Posttraumatic Stress Disorder Symptoms Contribute to Staff Perceived Irritability, Anger, and Aggression after TBI in a Longitudinal Veteran Cohort: A VA TBI Model Systems Study

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Running head: PTSD AND ANGER AFTER TBI

Posttraumatic Stress Disorder Symptoms Contribute to Staff Perceived Irritability, Anger, and Aggression after TBI in a Longitudinal Veteran Cohort: A VA TBI Model Systems Study

Objective: Examine the relationship between staff perceived irritability, anger, and aggression (IAA) and posttraumatic stress disorder (PTSD) in veterans with traumatic brain injury (TBI) of all severity levels.

Design: Longitudinal cohort design.

Setting: Veterans Affairs Polytrauma Transitional Rehabilitation Programs.

Participants: Veterans and service members with TBI of all severity levels enrolled in the Veterans Affairs Polytrauma Rehabilitation Centers' Traumatic Brain Injury Model System national database (N = 240).

Interventions: Not applicable.

Main Outcome Measure: Univariable and multivariable logistic regression modeling was used to examine the association between IAA and potential risk factors, including PTSD symptoms. IAA was measured as a single construct using an item from the Mayo-Portland Adaptability Inventory-4 that was rated by a program staff member at admission and discharge from the inpatient rehabilitation program. PTSD symptoms were assessed using the PTSD Checklist—Civilian Version.

Results: PTSD symptoms uniquely predicted program staff rated IAA at discharge even after controlling for severity of TBI, age, male gender, education, and annual earning. The model explained 19% of the variance in IAA.

Conclusions: When TBI severity and PTSD symptoms were considered simultaneously in a sample of veterans, only PTSD symptoms predicted staff-rated IAA. Given the negative

outcomes linked with IAA, Veterans may benefit from assessment and treatment of PTSD symptoms within rehabilitation settings.

Keywords: traumatic brain injury; posttraumatic stress disorder; anger; irritability; aggression; veterans; service members

Abbreviations

GCS Glasgow Coma Scale

IAA Irritability, anger, and aggression

MPAI-4 Mayo-Portland Adaptability Inventory-4

PCL-C PTSD Checklist – Civilian Version

PRC Polytrauma Rehabilitation Center

PTA Posttraumatic amnesia

PTRP Polytrauma Transitional Rehabilitation Programs

PTSD Posttraumatic stress disorder

ROC Receiver operating characteristic

TFC Time to follow commands

TBI Traumatic brain injury

TBIMS TBI Model Systems

VA Veterans Affairs

Irritability, anger, and aggression (IAA) are relatively common symptoms reported after traumatic brain injury (TBI[1]) and/or posttraumatic stress disorder (PTSD[2]). Irritability and anger pertain to emotional responses while aggression is an actual behavior intended to harm another. Although these constructs are distinct, they are interrelated and have not always been well-delineated in the TBI literature. Consequently, IAA will often be referred to as a collective construct throughout the manuscript. IAA can lead to devastating interpersonal, legal, and medical consequences for both victims and perpetrators.[3] Family members and medical staff report distress and burnout related to managing patients' IAA.[4] Additionally, staff may not refer patients who display IAA to needed services due to safety concerns for other patients and staff.[5] Patients with IAA may also have difficulty reintegrating into the community, reducing social support.[6] Finally, IAA can endure without treatment; therefore, understanding variables related to IAA is vitally important to assist patients with TBI achieve maximum rehabilitation outcomes.[4]

Executive dysfunction, or impairment in capacity to engage in autonomous, purposive, self-serving behavior,[7] is a problem observed in TBI, PTSD, and IAA.[8] Executive dysfunction is indicated by disinhibition and poor behavioral performance on neuropsychological tasks, generally complemented by prefrontal cortex activation changes observed in neuroimaging studies.[8] Emotional stimuli which trigger a limbic reaction can be downregulated by prefrontal cortex engagement which is imperative to manage PTSD symptoms.[9] When prefrontal cortical function is impaired, this region may not provide the necessary emotional control, resulting in IAA. Consistently, veterans who sustained penetrating TBIs in frontal lobe regions were rated as more aggressive than those who sustained TBIs affecting other brain regions and healthy controls.[10] It should be noted that neither the size of the lesion nor seizures were related to

aggression; however, family dynamics were, indicating social and psychological factors also contribute to IAA.

