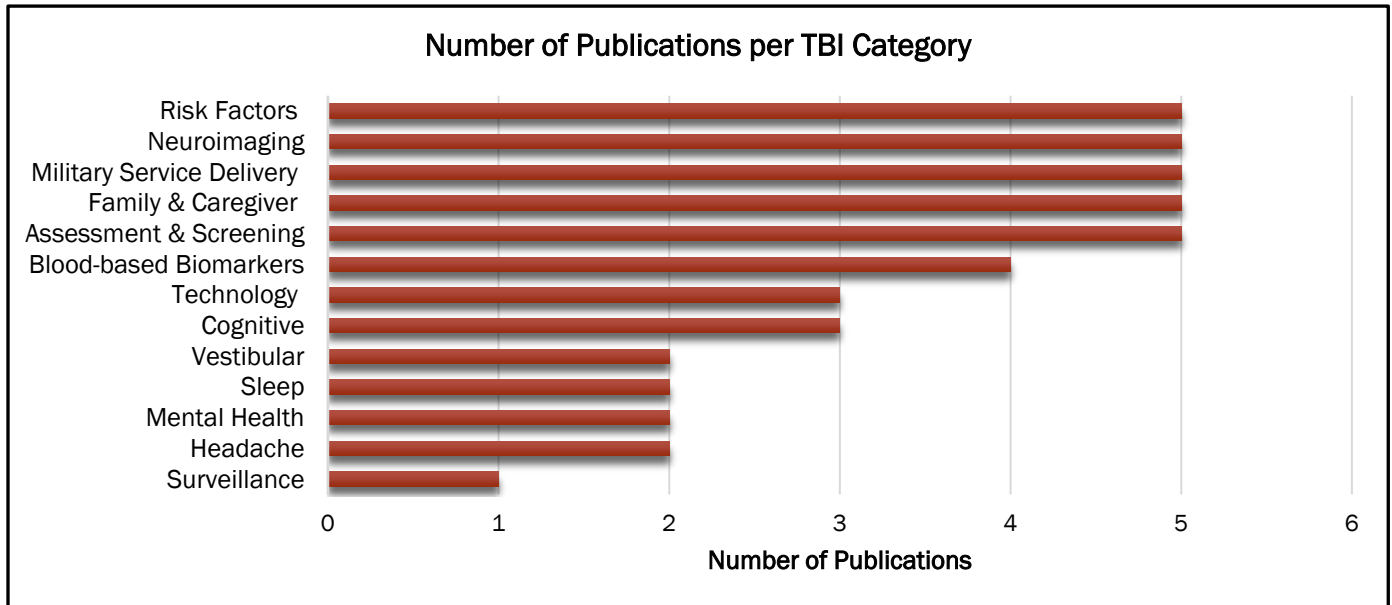
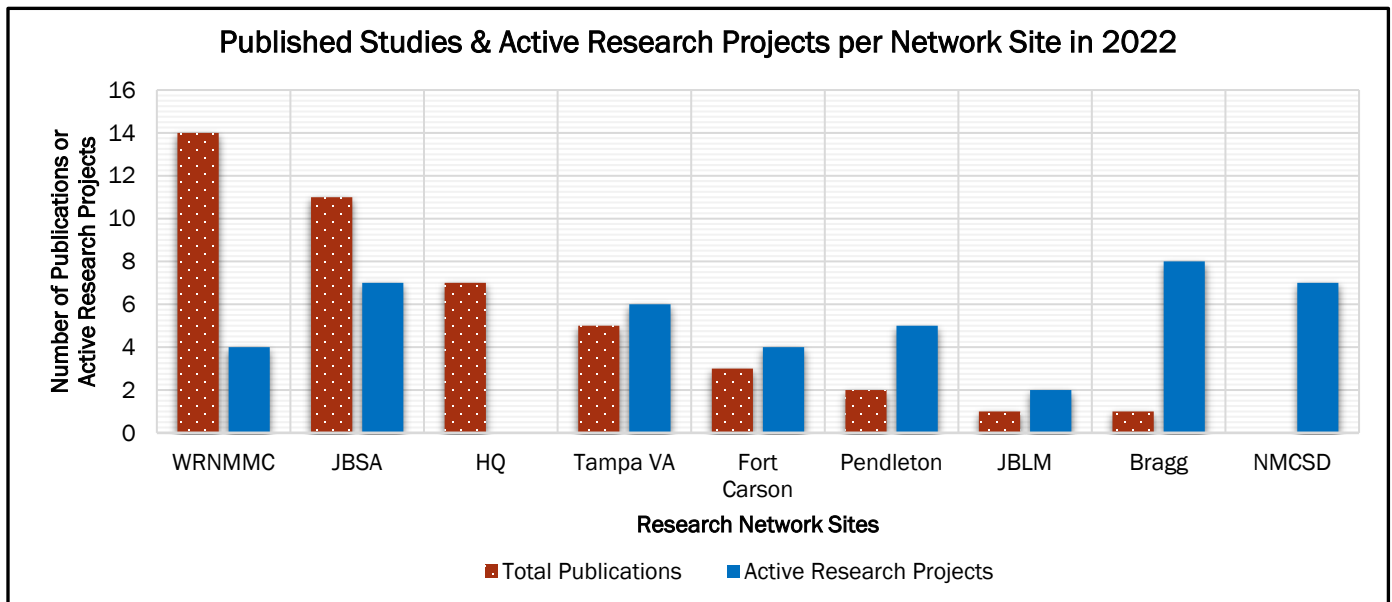


Figure 2: Comparison of Articles Published vs Active Research Projects During 2022



Note: Only lead sites are reflected in this metric. Collaboration on an article or project is not reflected in a site's total.

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Figure 3: Number of Articles Published Under the TBICoE Research Portfolio During 2022

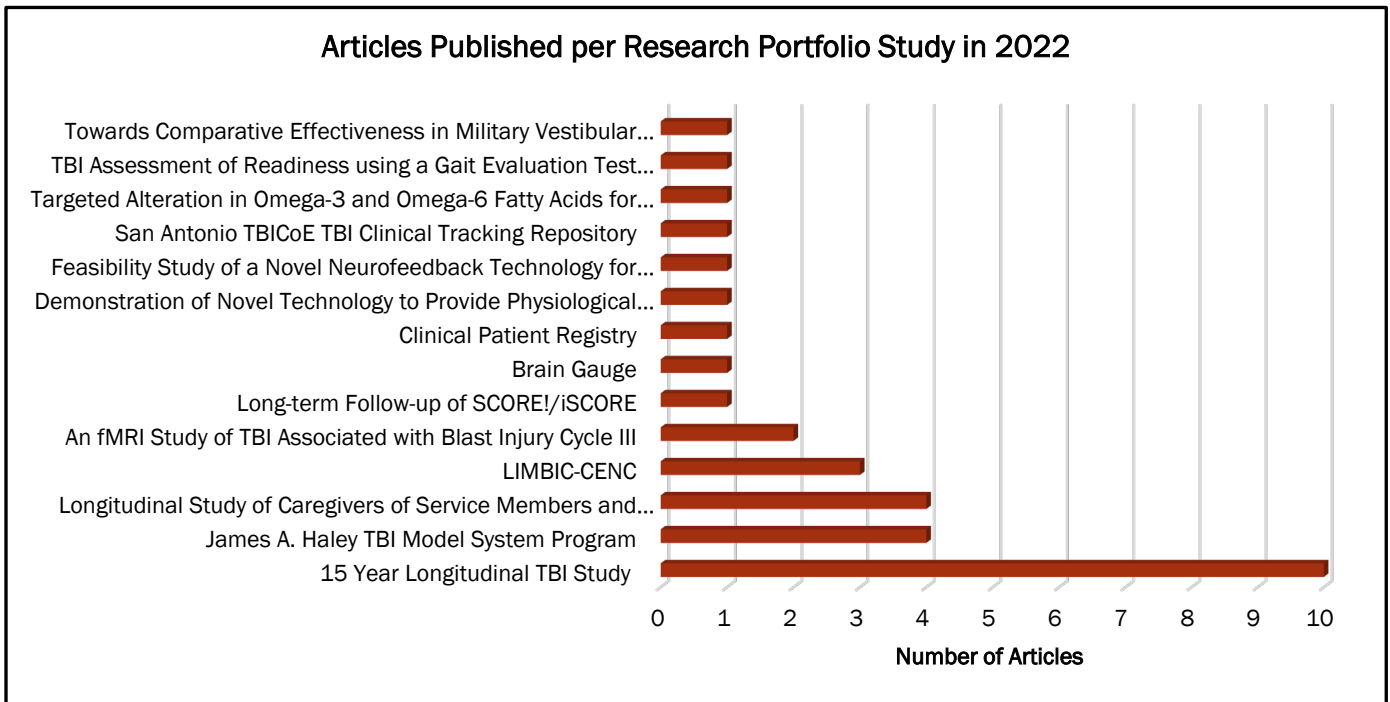
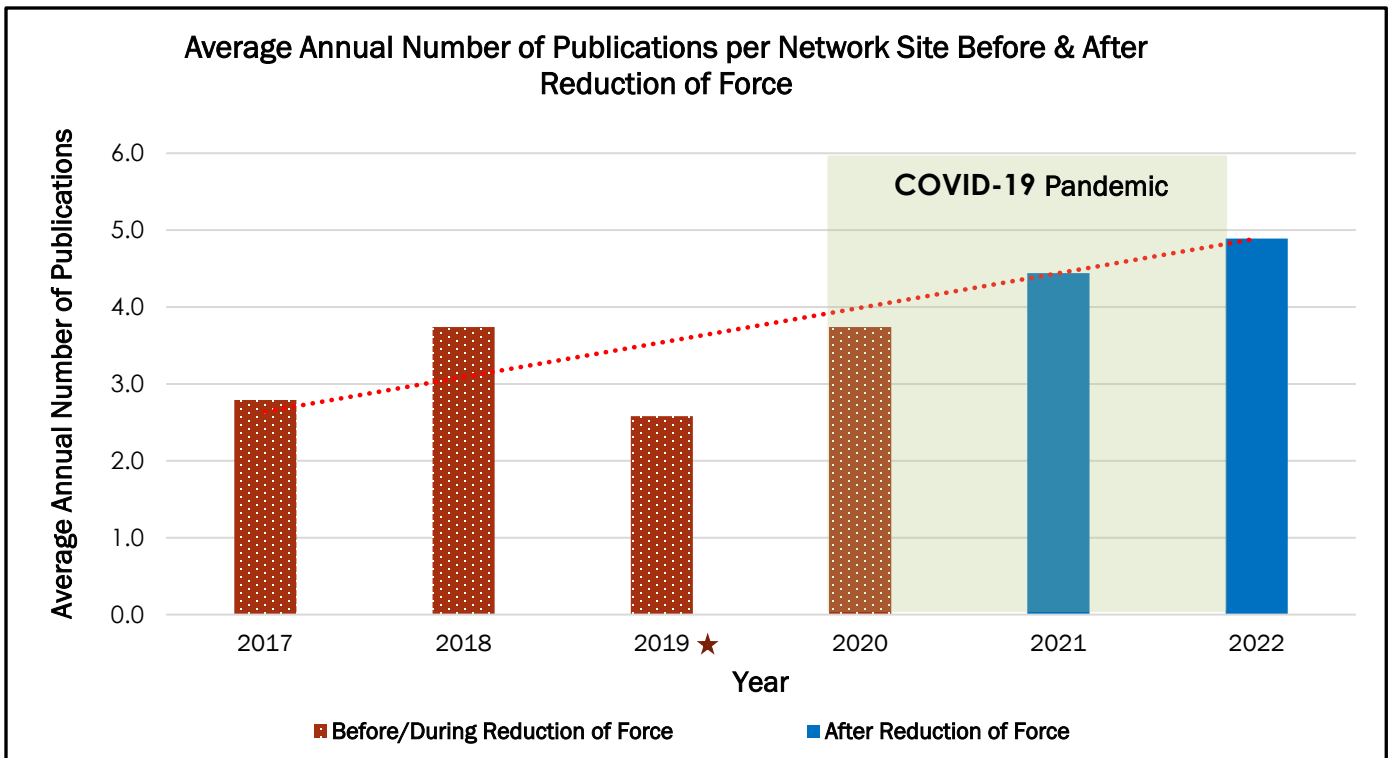


Figure 4: Annual Average Number of Publications per Research Network Site Before and After the Reduction of Force (closure of 10 network sites).



Note: The dotted line reflects the change in annual number of publications per site over time. The star indicates what year the reduction of force began.

