HHS Public Access

Author manuscript

Vision Res. Author manuscript; available in PMC 2022 September 01.

Published in final edited form as:

Vision Res. 2021 September ; 186: 1–12. doi:10.1016/j.visres.2021.04.004.

Blast Mild Traumatic Brain Injury is Associated with Increased Myopia and Chronic Convergence Insufficiency

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Abstract

While chronic visual symptom complaints are common among Veterans with a history of mild traumatic brain injury (mTBI), research is still ongoing to characterize the pattern of visual deficits that is most strongly associated with mTBI and specifically, the impact of blast-related mTBI on visual functioning. One area that has not been well explored is the potential impact of blast mTBI on refractive error. While myopic shifts have been documented following head injuries in civilian populations, posttraumatic myopic shifts have not been explored in participants with military mTBI. This study investigated the impact of blast mTBIs on a range of visual function measures including distance acuity and refractive error, in a well-characterized cohort of thirty-one Post-9/11 veterans for whom detailed clinical interviews regarding military and TBI history were available. Seventeen participants had a history of blast-related mTBI (blast mTBI+ group) while 14 did not (blast mTBI− group). Results show an increased frequency of convergence insufficiency and myopia in the blast mTBI+ group relative to the blast mTBI− group. Linear regression analyses further show that deficits in distance acuity and refractive error are associated with the number of blast mTBIs during military service but not the number of non-blast mTBIs or the number of lifetime non-blast TBIs and cannot be accounted for by PTSD. These results are consistent with long-lasting damage following blast mTBI to subcortical visual structures that

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CRediT Author Statement

Francesca Fortenbaugh: Conceptualization, Software, Formal analysis, Visualization, Writing – Original Draft **Jennifer Gustafson:** Conceptualization, Methodology, Investigation, Formal Analysis, Writing – Original Draft **Jennifer Fonda:** Conceptualization, Software, Formal analysis, Writing – Original Draft **Catherine Fortier:** Conceptualization, Methodology, Investigation, Writing – Original Draft **William Milberg:** Conceptualization, Methodology, Supervision, Funding acquisition, Writing – Original Draft **Regina McGlinchey:** Conceptualization, Methodology, Supervision, Funding acquisition, Writing – Original Draft

support both vergence movements and the accommodative functions needed to see clearly objects at varying distances.

Keywords

traumatic brain injury; distance acuity; myopia; accommodation; convergence; posttraumatic pseudomyopia; posttraumatic stress disorder

1. Introduction

Hundreds of thousands of active duty servicemen and Post-9/11 Veterans who served in the recent military conflicts from 2001 to the present have been diagnosed with a traumatic brain injury (TBI). Among those with TBI during deployment, the majority are mild TBIs (mTBI) and are related to blast exposure (Rigg & Mooney, 2011). Additionally, many veterans experience multiple TBIs due to blast and/or blunt force trauma during their military service (Greer, Sayer, Kramer, Koeller, & Velasquez, 2016; Hoge et al., 2004; Lindquist, Love, & Elbogen, 2017). Blast waves expose individuals not only to the inertial or shearing forces experienced during blunt force trauma, but also spallation and implosion forces from blast pressure waves which can damage tissue (DeWalt & Eldred, 2017; Wolf, Bebarta, Bonnett, Pons, & Cantrill, 2009). Given the prevalence of blast exposures in recent decades, the negative impact on these veterans' quality of life after service (Lemke, Cockerham, Glynn-Milley, & Cockerham, 2013), and the long-term healthcare costs of caring for veterans with a history of blast related TBI, understanding acute and chronic pathologies related to blast exposure is an important public health issue. This is particularly true for the visual system with a recent study estimating that overall economic cost of treatments, benefits, and lost productivity due to military eye injuries and vision impairment from TBI is over $2 billion dollars annually (Frick & Singman, 2019). Ocular trauma and visual dysfunction are two of the more common injuries following blast exposures in the current conflicts (Dougherty, MacGregor, Han, Heltemes, & Galarneau, 2011; Weichel, Colyer, Bautista, Bower, & French, 2009), and tissue damage impacting both the retina and visual system can occur in the absence of penetrating injuries (Cockerham et al., 2011; DeWalt & Eldred, 2017; Sen, 2017). Additionally, it has been found that resultant visual deficits may not arise immediately following blast exposure but can emerge over time even in the case of mTBI without penetrating ocular injuries (Frick & Singman, 2019). As a result of emerging evidence that even mTBIs can have lasting negative impacts on the health and functioning of the visual system, there has been increased interest in identifying potential vision-related disorders associated with TBIs due to blast and blunt force trauma, the impact of repetitive or varying severity blast-related TBIs, and determining whether biomarkers can be assessed to aid targeted development of therapeutic interventions (Capó-Aponte, Beltran, Walsh, Cole, & Dumayas, 2018; Casto, Nedostup, & Byrne, 2012; Ciuffreda, Ludlam, Thiagarajan, Yadav, & Capo-Aponte, 2014).

Several studies of Post-9/11 veterans seen in VA Polytrauma clinics have found that TBI is associated with binocular vision, accommodation, oculomotor, and visual field deficits (Ciuffreda et al., 2014; Cockerham et al., 2009; Goodrich, Kirby, Cockerham, Ingalla, &

Lew, 2007; Goodrich et al., 2014). In particular, convergence and accommodative insufficiency appear to be some of the more frequent visual disturbances following TBI, including mTBI (Alvarez et al., 2012; Brahm et al., 2009; Ciuffreda et al., 2007; Goodrich et al., 2014; Thiagarajan, Ciuffreda, & Ludlam, 2011). Studies focusing on subacute deficits (<2months) following blast-induced mTBIs in the military have shown deficits in eye movements, vergence, accommodation, and reduced reading speed compared to control participants (Capó-Aponte, Urosevich, Temme, Tarbett, & Sanghera, 2012), while other studies have shown that both blast and non-blast mTBI are associated with chronic deficits including convergence and accommodation insufficiency over one year post injury (Capó-Aponte et al., 2017; Magone & Shin, 2014). Other lines of research have begun to highlight additional areas of visual dysfunction that may help to identify blast-related mTBI, including scattered regions of decreased sensitivity across the visual field (Walsh et al., 2015).

Another area of visual functioning that can be impacted following TBI is visual acuity (Flanagan, Velez, Gu, & Singman, in press; Frick & Singman, 2019). In studies of military populations, moderate/severe TBI has been associated with severe acuity loss (Brahm et al., 2009; Flanagan et al., in press) but to our knowledge, no study to date has reported an association between mTBI and changes in refractive error. In the civilian population, however, associations between TBI and myopic shifts in refractive error have been documented (Hughes, Treacy, Duignan, & Mullaney, 2017; Imburgia, Sorrentino, & Mularoni, 2017; Kowal, 1992; London, Wick, & Kirschen, 2003). Given these documented cases of myopic shifts following trauma in the civilian literature and the focus thus far on severe visual acuity deficits following TBI in the military, assessing whether blast-related mTBI is associated with milder changes in visual acuity, and specifically with myopic shifts, is a gap in our current understanding of long-term blast-related mTBI impacts on visual functioning.

The goal of the current study was to investigate visual functioning in a cohort of Post-9/11 Veterans with detailed information regarding the nature and frequency of mTBI from a validated semi-structured clinical interview (Fortier et al., 2014). In particular, we tested whether visual functioning differs across Veterans with and without a history of blast-related mTBI who were several years post-deployment. As reports to date have shown mixed results regarding the impact of mTBI on visual acuity in civilian and military populations and given evidence of dose-response effects of mTBIs on diffuse damage to the visual system, we further sought to examine whether multiple blast-related mTBIs were associated with worse visual acuity outcomes and if any dose-dependent effect was due to the number of mTBIs generally, regardless of source, or whether it is specific to blast-related mTBIs.