IAA can complicate the TBI rehabilitation process, and staff's perceptions of IAA can influence the services patients are offered.[3,4] In civilians with mild to severe TBIs, 74%, 39%, and 45% reported irritability, anger, and aggression, respectively,[5-6] which are higher than levels reported by healthy controls.[11] Service members with TBI (mostly of mild severity) also reported more anger than healthy service member controls.[13] While TBI severity predicts many outcomes (e.g. pace of recovery),[14,15] it is not associated with IAA rates in post-acute and chronic stages post-injury,[11,7-8] Nor does frequency of aggression appear to change over time (i.e., 3-60 months post-injury) across all TBI severity levels in civilians.[3,4,16,17] The injury is only one variable contributing to IAA in patients with TBI. Psychological factors, such as PTSD symptoms, may also contribute to IAA in patients who are in rehabilitation for neurological injuries.

PTSD is independently associated with IAA,[2,9] especially in veterans/service members.[2,10] IAA can be symptoms of PTSD, but veterans/service members with PTSD are a unique group because they have higher IAA levels compared to civilians with PTSD.[2] Within one year of returning from deployment, 48% of veterans with PTSD symptoms reported engaging in physical aggression.[20] Other psychological disorders, such as anxiety and depressive disorders, are not associated with IAA as PTSD is,[21] perhaps due to the severity of emotion dysregulation associated with PTSD.[22] When veterans engage in skills that activate the prefrontal lobe,[23] IAA can be decreased.[24] The association between PTSD and aggression is concerning, considering 14-30% of veterans endorse PTSD symptoms.[25-26]

While TBI and PTSD are independently associated with IAA, they are often comorbid. Estimates of co-occurring PTSD in civilian TBI samples ranged from 3-30%.[27] Rates of PTSD in

veteran samples with TBI (primarily mild severity) are estimated between 12-89% with variability depending on sample size, use of screens or diagnostic interviews, and study methodologies.[27] Despite high comorbidity and executive dysfunction found in both conditions, few studies have examined if PTSD increases IAA in TBI samples. In 96 civilians with severe TBI, 27% endorsed PTSD symptoms, and those with PTSD symptoms reported more irritability (84%) than patients without PTSD symptoms (31%).[28] In military samples, TBI and PTSD (self-reported; severity unknown) were both associated with physical aggression.[29] A major limitation of this sample included the inconclusive nature of the TBI and PTSD diagnoses as they were not confirmed with medical records, measures, or structured interviews. A study examining these constructs in a large, well-characterized military TBI cohort has not been conducted.

In summary, understanding predictors of IAA is vitally important because IAA can interfere with TBI recovery as staff and family members find it challenging to work with irritable, angry, and aggressive patients.[3] Few studies have examined how comorbid TBI and PTSD relate to staff perceived IAA or studied military samples. The literature that has focused on military samples generally examined mild TBI at the exclusion of moderate and severe TBI and found widely discrepant comorbidity estimates (12-89%).[27] The current study furthers the literature by examining a well-characterized cohort of veterans with TBI of all injury severity levels admitted for inpatient rehabilitation in the Veterans Affairs (VA) TBI Model Systems (TBIMS). This study is the first to examine the relationship of IAA to PTSD in a military TBI sample using standardized scales including clinician ratings of IAA, minimizing self-report bias.

Method

Participants and Setting

Participants were enrolled prospectively in the VA TBI Model Systems National Database-a multicenter, longitudinal study of TBI outcomes. All participants were age 18 or older and transferred to a rehabilitation program at one of five VA Polytrauma Rehabilitation Centers (redacted for review). See REDACTED et al.[30] for VA TBIMS inclusion and exclusion criteria. Analyses were conducted with a subset of TBIMS participants.

All participants in the TBIMS database who enrolled and discharged between 2010 and 2018 were considered for analysis. The primary measure of IAA was the Mayo-Portland Adaptability Inventory-4 (MPAI-4). Program staff rated participants on the MPAI-4 at admission and discharge from the VA Polytrauma Transitional Rehabilitation Programs (PTRP) for post-acute rehabilitation. PTRP are for service members/veterans with TBI that focus on community reintegration to home, work, school, or military service.[31] Individuals were excluded if missing the MPAI-4 or predictor variables. Individuals undergoing inpatient rehabilitation and not referred for PTRP were not considered for analysis as the MPAI-4 was not collected during acute inpatient rehabilitation.

Procedures

This study was a sub-study of the parent VA PRC TBIMS study which was approved by local IRBs at all five VA polytrauma centers. Participants or their proxies provided informed consent prior to data collection. The study conforms to all state and federal research regulations.

Data (e.g. demographics) were collected via interviews with participants or family members/PTRP staff familiar with participants. The MPAI-4 was completed by program staff; self-report measures were completed by study participants. Study staff reviewed medical records for injury characteristics and medical comorbidity information.