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Figure 5: Journals in which TBICoE Articles were Published in During 2022

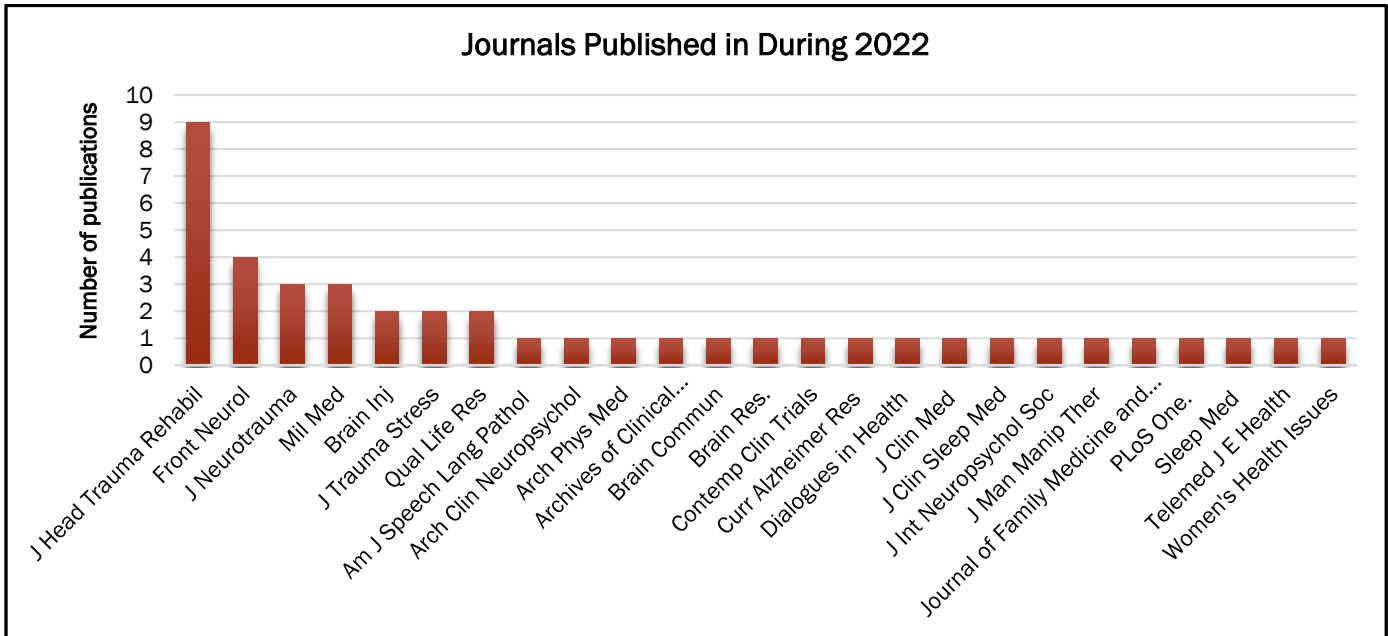


Table 1: Impact Factor for TBICoE Publications (by journal)

Journal	Impact Factor
Journal of Manual & Manipulative Therapy	1.43
Military Medicine	1.56
Brain Injury	2.17
Contemporary Clinical Trials	2.26
American Journal of Speech-Language Pathology	2.41
Journal of Family Medicine and Primary Care	3.02
Women's Health Issues	3.03
Journal of the International Neuropsychological Society	3.11
The Journal of Head Trauma Rehabilitation	3.12
PLoS One.	3.24
Brain Research	3.25
Quality of Life Research	3.44
Archives of Clinical Neuropsychology	3.45
Current Alzheimer Research	3.50
Journal of Traumatic Stress	3.95
Archives of Physical Medicine and Rehabilitation	4.06
Frontiers of Neurology	4.09
Journal of Clinical Sleep Medicine	4.32
Sleep Medicine	4.32
Brain Communications	4.40
Journal of Clinical Medicine	4.96
Science Reports	5.00
Telemedicine Journal and e-Health	5.03
Journal of Neurotrauma	5.27
Dialogues in Health	N/A

ARTICLE ABSTRACTS & POTENTIAL TBI CLINICAL IMPACT SUMMARIES

Assessment & Screening

1. *de Souza NL, Esopenko C, Jia Y, et al. Discriminating Mild Traumatic Brain Injury and Post-traumatic Stress Disorder Using Latent Neuroimaging and Neuropsychological Profiles in Active Duty Military Service Members [published online ahead of print, 2022 Dec 30]. J Head Trauma Rehabil. 2022;10.1097/HTR.0000000000000848. doi:10.1097/HTR.0000000000000848*

Site: JBSA

Abstract: Objective: Mild traumatic brain injury (mTBI) and post-traumatic stress disorder (PTSD) commonly occur among military service members and veterans and have heterogenous, but also overlapping symptom presentations, which often complicate the diagnoses of underlying impairments and development of effective treatment plans. Thus, we sought to examine whether the combination of whole brain gray matter (GM) and white matter (WM) structural measures with neuropsychological performance can aid in the classification of military personnel with mTBI and PTSD. **Methods:** Active duty US service members (n = 156; 87.8% male) with a history of mTBI, PTSD, combined mTBI+PTSD, or orthopedic injury completed a neuropsychological battery and T1- and diffusion-weighted structural neuroimaging. Cortical, subcortical, ventricular, and WM volumes and whole brain fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD), and axial diffusivity (AD) were calculated. Latent profile analyses were performed to determine how the GM and WM indicators, together with neuropsychological indicators, classified individuals. **Results:** For both GM and WM, respectively, a 4-profile model was the best fit. The GM model identified greater ventricular volumes in service members with cognitive symptoms, including those with a diagnosis of mTBI, either alone or with PTSD. The WM model identified reduced FA and elevated RD in those with psychological symptoms, including those with PTSD or mTBI and comorbid PTSD. However, contrary to expectation, a global neural signature unique to those with comorbid mTBI and PTSD was not identified. **Conclusions:** The findings demonstrate that neuropsychological performance alone is more robust in differentiating active duty service members with mTBI and PTSD, whereas global neuroimaging measures do not reliably differentiate between these groups.

Potential TBI Clinical Impact: A TBICoE researcher at JBSA contributed to a study aimed at determining if gray matter (GM) and white matter (WM) DTI measurements could aid in the neuropsychological classification of active duty service members with mTBI, PTSD, or both conditions. The findings demonstrated that GM and WM neuroimaging in combination with neuropsychological measures do not provide any additional benefit for identifying SMs with mTBI, PTSD, or comorbid presentation compared with neuropsychological tests alone.

2. Hoover PJ, Nix CA, Llop JZ, Lu LH, Bowles AO, Caban JJ. *Correlations Between the Neurobehavioral Symptom Inventory and Other Commonly Used Questionnaires for Traumatic Brain Injury [published online ahead of print, 2022 Jan 12]. Mil Med. 2022;usab559. doi:10.1093/milmed/usab559*

Site: JBSA

Abstract: Objective: To evaluate the correlations between the Neurobehavioral Symptom Inventory (NSI) and other questionnaires commonly administered within military traumatic brain injury clinics. **Setting:** Military outpatient traumatic brain injury clinics. **Participants:** In total, 15,428 active duty service members who completed 24,162 NSI questionnaires between March 2009 and May 2020. **Design:** Observational retrospective analysis of questionnaires collected as part of standard clinical care. **Main Measures:** NSI, Post-Traumatic Stress Disorder Checklist for DSM-V and Military Version, Patient Health Questionnaire (PHQ), Generalized Anxiety Disorder, Headache Impact Test (HIT-6), Insomnia Severity Index (ISI), Epworth Sleepiness Scale (ESS), Activities-Specific Balance Confidence Scale (ABC), Dizziness Handicap Inventory (DHI), Alcohol Use Disorders Identification Test (AUDIT), and the World Health Organization Quality of Life Instrument-Abbreviated Version. Only questionnaires completed on the same date as the NSI were examined. **Results:** The total NSI score was moderately to strongly correlated with all questionnaires except for the AUDIT. The strongest correlation was between the NSI Affective Score and the PHQ9 ($r = 0.86$). The NSI Vestibular Score was moderately correlated with the ABC ($r = -0.55$) and strongly correlated with the DHI ($r = 0.77$). At the item level, the HIT-6 showed strong correlation with NSI headache ($r = 0.80$), the ISI was strongly correlated with NSI difficulty sleeping ($r = 0.63$), and the ESS was moderately correlated with NSI fatigue ($r = 0.39$). **Conclusions:** Clinicians and health care administrators can use the correlations reported in this study to determine if questionnaires add incremental value for their clinic as well as to make more informed decisions regarding which questionnaires to administer.

Potential TBI Clinical Impact: TBICoE JBSA and colleagues measured the correlation between the Neurobehavioral Symptom Inventory (NSI) and other commonly administered questionnaires and found that the total NSI score was correlated with all questionnaires except the Alcohol Use Disorders Identification Test (AUDIT), suggesting that similar information is collected with the most commonly used TBI and PTSD questionnaires. These findings may assist clinicians and health care administrators in determining which questionnaires to include and exclude in their questionnaire batteries.

3. Llop JZ, Hoover PJ, Nix CA, Lu LH, Bowles AO, Caban JJ. *NSI and PCL-5 Normative Tables for Active Duty Service Members Affected by Traumatic Brain Injury [published online ahead of print, 2022 Jul 7]. Mil Med. 2022;usac189. doi:10.1093/milmed/usac189*

Site: JBSA

Abstract: Many service members (SMs) have been diagnosed with traumatic brain injury. Currently, military treatment facilities do not have access to established normative tables which can assist clinicians in gauging and comparing patient-reported symptoms. The aim of this study is to provide average scores for both the Neurobehavioral Symptom Inventory (NSI) and Post-traumatic Stress Disorder Checklist for DSM-V (PCL-5) for active duty SMs based upon varying demographic groups. **Methods:** Average scores were calculated for both the NSI and PCL-5 surveys from SMs who attended a military outpatient traumatic brain injury clinic. For this analysis, only the initial surveys

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for each SM were considered. The identifying demographics included age group, gender, grade, and race. **Results:** Four normative tables were created to show the average scores of both the NSI and PCL-5 surveys grouped by demographics. The tables are grouped by Age Group/Gender/Race and Grade/Gender/Race. **Conclusion:** Clinicians and health care administrators can use the scores reported in this study to determine where SM NSI or PCL-5 scores fall within the average for their demographic group.

Potential TBI Clinical Impact: TBICoE JBSA and colleagues examined the relationship between NSI/PCL-5 scores and demographics of patients with TBI and created four normative tables with average scores from both surveys grouped by demographics. The results of this study provide tools that clinicians who see and treat active duty service members can use to gauge how their patients' self-reported symptom severity compare with peers of similar demographics.

4. *Scarlett E, Lu LH, Cummings LD, Bowles AO. Neurobehavioral Symptom Inventory Item-Level Change Complements the Reliable Change Method [published online ahead of print, 2022 Dec 30]. J Head Trauma Rehabil. 2022;10.1097/HTR.0000000000000850. doi:10.1097/HTR.0000000000000850*

Site: JBSA

Abstract: Objective: To determine correspondence between the statistically derived 8-point reliable change index for the Neurobehavioral Symptom Inventory (NSI) against clinically significant item-level change in symptom severity from intake to discharge for mild traumatic brain injury (mTBI). **Setting:** Brain Injury Rehabilitation Service at Brooke Army Medical Center, Fort Sam Houston, San Antonio, Texas. **Patients:** In total, 655 active duty service members with a diagnosis of mTBI who received treatment and completed self-report measures between 2007 and 2020. **Design:** Observational retrospective analysis of outpatient clinical outcomes data. **Main Measures:** NSI total score change was used to divide patients into responder and nonresponders based on whether they met an 8-point decrease between intake and discharge. In addition, patients who had at least one NSI item that changed from a rating of 3 (severe) or 4 (very severe) at intake to a rating of 0 (none) or 1 (mild) at discharge were coded as an individual with significant item-level change. **Results:** Forty-five percent of the sample had significant item-level change and were classified as responders according to the reliable change method. Eight percent of the sample had significant item level change but did not meet the 8-point reliable change threshold. Fifteen percent of the sample did not experience significant item-level change but were classified as responders according to reliable change. Thirty-one percent did not meet either method's criterion for change. Classification agreement between the reliable change and item-level change methods was 76%, which was statistically significant ($\chi^2 1= 181.32, P < .001$). **Conclusion:** There is good correspondence between reliable change and item-level change on the NSI in this population. Reliable change is easily calculated and thus much more accessible than the item-level change method. There may be some situations where calculating item-level change may be helpful.

Potential TBI Clinical Impact: A TBICoE researcher at JBSA contributed to a process improvement study examining how reliable change on the Neurobehavioral Symptom Inventory (NSI) total score corresponded to a change at an NSI item level in active duty service members with mTBI. 76% of the time, reliable change and item level change methods matched classification of patients as responders or non-responders. Both methods had a 90% correspondence rate in detecting a decline

in NSI score. While both methods demonstrated utility, clinically, reliable change could be a more efficient way to detect a treatment response.

5. *Turner SM, Sloley SS, Bailie JM, Babakhanyan I, Gregory E. Perspectives on Development of Measures to Estimate Career Blast Exposure History in Service Members and Veterans. Front Neurol. 2022;13:835752. Published 2022 Apr 6. doi:10.3389/fneur.2022.835752*

Site: HQ

Abstract: The Department of Defense (DOD) has recently prioritized the investigation of the acute and chronic adverse brain health and performance effects of low-level blast (LLB) generated by the use of weapons systems. While acute exposure can be quantified by sensor technology, career exposure has no widely accepted and validated measure for characterization. Currently, distinct research groups are developing and validating four promising measures to estimate career blast exposure history: the Salisbury Blast Interview, Blast Exposure Threshold Survey, Blast Ordinance and Occupational Exposure Measure, and the Blast Frequency and Symptom Severity. Each measure offers an assessment of blast history that is uniquely beneficial to addressing specific research questions. However, use of divergent strategies is not efficient to accelerate the field's understanding of the impact of career exposure and service-connected health outcomes. As a DOD-wide solution, collaboration across these groups is required to develop a tool(s) that can be standardized across research studies and, ultimately, pared down to be implemented in clinical settings. Here, we overview the current four measures and provide a perspective on the way forward for optimization and/or combination in support of this solution.

Potential TBI Clinical Impact: TBICoE staff supporting NDAA FY18 Section 734 reviewed four blast exposure history measures currently being developed and provided recommendations for a unified approach toward development and optimization of these tool(s) for research and/or clinical settings. This manuscript highlights the importance of collaboration across U.S DOD and VA subject matter experts in streamlining metric development toward a measure of blast exposure history that can be implemented as a DOD-wide solution.

Blood-based Biomarkers

1. *Guedes VA, Lange RT, Lippa SM, et al. Extracellular vesicle neurofilament light is elevated within the first 12-months following traumatic brain injury in a U.S military population. Sci Rep. 2022;12(1):4002. Published 2022 Mar 7. doi:10.1038/s41598-022-05772-0*

Site: WRNMMC

Abstract: Traumatic brain injury (TBI) can be associated with long-term neurobehavioral symptoms. Here, we examined levels of neurofilament light chain (NFL) and glial fibrillary acidic protein (GFAP) in extracellular vesicles isolated from blood, and their relationship with TBI severity and neurobehavioral symptom reporting. Participants were 218 service members and veterans who sustained uncomplicated mild TBIs (mTBI, n = 107); complicated mild, moderate, or severe TBIs (STBI, n = 66); or Injured controls (IC, orthopedic injury without TBI, n = 45). Within one year after

injury, but not after, NfL was higher in the STBI group than mTBI ($p = 0.001$, $d = 0.66$) and IC ($p = 0.001$, $d = 0.35$) groups, which remained after controlling for demographics and injury characteristics. NfL also discriminated the STBI group from IC (AUC:77.5%, $p < 0.001$) and mTBI (AUC:76.1%, $p < 0.001$) groups. No other group differences were observed for NfL or GFAP at either timepoint. NfL correlated with post-concussion symptoms ($r(s) = -0.38$, $p = 0.04$) in the mTBI group, and with PTSD symptoms in mTBI ($r(s) = -0.43$, $p = 0.021$) and STBI groups ($r(s) = -0.40$, $p = 0.024$) within one year after injury, which was not confirmed in regression models. Our results suggest the potential of NfL, a protein previously linked to axonal damage, as a diagnostic biomarker that distinguishes TBI severity within the first year after injury.