2. Methods

2.1. Participants.

The thirty-one participants (62 eyes; 29 males) included in this study were recruited from the Translational Research Center for Traumatic Brain Injury and Stress Disorders (TRACTS) longitudinal cohort study which includes community-dwelling Post-9/11 veterans recruited primarily from the Greater Boston Metropolitan area and New England (McGlinchey, Milberg, Fonda, & Fortier, 2017). The mean age of the participants was 37.0 ±

9.9 years (range: 26 – 63 years). General inclusion criteria for the TRACTS cohort was that participants were Post-9/11 service members between 18 and 65 years of age. General exclusion criteria for the TRACTS cohort included prior seizure disorders, cognitive disorder due to general medical conditions, and/or neurological illness unrelated to TBI; active suicidal and/or homicidal ideation requiring intervention; or a current diagnosis of bipolar disorder or psychotic disorder unrelated to PTSD. For the current study, participants were additionally excluded if they had a history of retinal or ocular disease, open globe injuries due to trauma, or history of moderate/severe TBI. Participants were not preselected based on history of mild traumatic brain injury. The optometric assessments outlined in this study were appended to the standard one-year or five-year follow-up assessments completed by all TRACTS cohort participants. The additional optometric assessments were completed by eligible participants completing follow-up assessments between July 2015 and April 2017 based on the availability of space in the optometry clinic during their visit. This study was approved by the VA Boston Healthcare System internal review board, and all participants completed written informed consent before testing.

2.2. Materials and Procedure

All background and behavioral measures outside the optometric assessments in this study were collected during the testing battery completed by all participants in the TRACTS cohort study. These assessments were completed prior to the optometric exam. All TRACTS cohort participants complete 1) self-report measures of lifetime trauma history, military experiences, and deployments, 2) comprehensive psychiatric and neuropsychological assessments, 3) biological measurements including structural and functional magnetic resonance imaging, and 4) medical evaluations including samples for blood chemistry and genetic assessments (McGlinchey et al., 2017). We outline below the assessments included in the current study.

2.2.1 TRACTS Measures.—Demographic information on age, race/ethnicity, gender, and military/deployment experience was collected through self-report and questionnaires administered at baseline and follow-up assessments. Combat exposure was measured using the Deployment Risk and Resilience Inventory (DRRI): Combat Experience Scale (King, King, Vogt, Knight, & Samper, 2006). The DRRI combat module is a 16-item self-report questionnaire using a Likert scale range of 0–4, with higher scores indicating greater amount of combat experiences. The Neurobehavioral Symptom Inventory (NSI: Cicerone & Kalmar, 1995) is a 22-item questionnaire that asks participants to report on symptom severity for common symptoms associated with traumatic brain injury (vestibular, somatosensory, cognitive, and affective) during the last two weeks using a Likert scale range of 0–4; 0 indicating issues were rarely if ever present, while a score of 4 represents very severe perceived disruption. Within this measure two questions directly query an individual’s perceived visual status. The first question asks participants to rate general vision problems including blurry vision or trouble seeing. The second question asks participants to rate their level of photosensitivity. Post-traumatic stress was assessed using the Clinician Administered PTSD Scale (CAPS: Blake et al., 1990). The CAPS provided both a continuous score of PTSD current symptom severity and a diagnostic determination of PTSD status using the DSM-IV criteria (Weathers, Ruscio, & Keane, 1999). All diagnostic interviews in the TRACTS battery were completed by doctoral-level psychologists, with cases reviewed by at least three doctoral-level psychologists/psychiatrists to achieve consensus.

Boston Assessment of TBI-Lifetime (BAT-L): History of traumatic brain injury was assessed using the Boston Assessment of TBI-Lifetime (BAT-L; Fortier et al., 2014). This semi-structured clinical interview used a forensic approach to assess a participant's history of TBI that occurred during three epochs: pre-deployment, during deployment, and post-deployment. Using criteria outlined by the Department of Defense, the BAT-L defined a history of mild TBI (mTBI) as a period of self-reported loss of consciousness that lasted less than 30 minutes, and/or posttraumatic amnesia that lasted less than 24 hours, and/or altered mental status that lasted less than 24 hours following a credible injury mechanism that occurred during military service. (U.S. Department of Veterans Affairs and U.S. Department of Defence, 2009). Both the number of mTBIs and the severity of mTBIs was recorded. The BAT-L further assessed exposures to blast during military service and divides exposure into three distance categories as a proxy for blast severity (<10m, 11–25m, and 26–100m). For the current study, we classified close-blast exposures as <10 meters from detonation (Robinson et al., 2015). Using information from participants about the events at the time of injury, mTBIs were classified as either blast-related or non-blast related mTBIs. We note that classification of a blast mTBI requires both exposure to a blast and co-occurring acute neurological symptom(s) meeting the mTBI criteria outlined above. Depending on the magnitude of the blast, blast mTBIs can occur as a result of blast exposure at any of the three distance categories. Conversely, close blast exposures do not necessarily indicate a mTBIs occurred, as veterans can be exposed to close blast events without experiencing acute symptoms of mTBI. Information was also combined across the three epochs to derive a score of the number of lifetime mTBIs. Previous studies have demonstrated strong interrater reliability for the BAT-L (kappa >0.88) and strong correspondence with other standardized measurements of TBI history (Fortier et al., 2014; Fortier, Amick, Kenna, Milberg, & McGlinchey, 2015; McGlinchey et al., 2017).

For the purpose of this study, we defined three classes of mTBIs based on information derived from the BAT-L. This included the number of blast-related mTBIs during military service (blast mTBI), the number of mTBIs due to blunt-force trauma during military service (non-blast mTBI), and the number of non-blast lifetime mTBIs which included all mTBIs due to blunt force trauma before, during, and after military service (lifetime non-blast mTBI). For the group-level analyses we divided participants into two groups: the blast mTBI+ group, which included all participants with a history of at least one blast-related mTBI, and the blast mTBI− group, which included all other participants. Thus, the blast mTBI− group included participants with either no history of mTBI or a positive history of mTBIs due to blunt force trauma.

2.2.2 Optometric Assessments—Testing of visual function was conducted in the VA Boston Healthcare System, Jamaica Plain Campus Optometry Clinic and took approximately 30 minutes to complete. The optometrist who completed these assessments (author J.G.) was blind to participants TBI status and blast exposure at the time of data collection. All assessments followed approaches used in standard clinical practice. Participants' pupils were not dilated during the exam due to time constraints and to allow for measurements of accommodation and vergence functions. Below we outline the visual function assessments addressed in the current study. Participants also completed an assessment of retinal health at the end of the examination including fundus photography and optical coherence tomography scans (data not reported here).

Visual examination included assessments of visual acuity and refractive error, oculomotor function, accommodation, binocular visual function, and undilated ocular health. Distance and near visual acuity were measured monocularly with participant's habitual corrective lenses if needed using a standard high contrast Snellen visual acuity chart (Reichert ClearChart® 2 Digital Acuity System, Depew, NY, USA). Pinhole acuity was measured monocularly using a multihole pinhole occluder to assess for visual acuity deficits due to refractive error. Retinoscopy was used to obtain objective measurements of the refractive error in diopters for each eye using standard clinical technique. A retinoscope was used to shine light into the eye and observe the reflex off the retina as neutralizing lenses were placed in front of the eye. The resulting refractive error was used to classify each eye as myopic if spherical equivalence was ≤ -0.5 diopters (D). This cutoff was chosen to align with previous epidemiological studies of myopia in the general population (Foster & Jiang, 2014; Holden et al., 2016; Vitale, Sperduto, & Ferris, 2009). Refractive error is typically taken from one eye for this classification (Vitale et al., 2009); however, given that head traumas may have unilateral impacts on visual function, classifications were made for each eye separately.