Measures

Demographic and injury characteristics. Demographic information and TBI characteristics were obtained at study enrollment from medical records and self or proxy report (Redacted for review[32]). TBI severity was classified as mild, moderate, or severe based on the most severe metric available (i.e. Glasgow Coma Scale score, time to follow commands, or duration of altered consciousness/posttraumatic amnesia; Table 1).

PTSD symptoms at admission to PTRP. PTSD Checklist—Civilian Version (PCL-C[33]) is a 17-item self-report measure of how much individuals were bothered by PTSD symptoms in the past month. Responses range from 1 (not at all) to 5 (extremely). We examined the percent of the sample that likely had a PTSD diagnoses based on scores of 50 or greater.[34] We also examined results while classifying those with PTSD as meeting cluster cutoffs of scores of 3 or more on at least 1 symptom from each Cluster B and C, and at least two symptoms from each Cluster D and E. Cronbach's alpha for current sample = 0.95.

IAA at admission and discharge. The 29-item Mayo-Portland Adaptability Inventory (MPAI-4[35]) assesses how a person with TBI is experiencing problems in areas such as abilities, adjustment, and relationships. To evaluate level of IAA at PTRP admission and discharge, program staff rated item #15 using clinical team consensus. All patient behavior which the Veteran displayed in front of the program staff was used to develop the score. Admission MPAI-4 was rated after 2-3 weeks of PTRP treatment, and discharge ratings reflect participant status over 2-3 weeks prior to discharge. Item #15 asks program staff to rate the level at which the patient experiences "Irritability, anger, aggression: Verbal or physical expressions of anger." Answer choices include: 0 (None); 1 (Mild problems but does not interfere with activities; may use assistive device or medication); 2 (Mild problems, interferes with activities 5-24% of the time); 3 (Moderate problems; interferes with activities 25-75% of the time); 4 (Severe problems;

interferes with activities more than 75% of the time). Total scores were used in the regression model, and scores of 1 or greater on item #15 indicated IAA at admission and discharge.

Data analysis.

Statistical software R v3.5.0 was used for analyses (R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics were expressed as quantiles or percentages. Group comparisons were made using Wilcoxon rank-sum tests (continuous variables) and chi-square tests (categorical variables). IAA was the outcome variable and dichotomized to yes (MPAI-4#15>=1) or no (MPAI-4#15<1). A univariable logistic regression model was fit for the binary outcome to evaluate bivariate associations between IAA and each risk factor. A multivariable logistic regression model was then fit for the binary outcome as a function of all risk factors. Covariates for the multivariable model included age at index TBI, male gender, years of education, annual earnings prior to TBI, and days since sustaining TBI, as these variables were associated with IAA in TBI samples (Baguley, 2006).[16] Redundancy analyses checked for collinearity among risk factors; no risk factors were identified as redundant. Nagelkerke R^2 measures how well the model predicted IAA, with a higher R^2 indicating a better predicting model.[36] Discrimination index (area under the receiver operating characteristic curve) measured how well the model discriminated IAA, with higher scores indicating better discrimination.

Results

At the time of analyses (December 2018), 348 participants were enrolled in the VA PRC TBIMS database and admitted to PTRP. Individuals missing the primary outcome (MPAI-4) at admission (n=29) or discharge (n=18) or PCL-C at admission (n=62) were excluded. The final

sample consisted of 240 veterans (Figure 1); 34 (14%) met the study definition of PTSD (PCL score of 50 or more) comorbid with TBI (TBI+PTSD).

Table 2 describes characteristics of the overall sample and subgroups (TBI vs TBI+PTSD). The overall sample was primarily male (94%), single (46%), with a median age of 29 years. Participants with TBI+PTSD were significantly older (median age 34) compared to the TBI only participants (median age 28; p=.013). Participants identified as white (62%), Hispanic (15%), black (10%), and other ethnicities, with no significant differences observed across subgroups.

Most of the participants had more than a high school diploma (62%) with no differences between subgroups. However, a larger proportion of the TBI+PTSD group had an annual income over $50,000 (48%) compared to the TBI only group (26%; p<.05). TBI+PTSD participants served longer in the military (median of 8 years) compared to TBI only (median of 4 years; p<.05) with no differences in TBI occurring during deployment across the subgroups.