Potential TBI Clinical Impact: This TBICoE 15-Year Natural History of TBI Study examined the relationship between blood biomarkers neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP), and TBI severity and neurobehavioral symptoms. They found that those with complicated mild, moderate, or severe TBI had higher levels of NfL within 12 months of injury, as well as a correlation with NfL and post-concussion and PTSD symptoms. While the findings in this study support the potential of NfL as a diagnostic biomarker to discriminate TBI severity and provide insight into underlying pathology, additional studies are needed to validate its clinical utility

2. Lange RT, Lippa S, Brickell TA, Gill J, French LM. Serum Tau, Neurofilament Light Chain, Glial Fibrillary Acidic Protein, and Ubiquitin Carboxyl-Terminal Hydrolase L1 Are Associated with the Chronic Deterioration of Neurobehavioral Symptoms after Traumatic Brain Injury [published online ahead of print, 2022 Oct 18]. J Neurotrauma. 2022;10.1089/neu.2022.0249. doi:10.1089/neu.2022.0249

Site: WRNMMC

Abstract: The purpose of this study was to examine the association of serum tau, neurofilament light chain (NfL), glial fibrillary acidic protein (GFAP), and ubiquitin carboxy-terminal hydrolase L1 (UCHL-1) concentrations evaluated within the first 12 months after a military-related TBI, with longitudinal changes in neurobehavioral functioning extending two or more years post-injury. Participants were 84 United States service members and veterans (SMVs) prospectively enrolled in the Defense and Veterans Brain Injury Center of Excellence/Traumatic Brain Injury Center 15-Year Longitudinal TBI Study, separated into three discreet groups: (a) uncomplicated mild TBI (mTBI; $n = 28$), (b) complicated mild, moderate, severe, and penetrating TBI combined (STBI; $n = 29$), and (c) non-injured controls (NIC, $n = 27$). Participants completed a battery of self-report neurobehavioral symptom measures (e.g., depression, post-traumatic stress disorder [PTSD], post-concussion, anxiety, somatic, cognitive, and neurological symptoms) within 12 months of injury (baseline), and then again at two or more years post-injury (follow-up). At baseline, participants also completed a blood draw to determine serum concentrations of tau, NfL, GFAP, and UCHL-1 using an ultra-sensitivity assay method. In the mTBI and STBI groups (using hierarchical regression analyses), (1) baseline tau concentrations predicted the deterioration of neurobehavioral symptoms from baseline to follow-up on measures of anxiety, PTSD, depression, post-concussion, somatic, and neurological symptoms (accounting for 10-28% of the variance); (2) NfL predicted the deterioration of depression, post-concussion, somatic, cognitive, and neurological symptoms (10-32% variance); (3) GFAP predicted the deterioration of post-concussion, PTSD, depression, anxiety, somatic, neurological, and cognitive symptoms (11-43% variance); and (4) UCHL-1 predicted the deterioration of anxiety, somatic, and neurological symptoms (10-16% variance). In the NIC group, no meaningful associations were found between baseline biomarker concentrations and the deterioration of

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neurobehavioral symptoms on the majority of measures. This study reports that elevated tau, NfL, GFAP, and UCHL-1 concentrations within the first 12 months of injury are associated with the deterioration of neurobehavioral symptoms that extends to the chronic phase of recovery after a TBI. These findings suggest that a blood-based panel including these biomarkers could be a useful prognostic tool to identifying those individuals at risk of poor future outcome after TBI.

Potential TBI Clinical Impact: This TBICoE 15-Year Longitudinal TBI Study examined the association of blood-based biomarkers within the first 12 months following a military-related TBI and longitudinal changes in neurobehavioral functioning. Elevated tau, NfL, GFAP, and UCHL-1 blood levels were found within the first 12 months after injury among those with deterioration of neurobehavioral symptoms that extended to the chronic stages of recovery. The authors suggest that a blood-based panel including these biomarkers may be a useful objective tool to identify SMVs at risk for poor outcomes after TBI.

3. Lippa SM, Gill J, Brickell TA, Guedes VA, French LM, Lange RT. Blood Biomarkers Predict Future Cognitive Decline after Military-Related Traumatic Brain Injury. *Curr Alzheimer Res.* 2022;19(5):351-363. doi:10.2174/1567205019666220330144432

Site: WRNMMC

Abstract: Traumatic brain injury (TBI) has been associated with increased likelihood of late-life dementia; however, the mechanisms driving this relationship are elusive. Blood-based biomarkers may provide insight into these mechanisms and serve as useful prognostic indicators of cognitive recovery or decline following a TBI. The aim of this study was to examine blood biomarkers within one year of TBI and explore their relationship with cognitive decline. Service members and veterans (n=224) without injury (n=77), or with history of bodily injury (n=37), uncomplicated mild TBI (n=55), or more severe TBI (n=55), underwent a blood draw and neuropsychological assessment within one year of their injury as part of a case-control study. A subsample (n=87) completed follow-up cognitive assessment. In the more severe TBI group, baseline glial fibrillary acidic protein (p=.008) and ubiquitin C-terminal hydrolase-L1 (p=.026) were associated with processing speed at baseline, and baseline ubiquitin C-terminal hydrolase-L1 predicted change in immediate (R²Δ=.244, p=.005) and delayed memory (R²Δ=.390, p=.003) over time. In the mild TBI group, higher baseline tau predicted greater negative change in perceptual reasoning (R²Δ=.188, p=.033) and executive functioning (R²Δ=.298, p=.007); higher baseline neurofilament light predicted greater negative change in perceptual reasoning (R²Δ=.211, p=.012). Baseline ubiquitin C-terminal hydrolase-L1 strongly predicted memory decline in the more severe TBI group, while tau and neurofilament light strongly predicted decline in the mild TBI group. A panel including these biomarkers could be particularly helpful in identifying those at risk for future cognitive decline following TBI.

Potential TBI Clinical Impact: TBICoE 15-Year Longitudinal TBI Study colleagues examined the relationship between blood biomarkers within one year of TBI and cognitive decline and found that elevated levels of ubiquitin C-terminal hydrolase-L1 (UCH-L1) strongly predicted memory decline in the more severe TBI group, while elevated levels of tau and neurofilament light strongly predicted decline in the mTBI group. Given that this study only examined individuals one year post-TBI, a longer follow-up is needed before a panel of biomarkers can be validated for use to predict the risk of cognitive decline after a TBI.

4. *Lippa SM, Lange RT, Dalgard CL, et al. APOE Is Associated With Serum Tau Following Uncomplicated Mild Traumatic Brain Injury. Front Neurol. 2022;13:816625. Published 2022 Jul 14. doi:10.3389/fneur.2022.816625*

Site: WRNMMC

Abstract: APOE e4 has been linked to poor outcome following traumatic brain injury (TBI); however, the mechanisms behind this relationship are unclear. Few studies have investigated the relationship between the APOE genotype and established brain related protein biomarkers following TBI. The purpose of this study was to examine this relationship in service members and veterans (SMVs) following TBI. **Methods:** Participants were 209 SMVs [124 uncomplicated mild TBI (mTBI); 85 complicated mild, moderate, severe, or penetrating TBI (mod-sev TBI)] prospectively enrolled in the DVVIC-TBICoE 15-Year Longitudinal TBI Study. APOE genotyping was undertaken using non-fasting blood serum samples. Participants were divided into three groups: APOE e2+, APOE e3/e3, and APOE e4+. **Results:** In participants with mTBI, those with the APOE e2 allele had significantly lower levels of tau than those with APOE e4 ($p = 0.005$, $r = 0.43$, medium-large effect size). Those with APOE e3/e3 trended toward having higher tau than those APOE e2+ ($p = 0.076$, $r = 0.20$, small-medium effect size) and lower tau than those with APOE e4+ ($p = 0.062$, $r = 0.21$, small-medium effect size). There were no significant differences in biomarkers based on APOE in the mod-sev TBI group. **Discussion:** This study is the first to demonstrate APOE genotype is related to serum tau levels following a mTBI, extending prior findings to human serum following mTBI. In addition to higher serum tau levels in APOE e4 carriers, lower tau levels were observed in APOE e2 carriers, suggesting a possible protective effect.

Potential TBI Clinical Impact: This TBICoE 15-Year Longitudinal TBI Study examined the relationship between the APOE genotypes and brain related protein biomarkers after TBI and found higher serum tau levels in APOE e4 carriers and lower tau levels in APOE e2 carriers for those with an mTBI. This relationship did not exist in the moderate-severe TBI group. This study demonstrated a relationship between APOE alleles and serum tau levels following mTBI, suggesting a possible protective effect for carriers of the APOE e2 gene. Given the known association of elevated tau levels and TBI injury severity, it may be assumed that the APOE e4 allele is a risk factor for more severe TBI.

Cognitive

1. *Kennedy JE, Cooper DB, Curtiss G, et al. Research Letter: Long-Term Outcomes Following Cognitive Rehabilitation for Mild Traumatic Brain Injury: A 5-Year Follow-Up of a Cohort From the SCORE Randomized Clinical Trial. J Head Trauma Rehabil. 2022;37(6):390-395. doi:10.1097/HTR.0000000000000800*

Site: JBSA

Abstract: Objective: To examine the functioning of military service members 5 years after completing a randomized controlled trial (RCT) of cognitive rehabilitation for mild traumatic brain injury (mTBI). **Setting:** Home-based telephonic interview and internet-based self-ratings. **Participants:** Sixty-nine of the 126 (55%) active duty service members who were enrolled in a 4-arm RCT of cognitive rehabilitation 3 to 24 months after mTBI and were successfully contacted by phone 5 years later.

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Original and 5-year follow-up participants in each of 4 RCT treatment arms included: psychoeducation (n = 32 original, n = 17 follow-up), computer (n = 30 original, n = 11 follow-up), therapist-directed (n = 30 original, n = 23 follow-up), integrated (n = 34 original, n = 18 follow-up). **Design:** Inception cohort evaluated 5 years after completion of an RCT of cognitive rehabilitation. **Main Measures:** Post-concussion symptoms (Neurobehavioral Symptom Inventory total score), psychological distress (Symptom Checklist-90-revised Global Severity Index score), and functional cognitive/behavioral symptoms (Key Behaviors Change Inventory total average score). **Results:** Participants' post-concussive symptoms and psychological distress improved at the 5-year follow-up. Functional cognitive/behavioral symptoms were not significantly improved, but therapeutic gains were maintained across time, to 5 years after completing the RCT. **Conclusion:** In this sample of military personnel, post-concussive symptoms and psychological distress significantly improved from post-treatment to 5 years after cognitive rehabilitation, regardless of treatment arm. Functional cognitive/behavioral symptoms significantly improved with treatment while treatment gains were maintained at the 5-year follow-up. Replication of these results with a larger sample and interim data between 18 weeks and 5 years post-treatment is needed.

Potential TBI Clinical Impact: TBICoE JBSA researchers and collaborators examined outcomes in military SMs 5 years after completing a randomized controlled trial of cognitive rehabilitation for mTBI and found that post-concussion symptoms and psychological distress improved while functional cognitive/behavioral symptoms remained the same. Therapeutic gains were maintained over time. The results suggest that completion of a structured, interdisciplinary outpatient rehabilitation treatment for SMs with persistent cognitive symptoms may benefit mTBI patients and contribute to their recovery.

- 2. Lu LH, Reid MW, Troyanskaya M, Scheibel RS, Muncy C, Kennedy JE. Close proximity to blast: No long-term or lasting effect on cognitive performance in service members with and without TBI during blast exposure [published online ahead of print, 2022 Oct 6]. J Int Neuropsychol Soc. 2022;1-10. doi:10.1017/S1355617722000558*

Site: JBSA

Abstract: Objective: Blast related characteristics may contribute to the diversity of findings on whether mild traumatic brain injury sustained during war zone deployment has lasting cognitive effects. This study aims to evaluate whether a history of blast exposure at close proximity, defined as exposure within 30 feet, has long-term or lasting influences on cognitive outcomes among current and former military personnel. **Methods:** One hundred participants were assigned to one of three groups based on a self-report history of blast exposure during combat deployments: 47 close blast, 14 non-close blast, and 39 comparison participants without blast exposure. Working memory, processing speed, verbal learning/memory, and cognitive flexibility were evaluated using standard neuropsychological tests. In addition, assessment of combat exposure and current post-concussive, post-traumatic stress, and depressive symptoms, and headache was performed via self-report measures. Variables that differed between groups were controlled as covariates. **Results:** No group differences survived Bonferroni correction for family-wise error rate; the close blast group did not differ from non-close blast and comparison groups on measures of working memory, processing speed, verbal learning/memory, or cognitive flexibility. Controlling for covariates did not alter these results. **Conclusion:** No evidence emerged to suggest that a history of close blast exposure was associated with decreased cognitive performance when comparisons were made with the other

groups. Limited characterization of blast contexts experienced, self-report of blast distance, and heterogeneity of injury severity within the groups are the main limitations of this study.

Potential TBI Clinical Impact: TBICoE researchers at JBSA investigated the potential impact of close-proximity blast exposure, defined as within 30 ft, and long-term cognitive outcomes post-deployment. In the absence of PTS severity and after controlling for covariates (i.e., time since blast exposure, demographics, months since deployment, etc.), exposure to close blast did not appear to increase the risk for poor cognitive outcomes within working memory, processing speed, verbal learning, and cognitive flexibility domains. While this study did not clearly establish that distance to blast was a risk factor for cognitive impairment, the environment in which an mTBI was sustained should still be considered when treating patients with PTSD symptoms and cognitive complaints. Future studies that incorporate cognitive performance data pre-injury will further help shape our understanding of blast exposure risk and may help improve treatment for SMVs with PTSD symptoms and cognitive complaints.