Ocular alignment at distance and near was assessed using cover test; unilateral (to assess for strabismus), alternating (to determine magnitude), then repeat of unilateral (to assess for breakdown to an intermittent strabismus). An isolated 20/30 equivalent letter at 6m and 40 cm was utilized to assess ocular alignment at far and near distances, respectively. The ocular alignment was neutralized with a prism bar. Fixation was assessed using direct observation. Saccadic and pursuit eye movements were assessed using the Northeastern State University College of Optometry Oculomotor Test (NSUCO). The NSUCO is a direct observation assessment of saccades (Garzia, Richman, Nicholson, & Gaines, 1990; Maples & Ficklin, 1988). This test provides three sub-scores for each type of eye movements: assessments of whether head and body movements were noted while completing eye movements, the ability to complete the testing battery, and the overall accuracy of the eye movements. Scores were compared to age and gender normative values to determine if overall saccadic/pursuit eye movements fall within the normal range and a dichotomous code was used to indicate if measured values were inside/outside of the normative ranges (Maples, Atchley, & Ficklin, 1992).

Accommodative amplitude was assessed monocularly using an Accommodative Rule with a target consisting of high contrast 20/30 letters (Convergence Insufficiency Treatment Study Group, 2008; Scheiman & Wick, 2008). The measured findings in addition to the participant's refractive error, was used to determine the total accommodative amplitude. Scores were again compared to age-adjusted normative values to determine if the participant's scores fell at or above the age-adjusted minimum expected amplitude of accommodation and coded to indicate if they fell inside/outside the normative ranges.

Evaluation of convergence amplitudes were assessed with positive fusional vergence and near point of convergence tests. Positive fusional vergence was induced using a horizontal prism bar in the base out orientation. A high contrast 20/30 letter on a fixation stick was presented in front of the participant and the amplitudes with which participants were able to maintain clear, single, binocular vision was recorded where the amplitude was first increased and then decreased (Scheiman & Wick, 2008). This included measurements of the amplitude at which binocular vision was disrupted (break point) and measurements of when binocular vision returned to clear, single state (recovery point). Near point of convergence was assessed using an Accommodative Rule with a target consisting of a single column of 20/50 letters and repeated three times (Convergence Insufficiency Treatment Study Group, 2008; Scheiman & Wick, 2008). Here the target was initially positioned approximately 40cm in front of the participant and was moved slowly towards the participant. The distance at which the participant reported diplopia was recorded as the break point. The target was then moved slowly away from the participant and the distance at which the target became single again was recorded as the recovery point. Break and recovery points were then compared to normative values and coded to indicate if they fell inside/outside the normative ranges.

2.3. Statistical Analyses

Statistical analyses were completed using SPSS v.25 and Matlab (Mathworks, Natick, MA). Group-level statistics were calculated to test for differences in demographics and visual function assessments across participants with and without a history of blast mTBI. Fisher's Exact test with unadjusted odds ratios and 95% confidence intervals was calculated to test for differences in the frequency of participants showing abnormal age-adjusted values on visual function tests across the two groups as expected table counts were less than five for several variables using Pearson χ^2 test. For continuous variables, t-tests were calculated to test for between-group differences. As the three measures of resolving power were tested monocularly, data was combined across the two eyes. For these assessments, between-group differences were assessed using a linear mixed-effects model with blast mTBI group as a fixed factor, eye (left/right) as a repeated measure, and subject as a random intercept. The dependent variables were the refractive error measure in diopters and the denominator of the Snellen fraction for the distance and near acuities. For myopic classification, a logistic regression using a generalized linear model was calculated with blast mTBI group as a fixed factor, eye (left/right) as a repeated measure, and subject as a random intercept. Walds test were used to test significance for the blast mTBI factor and to calculate the odds ratio and 95% confidence interval for this parameter.

To determine whether the number of mTBIs was associated with increased myopia, and if this relationship was specific to blast mTBI, linear mixed-effects models were calculated. In separate models, the dependent variable was the three measures of resolving power: near acuity, distance acuity, and refractive error scores. For each of these measures, three models were calculated that varied in how the number of mTBIs were calculated. In the first model the number of blast mTBIs was included as the mTBI predictor variable. In the second model, the number of non-blast mTBIs during military service was used as the mTBI predictor variable. Finally, as many veterans have histories of civilian mTBIs both prior to or after military service (e.g. car or sports accidents), the third model included the number of lifetime non-blast mTBIs as the mTBI predictor variable. In all models, the age of participants and the number of mTBIs were included as fixed factors, along with the eye tested (left/right) as a repeated measure. For the near and distance acuity models, pinhole acuity was also included as a fixed factor. Pinhole acuity was included to control for acuity issues due to non-refractive error (e.g., damage to optic nerve, visual cortex) as pinhole assessments are expected to remain poor in these cases but return to 20/20 when the origin is refractive in nature. If mTBI is associated with increased myopia, it was predicted the number of mTBIs would be a significant predictor in the distance acuity model but have minimal impact on the near acuity model, and a significant negative association would be seen between refractive error and the number of mTBIs. Subject was included as a random intercept in all models.

To further assess the relationship between repeated mTBIs and the resolving power measures, separate leave-one-subject out cross-validation linear regression models were also run on the data in nine separate regression models (3 measures of the number of mTBIs x 3 resolving power assessments). As before, age and pinhole acuity were included as covariates for the near and distance acuity measures while only age was included as a covariate in the refractive error model. First, all measures were z-transformed to allow for comparison of the relative prediction value of each independent variable. Then, each of the 62 data points was left out of the sample once and a linear regression model was calculated on the remaining 61 data points. Using the coefficient weights from this model and the parameter values for the left-out data point, a predicted acuity or refractive error score was calculated. After this iterative process was run for all data points, the correlation between the observed and predicted scores was calculated using Spearman rho. For descriptive purposes, average standardized beta weights were calculated for each of the predictor variables across all 62 iterations.

3. Results

Within the sample, 17 participants had a history of blast mild TBI (blast mTBI+ group) during their military service and 14 participants did not (blast mTBI− group). Table 1 provides details regarding the events leading to the blast mTBI collected during the BAT-L assessment. Within the blast mTBI+ group, 7 (47%) participants also had a history of at least one non-blast mTBI during their lifetime. Within the blast mTBI− group, 3 (21%) participants had a history of non-blast mTBI during their military service and 6 (43%) participants had at least one non-blast mTBI during their lifetime. Across the 23 participants with at least one lifetime mTBI (blast or blunt force trauma), the average time since their last mTBI was 8.1 years (range: 2–35 years). Table 2 shows demographic details for all participants in this study and comparisons of measures across the blast mTBI− and blast mTBI+ groups. As seen in Table 2, the two groups were well-matched in terms of gender, age, and number of deployments. The blast mTBI+ groups showed greater levels of combat experience, more lifetime non-blast mTBIs over their lifetime, and a trend toward more severe current PTSD symptoms, but not a significant increase in the frequency of current

PTSD diagnoses. While the two groups did not differ in the number of non-blast mTBIs during military service, there was also a trend for the blast mTBI+ group to have a greater number of close blast exposures. Overall, the blast mTBI+ group did not endorse more severe TBI neurobehavioral symptoms on the composite score of the NSI questionnaire or in the specific domain of photosensitivity. However, the blast mTBI+ group did endorse more severe symptoms of blurry vision or trouble seeing in the last two weeks.

Table 3 shows the results of the optometric assessments and comparisons across the group of participants with and without a history of blast mTBI. As seen in Table 3, participants across the two groups showed comparable near acuity scores but the blast mTBI+ group overall showed greater deficits on the distance acuity test. While refractive error did not significantly differ across the two groups, a greater proportion of eyes in the blast mTBI group were classified as myopic, or having a refractive error ≤ −0.5D. Results of the generalized linear model showed that blast mTBI was associated with a significantly higher odds of myopic classification (OR = 6.294 (95%CI: 1.97–20.12); $\chi^2 = 9.623$, p=0.002). For all four resolving power measures, no significant differences were found across the left and right eyes ($p > 0.064$ for all).

No difference was observed across the two groups for eye movements, ocular alignment, or accommodation. A greater proportion of the blast mTBI+ group showed deficits on near point of convergence (70.6% vs. 26.7% for both break and recovery scores) while no difference was seen in positive fusional vergence measures. Of note, only one participant in each group showed an esophoria eye position at distance. In the near position, two participants in the blast mTBI− and three participants in the blast mTBI+ showed an esophoria. No participants showed an esotropia in either the near or far positions. For pinhole acuity scores, all but one participant had a pinhole acuity measured at 20/20, with the one participant showing a 20/25 pinhole acuity score.