Examination across injury severity indices resulted in most of the sample classified with severe TBI (79%). However, TBI+PTSD participants had a larger proportion sustaining mild TBI (29%) compared to the TBI only group (7%, p<.01). Motor vehicle accidents were the primary injury mechanism, and injury mechanisms varied across the subgroups (although not statistically significant) with more non-traditional injuries (39% classified as other) sustained by the TBI+PTSD group. Time elapsed since injury to PTRP admission was longer for the TBI+PTSD subgroup (median 141 days) compared to the TBI only group (median 79 days; p<.01) with no significant differences observed in overall program length of stay. There were no statistical differences in results when the TBI+PTSD subgroup was classified with cluster scores (versus a total score of 50 or more) on the PCL-C.

Table 3 summarizes PCL-C and MPAI-4 data for the overall sample and subgroups. As stated, 14% endorsed symptoms on the PCL-C (score of 50 or more) consistent with a potential PTSD diagnosis at the time of PTRP admission. At PTRP admission, clinician rated 67% of the sample having at least mild IAA which was reduced to 53% at discharge. Only 2% of the participants had severe IAA at admission which dropped to 1% at discharge. TBI+PTSD participants were more likely to be rated with moderate to severe IAA (30%) compared to TBI only participants (13%, $p<.01$) on admission. No difference in IAA across subgroups was observed at discharge (see Table 3).

Table 4 displays univariate relationships between IAA and demographics, TBI characteristics, and PTSD symptoms. For every one-point increase on the PCL-C, odds of being rated with IAA increased by 3% ($p<.01$). No other significant univariate relationships were observed. A similar pattern was observed in a multivariable model wherein the effects were adjusted for the presence of other model variables. Similarly, the PCL-C was the only significant predictor with a one-point PCL-C increase resulting in a 4% increased likelihood of being rated with IAA ($p<.01$; Nagelkerke $R^2 = 19\%$; C index = 72%).

Discussion

Veterans with PTSD[37] or TBI[13] are at an increased risk of IAA compared to veterans without these conditions. This study examined how PTSD symptoms related to IAA in veterans with detailed injury characterization and predominantly severe TBI. It is imperative to understand risk factors for staff perceived IAA, as staff are the gatekeepers to services that can increase the chances of successful rehabilitation, community integration, and life satisfaction.

Fourteen percent of our sample endorsed symptoms consistent with a PTSD diagnosis, similar to estimates of veterans who are receiving VA health care.[38] In our TBI sample, there

were significant differences in demographic and injury characteristics for those who endorsed PTSD symptom compared to those who did not. Those with PTSD and TBI were older, had higher income, and had served more time on active duty. Additionally, those with PTSD were more likely to have a TBI in the mild range and a longer time between TBI and PTRP admission. These differences, particularly time on active duty, mild TBI severity, and longer duration before PTRP, could have contributed to the development of PTSD, as these veterans had more opportunity for trauma exposure while serving. Then they may have delayed seeking services, as avoidance is a symptom of PTSD.

Regarding IAA, the current results demonstrated that in a program designed to assist veterans in returning to the least restrictive environment available, program staff rated most veterans as having at least mild IAA and few veterans as having severe IAA. These findings are consistent with previous literature demonstrating IAA is common in TBI samples,[11] yet our results suggest that staff considered few veterans recovering from TBI severely impaired by IAA. Of note, these veterans could have received treatment for PTSD in PTRP, which would explain why no differences in IAA remained between those with PTSD+TBI and those with TBI at discharge.

In the multivariable model, PTSD at admission was the only predictor associated with IAA at discharge, even after adding variables to the model that are predictors of IAA in the literature. Patients with PTSD have hypoactivation in the prefrontal cortex and hyperactivation in the amygdala, suggesting extreme emotional responses (e.g. fear, anger) originating in the amygdala are not effectively regulated by the prefrontal cortex.[39] This same decreased activity in the prefrontal cortex and ineffective emotion regulation can result in IAA,[22,39] which may be accounting for the present findings. Finding that PTSD symptoms predict staff reported IAA in a

neurologically impaired sample is important because there are effective PTSD treatments, such as Cognitive Processing Therapy[40] and Prolonged Exposure.[41] However, veterans with PTSD may be hesitant to initiate these treatments due to concerns about being unable to manage emotions that may arise.[42] Other treatments that can assist in reducing IAA include psychotherapies that teach emotion regulation skills.[12,24] Staff and veterans may benefit from knowing PTSD symptoms contribute to IAA, there are effective PTSD and emotion regulation treatments, and veterans may need encouragement to initiate these treatments.

The lack of statistical significance of other IAA predictors found in previous literature may be due to restricted variance in our sample, such as 94% of the sample being male. However, the findings are striking as the sample mainly consisted of individuals who sustained severe TBIs. This suggests that mental health symptoms are an important consideration even in neurologically impaired samples who are in rehabilitation programs to improve their physical functioning. Finally, the predictors accounted for 19% of the variance in IAA, suggesting important factors remain unexplored.