3. Myers JR, Solomon NP, Lange RT, et al. Analysis of Discourse Production to Assess Cognitive Communication Deficits Following Mild Traumatic Brain Injury With and Without Post-traumatic Stress. Am J Speech Lang Pathol. 2022;31(1):84-98. doi:10.1044/2021_AJSLP-20-00281

Site: WRNMMC

Abstract: Cognitive communication deficits can be difficult to assess in individuals with mild traumatic brain injury (mTBI). However, the use of discourse analysis as a direct and sensitive metric of cognitive communication skills has shown promising clinical utility for other TBI severity levels. This exploratory study investigated discourse production in service members and veterans (SMVs) with uncomplicated mTBI with and without post-traumatic stress disorder (PTSD) and SMVs with neither mTBI or PTSD. **Methods:** Fifteen SMVs with mTBI and PTSD, 26 with mTBI, and 25 controls with no brain injury (NBI) and without PTSD were given a wordless picture story to elicit spontaneous discourse. Discourse samples were analyzed for global coherence, word count, the use of negative emotion words, cognitive process words, nonfluencies, and story completeness. **Results:** Results revealed a significant difference between the mTBI (Mdn = 3.33) and NBI (Mdn = 3.50) groups, $\chi(2)(3) = 6.044$, $p = .017$, $\epsilon(2) = .03$, for global coherence. Word count differed significantly between the mTBI + PTSD (Mdn = 135) and NBI (Mdn = 195) groups, $\chi(2)(3) = 7.968$, $p = .006$, $\epsilon(2) = .06$. No other group differences were observed. **Discussion:** Structural features of discourse production may serve as potential markers of cognitive communication deficits in mTBI. Furthermore, PTSD may contribute to verbal fluency deficits in individuals with mTBI. Additional research is needed to develop discourse-related measures that are more sensitive to the effects of mTBI and PTSD.

Potential Clinical Impact: The TBICoE 15-Year Natural History of TBI Study examined differences in discourse production in SMVs with mTBI, mTBI + PTSD, and those with no brain injury (NBI), and found significant differences in global coherence and word count among those with mTBI and mTBI + PTSD respectively. Tools that provide clinicians with diagnostic insight into SMV's discourse production abilities may result in more precise treatment care plans and an objective means for monitoring treatment progress.

Family & Caregiver

1. *Brickell TA, French LM, Wright MM, Lange RT. Aggression in Military Members With Mild Traumatic Brain Injury and Post-Traumatic Stress Disorder Is Associated With Intimate Partner Health-Related Quality of Life. Womens Health Issues. 2022;32(5):526-533. doi:10.1016/j.whi.2022.04.003*

Site: WRNMMC

Abstract: We aimed to examine the relationship between service member/veteran (SMV) aggression and health-related quality of life (HRQOL) in their intimate partners. **Methods:** This prospective cohort study included 201 female intimate partner caregivers of post-9/11 male SMVs with a diagnosis of uncomplicated mild traumatic brain injury and post-traumatic stress disorder from a military treatment facility. Caregivers completed 17 HRQOL measures and rated the level the SMV experiences problems with verbal or physical expressions of irritability, anger, or aggression on the Mayo–Portland Adaptability Inventory, 4th edition. Caregivers were classified into three SMV Aggression groups: i) none or very mild (n = 53); ii) mild (n = 47); and iii) moderate or severe (n = 101). HRQOL scores were classified as clinically elevated using a cutoff of 60T or higher. **Results:** Using χ^2 analysis, the moderate or severe group had a significantly higher proportion of clinically elevated scores on 15 HRQOL measures compared with the none or very mild group, and six measures compared with the mild group. The mild group had higher scores on two measures compared with the none or very mild group. Using analysis of covariance (and controlling for caregiver strain), the moderate or severe group had significantly higher scores on 11 HRQOL measures compared with the none or very mild group, and two measures compared with the mild group. The mild group had higher scores on five measures compared with the none or very mild group. **Conclusions:** Many caregivers who report moderate to severe SMV aggression after a traumatic brain injury, report poor HRQOL beyond the strain of care provision. Traumatic brain injury and post-traumatic stress disorder programs should screen for and treat SMV aggression, and attend to the health needs of their caregivers.

Potential TBI Clinical Impact: This TBICoE 15-Year Longitudinal TBI Study examined the association of aggression in SMVs with comorbid mTBI and PTSD and health-related quality of life (HRQOL) in their caregiver partners. The study found that high scores of aggression were associated with worse HRQOL in caregivers, highlighting an area of focus for caregiver health.

2. *Brickell TA, Wright MM, Ferdosi H, French LM, Lange RT. Pain interference and health-related quality of life in caregivers of service members and veterans with traumatic brain injury and mental health comorbidity. Qual Life Res. 2022;31(10):3031-3039. doi:10.1007/s11136-022-03153-8*

Site: WRNMMC

Abstract: Objective: To examine (1) the relationship between caregiver pain interference with caregiver health-related quality of life (HRQOL), caregiver age, and service member/veteran (SMV) functional ability, and (2) change in caregiver pain interference longitudinally over 5 years. **Methods:** Participants were 347 caregivers of SMVs diagnosed with traumatic brain injury (TBI). Caregivers completed the SF-12v2 Health Survey Bodily Pain scale at an initial baseline evaluation and up to

four annual follow-up evaluations. Caregivers were divided into three pain interference groups: High Pain Interference (n = 104), Neutral Pain Interference (n = 117), and Low Pain Interference (n = 126). Caregivers also completed 15 HRQOL measures and a measure of SMV functional ability. **Results:** The High Pain Interference group reported more clinically elevated scores on 13 measures compared to the Low Pain Interference group, and seven measures compared to the Neutral Pain Interference group. The Neutral Pain Interference group had more clinically elevated scores on three measures compared to the Low Pain Interference group. The High and Neutral Pain Interference groups were older than the Low Pain Interference group. Parent caregivers were older than intimate partner/sibling caregivers, but did not report worse pain interference. Caregiver age, and measures of Fatigue, Strain, Perceived Rejection, and Economic QOL were the strongest predictors of pain interference ($p < .001$), accounting for 28.2% of the variance. There was minimal change in Bodily Pain scores over five years. The interaction of time and age was not significant ($X(2) = 2.7, p = .61$). **Conclusion:** It is important to examine pain in the context of HRQOL in caregivers, regardless of age.

Potential TBI Clinical Impact: TBICoE 15-Year Longitudinal TBI Study and TBICoE HQ colleagues examined caregiver pain interference and its relationship with health-related quality of life (HRQOL), caregiver age, and SMV functional ability, and found that 30% of caregivers in this study reported significant pain impairment and poor HRQOL. These findings emphasize the need to assess caregivers for pain and offer appropriate treatments in order to improve their quality of life.

3. Brickell TA, Lippa SM, Wright MM, et al. Is Traumatic Brain Injury Severity in Service Members and Veterans Related to Health-Related Quality of Life in Their Caregivers?. *J Head Trauma Rehabil.* 2022;37(6):338-349. doi:10.1097/HTR.0000000000000802

Site: WRNMMC

Abstract: Objective: To examine the relationship between service member/veteran (SMV) traumatic brain injury (TBI) severity with caregiver health-related quality of life (HRQOL). **Setting:** Military treatment facility. **Participants:** Caregivers (N = 316) of SMVs following a TBI divided into 2 groups based on SMV TBI severity: (1) caregivers of SMVs following an uncomplicated mild TBI (mTBI Caregiver group, n = 246), and (2) caregivers of SMVs following a complicated mild, moderate, severe, or penetrating TBI (STBI Caregiver group, n = 70). The STBI Caregiver group was further divided into 2 subgroups: Parent (n = 21) versus Intimate Partner (n = 49). The mTBI Caregiver group consisted of intimate partners. **Design:** Prospective cohort. **Main Measures:** Caregivers completed 15 HRQOL measures. **Results:** Using analysis of variance and chi-square analysis, the mTBI Caregiver group reported worse scores on 12 HRQOL measures and more clinically elevated scores for 6 of 15 comparisons than the STBI Caregiver group. The uncomplicated mTBI Caregiver group also reported worse scores on 10 HRQOL measures than intimate partners in the STBI Caregiver group and 5 measures than parents in the STBI Caregiver group. Parents reported worse scores on 3 measures than intimate partners in the STBI Caregiver group. The uncomplicated mTBI Caregiver group reported more clinically elevated scores for 7 of 15 comparisons than intimate partners in the STBI Caregiver group. **Conclusion:** Intimate partner caregivers of an SMV following a remote uncomplicated mTBI reported worse HRQOL than intimate partners and parent caregivers of an SMV following a more severe TBI, mostly likely due to SMV physical and mental health comorbidities. Interventions that focus on the SMV's TBI and other comorbidities, the caregiver's behavioral health problems, and the relationship and family factors that interact with each other will likely have the most success in improving individual and family outcomes for military families.

Potential TBI Clinical Impact: This TBICoE 15-Year Longitudinal TBI Study examined the relationship between SMVs TBI severity and caregiver health-related quality of life (HRQOL) and found that caregivers of SMVs with less severe TBI reported worse HRQOL than those with more severe TBI. Researchers in this study suggest this finding is likely due to comorbid conditions that coexist with less severe TBIs. Clinicians should continue to assess caregiver needs, regardless of severity of the SMVs TBI. The study further suggests interventions that focus on SMVs TBI and other comorbidities, the caregiver's behavioral health, and family factors that interact with each other to optimize SMV and military family outcomes.

4. *Finn JA, Klocksieben FA, Smith AN, et al. Family Needs After Traumatic Brain Injury: A VA TBI Model Systems Study. J Head Trauma Rehabil. 2022;37(6):327-337. doi:10.1097/HTR.0000000000000799*

Site: Tampa VA

Abstract: Objective: To describe the self-reported needs of family caregivers of service members and veterans (SMVs) who sustained a traumatic brain injury (TBI) and to identify predictors of the unmet family caregiver needs. **Setting:** Five Department of Veterans Affairs (VA) Polytrauma Rehabilitation Centers (PRCs). **Participants:** Family caregivers of SMVs enrolled in the VA PRC TBI Model Systems (TBIMS) national database who were within their first 5 years post-TBI (n = 427). **Design:** Observational study. **Main outcome measure:** The Family Needs Questionnaire-Revised (FNQ-R) was completed by each SMV's designated caregiver. **Analyses:** Descriptive analyses were conducted on the FNQ-R responses at the item, domain, and total score levels. Unadjusted univariable and adjusted multivariable regression models were fitted to identify predictors of total unmet needs and unmet family need domains. **Results:** FNQ-R item-level and domain-level descriptive results indicated that health information was the most frequently met need domain. In contrast, emotional and instrumental support domains were the least often met. On average, family caregivers reported that 59.2% of the 37 FNQ-R needs were met at the time of the follow-up assessment. Regression models indicated that both the number of SMV-perceived environmental barriers and whether the SMV received mental health treatment within the past year predicted the number of unmet FNQ-R needs. SMV-reported environmental barriers predicted increased unmet needs in all 6 family caregiver domains, and SMV mental health treatment in the past year predicted more unmet family caregiver emotional support, community support, and professional support needs. **Conclusions:** The current findings can be used to inform policy and programming for VA and Department of Defense to proactively address the specific needs of families and caregivers experienced in the first 5 years post-TBI.

Potential TBI Clinical Impact: TBICoE Tampa VA and TBIMS colleagues in this study identified predictors of unmet family caregiver needs based on The Family Needs Questionnaire-Revised (FNQ-R), and found that while most received health information, more efforts may need to be given towards emotional and instrumental support. "Instrumental support" refers to offering help or assistance in a tangible and/or physical way and in this study was measured as time for rest, socializing with friends, and focusing on personal and household responsibilities. These findings have the potential to inform policy and programming for the VA and DOD to address specific needs of families and caregivers of SMVs in the first 5 years post-TBI.

5. *Brickell, T. A., Wright, M. M., Sullivan, J. K., Varbedian, N. V., Nose, K. A., Rather, L. M., Tien, N. K., French, L. M., & Lange, R. T. (2022). Caregiver sleep impairment and service member and veteran adjustment following traumatic brain injury is related to caregiver health-related quality of life. Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine, 18(11), 2577–2588. <https://doi.org/10.5664/jcsm.10164>*

Site: WRNMMC

Abstract: Objective: To examine the relationship between caregiver sleep impairment and/or service member/veteran (SMV) adjustment post-traumatic brain injury (TBI), with caregiver health-related quality of life (HRQOL). **Methods:** Caregivers (N=283) completed 18 measures of HRQOL, sleep impairment, and SMV adjustment. Caregivers were classified into four sleep impairment/SMV adjustment groups: [1] Good Sleep/Good Adjustment (n=43), [2] Good Sleep/Poor Adjustment (n=39), [3] Poor Sleep/Good Adjustment (n=55), and [4] Poor Sleep/Poor Adjustment (n=146). **Results:** The Poor Sleep/Poor Adjustment group reported significantly worse scores on most HRQOL measures and a higher prevalence of clinically elevated scores (≥ 60) on the majority of comparisons compared to the other three groups. The Good Sleep/Poor Adjustment and Poor Sleep/Good Adjustment groups reported worse scores on the majority of the HRQOL measures and a higher prevalence of clinically elevated scores on seven comparisons compared to the Good Sleep/Good Adjustment group. Fewer differences were found between the Good Sleep/Poor Adjustment and Poor Sleep/Good Adjustment groups. The Poor Sleep/Poor Adjustment group reported a higher prevalence of severe ratings for SMV Irritability, Anger, and Aggression compared to the Good Sleep/Poor Adjustment group. **Conclusions:** While the presence of either caregiver sleep impairment or poor SMV adjustment singularly was associated with worse caregiver HRQOL, the presence of both sleep impairment and poor SMV adjustment was associated with further impairment in HRQOL. Caregivers could benefit from sleep intervention. Treatment of SMVs neurobehavioral problems may improve the SMV's recovery, and lessen sleep problems, distress, and burden among their caregivers.

Potential TBI Clinical Impact: This TBICoE 15-Year Longitudinal TBI Study examined the relationship between caregiver sleep impairment and/or SMV adjustment post-TBI, with caregiver health-related quality of life (HRQOL) and found that caregiver sleep impairment or poor SMV adjustment was associated with worse caregiver HRQOL and when occurring together, was associated with further HRQOL impairment. Caregivers should be evaluated and, if necessary, treated for sleep disturbances in addition to their SMVs.