While the primary aim of the current study was to examine the impact of blast mTBI on visual functioning, Post-9/11 veterans often experience multiple mTBIs from differing sources during their military service and over their lifetime (Fortier et al., 2014; Lindquist et al., 2017; McGlinchey et al., 2017) and this is reflected in the types of mTBIs observed in the current cohort. Therefore, to further explore the impact of multiple mTBIs on visual acuity and whether specific types of mTBIs may be more associated with acuity deficits, linear mixed-effects regression models were calculated to determine if differences in resolving power (e.g., acuity and refractive error) across participants is associated with the number and/or type of mTBI. Results of these models show a link between increased myopia and the number of blast mTBIs in our cohort (Table 4). This association is seen first in the regression models predicting near and distance acuity scores. While the number of blast mTBIs was found to be significantly associated with poorer distance acuity scores, it was not associated with near acuity scores. Indeed, near acuity scores were only associated with the age of participants, as expected due to presbyopia. For both near and distance acuity, the number of non-blast military or lifetime mTBIs was not associated with acuity scores. The selective impairment of distance vision associated with blast mTBIs seen in the acuity score measures matches the results seen in the regression analyses conducted on refractive error. As seen in Table 4 and Figure 1, the number of blast mTBIs but not the number of non-blast mTBIs was found to be negatively associated with refractive error (B = −0.872, p = 0.027). This result indicates that each blast mTBI was associated with a −0.872D shift in refractive error. As with the distance acuity scores, refractive error was not associated with the number of non-blast military or lifetime mTBIs.

To further characterize the association between acuity and the number of mTBIs, separate linear regressions were calculated for near/far acuity and refractive error measurements across the three assessments of number of mTBIs using leave-one-subject-out cross-validation. Results of these analyses (Table 5) show that near acuity scores are predominantly predicted by the age of participants with standardized betas greater than 0.3. In contrast, standardized beta values for the age of participants are all less than 0.1 when predicting distance acuity scores. For both the distance acuity and refractive error scores, a significant association between observed and predicted scores was only seen when the number of blast mTBIs was used as a predictor variable (Distance Acuity: $\rho = 0.31$, $p = 0.013$; Refractive Error: $\rho = 0.32$, $p = 0.010$), indicating a selective association between blast mTBIs and myopia rather than global deficits in resolving power (e.g., astigmatism). In the distance acuity model, age is seen to provide little information about the acuity scores across participants while both the number of blast mTBIs and pinhole acuity explain the most variance. As noted above, only one participant did not have a pinhole acuity of 20/20, with this participant's pinhole acuity measured at 20/25. Rerunning the analyses without pinhole as a predictor variable shows similar standardized parameter estimates for the number of blast mTBIs and overall association between observed and predicted distance acuity values (# mTBI: $\beta = 0.4167$; overall model: $\rho = 0.3018$, $p = 0.017$). As seen in Table 5, for the refractive error model, the number of blast mTBIs provides a relatively larger contribution to the model than the age of the participants ($\beta = -0.382$ vs. 0.206). However, as seen in Figure 1 and the standardized beta value, the age of participants shows a slight positive relationship with refractive error with the largest myopic refractive error scores occurring in participants under 40 years of age. This subtle relationship between the age of participants and refractive error scores may explain why group-level differences were not seen in refractive error scores in the analysis presented in Table 3.

PTSD Status and Self-Reported Neurobehavioral Symptoms.

While the previous analyses show that blast mTBIs were associated with increased myopia and convergence insufficiency, previous work has shown that Veterans with comorbid PTSD and TBI report higher levels of subjective visual symptoms compared to Veterans with TBI alone even when objective tests show no difference in oculomotor or binocular visual function (Goodrich et al., 2014). As seen in Table 2, participants in the blast mTBI+ group reported more severe visual symptoms on the NSI questionnaire when asked about visual impairments including blurry vision and trouble seeing while no difference was found in the self-reported severity of photosensitivity across the two groups. As over half of the current cohort of participants had a current diagnosis of PTSD at the time of testing, we first tested whether PTSD diagnoses and current PTSD symptom severity were also related to self-reported visual symptoms on the NSI questionnaire. Comparing across participants with and without a current diagnosis of PTSD, participants with PTSD reported more severe visual symptoms ($t(29) = 3.299$, $p = 0.003$), more severe issues with photophobia ($t(29) = 3.216$, p

= 0.003), and higher overall total scores across all domains in the NSI ($t(29) = 4.354$, $p < 0.001$) compared to participants without a current PTSD diagnosis. Spearman rho correlations further showed that the degree of current PTSD symptom severity was positively correlated with both the severity of visual symptoms reported by participants ($\rho = 0.626$, $p < 0.001$) and the severity of photosensitivity symptoms ($\rho = 0.699$, $p < 0.001$). Thus, both a positive diagnosis and higher PTSD symptom severity were associated with reports of more severe visual symptoms (see Figure 2).

As a trend toward more severe current PTSD symptoms was seen in the blast mTBI group (see Table 2), a final set of control analyses were calculated to determine if PTSD diagnosis was statistically interchangeable with a positive history of blast mTBI in the between group analyses of visual functioning. Repeating the between group analyses presented in Table 3 but separating the groups according to PTSD diagnosis, no statistical differences were seen in visual function measures across the participants with and without a current diagnosis of PTSD including distance acuity ($B = -2.98$, $t(29) = -1.25$, $p = 0.221$), refractive error ($B = 0.45$, $t(29) = -0.80$, $p = 0.429$), or near point of convergence ($p = 0.285$ for both break point and recovery). Finally, replacing the number of blast mTBIs with current PTSD severity in the linear mixed effects models showed that PTSD symptom severity was not associated with either refractive error ($B = -0.006$, $t(28) = -0.639$, $p = 0.528$) or distance acuity scores ($B = 0.064$, $t(28) = 1.719$, $p = 0.097$). Collectively, these results replicate the pattern seen in Goodrich et al. (2014), with both PTSD diagnosis and higher PTSD symptom severity being associated with more severe reports of visual symptoms but not with the testing outcomes measuring resolving power, oculomotor or binocular visual function. Importantly, these final results demonstrate that current PTSD status is not able to account for the association seen between blast mTBI and increased myopia or rates of convergence insufficiency in the current cohort.

4. Discussion

The results of the current study show that in our cohort of participants, history of blast mTBI is associated with an increased frequency of convergence insufficiency and increased myopia, even years after injury. Roughly 70% of participants with a history of blast mTBI (blast mTBI+ group) showed deficits on near point of convergence compared with 27% of participants without a history of blast mTBI (blast mTBI− group). The relatively high proportion of near point of convergence deficits in the blast mTBI− group is perhaps not surprising given 3/14 (21%) of this group had a history of blunt force mTBI during military service, and 6/14 (43%) had a history of blunt force mTBI during their lifetime, and there are frequent reports in the literature that mTBI in general is associated with convergence insufficiency (Cockerham et al., 2009; Goodrich et al., 2007). The relative increase in the frequency of convergence insufficiency in our blast mTBI cohort is also consistent with recent work showing an association between blast mTBI and higher rates of deficits in vergence functions in active-duty service members and Post-9/11 veterans (Capó-Aponte et al., 2017; Capó-Aponte et al., 2012; Magone & Shin, 2014). While convergence and accommodation dysfunction have been well-documented within the first year post-injury, relatively few studies have documented their persistence several years post-injury (Capó-Aponte et al., 2017). Our finding of increased deficits in convergence abilities in a cohort of community-dwelling Post-9/11 veterans all several years post-injury therefore adds to the literature in highlighting the chronic and pervasive nature of these deficits.