Study Limitations and Strengths

Limitations of the study include using a single item to assess for IAA, which is less reliable than a total scale and does not allow for distinctions to be made between anger, irritability, and aggression. Factors that contribute to these variables may differ. Additionally, we were not able to control for medication effects on IAA. Veterans completed self-report measures of PTSD symptoms; diagnostic interviews would strengthen this research. Finally, the sample is unique in that it involves veterans who may differ from civilians in terms of PTSD symptoms, recovery from TBI, and IAA.

Strengths of the study included an adequate sample size allowing examination of PTSD symptoms in addition to common IAA covariates. Program staff rated veterans' IAA, which is more objective than self-report of socially undesirably behaviors. Longitudinally monitoring IAA over the duration of rehabilitation is a strength over more common cross-sectional studies. Finally, our sample contained moderate and severe TBI, while most PTSD and TBI literature has focused on mild TBI.

Conclusions

PTSD symptoms predicted IAA in veterans with severe TBI. Clinical implications include assessing for and treating mental health symptoms in individuals being in rehabilitation for neurological injuries. Integrating mental health staff within interdisciplinary teams at rehabilitation centers would be one way to assist these veterans. PTSD symptom measures are brief and may be utilized as low-burden predictive measures to identify IAA risk. Treatments options for these veterans include PTSD treatments and treatments that teach individuals with TBI and PTSD how to regulate their emotions.

References

1. Hesdorffer DC, Rauch SL, Tamminga CA. Long-term psychiatric outcomes following traumatic brain injury: a review of the literature. *J Head Trauma Rehabil*. 2009;24(6):452-459. doi:10.1097/HTR.0b013e3181c133fd.
2. Orth U, Wieland E. Anger, hostility, and posttraumatic stress disorder in trauma-exposed adults: a meta-analysis. *J Consult Clin Psychol*. 2006;74(4):698-706. doi:10.1037/0022-006X.74.4.698.
3. Kim E. Agitation, aggression, and disinhibition syndromes after traumatic brain injury. *NeuroRehabiliation.* 2002;17(4):297-310.
4. Kelly G, Parry A. Managing challenging behaviour of people with acquired brain injury in community settings: The first 7 years of a specialist clinical service. *Brain Impair*. 2008;9:293-304. doi:10.1375/brim.9.3.293
5. Watson C, Rutterford NA, Shortland D, Williamson N, Alderman N. Reduction of chronic aggressive behaviour 10 years after brain injury. *Brain Inj.* 2001;15(11):1003-1015. doi:10.1080/02699050010022662
6. Winkler D, Unsworth C, Sloan S. Factors that lead to successful community integration following severe traumatic brain injury. *J Head Trauma Rehabil*. 2006;21(1):8-21. doi:10.1097/00001199-200601000-00002
7. Lezak MD, Howieson DB, Loring DW, Fischer JS. *Neuropsychological Assessment.* New York, NY: Oxford University Press; 2004.
8. Brenner LA. Neuropsychological and neuroimaging findings in traumatic brain injury and post-traumatic stress disorder. *Dialogues Clin Neurosci.* 2011;13(3):311-323.

9. Koenigs M, Grafman J. Posttraumatic stress disorder: the role of medial prefront cortex and amygdala. *Neuroscientist*. 2009;15(5):540-548. doi:10.1177/1073858409333072.
10. Grafman J, Schwab K, Warden D, Pridgen A, Brown HR, Salazar AM. Frontal lobe injuries, violence, and aggression: A report of the Vietnam Head Injury Study. *Neurology.* 1996;46(5):1231-1238. doi:10.1212/wnl.46.5.1231
11. Rao V, Rosenberg P, Bertrand M, et al. Aggression after traumatic brain injury: prevalence and correlates. *J Neuropsychiatry Clin Neurosci.* 2009;21(4):420. doi:10.1176/jnp.2009.21.4.420
12. Neumann D, Malec JF, Hammond FM. The relations of self-reported aggression to alexithymia, depression, and anxiety after traumatic brain injury. *J Head Trauma Rehabil.* 2017;32(3):205. doi:10.1097/HTR.0000000000000261.
13. Bailie JM, Cole WR, Ivins B, et al. The experience, expression, and control of anger following traumatic brain injury in a military sample. *J Head Trauma Rehabil.* 2015;30(1):12-20. doi:10.1097/HTR.0000000000000024
14. Walker WC, Stromberg KA, Marwitz JH, et al. Predicting Long-Term Global Outcome after Traumatic Brain Injury: Development of a Practical Prognostic Tool Using the Traumatic Brain Injury Model Systems National Database. *J Neurotrauma.* 2018;35(14);1587-1595. doi.org/10.1089/neu.2017.5359
15. Corrigan JD, Horn SD, Barrett RS, et al. Effects of patient preinjury and injury characteristics on acute rehabilitation outcomes for traumatic brain injury. *Arch Phys Med Rehab.* 2015;96(s Suppl 3):S209-21. doi:10.1016/j.apmr.2015.03.026