Headache

1. *Faurot, K. R., Cole, W. R., MacIntosh, B. A., Dunlap, M., Moore, C. B., Roberson, B., Guerra, M., Domenichiello, A. F., Palsson, O., Rivera, W., Nothwehr, A., Arrieux, J., Russell, K., Jones, C., Werner, J. K., Clark, R., Diaz-Arrastia, R., Suchindran, C., Mann, J. D., Ramsden, C. E., ... Kenney, K. (2022). Targeted dietary interventions to reduce pain in persistent post-traumatic headache among service members: Protocol for a randomized, controlled parallel-group trial. *Contemporary clinical trials, 119, 106851.*
<https://doi.org/10.1016/j.cct.2022.106851>*

Site: Bragg

Abstract: Post-traumatic headache (PTH) is common after traumatic brain injury (TBI), especially among active duty service members (SMs), affecting up to 35% of patients with chronic TBI. Persistent PTH is disabling and frequently unresponsive to treatment and is often migrainous. Here, we describe a trial assessing whether dietary modifications to increase n-3 eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and reduce n-6 linoleic acid (LA), will alter nociceptive lipid mediators and result in clinical improvements in persistent PTH. **Methods:** This prospective, randomized, controlled trial tests the efficacy, safety, and biochemical effects of targeted, controlled alterations in dietary n-3 and n-6 fatty acids in 122 adult SMs and military health care beneficiaries with diagnosed TBI associated with actively managed persistent frequent (>8 /month) PTH with migraine. Following a 4-week baseline, participants are randomized to one of two equally intensive dietary regimens for 12 additional weeks: 1) increased n-3 EPA + DHA with low n-6 LA (H3L6); 2) usual US dietary content of n-3 and n-6 fatty acids (Control). During the intervention, participants receive diet arm-specific study oils and foods sufficient for 75% of caloric needs and comprehensive dietary counseling. Participants complete daily headache diaries throughout the intervention. Clinical outcomes, including the Headache Impact Test (HIT-6), headache hours per day, circulating blood fatty acid levels, and bioactive metabolites, are measured pre-randomization and at 6 and 12 weeks. Planned primary analyses include pre-post comparisons of treatment groups on clinical measures using ANCOVA and mixed-effects models. Similar approaches to explore biochemical and exploratory clinical outcomes are planned.

Potential TBI Clinical Impact: TBICoE Fort Bragg and colleagues described the methods and rationale for investigating the effects of targeted dietary interventions for post-traumatic headache (PTH) management in SMs with TBI. This study may help to identify dietary interventions that could improve PTH and other clinical outcomes for the SM.

2. *Hammerle, M. H., Lu, L. H., Thomas, L. C., Swan, A. A., Hoppes, C. W., Nelson, J. T., & Treleven, J. M. (2022). Possible autonomic or cranial nerve symptoms triggered during sustained neck rotation in persistent headache post-concussion: a retrospective observational cross-sectional study. *The Journal of manual & manipulative therapy, 1-11.* Advance online publication. <https://doi.org/10.1080/10669817.2022.2085850>*

Site: JBSA

Abstract: Objective: To examine and categorize symptoms occurring within 60 s 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 TBI Clinical Impact: TBICoE JBSA participated in a study which explored the hypothesis that a prolonged vertebrobasilar insufficiency (VBI) test in military SMs with persistent post-traumatic headache may be sensitive to more relevant symptoms than the standard administration time (10 seconds). Using the longer test administration (60 seconds), 81.3% of patients reported at least one symptom. The results suggest a potential autonomic/cranial nerve origin rather than vascular origin of these symptoms. By establishing the anatomical or biomechanical origin of these symptoms, it may guide clinicians to more effective assessments and interventions for post-concussion headaches.

Mental Health

1. *Remigio-Baker RA, Hungerford LD, Lee-Tauler SY, et al. Disparities in mental health symptoms recovery across race/ethnicity and education level following mild traumatic brain injury. Dialogues in Health. 2022/12/01/ 2022;1:100048. doi:<https://doi.org/10.1016/j.dialog.2022.100048>*

Site: HQ

Abstract: Purpose: The purpose of this study was to investigate the relationship between race/ethnicity and post-concussive mental health (i.e., depressive, post-traumatic stress disorder [PTSD]) and neurobehavioral symptoms among service members, and whether this association differed by education level. **Methods:** The study sample consisted of 524 patients from a multidisciplinary US military outpatient treatment facility for post-concussive symptoms. Poisson regression with robust error variance was utilized to investigate outcome (i.e., clinically-elevated depressive [Patient Health Questionnaire-8 ≥ 15], PTSD [PTSD Checklist, DSM V ≥ 38] and neurobehavioral [Neurobehavioral Symptom Inventory >75th percentile] symptoms at admission and last follow-up in this cohort study. Modification by education level (low [no college degree] vs. high [associate's degree or higher]) was additionally evaluated. **Results:** The relationship between race/ethnicity and mental health/neurobehavioral symptoms varied by education level (p-interaction:

depressive symptoms = 0.002, PTSD symptoms = 0.035, neurobehavioral symptoms = 0.040). Specifically, non-Whites were at a significantly higher prevalence for clinically-elevated depressive symptoms post-treatment than Whites, but only among those with higher education level (PR = 2.22, CI = 1.37–3.59). A similar trend was demonstrated for PTSD and neurobehavioral symptoms.

Conclusion: Military health care may need to increase depression-focused treatment options that are acceptable for racial/ethnic minority patients, particularly those with higher education, while they are recovering from comorbid traumatic brain injury.

Potential TBI Clinical Impact: TBICoE researchers from HQ and across the network conducted a study to investigate whether there are differences in the level of depressive and PTSD symptomatology post-concussion by race/ethnicity among SMs. The results demonstrated that racial/ethnic disparities in the recovery of depressive and neurobehavioral symptoms varied by the level of education, with non-whites in the study at a significantly higher prevalence for clinically-elevated depressive symptoms post-treatment compared to whites among those with a higher education level. Clinicians within the MHS should be aware of the varying rates of PCS based on race/ethnicity and education and then tailor their assessments and treatment plans accordingly.

- 2. Esopenko C, de Souza NL, Jia Y, et al. Latent Neuropsychological Profiles to Discriminate Mild Traumatic Brain Injury and Post-traumatic Stress Disorder in Active Duty Service Members. J Head Trauma Rehabil. 2022;37(6):E438-E448. doi:10.1097/HTR.0000000000000779*

Site: JBSA

Abstract: Objective: To determine whether cognitive and psychological symptom profiles differentiate clinical diagnostic classifications (eg, history of mild traumatic brain injury [mTBI] and post-traumatic stress disorder [PTSD]) in military personnel. **Methods:** U.S. active duty service members (N = 209, 89% male) with a history of mTBI (n = 56), current PTSD (n = 23), combined mTBI + PTSD (n = 70), or orthopedic injury controls (n = 60) completed a neuropsychological battery assessing cognitive and psychological functioning. Latent profile analysis was performed to determine how neuropsychological outcomes of individuals clustered together. Diagnostic classifications (ie, mTBI, PTSD, mTBI + PTSD, and orthopedic injury controls) within each symptom profile were examined. **Results:** A 5-profile model had the best fit. The profiles differentiated subgroups with high (34.0%) or normal (21.5%) cognitive and psychological functioning, cognitive symptoms (19.1%), psychological symptoms (15.3%), and combined cognitive and psychological symptoms (10.0%). The symptom profiles differentiated participants as would generally be expected. Participants with PTSD were mainly represented in the psychological symptom subgroup, while orthopedic injury controls were mainly represented in the high-functioning subgroup. Further, approximately 79% of participants with comorbid mTBI and PTSD were represented in a symptomatic group (~24% = cognitive symptoms, ~29% = psychological symptoms, and 26% = combined cognitive/psychological symptoms). Our results also showed that approximately 70% of military personnel with a history of mTBI were represented in the high- and normal-functioning groups. **Conclusions:** These results demonstrate both overlapping and heterogeneous symptom and performance profiles in military personnel with a history of mTBI, PTSD, and/or mTBI + PTSD. The overlapping profiles may underscore why these diagnoses are often difficult to diagnose and treat, but suggest that advanced statistical models may aid in identifying profiles representing symptom and cognitive performance impairments within patient groups and enable identification of more effective treatment targets.

Potential TBI Clinical Impact: TBICoE JBSA examined whether neuropsychological profiles differentiated mTBI and PTSD in military personnel and found that those with mTBI only were represented in the high to normal functioning group, those with mTBI + PTSD in the symptomatic group, and those with PTSD only in the psychological group. If these findings are replicated, the use of statistical models could help identify profiles indicative of TBI vs PTSD allowing for more effective tailored interventions for these patients.

Military Service Delivery

1. *Colvin MK, Roebuck-Spencer TM, Sperling SA, et al. Linking Patient-Centered Outcomes to Neuropsychological Practice: A Conceptual Framework and Opportunities for Research. Arch Clin Neuropsychol. 2022;37(6):1091-1102. doi:10.1093/arclin/acac015*

Site: Pendleton

Abstract: In the current health care climate, reimbursement for services is increasingly linked to the ability to demonstrate beneficial patient outcomes. Neuropsychology faces some unique challenges in outcomes research, namely, that neuropsychologists often do not follow patients over time and the effect of neuropsychological services on patient outcomes may not be fully realized until under another provider's care. Yet there is an urgent need for empirical evidence linking neuropsychological practice to positive patient outcomes. To provide a framework for this research, we define a core set of patient-centered outcomes and neuropsychological processes that apply across practice settings and patient populations. Within each area, we review the available existing literature on neuropsychological outcomes, identifying substantial gaps in the literature for future research. This work will be critical for the field to demonstrate the benefit of neuropsychological services, to continue to advocate effectively for reimbursement, and to ensure high-quality patient care.

Potential TBI Clinical Impact: A TBICoE researcher at Camp Pendleton collaborated with fellow National Academy of Neuropsychology Policy and Planning committee members to provide a framework to guide future research to generate empirical evidence on the benefits of neuropsychological practice on patient outcomes. Neuropsychological services can support or improve differential diagnosis, assessing change over time, treatment planning, patient/caregiver feedback, and patient referrals, all of which may improve patient-centered outcomes such as quality of life, functional independence, treatment adherence, safety, and caregiver knowledge, but a more direct link between services and outcomes is warranted. Given the integral role neuropsychologists serve in treating military TBI, pursuing such research will support evidence-based care for a greater number of service members and promote better outcomes for our Warfighters.

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- 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 [published online ahead of print, 2022 Oct 18]. Arch Phys Med Rehabil. 2022;S0003-9993(22)01659-8. doi:10.1016/j.apmr.2022.09.020*

Site: Tampa VA

Abstract: Objective: To compare barriers and facilitators to accessing health care services among service members and veterans (SMVs) by traumatic brain injury (TBI) severity groups.

Design: Qualitative descriptive study guided by an access to health care services conceptual framework. **Setting:** Five Veterans Affairs (VA) polytrauma rehabilitation centers. **Participants:** SMVs (N=55, including 10 caregivers as proxies) ≥2 years post-TBI recruited from the VA TBI Model Systems 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 SMVs 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. SMVs 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 SMV health outcomes. Findings support current policy and practice efforts to facilitate health care access for SMVs with TBI but highlight the need for tailored approaches for those with greater disability.

Potential TBI Clinical Impact: TBICoE researchers at the Tampa VA contributed to a TBI Model System study examining facilitators and barriers in accessing health care services among SMVs by TBI severity groups. Results demonstrated that facilitators and barriers to accessing health care varied by TBI severity, representing a possible link between health care access and SMV health outcomes. The study findings suggest injury severity level is critical to consider in future quality improvement and policy efforts within the DOD and VA network.

- Lindberg MA, Moy Martin EM, Marion DW. Military Traumatic Brain Injury: The History, Impact, and Future. J Neurotrauma. 2022;39(17-18):1133-1145. doi:10.1089/neu.2022.0103*

Site: HQ

Abstract: This review examines how lessons learned from United States military conflicts, beginning with the United States Civil War through the engagements in Iraq and Afghanistan, have shaped current traumatic brain injury (TBI) care in the United States military, influenced congressional mandates and directives, and led to best practices in caring for the warfighter. Prior to the most recent war, emphasis was placed on improving the surgical and medical care of service members (SM) with severe and especially penetrating brain injuries. However, during the Iraq and Afghanistan conflicts, also known as the Global War on Terrorism (GWOT), blast injury from improvised explosive

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devices most often caused mild TBI (mTBI), an injury that was not always recognized and was labelled the "signature wound" of the GWOT. This has led to extensive research on objective diagnostic technologies for mTBI, the association of mTBI with post-traumatic stress disorder (PTSD), and the long term consequences of mTBI. Here we summarize the key findings and most important advances from those efforts, and discuss the way forward regarding future military conflicts.

Potential TBI Clinical Impact: TBICoE Research HQ examined how lessons learned from U.S military conflicts have shaped current TBI clinical care and led to best practices in caring for the warfighter, as well as their influence on Congressional mandates and directives. While the manuscript describes key findings from all major conflicts since the Civil War, it emphasizes the lessons learned from the Global War on Terrorism, and the impact of special initiatives within the DOD that have dramatically reduced the morbidity and mortality following combat related TBI.

4. *Lindberg MA, Sloley SS, Ivins BJ, Marion DW, Moy Martin EM. Military TBI-What civilian primary care providers should know. J Family Med Prim Care. 2021;10(12):4391-4397. doi:10.4103/jfmpc.jfmpc_98_21*

Site: HQ

Abstract: In June 2019, the Department of Veterans Affairs (VA) launched the VA Mission Act, which expanded veterans' health care access to the private sector. Since civilian primary care providers may see more veterans in their practice, it will be important to understand the unique experiences, comorbidities, and culture of this population in order to provide optimal care. Military service members (SMs) are at an increased risk for traumatic brain injury (TBI), and comorbidities, such as post-traumatic stress disorder (PTSD), increasing the likelihood of prolonged symptoms. Military training and repetitive low-level blast exposure may cause symptoms similar to TBI or increase long-term negative effects in SMs. Military culture often has a strong influence in this population. Those who serve in the military identify with military values and have a strong team mentality, which places emphasis on the mission above all else, not accepting defeat, and not ever leaving a fellow SM behind. These values can impact the way a SMVs seeks care and/or communicates with his or her health care provider. Taking a detailed history to understand how these factors apply, as well as screening for mental health comorbidities, are recommended. Understanding the military cultural influences can assist in promoting a stronger therapeutic alliance and encourage more open communication. Ultimately, it is the trusting and respectful relationship between the SMVs and the provider that will determine the most effective treatment and result in the most effective resolution of TBI and comorbid symptoms.