The main novel finding of the current study is the observed association between a positive history of blast mTBI and greater myopia. This association is seen in both the group-level analyses and the regression analyses examining the impact of repetitive blast mTBI on acuity thresholds and refractive error. In the group-level comparisons, we observed greater distance acuity deficits in the blast mTBI group along with a higher proportion of this sample being classified as myopic based on refractive error (Table 3). Recent epidemiological studies have found myopia prevalence rates of 41.6% for individuals 12 to 56 years of age in the United States (Vitale et al., 2009), 38% for active duty service members in the U.S. Armed Forces (Reynolds, Taubman, & Stahlman, 2019), and 25% worldwide, with the potential to increase upwards of 50% by 2050 (Holden et al., 2016). Our finding that 42% of the eyes in the blast mTBI− group were classified as being myopic broadly matches the current estimated prevalence rates in the United States. For the blast mTBI+ group, however, we find nearly a doubling in the frequency of myopia with 82% of all eyes (28/34) classified as myopic, far outside current estimates of prevalence rates in the United States and within the U.S. military.

In addition to the group-level differences, we found a positive association between the number of blast mTBIs and the degree of myopia in our sample (Tables 4 & 5). This is seen when comparing the regression models for near and distance acuity, which showed that the number of blast mTBIs was associated with worse distance acuity scores but was not related to near acuity scores. Importantly, regression models for the two acuity measures included pinhole acuity as a covariate to control for nonrefractive issues. While myopia is most often classified based on refractive error, myopia also presents in distance acuity scores and has been classified through distance acuity measurements in previous studies (Vitale et al., 2009). Additionally, the fact that associations were selectively seen with distance acuity but not near acuity scores helps to rule out disorders such as astigmatism which would be expected to impact acuity at both near and far distances. Importantly, the present results also showed that the number of blast mTBIs was negatively associated with lens power in the refractive error models, providing another measure indicating that blast mTBIs are associated with increased myopia. These associations with distance acuity and refractive error were not replicated using either the number of blunt force mTBIs during military service or the number of blunt force mTBIs across the lifespan. These results suggest both an association between repetitive blast mTBIs and increased myopia as well as some level of specificity in the etiology of mTBI and the resulting impact on resolving power. While it is well documented that service members in the recent conflicts often experience multiple mTBIs during their deployments (Greer et al., 2016; Hoge et al., 2004; Lindquist et al., 2017), and greater deficits in visual function have been shown to be associated with single-event TBIs of greater severity (Brahm et al., 2009; Dougherty et al., 2011; Reynolds, Barker, Merezhinskaya, Oh, & Stahlman, 2019), the impact and potential dose-response effect of repetitive mTBIs on visual functioning remains understudied. The current findings cannot fully dissociate the role of TBI severity from the number of mTBIs, as it is possible that veterans with a history of multiple mTBIs may also experience more severe mTBIs on any given occasion. Additionally, while the number of close-blast exposures (i.e., blasts occurring within 10 meters of an individual) was not significantly different across the two groups, a trend was observed with participants in the blast mTBI− groups having a history of 0–1 close blast exposures while participants in the blast mTBI+ group had a mean of 4 close blast exposures. Close-blast exposures do not necessarily lead to mTBIs, but it is possible that more frequent exposure to low-level blast waves in the blast mTBI+ group impacted the current finding. At least one study in humans has shown that repetitive exposure to low-level blasts not leading to mTBI was associated with increased prevalence of visual field defects in active duty service members over a two year period compared to controls (Capó-Aponte et al., 2015), a finding consistent with other lines of research looking at the impact of blast mTBI on visual field sensitivity (Walsh et al., 2015). Another study has shown that having a history of more than one blast mTBI increases the likelihood of chronic visual function deficits over a year post injury (Magone & Shin, 2014). Additionally, animal studies on the effects of blast exposures on the visual system (Choi et al., 2015; Vest, Bernardo-Colón, Watkins, Kim, & Rex, 2019) have documented cumulative dysfunctions due to repetitive blast exposures. Collectively, these studies along with the current results, point to the need for more work to be done to understand the impact that multiple mTBIs, whether due to blast or blunt force trauma, have on long-term visual functioning.

Several lines of research have begun to unravel the mechanisms leading to deficits in visual functioning following mTBI, and in particular, blast mTBI. Blast TBI is generally associated with both diffuse axonal injury due to shearing forces that can damage long-range nerve fiber tracts at the time of injury (Davenport, Lim, Armstrong, & Sponheim, 2012; Magnuson, Leonessa, & Ling, 2012) as well as progressive neuronal degeneration due to neuroinflammatory responses that continue post-injury (Lozano et al., 2015). Concerning the visual system, these pathological changes can impact visual functioning in the absence of ocular injury by damaging the retina, optic nerve, and the cranial nerves that underly oculomotor functioning, as well as the cortical and subcortical structures that support visual perception (Allen et al., 2018; DeWalt & Eldred, 2017; Dutca et al., 2014; Kelts, 2010; Petras, Bauman, & Elsayed, 1997). Recent work in animal models has shown chronic deficits in contrast sensitivity and spatial frequency sensitivity in rats months after exposure to a single acoustic blast (Allen et al., 2018). Given the multiple systems involved in supporting typical visual functions (Palmer, 1999; Wandell, Brewer, & Dougherty, 2005), it is not surprising that a myriad of visual function deficits have been found in patients with blast TBI across the literature.

Focusing on our novel finding of increased myopia in the blast mTBI+ group, clinical studies of TBI and visual acuity loss without direct orbital trauma suggest two primary mechanisms that may underly the observed changes in acuity. The first, indirect traumatic optic neuropathy, involves indirect damage to the optic nerve from blunt or blast forces associated with a TBI (Singman et al., 2016; Wang, Hamm, & Povlishock, 2011). One recent study used optical coherence tomography to assess retinal thickness in a group of veterans with a history of mTBI and persistent posttraumatic headaches and found evidence for thinning in the peripapillary retinal nerve fiber layer indicative of a mild optic neuropathy (J. W. Chan, Hills, Bakall, & Fernandez, 2019). While vision loss due to indirect traumatic optic neuropathy can be delayed from the time of injury (Atkins, Newman, & Biousse, 2008), there are two findings from the current study that suggest indirect traumatic optic neuropathy is unlikely to explain the current acuity findings. First, one would expect global reductions in acuity with this type of injury rather than the systematic shift toward myopia observed. Second, pinhole acuity measures would not have been normal if the acuity issues were primarily driven by damage to the optic nerve or retina. As pinhole acuity was 20/20 for all participants but one, and this participant showed only a mild acuity decrease at 20/25, it is more likely that the current findings are refractive in nature. An alternative theory is that differences in refractive error are driven by a mild form of posttraumatic pseudomyopia. Blur-driven accommodation is controlled by a network of cortical and subcortical regions including areas in occipital, cerebellar, and parietal regions, the superior colliculus, Edinger-Westphal nucleus and cranial nerve III (Green, Optom, Szymanowicz, Ludlam, & Neera Kapoor, 2010). It has been proposed that damage to these regions, and in particular the subcortical regions and cranial nerve III, can lead to accommodative excess, preventing accommodation from relaxing when viewing distant stimuli (London et al., 2003). Posttraumatic pseudomyopia has been documented in civilian patients with acquired brain injuries from neurological events (e.g., stroke) or TBI (e.g., car accidents) (R. P. Chan & Trobe, 2002; London et al., 2003), yet to our knowledge, no research has investigated the presence of posttraumatic pseudomyopia following combat-related TBI including blast mTBI. While one study found 19% of 161 head injury patients referred for clinical assessments due to persistent visual symptoms were diagnosed with pseudomyopia (Kowal, 1992), another study of 51 patients with TBI found only 4% were diagnosed with pseudomyopia (Ciuffreda et al., 2007). While the overall prevalence of posttraumatic pseudomyopia is unknown, most case reports of this disorder have included patients with moderate or severe types of acquired brain injury. However, two recent case reports have documented posttraumatic pseudomyopia following whiplash due to a car accident, suggesting that this syndrome can occur following milder cases of TBI (Hughes et al., 2017; Imburgia et al., 2017). Accommodative excess in posttraumatic pseudomyopia is associated with subjective myopic shifts in refractive error that do not persist under cycloplegia, and are not accompanied by miosis or strong convergence responses as seen in spasm of the near reflex (London et al., 2003). As no cycloplegic exams were completed in the current study, it is not possible to determine whether the myopic shifts observed in the blast mTBI+ group remain under cyloplegia, but we note that miosis was not overtly observed during clinical exams and esophorias in the distance position were both infrequent and equivalent across groups. A future area of research is therefore to include cycloplegic exams in the current battery of optometric assessments and determine whether repetitive mTBIs from blast may lead to mild forms of posttraumtic pseudomyopia.

