MILITARY MEDICINE, 183, 11/12:e564, 2018

Visual Dysfunction and Associated Co-morbidities as Predictors of Mild Traumatic Brain Injury Seen Among Veterans in Non-VA Facilities: Implications for Clinical Practice

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ABSTRACT Introduction: Traumatic brain injury (TBI) and post-traumatic stress disorder are considered the signature injuries of the Iraq and Afghanistan conflicts. With the extensive use of improvised explosive devices by the enemy, the concussive effects from blast have a greater potential to cause mild TBI (mTBI) in military Service Members. These mTBI can be associated with other physical and psychological health problems, including mTBI-induced visual processing and eye movement dysfunctions. Our study assessed if any visual dysfunctions existed in those surveyed in non-Veterans Administration (VA) facilities who had suffered mTBI (concussive effect), in addition to the presence of concussion-related co-morbidities. Materials and Methods: As part of a larger study involving veterans from different service eras, we surveyed 235 Veterans who had served during the Iraq and/or Afghanistan conflict era. Data for the study were collected using diagnostic telephone interviews of these veterans who were outpatients of the Geisinger Health System. We assess visual dysfunction in this sample and compare visual dysfunctions of those who had suffered a mTBI (concussive effect), as well as co-morbidities, with those in the cohort who had not suffered concussion effects. Results: Of those veterans who experienced visual dysfunctions, our results reflected that the visual symptoms were significant for concussion with the subjects surveyed, even though all had experienced a mTBI event greater than five years ago. Although we did find an association with concussion and visual symptoms, the association for concussion was strongest with the finding of greater than or equal to three current TBI symptoms, therefore we found this to be the best predictor of previous concussion among the veterans. Conclusions: Veterans from the Iraq/Afghanistan era who had suffered concussive blast effects (mTBI) can present with covert visual dysfunction as well as additional physical and psychological health problems. The primary eye care providers, especially those in a non-military/VA facility, who encounter these veterans need to be aware of the predictors of mTBI, with the aim of uncovering visual dysfunctions and other associated co-morbidities.

INTRODUCTION

Traumatic brain injury (TBI) is a significant public health issue in both the civilian population and the U.S. military forces,[1] including Warfighters serving in a Reserve or National Guard unit. As these Service Members return to their civilian lives, the concern exists that they do not have the same level of visibility for their injuries as those who are treated in a military treatment facility or Veterans Administration (VA) clinical facility.

TBI is delineated as a brain trauma resulting from an external force and/or acceleration–deceleration mechanism, including blasts, falls, direct impacts, and motor vehicle accidents, often with an alteration in mental status. Warfighters who have sustained a mild TBI (mTBI) and associated co-morbid somatic, cognitive, and affective symptoms, including post-traumatic stress disorder (PTSD), can be more difficult to diagnose than those who have suffered moderate to severe TBI.[2] Therefore, the proper identification of milder forms of TBI is important when providing optimal care for this population.

Over the course of time, the conflicts in Iraq (Operation Iraqi Freedom; Operation New Dawn), Afghanistan (Operation Enduring Freedom), and the joint campaign in Iraq and in Syria (Operation Inherent Resolve) have accounted for a significant increase in the occurrence of concussive TBI (cTBI) and mTBI among military personnel as a result of contact with enemy forces or weapon systems – mortars, improvised explosive devices (IEDs), rocket-propelled grenades – and from head impacts from accidents caused by enemy action, equipment failure, or other factors.

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doi: 10.1093/milmed/usy102

The Department of Veterans Affairs/Department of Defense define TBI as "a traumatically induced structural injury and/or physiological disruption of brain function as a result of an external force that is indicated by new onset or worsening of at least one of the following clinical signs, immediately following the event—any period of loss of or a decreased level of consciousness (LOC), any loss of memory for events immediately before or after the injury (post-traumatic amnesia [PTA]), any alteration in mental state at the time of the injury (confusion, disorientation, slowed thinking, etc.), neurological deficits (weakness, loss of balance, change in vision, praxis, paresis/plegia, sensory loss, aphasia, etc.) that may or may not be transient, and/or intracranial lesion".[3]