Potential TBI Clinical Impact: In this paper, TBICoE Research HQ colleagues highlight the unique aspects of military experiences, culture, and comorbidities that can influence TBI symptoms and treatment seeking behaviors. The authors provide suggestions on what primary care providers in the private sector should know about military TBI to optimize care in this population.

5. *Nix CA, Cummings LD, Lu LH, Bowles AO. Characteristics of Responders and Nonresponders in a Military Post-concussion Rehabilitation Program. J Head Trauma Rehabil. 2022;37(6):E458-E466. doi:10.1097/HTR.0000000000000792*

Site: JBSA

Abstract: Objective: To characterize treatment responders and non-responders as measured by the Neurobehavioral Symptom Inventory (NSI) in order to understand whether certain traits in our patient population would characterize favorable response. **Setting:** Brain Injury Rehabilitation Service at Brooke Army Medical Center, Fort Sam Houston, San Antonio, Texas. **Patients:** In total, 655 active-duty military patients with a diagnosis of mild traumatic brain injury (mTBI) who received treatment between 2007 and 2020 and completed self-report measures as part of routine care. **Design:** Observational retrospective analysis of outpatient clinical outcomes data. **Main measures:** The primary outcome measure was the NSI, divided into the responder and non-responder groups. Responders were defined by reliable change in NSI total score (decrease of ≥ 8 points from intake to discharge). **Findings:** Responders (n = 395) reported a higher level of symptom burden at intake on the NSI. Women responded proportionally more (70%) than men (58%). After treatment, responders reported improvements on all measures evaluated while non-responders reported no change or slightly worse symptoms. Logistic regression analysis showed that post-traumatic stress symptoms at intake decreased odds of favorable treatment response while satisfaction with social relationships increased odds of favorable treatment response. **Conclusion:** The results from this process improvement project suggested that post-traumatic symptoms warrant programmatic attention in TBI clinics while social relationships may be a protective factor that can be capitalized to enhance troop readiness. Systematic examination of these characteristics should be conducted on a larger population within the military health system.

Potential Clinical Impact: TBICoE JBSA conducted a process improvement project to characterize treatment responders and non-responders after symptom-targeted treatment of post-concussive symptoms and found that PTSD symptoms decreased the odds of favorable treatment response, while satisfaction with social relationships increased the odds of a favorable treatment response. This project is an initial step in understanding how specific factors impact treatment response, as well as identifying “protective” factors that may be utilized to enhance troop readiness.

Neuroimaging

1. *Adamson MM, Main K, Harris OA, Kang X. Sex differences in cortical thickness and diffusion properties in patients with traumatic brain injury: a pilot study. Brain Inj. 2022;36(4):488-502. doi:10.1080/02699052.2022.2034046*

Site: HQ

Abstract: Cortical thickness and diffusion properties are important measures of gray and white matter integrity in those with traumatic brain injury (TBI). Many studies show that healthy adult females have greater cortical thickness than males across numerous brain sites. In this study, we explored this sex difference in patients with TBI. **Methods:** Participants consisted of 32 patients with TBI and 21 neurologically healthy controls. All were scanned by magnetic resonance imaging (MRI).

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Differences in cortical thickness and diffusion properties were examined between groups (i.e., TBI/control, male/female). **Results:** Patients with TBI had more cortical thinning (both hemispheres) compared to controls. They also showed decreased fractional anisotropy (FA) for several major white matter tracts. Healthy females had significantly greater cortical thickness compared to healthy males. However, this difference was smaller among the patients with TBI. We found no sex differences in diffusion properties. There were moderate correlations between cortical thickness, diffusion properties, and cognitive performance, as measured by the Trail Making Test B. **Conclusion:** These findings contribute to a growing discussion on sex differences in cortical thickness and diffusion properties. Sexual dimorphism could necessitate different clinical profiles, targets, and rehabilitation strategies in patients with TBI.

Potential TBI Clinical Impact: A TBICoE Research HQ staff and Palo Alto colleagues examined sex differences in cortical thickness and diffusion properties among patients with and without TBI. Sex differences in cortical thickness in both TBI and control groups were observed. These findings suggest that cortical thickness and diffusion properties may serve as useful biomarkers for TBI assessment if and when universal metrics and normative data are established for clinical use.

2. Hershaw JN, Hill-Pearson CA. Changes in EEG Activity Following Live Z-Score Training Predict Changes in Persistent Post-concussive Symptoms: An Exploratory Analysis. Front Neurol. 2022;13:714913. Published 2022 Mar 21. doi:10.3389/fneur.2022.714913

Site: Fort Carson

Abstract: A specific variant of neurofeedback therapy (NFT), Live Z-Score Training (LZT), can be configured to not target specific EEG frequencies, networks, or regions of the brain, thereby permitting implicit and flexible modulation of EEG activity. In this exploratory analysis, the relationship between post-LZT changes in EEG activity and self-reported symptom reduction is evaluated in a sample of patients with persistent post-concussive symptoms (PPCS). Penalized regressions were used to identify EEG metrics associated with changes in physical, cognitive, and affective symptoms; the predictive capacity of EEG variables selected by the penalized regressions were subsequently validated using linear regression models. Post-treatment changes in theta/alpha ratio predicted reduction in pain intensity and cognitive symptoms and changes in beta-related power metrics predicted improvements in affective symptoms. No EEG changes were associated with changes in a majority of physical symptoms. These data highlight the potential for NFT to target specific EEG patterns to provide greater treatment precision for PPCS patients. This exploratory analysis is intended to promote the refinement of NFT treatment protocols to improve outcomes for patients with PPCS.

Potential TBI Clinical Impact: TBICoE Fort Carson evaluated the relationship between a specific variant of neurofeedback therapy (NFT) (i.e., Live Z-Score Training), changes in EEG activity, and self-reported persistent post-concussive symptoms (PPCS); and found that post-treatment changes predicted improvements in cognitive and affective symptoms. Further study is needed to provide insight into causality and determine the magnitude of EEG activity for clinically meaningful symptom improvement. These findings provide considerations for the future development and refinement of NFT protocols for PPCS.

3. *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 [published online ahead of print, 2022 Oct 18]. J Neurotrauma. 2022;10.1089/neu.2022.0276. doi:10.1089/neu.2022.0276*

Site: WRNMMC

Abstract: The extant literature investigating the relationship between diffusion tensor imaging (DTI) and cognition following traumatic brain injury (TBI) is limited by small sample sizes and inappropriate control groups. The present study examined DTI metric differences between service members and veterans (SMVs) with bodily injury (Trauma Control; TC), uncomplicated mild TBI (mTBI), complicated mild TBI (compTBI), and severe-moderate TBI combined (smTBI), and how DTI metrics related to cognition within each group. Participants were 226 SMVs (56 TC, 112 mTBI, 29 compTBI, 29 smTBI) with valid neuropsychological testing and DTI at least 11 months post-injury. 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 $ps < 0.05$; $rs = 0.17$ 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 ($|rs|$: 0.43 to 0.66 ; $ps < 0.05$), and/or Delayed Memory ($|rs|$: 0.41 to 0.67 ; $ps < 0.05$). 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 uncinata fasciculus MD and RD. In contrast, there were no significant relationships between DTI metrics and cognition/emotional functioning within the mTBI or TC groups. 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 TBI Clinical Impact: This TBICoE 15-Year Longitudinal TBI Study examined a large sample of SMVs to demonstrate the potential relationship between neuroimaging results and cognitive performance following TBI. Findings suggest a dose-response relationship between TBI severity, white matter integrity and cognitive performance. The group with moderate-severe TBI had significantly reduced white matter integrity compared to those participants with mTBI and non-TBI trauma control groups. The white matter injury they detected was related to worse processing speed and delayed memory at one year or more after injury. Utilization of DTI protocols may eventually provide data on areas of the brain associated with specific cognitive deficits seen after TBI.

4. *Runyan A, Philippi CL, Pessin S, et al. Comparing resting-state connectivity of working memory networks in U.S. Service members with mild traumatic brain injury and post-traumatic stress disorder. Brain Res. 2022;1796:148099. doi:10.1016/j.brainres.2022.148099*

Site: JBSA

Abstract: Mild traumatic brain injury (mTBI) and post-traumatic stress disorder (PTSD) are prevalent among military populations, and both have been associated with working memory (WM)

impairments. Previous resting-state functional connectivity (rsFC) research conducted separately in PTSD and mTBI populations suggests that there may be similar and distinct abnormalities in WM-related networks. However, no studies have compared rsFC of WM brain regions in participants with mTBI versus PTSD. We used resting-state fMRI to investigate rsFC of WM networks in U.S. service members (n = 127; ages 18-59) with mTBI only (n = 46), PTSD only (n = 24), and an orthopedically injured (OI) control group (n = 57). We conducted voxelwise rsFC analyses with WM brain regions to test for differences in WM network connectivity in mTBI versus PTSD. Results revealed reduced rsFC between ventrolateral prefrontal cortex (vlPFC), lateral premotor cortex, and dorsolateral prefrontal cortex (dlPFC) WM regions and brain regions in the dorsal attention and somatomotor networks in both mTBI and PTSD groups versus controls. When compared to those with mTBI, individuals with PTSD had lower rsFC between both the lateral premotor WM seed region and middle occipital gyrus as well as between the dlPFC WM seed region and paracentral lobule. Interestingly, only vlPFC connectivity was significantly associated with WM performance across the samples. In conclusion, we found primarily overlapping patterns of reduced rsFC in WM brain regions in both mTBI and PTSD groups. Our finding of decreased vlPFC connectivity associated with WM is consistent with previous clinical and neuroimaging studies. Overall, these results provide support for shared neural substrates of WM in individuals with either mTBI or PTSD.

Potential TBI Clinical Impact: TBICoE researchers at JBSA contributed to a study investigating neuroimaging difference in working memory network regions in SMs with mTBI compared with those with PTSD. Results of the study showed similar patterns of reduced resting-state functional connectivity in the working memory brain regions of both groups, which suggest that the neural mechanisms contributing to cognitive symptoms in mTBI and PTSD may be similar. This finding may inform behavioral and neurostimulation interventions for treating WM impairments in SMs with mTBI and PTSD, however, more studies are needed to test their effect.

5. *Yeh PH, Lippa SM, Brickell TA, Ollinger J, French LM, Lange RT. Longitudinal changes of white matter microstructure following traumatic brain injury in U.S. military service members. Brain Commun. 2022;4(3):fcac132. Published 2022 May 27. doi:10.1093/braincomms/fcac132*

Site: WRNMMC

Abstract: The purpose of this study was to analyze quantitative diffusion tensor imaging measures across the spectrum of traumatic brain injury severity and evaluate their trajectories in military service members. Participants were 96 U.S. military service members and veterans who had sustained a mild traumatic brain injury [including complicated mild traumatic brain injury (n = 16) and uncomplicated mild traumatic brain injury (n = 68)], moderate-severe traumatic brain injury (n = 12), and controls (with or without orthopaedic injury, n = 39). All participants had been scanned at least twice, with some receiving up to five scans. Both whole brain voxel-wise analysis and tract-of-interest analysis were applied to assess the group differences of diffusion tensor imaging metrics, and their trajectories between time points of scans and days since injury. Linear mixed modelling was applied to evaluate cross-sectional and longitudinal diffusion tensor imaging metrics changes within and between groups using both tract-of-interest and voxel-wise analyses. Participants with moderate to severe traumatic brain injury had larger white matter disruption both in superficial subcortical and deep white matter, mainly over the anterior part of cerebrum, than those with mild traumatic brain injury, both complicated and uncomplicated, and there was no evidence of recovery over the period of follow-ups in moderate-severe traumatic brain injury, but deterioration was

possible. Participants with mild traumatic brain injury had white matter microstructural changes, mainly in deep central white matter over the posterior part of cerebrum, with more spatial involvement in complicated mild traumatic brain injury (e.g. astrocytosis with glial processes and glial scarring). Our results did not replicate 'V-shaped' trajectories in diffusion tensor imaging metrics, which were revealed in a previous study assessing the sub-acute stage of brain injury in service members and veterans following military combat concussion. In addition, non-traumatic brain injury controls, though not demonstrating any evidence of sustaining a traumatic brain injury, might have transient white matter changes with recovery afterward. Our results suggest that white matter integrity following a remote traumatic brain injury may change as a result of different underlying mechanisms at the microstructural level, which can have a significant consequence on the long-term well beings of service members and veterans. In conclusion, longitudinal diffusion tensor imaging improves our understanding of the mechanisms of white matter microstructural changes across the spectrum of traumatic brain injury severity. The quantitative metrics can be useful as guidelines in monitoring the long-term recovery.

Potential TBI Clinical Impact: This TBICoE 15-Year Longitudinal TBI Study analyzed longitudinal trajectories in diffusion tensor imaging measures across TBI severities, and found that those with moderate to severe TBI had larger white matter microstructural changes in certain regions with no evidence of recovery over the follow-up period (2 years.) compared with mTBI groups. Characterizing microarchitectural changes over time could potentially be used to predict long-term recovery or deterioration.