Due to time limitations in the testing session, the present battery represents a subset of potential tests available to measure visual functioning. This subset of measures were chosen because they are well-established, follow established clinical guidelines proposed for examining visual functioning in patients with mTBI (Goodrich et al., 2013), and are readily available in most optometry clinics. However, additional measures have been proposed for objective testing of visual function in patients with mTBI, including electrophysiological assessments (e.g., visual-evoked potentials, electroretinography), pupillography, and computerized assessments of oculomotor function such as eye-movement assessments during reading or measuring peak velocity of vergence/accommodative movements

(Ciuffreda & Ludlam, 2011). Adding additional computerized measures of oculomotor function and integrating electrophysiological recordings into the current battery of tests is another area of future research that will help to validate the current findings across multiple measures of functioning and may help to elucidate the neurobiological basis of the deficits seen in the current study.

There are several limitations with the current study. First, the cross-sectional nature of the current study prevents studying how changes in acuity evolve over time. This is a limitation to the majority of studies looking at the relationship between TBI and visual function in humans and there is generally a need for more longitudinal assessments on the impact of mTBI on visual functioning to characterize the long-term impacts. Post-9/11 veterans are the youngest veteran cohort with a median age of 37 years (Vespa, 2020). Given the current high cost of caring for veterans within this cohort who have ocular trauma and/or visual dysfunction (Frick & Singman, 2019), evidence for accelerated aging processes associated with blast exposures (Trotter, Robinson, Milberg, McGlinchey, & Salat, 2015), and the potential interaction of these factors with normal aging processes across the visual system (Owsley, 2011), there is a compelling need for comprehensive longitudinal assessments of how visual functions may change over time in this population to aid in developing treatment options, reduce healthcare burden, and improve overall quality of life for these veterans. Second, Post-9/11 veterans are a highly polymorbid population and along with TBI, psychiatric and behavioral conditions such as posttraumatic stress disorder, depression, sleep disorders, chronic pain, and substance use disorders can all contribute to deficits in overall functioning (Amick et al., 2018; Fortenbaugh et al., 2020; Lippa et al., 2015) with PTSD being the most prominent contributor to functional disabilities (Fortenbaugh et al., 2020). As previous research has shown that comorbid PTSD and mTBI is associated with higher subjective reports of visual symptoms than mTBI alone (Goodrich et al., 2014), we completed several control analyses demonstrating that current PTSD diagnosis or PTSD symptom severity scores are unable to account for the deficits in visual functioning observed in the blast mTBI+ group. However, given the smaller sample size in the current study relative to the sample size in Goodrich et al., 2014, we were unable to define groups to directly compare those with blast mTBI+ and PTSD to those with just blast mTBI+. Additional work with large enough sample sizes to allow for these types of comparisons as well as consideration of other common comorbidities in this population such as depression is warranted given the heterogenous nature of this population.

Beyond controlling for common comorbidities, larger scale replications would allow for a more precise delineation of what impacts of mTBIs are most strongly associated with different etiologies (e.g., blast vs. blunt force trauma) and the impact of multiple mTBIs over months, years, or decades, on visual functioning. As seen in Table 1, blast mTBI events were highly variable across participants. The most common cause of blast mTBI was improvised explosive devices (IED) and 67% of the events occurred when participants were in vehicles. However, even for IED blast exposures while participants were in vehicles, both the direction and distance of the blast varied across participants. Both animal models (Allen et al., 2018) and biomechanical simulation studies (Notghi et al., 2017) have demonstrated that the impact of blast pressure waves on the visual system depends on multiple factors including the distance and direction of the blast wave relative to an individual and can be moderated by various types of protective gear worn at the time. While Table 1 presents information regarding the events surrounding blast mTBIs at a descriptive level, inclusion of details such as this in larger studies may help to determine whether certain environmental conditions beyond just the magnitude of the detonation are predictive of specific types of visual impairments, whether lateralized deficits are seen when explosions occur primarily to the left or right side, or if other environmental details can provide clinically relevant information for diagnosing and monitoring visual function over time in patients with a history of blast mTBI.

Finally, the present study is limited in terms of the gender distribution of the participants. Indeed, the blast mTBI+ group had no female participants. This is not necessarily unexpected in a random sampling of Post-9/11 Veterans. All OEF/OIF veterans entering the VA have been screened for potential TBI since 2007. Only 13% of that population are female, and it is unreported in a public platform how many of those go on to screen positive (Amara et al., 2014), A separate study has reported that only 2% of service members critically injured in theater between 2002 and 2011 were female (Chin & Zeber, 2020). While female veterans are less likely to experience mTBIs during deployment, and in particular, less likely to experience a mTBI due to blast exposure, women are and have been deployed to forward positions in the current conflicts and experienced TBIs of all severity levels due to blast exposures. There is a growing recognition that women are under-represented in studies of combat-related TBIs in this veteran population and additional work is needed to understand whether gender differences exist in regards to long term sequalae related to TBI (Cogan, McCaughey, & Scholten, 2020).

In conclusion, the results of the present study show evidence for a novel indicator of blast mTBI on visual function, namely, increased myopia. While additional work is needed to understand the underlying cause of this difference in acuity, the additional finding of chronic convergence insufficiency years post-injury suggests that damage to subcortical structures that underly oculomotor functions may play a role. As most studies of visual function and TBI to date have only considered best-corrected acuity measures in their analyses, the present results point to a potential novel biomarker of blast mTBI that deserves further exploration and may help to account for some of the many visual symptoms reported by veterans with a history of mTBI.

Acknowledgments

This research was supported by the Department of Veterans Affairs (VA) through the Translational Research Center for TBI and Stress Disorders (TRACTS), a VA Rehabilitation Research & Development Traumatic Brain Injury National Research Center (B3001-C), a Career Development Award from the Department of Veterans Affairs Rehabilitation Research and Development (1IK2RX002268) to F.C.F, a VA Clinical Science Research & Development Merit Review (CX01327) to R.E.M, and a National Institute of Health NCCIH grant (R21 AT009430-01) to W.P.M. The contents within do not represent the views of the Department of Veterans Affairs or the United States government.

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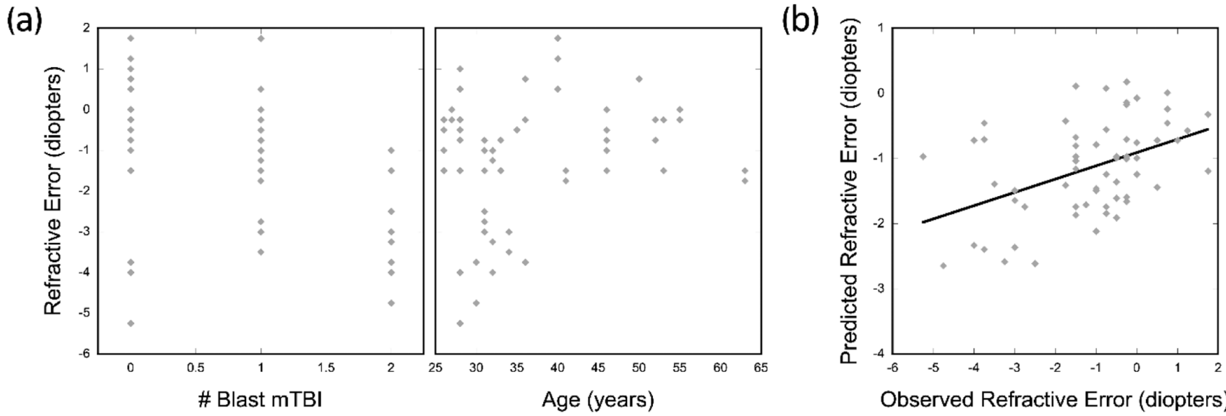

Figure 1.