16. Baguley IJ, Cooper J, Felmingham K. Aggressive behavior following traumatic brain injury: how common is common? *J Head Trauma Rehabil.* 2006;21(1):45-56. doi:10.1097/00001199-200601000-00005

17. Roy D, Vaishnavi S, Han D, Rao V. Correlates and prevalence of aggression at six months and one year after first-time traumatic brain injury. *J Neuropsychiatry Clin Neurosci.* 2017;29(4):334-342. doi:10.1176/appi.neuropsych.16050088

18. Taft CT, Watkins LE, Stafford J, Street AE, Monson CM. Posttraumatic stress disorder and intimate relationship problems: A meta-analysis. *J Consult Clin Psychol.* 2011;79(1): 22-33. doi:10.1037/a0022196

19. Marshall AD, Panuzio J, Taft CT. Intimate partner violence among military veterans and active duty servicemen. *Clin Psychol Rev.* 2005;25(7):862-876. doi:10.1016/j.cpr.2005.05.009

20. Elbogen EB, Johnson SC, Wagner HR, Sullivan C, Taft CT, Beckham JC. Violent behavior and post-traumatic stress disorder in US Iraq and Afghanistan veterans. *Br J Psychiatry.* 2014;204(5):368-375. doi:10.1192/bjp.bp.113.134627

21. Rueve ME, Welton RS. Violence and mental illness. *Psychiatry (Edgmont).* 2008;5(5):34-48.

22. Miles SR, Sharp C, Tharp AT, et al. Emotion dysregulation as an underlying mechanism of impulsive aggression: Reviewing empirical data to inform treatments for veterans who perpetrate violence. *Aggress Violent Behav.* 2017;34:147-153. doi:10.1016/j.avb.2017.01.017

23. Lee T-W, Xue S-W. Does emotion regulation engage the same neural circuit as working memory? A meta-analytical comparison between cognitive reappraisal of negative emotion and 2-back working memory task. *PLoS ONE.* 2018;13(9):e0203753. doi:10.1371/journal.pone.0203753

24. Miles SR, Thompson KE, Stanley M, Kent TA. Single session emotion regulation skills training to reduce aggression in combat veterans: A clinical innovation case study. *Psychol Serv.* 2016;13(2):170-177. doi:10.1037/ser0000071.

25. Dursa E, Reinhard M, Barth S, Schneiderman A. Prevalence of a positive screen for PTSD Among OEF/OIF and OEF/OIF-Era veterans in a large population-based cohort. *J Trauma Street.* 2014:27(5):542-549. doi:10.1002/jts.21956.

26. Dohrenwend BP, Turner JB, Turse NA, Adams BG, Koenen KC, Marshall R. The psychological risks of Vietnam for U.S. veterans: A revision with new data and methods. *Science.* 2006;313(5789):979-982. doi:10.1126/science.1128944.

27. Bahraini NH, Breshears RE, Hernández TD, Schneider AL, Forster JE, Brenner LA. Traumatic brain injury and posttraumatic stress disorder. *Psychiatr Clin North Am.* 2014;37(1):55-75. doi.org/10.1016/j.psc.2013.11.002

28. Bryant RA, Marosszeky JE, Crooks J, Baguley IJ, Gurka JA. Posttraumatic stress disorder and psychosocial functioning after severe traumatic brain injury. *J Nerv Ment Dis.* 2001;189(2):109-113. doi:10.1097/NMD.0b013e3181b97a75

29. Gallaway MS, Fink DS, Millikan AM, Bell MR. Factors associated with physical aggression among US Army soldiers. *Aggress Behav.* 2012;38(5):357-367. doi:10.1002/ab.21436.