Risk Factors

1. *Gius BK, Fournier LF, Reljic T, et al. Associations Between Sociodemographic, Mental Health, and Mild Traumatic Brain Injury Characteristics With Lifetime History of Criminal Justice Involvement in Combat Veterans and Service Members [published online ahead of print, 2022 Aug 27]. Mil Med. 2022;usac257. doi:10.1093/milmed/usac257*

Site: Tampa VA

Abstract: Introduction: Veterans and service members (SMV) may have more risk factors for arrest and felony incarceration (e.g., post-traumatic stress disorder and at-risk substance use) but also more protective factors (e.g., access to health care) to mitigate behaviors that may lead to arrest. As such, understanding which factors are associated with criminal justice involvement among SMV could inform prevention and treatment efforts. The current study examined relationships between lifetime history of arrests and felony incarceration and sociodemographic, psychological, and brain injury characteristics factors among combat SMV. **Materials and methods:** The current study was a secondary data analysis from the Chronic Effects of Neurotrauma Consortium multicenter cohort study, approved by local institutional review boards at each study site. Participants were SMV (N = 1,540) with combat exposure (19% active duty at time of enrollment) who were recruited from eight Department of Veterans Affairs and DOD medical centers and completed a baseline assessment. Participants were predominantly male (87%) and white (72%), with a mean age of 40 years (SD = 9.7). Most (81%) reported a history of at least one mild traumatic brain injury, with one-third of those experiencing three or more mild traumatic brain injuries (33%). Participants completed a self-report measure of lifetime arrest and felony incarceration history, a structured interview for all potential

concussive events, the post-traumatic stress disorder checklist for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V), and the Alcohol Use Disorders Identification Test-Consumption. Three groups were compared on self-reported level of lifetime history of criminal justice system involvement: (1) no history of arrest or incarceration (65%); (2) history of arrest but no felony incarceration (32%); and (3) history of felony incarceration (3%). **Results:** Ordinal regression analyses revealed that hazardous alcohol consumption ($\beta = .44$, $P < .001$; odds ratio = 1.56) was positively associated with increased criminal justice involvement after adjusting for all other variables. Being married or partnered ($\beta = -.44$, $P < .001$; odds ratio = 0.64) was negatively associated with decreased criminal justice involvement. **Conclusions:** The rate of lifetime arrest (35%) in this SMV sample was consistent with rates of arrests in the U.S. general population. One modifiable characteristic associated with lifetime arrest and felony incarceration was hazardous alcohol consumption. Alcohol use should be a top treatment target for SMV at risk for arrest and those with history of criminal justice involvement.

Potential TBI Clinical Impact: The TBICoE Tampa VA team contributed to a CENC study on the history of mTBI, and relevant sociodemographic and mental health factors as correlates of arrest and incarcerations in SMVs. Results indicated that mTBI was not associated with a history of criminal justice involvement, though hazardous alcohol consumption was related to lifetime arrest and felony incarceration. Of note, the arrest rate in this sample was consistent with the arrest rate in the U.S. general population. Screening for alcohol use and misuse may provide an opportunity for effective early intervention to reduce the rate of arrest and incarceration.

- 2. 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 [published online ahead of print, 2022 Oct 31]. J Trauma Stress. 2022;10.1002/jts.22892. doi:10.1002/jts.22892*

Site: WRNMMC

Abstract: This study aimed to identify risk factors predictive of the presence and persistence of post-traumatic stress disorder (PTSD) symptom reporting following traumatic brain injury (TBI). Participants were 1,301 U.S. service members and veterans (SMVs) divided into four groups: uncomplicated mild TBI (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). 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, $ps < .001$. These risk factors may be useful in identifying SMVs at risk for the development and/or persistence of PTSD symptoms who may need intervention.

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Potential TBI Clinical Impact: The TBICoE 15-Year Longitudinal TBI Study team sought to identify risk factors that are predictive of the presence and persistence of PTSD symptoms in SMVs following a TBI. In this study seven risk factors were statistically associated with the presence of DSM-IV criteria for PTSD, or which five were considered the most clinically useful: depressive symptom severity, lack of social participation, complaints of memory or attention problems, history of mTBI, and high level of combat exposure. Clinicians and SMVs would benefit from continued screening for these stated risk factors to help identify SMVs at an increased risk for the development and/or persistence of PTSD.

3. *Lange RT, French LM, Bailie JM, et al. Clinical utility of PTSD, resilience, sleep, and blast as risk factors to predict poor neurobehavioral functioning following traumatic brain injury: A longitudinal study in U.S. military service members. Qual Life Res. 2022;31(8):2411-2422. doi:10.1007/s11136-022-03092-4*

Site: WRNMMC

Abstract: Purpose: This study examined the clinical utility of post-traumatic stress disorder (PTSD), low resilience, poor sleep, and lifetime blast exposure as risk factors for predicting future neurobehavioral outcome following traumatic brain injury (TBI). **Methods:** Participants were 591 U.S. military service members and veterans who had sustained a TBI (n = 419) or orthopedic injury without TBI (n = 172). Participants completed the Neurobehavioral Symptom Inventory, PTSD Checklist, and the TBI-Quality of Life (TBI-QOL) scale at baseline and follow-up. **Results:** Using the four risk factors at baseline, 15 risk factor combinations were examined by calculating odds ratios to predict poor neurobehavioral outcome at follow-up (i.e., number of abnormal scores across five TBI-QOL scales [e.g., fatigue, depression]). The vast majority of risk factor combinations resulted in odds ratios that were considered to be clinically meaningful (i.e., ≥ 2.5) for predicting poor outcome. The risk factor combinations with the highest odds ratios included PTSD singularly, or in combination with poor sleep and/or low resilience (odds ratios = 4.3-72.4). However, poor sleep and low resilience were also strong predictors in the absence of PTSD (odds ratios = 3.1-29.8). **Conclusion:** PTSD, poor sleep, and low resilience, singularly or in combination, may be valuable risk factors that can be used clinically for targeted early interventions.

Potential TBI Clinical Impact: TBICoE 15-Year Longitudinal TBI Study colleagues found that risk factor combinations were clinically useful in predicting poor neurobehavioral outcomes. They identified PTSD, low resilience, poor sleep, and lifetime blast exposure as clinical markers of poor long-term neurobehavioral outcome after TBI. The findings suggest that these may serve as valuable risk factors to continue to routinely screen for, or begin to screen for, to provide a targeted treatment approach.

4. *Merritt VC, Brickell TA, Bailie JM, et al. Low resilience following traumatic brain injury is strongly associated with poor neurobehavioral functioning in U.S. military service members and veterans. Brain Inj. 2022;36(3):339-352. doi:10.1080/02699052.2022.2034183*

Site: WRNMMC

Abstract: The purpose of this study was to examine the relationship between resilience and self-reported neurobehavioral functioning following traumatic brain injury (TBI) in U.S. military service members and veterans (SMVs). A secondary objective was to examine the interaction between

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resilience and post-traumatic stress disorder (PTSD) on neurobehavioral functioning. **Methods:** Participants included 795 SMVs classified into four groups: Uncomplicated Mild TBI (mTBI; n=300); Complicated Mild, Moderate, Severe, or Penetrating TBI (STBI, n 162); Injured Controls (IC, n=185); and Non-injured Controls (NIC, n=148). Two independent cohorts were evaluated - those assessed within 1-year of injury and those assessed 10-years post-injury. SMVs completed self-report measures including the PTSD Checklist-Civilian version, Neurobehavioral Symptom Inventory, and TBI-Quality of Life. **Results:** Results showed that (1) lower resilience was strongly associated with poorer neurobehavioral functioning across all groups at 1-year and 10-years post-injury, and (2) PTSD and resilience had a robust influence on neurobehavioral functioning at both time periods post-injury, such that SMVs with PTSD and low resilience displayed the poorest neurobehavioral functioning. **Conclusion:** Results suggest that regardless of injury group and time since injury, resilience and PTSD strongly influence neurobehavioral functioning following TBI among SMVs. Future research evaluating interventions designed to enhance resilience in this population is indicated.

Potential TBI Clinical Impact: In this TBICoE 15-Year Natural History of TBI study, researcher examined resilience and self-reported neurobehavioral functioning after TBI, and found that lower resilience, as well as PTSD, was associated with worse neurobehavioral functioning at 1-year and 10-years post-injury. The results suggest that interventions to improve resiliency in SMVs may play a key role in equipping individuals with the training necessary to improve outcomes following a TBI.

5. Wachen JS, Mintz J, LoSavio ST, et al. The impact of prior head injury on outcomes following group and individual cognitive processing therapy among military personnel. J Trauma Stress. 2022;35(6):1684-1695. doi:10.1002/jts.22870

Site: JBSA

Abstract: This study examined the impact of a history of head injury (HHI) on post-traumatic stress disorder (PTSD) and depression symptoms in active duty military personnel following group and individual cognitive processing therapy (CPT). Data for these secondary analyses were drawn from a clinical trial comparing group and individual CPT. Service members (N = 268, 91.0% male) were randomized to 12 sessions of group (n = 133) or individual (n = 135) CPT. Most participants (57.1%) endorsed a deployment-related HHI, 92.8% of whom reported currently experiencing symptoms (CES) related to the head injury (i.e., HHI/CES). Patients classified as non-HHI/CES demonstrated large, significant improvements in PTSD symptom severity in both individual and group therapy, $d_s = 1.1$, $p < .001$. Patients with HHI/CES status showed similar significant improvements when randomized to individual CPT, $d = 1.4$, $p < .001$, but did not demonstrate significant improvements when randomized to group CPT, $d = 0.4$, $p = .060$. For participants classified as HHI/CES, individual CPT was significantly superior to group CPT, $d = 0.98$, $p = .003$. Symptoms of depression improved following treatment, with no significant differences by treatment delivery format or HHI/CES status. The findings of this clinical trial subgroup study demonstrate evidence that group CPT is less effective than individual CPT for service members classified as HHI/CES. The results suggest that HHI/CES status may be important to consider in selecting patients for group or individual CPT; additional research is needed to confirm the clinical implications of these findings.

Potential TBI Clinical Impact: TBICoE JBSA participated in a study examining the effects of history of head injury (HHI) on PTSD and depression symptoms following group and individual cognitive processing therapy (CPT), and found that those without HHI but experiencing current symptoms

benefitted from individual and group CPT, while those with HHI and current symptoms, benefitted mostly from individual CPT. Clinicians should be aware that, in one large clinical study at least, HHI and current symptom status had an impact on response to group vs individual CPT.

Sleep

1. *Silva MA, Lee JM, Garcia A, Dams-O'Connor K, Nakase-Richardson R. Research Letter: Impact of Obstructive Sleep Apnea Disease Duration on Neuropsychological Functioning After Traumatic Brain Injury: A Veterans Affairs TBI Model Systems Study. J Head Trauma Rehabil. 2022;37(6):E496-E501. doi:10.1097/HTR.0000000000000797*

Site: Tampa VA

Abstract: Objective: To examine the relationship between obstructive sleep apnea (OSA) disease duration and cognitive functioning in those with a history of traumatic brain injury (TBI). We hypothesized that longer OSA duration would predict poorer cognitive performance. **Setting:** Inpatient brain injury units at a Veterans Affairs (VA) Polytrauma Rehabilitation Center. **Participants:** Participants in the VA TBI Model Systems multicenter longitudinal study who enrolled in a modular substudy (April 15, 2018, to January 15, 2021) examining cognition following TBI. All participants had received inpatient rehabilitation for TBI and reported a diagnosis of OSA (n = 89, mean age = 40.8 years, 97% male, 81% White). Reported duration of OSA ranged from 2 to 7 years (mean = 4.2; SD = 3.9). **Design:** Retrospective analysis of prospective cohort, cross-sectional. **Main Measure:** Brief Test of Adult Cognition by Telephone (BTACT). **Results:** Controlling for age, education, and time to follow commands, OSA disease duration was negatively associated with delayed verbal memory ($R^2\Delta = 0.053$, $F(1,84) = 5.479$, $P = .022$). Performance in other cognitive domains was not significantly associated with OSA disease duration. **Conclusion:** This study provides preliminary evidence that longer duration of OSA (i.e. time since diagnosis) has a negative impact on verbal memory in those with a history of hospitalized TBI. This finding extends the literature (which focused on the general population) on the cognitive impact of OSA and is consistent with hypothesized mechanisms such as hippocampal damage and secondary impact of fatigue. Findings suggest that early OSA identification and treatment may be prudent for persons with TBI.

Potential TBI Clinical Impact: Tampa VA and TBIMS colleagues examined the impact of duration of obstructive sleep apnea (OSA) on cognitive functioning in those with a history of TBI, and found that OSA duration was negatively associated with delayed verbal memory. Identification of those with OSA and providing efficacious treatments may benefit SMVs with a history of TBI, but further study is needed to determine the effect of OSA treatment on cognitive functioning following TBI.

2. *Steward KA, Silva MA, Maduri P, et al. Obstructive sleep apnea is associated with worse cognitive outcomes in acute moderate-to-severe traumatic brain injury: A TBI Model Systems study. Sleep Med. 2022;100:454-461. doi:10.1016/j.sleep.2022.09.012*

Site: Tampa VA

Abstract: Objective: To examine the relationship between polysomnography-classified obstructive sleep apnea (OSA) severity and cognitive performance in acute moderate-to-severe traumatic brain injury (TBI). **Methods:** This was a cross-sectional, secondary analysis leveraging data from a clinical trial ([NCT03033901](#)) and TBI Model Systems. Sixty participants (mean age = 50 ± 18 y, 72% male,

67% white) with moderate-to-severe TBI from five civilian rehabilitation hospitals were assessed at one-month post-injury. Participants underwent Level 1 polysomnography. OSA severity was classified as mild, moderate, and severe using the Apnea-Hypopnea Index (AHI). Associations between OSA metrics of hypoxemia (nadir and total time spent below 90%) and AHI with cognition were examined. Cognition was assessed with the Brief Test of Adult Cognition by Telephone (BTACT), which is comprised of six subtests assessing verbal memory, attention/working memory, processing speed, language, and executive function. **Results:** Over three-quarters of this acute TBI sample (76.7%) were diagnosed with OSA (no OSA n = 14; mild OSA n = 19; moderate/severe OSA n = 27). After adjustment for age, gender, and education, those with OSA had worse processing speed, working memory, and executive functioning compared to those without OSA. Compared to those with moderate/severe OSA, those with mild OSA had worse working memory and executive function. **Conclusions:** OSA is highly prevalent during acute stages of TBI recovery, and even in mild cases is related to poorer cognitive performance, particularly in the domains of attention/working memory and executive functioning. Our results support the incorporation of OSA diagnostic tools and interventions into routine clinical care in rehabilitation settings.

Potential TBI Clinical Impact: The TBICoE Tampa VA team contributed to a study on untreated obstructive sleep apnea (OSA) which found that OSA was highly prevalent during the acute stages of recovery from moderate-severe TBI and was related to worse functional and cognitive outcomes. As this new area of research develops, clinicians should pay attention to OSA in SMVs, as it is a treatable disease with the potential to impair cognitive abilities after TBI.