(a) Two scatterplots showing refractive error scores as a function the number of blast mTBIs and the age of participants in years. (b) Scatterplot showing the association between the observed and predicted refractive error from the mixed-effects linear regression model using the number of blast mTBIs and age as predictors (see Table 4). The sold line shows the best fitting-regression line. Diamonds show individual data from each of the 62 eyes measured.

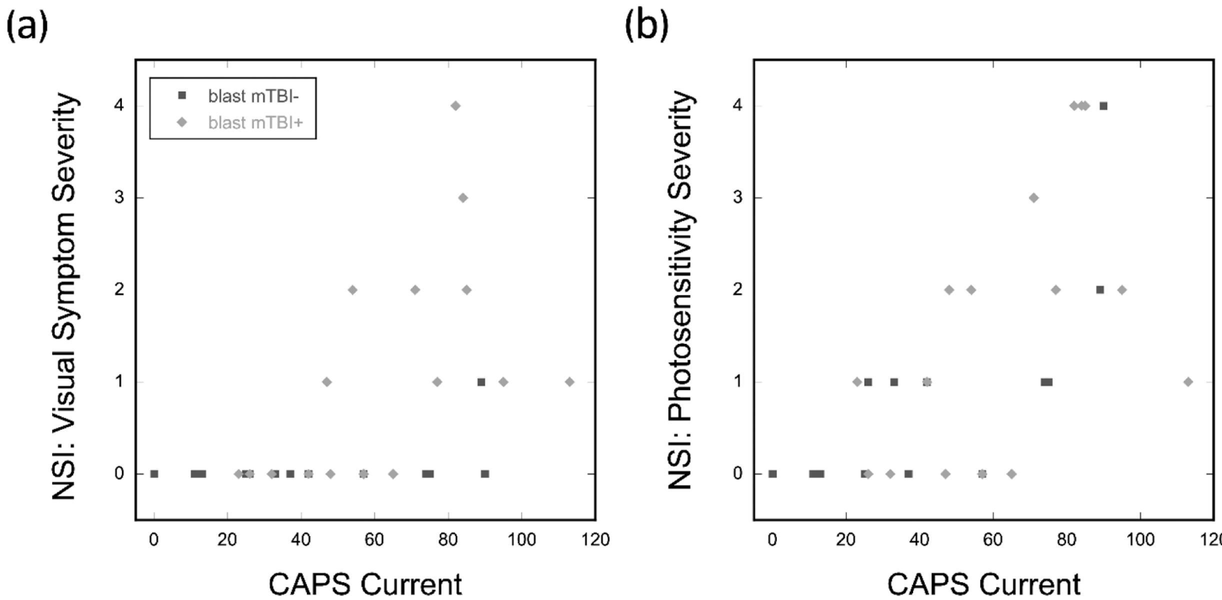

Figure 2.
Scatterplot showing the relationship between PTSD symptom severity measured using the CAPS current score and self-reported visual symptoms from the Neurobehavioral Symptom Inventory (NSI) including (a) NSI severity ratings of visual problems including blurry vision and trouble seeing and (b) NSI severity ratings of photosensitivity. Data from the 17 participants with a history of blast mTBI are shown as squares while data from the 14 participants without a history of blast mTBI are shown as diamonds.

Table 1.

Summary table of events surrounding blast-related mTBI for the seventeen participants in the bmTBI+ group. Multiple events are ordered based on severity, not chronology. Table includes participant's self-report of the source of the blast exposure, the approximate distance they were located from the detonation, the setting that they were located, and the direction that the blast wave approached them from.

	1st Blast mTBI Event			2nd Blast mTBI Event		
ID	Source of Blast	Estimated Distance (m)	Setting (Direction)	Source of Blast	Estimated Distance (m)	Setting (Direction)
1	Rocket	50	Open (Left)			
2	IED	50–75	Vehicle (Behind/Under)			
3	IED	10	Vehicle (Front)	Mortar	11–25	Building (Behind)
4	IED	10	Vehicle (Right)			
5	IED	0	Vehicle (Under)			
6	IED	4	Vehicle (Right)			
7	Land mine	0	Vehicle (Front/Right)			
8	Mortar	--	Open (Front)			
9	Training grenades	<2	Open (Left)			
10	Land mine	3	Combined (Right)	IED	2	Vehicle (Right)
11	IED	1	Vehicle (Front/Left)	IED	1	Vehicle (Front/Right)
12	IED	11–25	Combined (Front)			
13	Land mine	<10	Vehicle (Front/Left)			
14	IED	10	Vehicle (Front/Left)			
15	Mortar	10	Building (Front/Left)			
16	IED	15–20	Vehicle (Front/Right)	IED	0	Vehicle (Under)
17	Mortar	25	Open (Behind)			

* IED = improvised explosive devise; Vehicle/Building/Open = individual was inside an enclosed vehicle, in a building, or outside in open space at time of explosion; Combined = blast either threw individual out of vehicle or occurred while vehicle doors/turret opened; "--" = participant unable to provide detail due to posttraumatic amnesia

Table 2.

Participant demographics, TBI history, and current PTSD status for the total sample and by blast mTBI group. Gender and PTSD diagnosis show frequency and % of sample. All other variables show the mean ± 1 S.D.

	Total (N=31)	**Blast mTBI− (N=14)**	**Blast mTBI+ (N=17)**	**Statistical Test**
Age (years)	36.87±9.91	37.14±10.90	36.65±9.35	$t(29) = 0.14$, $p = 0.893$
Gender (male)[a]	29 (93.5%)	12 (85.7%)	17 (100%)	$p = 0.196$
# Non-Blast Military mTBI	0.42±0.72 (range: 0–3)	0.29±0.61 (range: 0–2)	0.53±0.80 (range: 0–3)	$t(29) = 0.94$, $p = 0.357$
# Lifetime mTBI	1.87±1.54 (range: 0–6)	1.07±1.73 (range: 0–6)	2.53±1.01 (range: 1–5)	$\mathbf{t(29) = 2.93}$, $\mathbf{p = 0.007}$
# Close Blast Exposure	2.58±5.85 (range: 0–30)	0.43±1.34 (range: 0–5)	4.35±7.44 (range: 0–30)	$t(29) = 1.94$, $p = 0.062$ OR = 2.44
PTSD	17 (54.8%)	6 (42.9%)	11(64.7%)	(0.57–10.45), $p = 0.289$
CAPS Current	52.12±29.21 (range: 0–100)	41.79±30.27 (range: 0–90)	60.76±26.1 (range: 20–100)	$t(29) = 1.87$, $p = 0.071$
# Deployments	1.77±1.41	1.57±1.65	1.94±1.20	$t(29) = 0.72$, $p = 0.476$
Deployment Duration (months)	15.84±11.40	11.79±9.49	19.18±12.01	$t(29) = 1.87$, $p = 0.072$
Combat Experience[b]	14.97±10.20	8.43±5.74	21.07±9.73	$\mathbf{t(27) = 4.22}$ $\mathbf{p = 0.001}$
NSI: Total	23.26±16.52	20.57±18.19	25.47±15.21	$t(29) = 0.82$, $p = 0.420$
NSI: Visual Issues	0.58±1.03	0.07±0.28	1.00±1.22	$\mathbf{t(29)=2.78}$, $\mathbf{p = 0.010}$
NSI: Photosentivity	1.19±1.38	0.79±1.12	1.53±1.50	$t(29)=1.53$, $p = 0.137$

Note:

(a) Odds ratio could not be calculated.

(b) Combat Experience scores were not available for two participants in the blast mTBI+ group.