30. Redacted for review

31. Duchnick JJ, Ropacki S, Yutsis M, Petska K, Pawlowski C. Polytrauma transitional rehabilitation programs: comprehensive rehabilitation for community integration after brain injury. *Psychol Serv.* 2015;12(3):313. doi:10.1037/ser0000034

32. Redacted for review

372 33. Weathers F, Litz B, Herman D, Huska J, Keane T. The PTSD Checklist (PCL): Reliability,
373 validity, and diagnostic utility. Paper presented at the Annual Convention of the International
374 Society for Traumatic Stress Studies, San Antonio, TX. 1993, Oct.
375 34. Blanchard EB, Jones-Alexander J, Buckley TC, Forneris CA. Psychometric properties of the
376 PTSD Checklist (PCL). *Behav Res Ther.* 1996;34(8):669-673. doi:10.1016/0005-
377 7967(96)00033-2.
378 35. Bellon K, Malec J, Kolakowsky-Hayner S. Mayo-Portland Adaptability Inventory-4. *J Head*
379 *Trauma Rehabil.* 2012;27(4):314-316. doi:10.1097/HTR.0b013e3182562f04.
380 36. Nagelkerke NJD. A note on a general definition of the coefficient of determination.
381 *Biometrika.* 1991;78(3):691-692. doi:10.1093/biomet/78.3.691
382 37. Jakupcak M, Conybeare D, Phelps L, et al. Anger, hostility, and aggression among Iraq and
383 Afghanistan war veterans reporting PTSD and subthreshold PTSD. *J Trauma Stress.*
384 2007;20(6):945-954. doi:10.1002/jts.20258
385 38. Tanielian T, Jaycox LH (Eds.) *Invisible Wounds of War: Psychological and Cognitive*
386 *Injuries, Their Consequences, and Services to Assist Recovery.* Santa Monica, CA: RAND
387 Corporation; 2008.
388 39. Shin LM, Rauch SL, Pitman RK. Amygdala, medial prefrontal cortex, and hippocampal
389 function in PTSD. *Ann N Y Acad Sci*. 2006;1071(1):67-79. doi:10.1196/annals.1364.007
390 40. Resick PA, Monson CM, Chard KM. *Cognitive Processing Therapy: Veteran/military*
391 *version.* Washington, DC: Department of Veterans' Affairs; 2010.
392 41. Foa EB, Hembree EA, Rothbaum BO. *Prolonged exposure therapy for PTSD: Emotional*
393 *processing of traumatic experiences.* Therapist Guide. Oxford, NY: Oxford University Press;
394 2007.

42. Hundt NE, Mott JM, Miles SR, Arney J, Cully JA, Stanley MA Veterans' perspectives on initiating evidence-based psychotherapy for PTSD. *Psychol Trauma.* 2015;7(6):539-546. doi:10.1037/tra0000035

Figure 1. Flow Chart of Participants

Table 1 Classification of TBI Severity

TBI Group	GCS	GCS-Motor Score	TFC	PTA	Imaging
Mild	13-15	6	0	0	Negative
Moderate	9-12	4-6	0	1-14	(either)
Severe	3-8	1-3	≥1	>15	(either)

Abbreviations: GCS, Glasgow Coma Scale. TFC, time to follow commands. PTA, posttraumatic amnesia.

Table 2 Descriptive statistics of study sample, TBI Only, and TBI+PTSD

	Study Sample (N=240)		TBI Only (n=206)		TBI+PTSD (n=34)		Difference between TBI Only and TBI+PTSD
	n*	Summary	n*	Summary	n*	Summary	P value
Male	240	94% (225)	206	95% (195)	34	88% (30)	0.152
Age	240	23;29;43	206	23;28;42	34	27;34;46	0.013
Years of education	240		206		34		0.248
High school diploma or less		38% (92)		40% (82)		29% (10)	
More than high school diploma		62% (148)		60% (124)		71% (24)	
Annual earnings	182		157		25		0.025
Below $50,000		71% (129)		74% (116)		52% (13)	
$50,000 and above		29% (53)		26% (41)		48% (12)	
Race/ethnicity	227		193		34		0.457
White		62% (140)		60% (116)		71% (24)	
Black		10% (23)		11% (22)		3% (1)	
Hispanic		15% (35)		16% (30)		15% (5)	
Other		13% (29)		13% (25)		12% (4)	
Marital status	240		206		34		0.223
Single		46% (111)		48% (99)		35% (12)	
Married		29% (70)		27% (56)		41% (14)	
Divorced/ separated		25% (59)		25% (51)		24% (8)	
Years in active duty	217	3;4;9	184	3;4;8	33	3;8;15	0.026
Cause of injury	238		205		33		0.121
Vehicular		54% (129)		56% (115)		42% (14)	
Fall		18% (42)		18% (37)		15% (5)	
Violence: penetrating		5% (12)		5% (11)		3% (1)	
Violence: blast		0% (0)		0% (0)		0% (0)	
Other		23% (55)		20% (42)		39% (13)	
Injured during deployment	240	12% (30)	206	13% (26)	34	12% (4)	0.889
Injury severity category (3-level)	223		192		31		<0.001
Mild		10% (22)		7% (13)		29% (9)	
Moderate		11% (24)		10% (20)		13% (4)	
Severe		79% (177)		83% (159)		58% (18)	
Days from injury to PTRP admission	240	58;84;135	206	56;79;124	34	77;141;735	<0.001
Length of PTRP stay	240	57;93;127	206	53;92;123	34	66;93;143	0.315

Abbreviations: PTRP, Polytrauma Transitional Rehabilitation Programs; PTSD, posttraumatic stress disorder; TBI, Traumatic brain injury.