Surveillance

1. *Hai T, Agimi Y, Stout K. Clusters of conditions among US service members diagnosed with mild TBI from 2017 through 2019. Front Neurol. 2022;13:976892. Published 2022 Nov 9. doi:10.3389/fneur.2022.976892*

Site: HQ

Abstract: Background: Many U.S. military service members (SMs) newly diagnosed with mild Traumatic Brain Injury (mTBI) may exhibit a range of symptoms and comorbidities, making for a complex patient profile that challenges clinicians and health care administrators. This study used clustering techniques to determine if conditions co-occurred as clusters among those newly injured with mTBI and up to one year post-injury. **Methods:** We measured the co-occurrence of 41 conditions among SMs diagnosed with mTBI within the acute phase, one or three months post-mTBI diagnosis, and chronic phase, one year post-mTBI diagnosis. Conditions were identified from the literature, clinical subject matter experts, and mTBI care guidelines. The presence of conditions were based on medical encounters recorded within the military health care data system. Through a two-step approach, we identified clusters. Principal component analysis (PCA) determined the optimal number of clusters, and hierarchical cluster analyses (HCA) identified the composition of clusters. Further, we explored how the composition of these clusters changed over time. **Results:** Of the 42,018 SMs with mTBI, 23,478 (55.9%) had at least one condition of interest one-month post-injury, 26,831 (63.9%) three months post-injury, and 29,860 (71.1%) one year post-injury. Across these three periods, six clusters were identified. One cluster included vision, cognitive, ear, and sleep disorders that occurred one month, three months, and one year post-injury. Another subgroup included psychological

conditions such as anxiety, depression, PTSD, and other emotional symptoms that co-occurred in the acute and chronic phases post-injury. Nausea and vomiting symptoms clustered with cervicogenic symptoms one month post-injury, but later shifted to other clusters. Vestibular disorders clustered with sleep disorders and headache disorders one-month post-injury and included numbness and neuropathic pain one year post-injury. Substance abuse symptoms, alcohol disorders, and suicidal attempt clustered one year post-injury in a fifth cluster. Speech disorders co-occurred with headache disorders one month and one year post-injury to form a sixth cluster. **Conclusion:** PCA and HCA identified six distinct subgroups among newly diagnosed mTBI patients during the acute and chronic phases post-injury. These subgroups may help clinicians better understand the complex profile of SMs newly diagnosed with mTBI.

Potential TBI Clinical Impact: The surveillance team at TBICoE HQ reviewed the medical encounters for 42,018 SMs to determine if conditions co-occurred as clusters among those newly injured with mTBI and up to one year post-injury. Six clusters were identified among newly diagnosed mTBI patients during the acute and chronic phases post-injury. Awareness of clusters can support the development and delivery of care by promoting early clinical interventions and help providers anticipate manifestation of overlapping conditions of their mTBI patients over time.

Technology

1. *Ivins BJ, Arrieux JP, Cole WR. An Initial Psychometric Analysis of the Brain Gauge Tactile-Based Test Battery and Its Potential for Clinical Use Assessing Patients With Acute Mild Traumatic Brain Injury. Arch Clin Neuropsychol. 2022;37(7):1564-1578. doi:10.1093/arclin/acac031*

Site: HQ

Abstract: A new brief computerized test battery that uses tactile stimulation, Brain Gauge (BG), has been proposed as a cognitive assessment aid and its developers have reported an almost perfect ability to distinguish acute mild traumatic brain injury (mTBI) patients from healthy controls. This investigation attempted to replicate those results and serve as an initial psychometrically and clinically focused analysis of BG. BG scores from 73 military service members (SM) assessed within 7 days after having a clinically diagnosed mTBI were compared to 100 healthy SMs. Mean scores were compared, score distributions were examined, and univariate and multivariate base rate analyses of low scores were performed. SMs with mTBI had statistically significantly worse performance on both BG Reaction Time (RT) tests and the Sequential Amplitude Discrimination test as reflected by higher mean RT and RT variability and higher minimum detectable amplitude difference. SMs with mTBI also had a significantly lower whole-battery composite (i.e., Cortical Metric Symptom Score). Larger proportions of SMs with mTBI had lower overall performance than controls. However, at most only 26.9% of those with mTBI performed at potentially clinically meaningful cutoffs that were defined as various numbers of low scores that were prevalent in no more than 10% of the control group, which is equivalent to specificity $\geq 90\%$ and sensitivity $\leq 26.9\%$ for mTBI. Our analysis did not replicate the high level of classification accuracy reported by BG's developers. Pending further psychometric development, BG may have limited clinical utility for assessing mTBI patients.

Potential TBI Clinical Impact: TBICoE HQ and Fort Bragg staff and collaborators from Womack AMC sought to evaluate Brain Gauge's (BG) diagnostic accuracy and provide preliminary military

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normative data. They were unable to replicate the high level of classification accuracy for acute mTBI reported by BG developers. At this time, BG lacks sufficient psychometric development for clinical or research use, but with further development it may attain a level of clinical utility similar to brief computerized cognitive test batteries, such as IMPACT and ANAM.

- 2. Rhea CK, Yamada M, Kuznetsov NA, et al. Neuromotor changes in participants with a concussion history can be detected with a custom smartphone app. PLoS One. 2022;17(12):e0278994. Published 2022 Dec 15. doi:10.1371/journal.pone.0278994*

Site: Pendleton

Abstract: Neuromotor dysfunction after a concussion is common, but balance tests used to assess neuromotor dysfunction are typically subjective. Current objective balance tests are either cost- or space-prohibitive, or utilize a static balance protocol, which may mask neuromotor dysfunction due to the simplicity of the task. To address this gap, our team developed an Android-based smartphone app (portable and cost-effective) that uses the sensors in the device (objective) to record movement profiles during a stepping-in-place task (dynamic movement). The purpose of this study was to examine the extent to which our custom smartphone app and protocol could discriminate neuromotor behavior between concussed and non-concussed participants. Data were collected at two university laboratories and two military sites. Participants included civilians and service members (N = 216) with and without a clinically diagnosed concussion. Kinematic and variability metrics were derived from a thigh angle time series while the participants completed a series of stepping-in-place tasks in three conditions: eyes open, eyes closed, and head shake. We observed that the standard deviation of the mean maximum angular velocity of the thigh was higher in the participants with a concussion history in the eyes closed and head shake conditions of the stepping-in-place task. Consistent with the optimal movement variability hypothesis, we showed that increased movement variability occurs in participants with a concussion history, for which our smartphone app and protocol were sensitive enough to capture.

Potential TBI Clinical Impact: TBICoE at Camp Pendleton contributed to a cross-sectional study, with both SM and civilians, investigating the extent to which a smartphone application could differentiate neuromotor behavior between concussed and non-concussed users during a dynamic balance test. Compared to users without a history of concussion, those with a history of concussion showed significant differences in movement variability when performing the test during eyes closed and head shake conditions. The app shows clinical promise as a portable, objective, and dynamic tool for concussion assessment. However further research is needed to test its sensitivity to more functional tasks under additional environmental conditions.

- 3. Uomoto JM, Skopp N, Jenkins-Guarnieri M, et al. Assessing the Clinical Utility of a Wearable Device for Physiological Monitoring of Heart Rate Variability in Military Service Members with Traumatic Brain Injury. Telemed J E Health. 2022;28(10):1496-1504. doi:10.1089/tmj.2021.0627*

Site: JBLM

Abstract: Autonomic dysfunction has been implicated as a consequence of traumatic brain injury (TBI). Heart rate variability (HRV) may be a viable measure of autonomic dysfunction that could

enhance rehabilitative interventions for individuals with TBI. This pilot study sought to assess the feasibility and validity of using the Zeriscope™ platform system in a real-world clinical setting to measure HRV in active duty service members with TBI who were participating in an intensive outpatient program. **Methods:** Twenty-five service members with a history of mild, moderate, or severe TBI were recruited from a military treatment facility. A baseline assessment was conducted in the cardiology clinic where point validity data were obtained by comparing a 5-min recording of a standard 12-lead electrocardiogram (ECG) output against the Zeriscope platform data. **Results:** Compared with the ECG device, the Zeriscope device had a concordance coefficient (r_c) of 0.16, falling below the standard deemed to represent acceptable accuracy in HR measurement (i.e., 0.80). Follow-up analyses excluding outliers did not significantly improve the concordance coefficient to an acceptable standard for the total participant sample. System Usability Survey responses showed that participants rated the Zeriscope system as easy to use and something that most people would learn to use quickly. **Conclusions:** This study demonstrated promise in ambulatory HRV measurement in a representative military TBI sample. Future research should include further refinement of such ambulatory devices to meet the specifications required for use in a military active duty TBI population.

Potential TBI Clinical Impact: TBICoE JBLM evaluated the feasibility of a wearable system (Zeriscope platform) for providing reliable and consistent heart rate variability (HRV) readings for military TBI patients, and found that the Zeriscope platform had high patient acceptance but insufficient accuracy. Although this study suggests the clinical feasibility and patient acceptance of the wearable system, a more reliable and consistent device must be developed before deploying it in a larger clinical setting.

Vestibular

1. *Vander Vegt CB, Hill-Pearson CA, Hershaw JN, Loftin MC, Bobula SA, Souvignier AR. A Comparison of Generalized and Individualized Vestibular Rehabilitation Therapy in a Military TBI Sample. J Head Trauma Rehabil. 2022;37(6):380-389. doi:10.1097/HTR.0000000000000777*

Site: Fort Carson

Abstract: Objective: To compare clinical outcomes between active duty service members receiving generalized versus individualized vestibular rehabilitation treatment (GVRT and IVRT, respectively) for persistent vestibular-related symptoms following mild traumatic brain injury (mTBI). **Setting:** An outpatient TBI rehabilitation clinic. **Participants:** Fifty-seven participants with persistent vestibular-related symptoms following mTBI were randomly assigned to the GVRT ($n = 28$) or IVRT ($n = 29$) group, stratified by dizziness-related impairment severity. Forty-two participants ($n = 21$ per group) completed the post-treatment evaluation and were included in analyses. **Design:** We employed a single-site, randomized, pre-/post-test experimental design. The GVRT program consisted of eight 45-minute group-based treatment sessions and IVRT consisted of three 30-minute one-on-one treatment sessions both to be completed within 8 weeks. Group assignment was not blinded to study personnel or participants. Research evaluations were completed approximately 2 weeks prior to treatment initiation and following treatment completion. **Main Measures:** Outcome measures included Dizziness Handicap Inventory (DHI) and Activities-specific Balance Confidence Scale (ABC)

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total scores, Sensory Organization Test (SOT) composite equilibrium and sensory input ratio scores, Head Shake SOT (HS-SOT) conditions 2 and 5, and horizontal and vertical Dynamic Visual Acuity. Separate mixed-effects models were used to compare clinical outcomes between the GVRT and IVRT groups. **Results:** Both groups demonstrated significant improvement from pre- to post-treatment on self-reported dizziness-related impairment (DHI [F(1,41) = 16.28, P < .001]) and balance performance with and without head movement (composite equilibrium score [F(1,41) = 16.58, P < .001, effect size [ES] = 0.43], somatosensory [F(1,41) = 6.79, P = .013, ES = 0.26], visual [F(1,41) = 6.49, P = .015, ES = 0.29], vestibular [F(1,41) = 22.31, P < .001, ES = 0.55], and HS-SOT condition 5 [F(1,38) = 23.98, P < .001, ES = 0.64]). Treatment effects did not differ between groups on any of the outcome measures. **Conclusion:** We provide preliminary evidence that differences in clinical outcomes do not exist between participants receiving generalized versus individualized VR. Further research is needed to determine comparative effectiveness between these 2 treatment approaches for persistent vestibular-related symptoms following mTBI.

Potential TBI Clinical Impact: TBICoE Fort Carson compared clinical vestibular outcomes of SMS following mTBI who received generalized (GVRT) versus individualized vestibular rehabilitation treatment (IVRT). Results showed significant improvements in dizziness-related impairments and balance performance regardless of treatment group assignment. Future research is needed to determine the comparative effectiveness of GVRT and IVRT, which may inform SMS' responses to these treatment approaches and effectiveness within different clinical settings after mTBI.

- 2. Wood NI, Hentig J, Hager M, et al. The Non-Concordance of Self-Reported and Performance-Based Measures of Vestibular Dysfunction in Military and Civilian Populations Following TBI. J Clin Med. 2022;11(11):2959. Published 2022 May 24. doi:10.3390/jcm11112959*

Site: Fort Carson

Abstract: As a predominately young, physically active, and generally healthy population, service members (SMS) with vestibular dysfunction following a TBI may not be accurately represented by the current civilian reference ranges on assessments of vestibular dysfunction. This study enrolled SMS who were referred for vestibular rehabilitation following a mild/moderate TBI. The participants self-reported vestibular dysfunction using the Activities-specific Balance Confidence (ABC) scale and the Dizziness Handicap Inventory (DHI) followed by evaluation of vestibular performance using computerized dynamic posturography sensory organizational test (CDP-SOT). Retrospective analysis of these outcomes comparing the study sample of SMS to the reported civilian samples revealed SMS self-reported lower vestibular dysfunction with significantly higher balance confidence (ABC: 77.11 ± 14.61 , p < 0.05) and lower dizziness (DHI: 37.75 ± 11.74 , p < 0.05) than civilians. However, the SMS underperformed in performance-based evaluations compared to civilians with significantly lower CDP-SOT composite and ratio scores (COMP: 68.46 ± 13.46 , p < 0.05; VIS: 81.36 ± 14.03 , p < 0.01; VEST: 55.63 ± 22.28 , p < 0.05; SOM: 90.46 ± 10.17 , p < 0.05). Correlational analyses identified significant relationships between the ABC and CDP-SOT composite ($r = 0.380$, p < 0.01) and ratio scores (VIS: $r = 0.266$, p < 0.05; VEST: $r = 0.352$, p < 0.01). These results highlight the importance of recognizing and understanding nuances in assessing vestibular dysfunction in SMS to ensure they have access to adequate care and rehabilitation prior to returning to duty.

Potential TBI Clinical Impact: TBICoE Fort Carson evaluated vestibular-related impairment measures in SMS after TBI and compared the measures with comparable civilian-reported outcomes. The study found differences in symptom burden and overall performance in vestibular function, as well as

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demographic differences. These findings highlight that outcomes may differ between SM and civilians following TBI and SMs may require care and rehabilitation that differ from the civilian population prior to their return to duty. It is possible that military culture impacted the results seen in the SM group, so future studies should attempt to address this limitation.