PTSD = current diagnosis of Posttraumatic Stress Disorder; CAPS Current = index of current PTSD symptom severity from Clinician Adminstered PTSD Scale; Combat Experience score derived from Deployment Risk and Resilience Inventory; NSI = Neurbehavioral Symptom Inventory

Table 3.

Group differences in visual function measures across participants with and without a history of blast-induced mTBI. Myopic classification shows the number of eyes with refractive error ≤ −0.5 Diopters. Frequencies for eye movement, ocular alignment, accommodation and convergence tests show the number of participants with abnormal age-adjusted values. All other variables show the mean ± 1 S.D. Test statistics show t-test or with odds ratio (OR) and 95% confidence interval.

Domain	Test	Blast mTBI−	Blast mTBI+	Statistical Test
Resolving Power[a]	Near Acuity	26.36±9.42	25.47±18.06	$t(29) = 0.22$, $p = 0.828$
	Distance Acuity	20.36±1.31	25.29±9.21	**$t(29) = -2.18$, $p = 0.038$**
	Refractive Error (diopters)	−0.71±1.69	−1.49±1.43	$t(29) = 1.41$, $p = 0.169$
	Myopic Classification	12 (42.9%)	28 (82.4%)	**OR = 6.29 (1.97–20.12), $p = 0.002$**
Eye Movements	Fixation[b]	0 (0.0%)	1 (5.9%)	$p = 1.0$
	Pursuit	3 (21.4%)	5 (29.4%)	OR = 1.53 (0.29–7.95), $p = 0.698$
	Saccades	2 (14.3%)	6 (35.3%)	OR = 3.27 (0.54–19.75), $p = 0.240$
Ocular Alignment	Near Cover Test	4 (28.6%)	6 (35.3%)	OR = 1.36 (0.30–6.28), $p = 1.0$
	Far Cover Test	1 (7.1%)	1 (5.9%)	OR = 0.81 (0.05–14.28), $p = 1.0$
Accommodation	Accommodative Amplitude	7 (50.0%)	3 (17.6%)	OR = 0.21 (0.04–1.09), $p = 0.121$
Convergence	Positive Fusional Vergence – Break (Δ diopters)	30.36±8.66	26.18±12.04	$t(29) = 1.09$, $p = 0.286$
	Positive Fusional Vergence – Recovery (Δ diopters)	22.57±6.93	20.47±9.23	$t(29) = 0.70$, $p = 0.487$
	Near Point Convergence – Break	3 (21.4%)	12 (70.6%)	**OR = 8.80 (1.69–45.76), $p = 0.011$**
	Near Point Convergence – Recovery	3 (21.4%)	12 (70.6%)	**OR = 8.80 (1.69–45.76), $p = 0.011$**

Note:

a) Data for the resolving power assessments was measured monocularly and combined across both eyes using a mixed-effects model for acuity and refractive error scores and a generalized linear model for myopic classification. For all models, Eye (left/right) was included as a repeated measure. Significance for the blast mTBI factor is reported in the table. Near and distance acuity were scored as the denominator of the Snellen fraction with base 20 feet. Refractive error is measured in diopters.

b) Odds ratio could not be calculated. Eye movement, ocular alignment, accommodation, and near point convergence measures show the number of participants with abnormal age-adjusted values. Positive fusional vergence scores show the mean break and recovery points in prism diopters.

Table 4.

Linear mixed-effects models when Near Acuity, Distance Acuity, or Refractive Error were used as the dependent variable. For each dependent variable, three measures were used to define the independent variable # mTBI: the number of blast-related mTBI during military service (top), the number of non-blast mTBI during military service (middle) and the total number of lifetime non-blast mTBI including pre-deployment, during deployment, and after deployment (bottom).

	Number of Blast Military mTBI								
	Near Acuity			**Distance Acuity**			**Refractive Error**		
	B	**95% CI**	***p***	**B**	**95% CI**	***p***	**B**	**95% CI**	***p***
Intercept	−5.887	−118.59 to 106.83	.917	−67.47	−104.18 to −30.75	.001	−1.903	−4.058 to 0.252	.081
Age	0.584	0.216 to 0.957	**.003**	0.074	−0.133 to 0.280	.471	0.033	−0.021 to 0.087	.217
Eye	3.668	−3.591 to 10.927	.310	0.934	−0.856 to 2.724	.295	0.250	−0.016 to 0.516	.064
# mTBI	−1.184	−6.371 to 4.004	.644	4.105	1.192 to 7.018	**.007**	−0.872	−1.634 to −0.109	**.027**
Pinhole	0.458	−5.179 to 6.095	.871	4.212	2.402 to 6.022	**<.001**			
	Number of Non-Blast Military mTBI								
	Near Acuity			**Distance Acuity**			**Refractive Error**		
	B	**95% CI**	***p***	**B**	**95% CI**	***p***	**B**	**95% CI**	***p***
Intercept	−10.653	−122.50 to 101.20	.849	−64.09	−101.64 to −25.55	.001	−2.859	−5.138 to −0.580	.016
Age	0.570	0.209 to 0.930	**.003**	0.066	−0.166 to 0.298	.566	0.039	−0.019 to 0.097	.180
Eye	3.622	−3.635 to 10.879	.316	0.941	−0.850 to 2.732	.291	0.250	−0.016 to 0.516	.064
# mTBI	−2.892	−7.873 to 2.089	.244	1.468	−1.729 to 4.664	.355	0.357	−0.446 to 1.160	.370
Pinhole	0.743	−4.858 to 6.345	.791	4.166	2.320 to 6.012	**<.001**			
	Number of Non-Blast Lifetime mTBI								
	Near Acuity			**Distance Acuity**			**Refractive Error**		
	B	**95% CI**	***p***	**B**	**95% CI**	***p***	**B**	**95% CI**	***p***
Intercept	−4.158	−116.52 to 108.91	.946	−64.52	−102.16 to −26.87	.001	−2.750	−5.163 to −0.336	.027
Age	0.602	0.235 to 0.984	**.002**	0.068	−0.169 to 0.304	.562	0.038	−0.021 to 0.098	.200
Eye	3.700	−3.556 to 10.967	.306	0.938	−0.853 to 2.729	.293	0.250	−0.016 to 0.516	.064
# mTBI	0.593	−2.136 to 3.322	.660	0.503	−1.230 to 2.236	.557	0.061	−0.376 to 0.498	.517
Pinhole	0.262	−5.387 to 5.911	.926	4.184	2.336 to 6.032	**<.001**			

Note: Age = Participant age was measured in years; Eye = right/left eye dichotomous variable with left as reference category; Pinhole = denominator of the Snellen fraction with base 20 feet from the pinhole acuity test. Near/Distance acuity dependent variables were defined as the denominator of the Snellen fraction with base 20 feet. Refractive error dependent variable was measured in diopters.

Table 5.

Results of the cross-validation linear regression analyses. Standardized beta weights were averaged across the 62 folds. Spearman rho correlations were calculated measuring the association between observed and predicted acuity scores. The same variables from Table 4 were used in these analyses.

		Average Standardized Beta (β)			
Resolution	**mTBI Measure**	**# mTBI**	**Age**	**Pinhole**	**Statistic**
Near Acuity	Military Blast	−0.057	0.390	0.036	**ρ = 0.53, *p* < 0.001**
	Military Non-Blast	−0.143	0.380	0.047	**ρ = 0.58, *p* < 0.001**
	Lifetime Non-Blast	0.064	0.407	0.026	**ρ = 0.50, *p* < 0.001**
Distance Acuity	Military Blast	0.388	0.095	0.443	**ρ = 0.31, *p* = 0.013**
	Military Non-Blast	0.134	0.083	0.453	ρ = −0.05, *p* = 0.673
	Lifetime Non-Blast	0.105	0.093	0.458	ρ = −0.11, *p* = 0.411
Refractive Error	Military Blast	−0.382	0.206		**ρ = 0.323, *p* = 0.010**
	Military Non-Blast	0.161	0.243		ρ = 0.086, *p* = 0.504
	Lifetime Non-Blast	0.119	0.253		ρ = 0.095, *p* = 0.464