Note. PTSD is defined as PCL-C >= 50. Summary statistics were expressed as quartiles (1st; median; 3rd) for continuous variables, and percentage (count) for categorical variables. Comparisons between groups

were made using Wilcoxon rank-sum tests for continuous variables and chi-square tests for categorical variables.
* n column is the count of observed records for each variable. For example, among 240 individuals in the study sample, 182 of them had data for annual earnings.

Table 3 PTSD symptoms and IAA of study sample, TBI Only, and TBI+PTSD

	Study Sample (N=240)		TBI Only (n=206)		TBI+PTSD (n=34)		Difference between TBI Only and TBI+PTSD
	n*	Summary	n*	Summary	n*	Summary	P value
PCL-C at admission	240	20;27;37	206	19;24;34	34	54;61;69	<0.001
Irritability, anger, and aggression at admission (MPAI-4 item 15)	240		206		34		<0.001
None		33% (79)		36% (74)		15% (5)	
Mild problem: without interference		23% (56)		23% (48)		24% (8)	
Mild problem: with interference		29% (69)		28% (58)		32% (11)	
Moderate problem		12% (30)		12% (24)		18% (6)	
Severe problem		2% (6)		1% (2)		12% (4)	
Irritability, anger, and aggression at discharge (MPAI-4 item 15)	240		206		34		0.052
None		47% (112)		50% (103)		26% (9)	
Mild problem: without interference		30% (71)		27% (55)		47% (16)	
Mild problem: with interference		17% (41)		16% (33)		24% (8)	
Moderate problem		6% (14)		6% (13)		3% (1)	
Severe problem		1% (2)		1% (2)		0% (0)	

Abbreviations: IAA, irritability, anger, and aggression; MPAI-4, Mayo-Portland Adaptability Inventory-4; PCL-C, PTSD Checklist – Civilian Version; PTSD, posttraumatic stress disorder; TBI, Traumatic brain injury.
Note. PTSD is defined as PCL-C >= 50. Summary statistics were expressed as quartiles (1st; median; 3rd) for continuous variables, and percentage (count) for categorical variables. Comparisons between groups were made using Wilcoxon rank-sum tests for continuous variables and chi-square tests for categorical variables.
* n column is the count of observed records for each variable.

Table 4 Relationships between IAA and Predictors

		Univariable Models		Multivariable Model	
Risk factor	Comparison	OR (95% CI)	p-value	aOR (95% CI)	p-value
PCL-C at PTRP admission	One score higher	1.03 (1.01, 1.05)	0.002	1.04 (1.01, 1.07)	0.004
Injury severity category (3-level)	Moderate vs. Mild	1.17 (0.36, 3.75)	0.796	3.81 (0.78, 18.64)	0.098
	Severe vs. Mild	0.86 (0.35, 2.10)	0.74	2.515 (0.73, 8.69)	0.145
Age at Index TBI	One year older	1.00 (0.98, 1.02)	0.716	0.98 (0.95, 1.01)	0.15
Male	Male vs. Female	0.39 (0.12, 1.27)	0.12	0.68 (0.18, 2.60)	0.574
Years of education	> high school vs. High school or less	1.24 (0.74, 2.09)	0.415	1.15 (0.57, 2.33)	0.701
Annual earnings prior to injury	>=$50,000 vs. < $50,000	1.30 (0.68, 2.49)	0.421	0.98 (0.45, 2.11)	0.954
Days from injury to admission	One day later	1.00 (1.00, 1.00)	0.062	1.00 (1.00, 1.01)	0.098
		Discrimination index		Nagelkerke R2	
		72.2%		19%	

Abbreviations: CI, confidence interval; aOR, adjusted odds ratio; OR, unadjusted odds ratio; PCL-C, PTSD Checklist – Civilian Version; PTRP, Polytrauma Transitional Rehabilitation Programs; TBI, Traumatic brain injury.

Figure 1. Flow Chart of Participants