The Department of Defense reported 370,688 cases of clinically confirmed TBI from 2000 to the second quarter of 2017, with mTBI accounting for 82.3% of all cases.[4] Similarly, the Centers for Disease Control and Prevention reported that TBI affects approximately 1.7 million people in the USA annually. The total combined rates of TBI-related hospitalizations, emergency department visits, and deaths climbed from a rate of 521.0 per 100,000 in 2001 to a rate of 823.7 per 100,000 in 2010, with mTBI accounting for at least 75% of all TBIs in the USA.[5]

Warfighters with mTBI are often identified only when overt head injuries are present, leaving the more subtle mTBI cases to go undiagnosed by the medical community, primarily due to the lack of objective assessment tools. Valid and objective biomarkers of acute mTBI are of particular importance in forward deployed situations for military clinicians to make accurate and immediate determination of return to duty status or evacuation for further evaluation. As such, mTBI continues to be a diagnostic challenge for the medical community primarily due to the lack of objective assessment tools.[6] Health care providers have also noted issues with diagnosing self-reported brain injury/concussion symptoms.[7]

Recent studies have examined objective assessments and subjective evaluations of visual functions as potential biomarkers for mTBI. A 2010 military mTBI diagnostics workshop highlighted the importance of finding biomarkers or diagnostic tests to expedite the diagnosis of warfighters suspected of having a concussion/mTBI.[8] Undiagnosed mTBI/concussions can jeopardize veterans' health, and expose injured warfighters to the potential effects of further concussions/brain injuries which have been shown to lead to further detrimental sequelae.[9]

Mild traumatic brain injuries are linked to visual impairment, even beyond the acute stage of injury, with the potential for long-term chronic effects to manifest. One of the first clinical studies which compared visual dysfunction in soldiers exposed to blast-related mTBI to deployed controls without TBI, found significant early visual dysfunction in these soldiers. The assessment was completed in the short term (15–45 d) after the blast-related mTBI occurred. The most common reported symptoms in this study were binocular vision problems, eye fatigue, and photophobia, although there were minimal or no reductions in visual acuity.[10] Visual symptoms have been found to persist in patients up to 2 yr after combat-related TBI.[11,12] In a retrospective study of routine eye exams in 31 veterans with blast-related mTBI, significant visual dysfunction was found in 68% of patients almost 6 yr after injury.[13]

Post-deployment members of the National Guard, Reserve and Individual Mobilization Augmentees (IMAs) may choose to not seek care in a VA clinical facility, due to employer provided health insurance, geographic, and other considerations. Injured Warfighters can face visual, mental and physical challenges after deployment, compounded if exposed to blast trauma, and these infirmities may be unreported by the patient. During a routine eye examination, which can also serve as a potential screening for mTBI, subtle or subclinical visual dysfunctions, as a consequence of mTBI, may go unrecognized.

In an effort to further assess this group in question, the present study was designed to assess the prevalence of visual symptoms, as well as co-morbidities, in Veterans of the Iraq and Afghanistan conflicts who suffered mTBI and were treated outside of either a VA clinical facility or a military treatment facility. One goal of our study was to see if a predictive model could be developed that could be useful in a clinical practice setting.

METHODS

As part of a larger study involving veterans from several service eras, we surveyed 235 veterans by telephone who had served during the Iraq and/or Afghanistan conflict.[14] As with the baseline survey, data for the TBI study were collected using diagnostic telephone interviews of these veterans who were outpatients of the Geisinger Clinic, a large, integrated health care organization in Pennsylvania, and one of largest integrated health services organizations in the USA involved in public health research.[15] Outcome measures were assessed for those who had a history of service related concussion, compared to veterans who did not using the 3-Question TBI Screen from Schwab et al.[16] Additional questions related to when they experienced the concussion and whether they ever received a deployment-related medical diagnosis of TBI or not (Appendix 1). As a previous study found five significant factors associated with PTSD, depression, and mental health service use among a group of veterans, (low self-esteem of the veteran, veteran's use of alcohol/drugs to cope, veteran's history of childhood adversity, high combat exposure, and low psychological resilience) our survey data were also collected related to PTSD, military history, combat exposure, mental health, perceived health status, sleep problems, and on other measures during the baseline survey.[17] The TBI interview also included 13 specific vision related questions (Appendix 2) based on The Brain Injury Vision Symptom Survey (BIVSS) Questionnaire, a 28-itemscaled survey designed to query vision behaviors related to: clarity, comfort, diplopia, depth perception, dry-eye, peripheral vision, and reading with individuals who have suffered mild-to-moderate brain injury.[18]

Statistical analyses include descriptive statistics and analyses assessing the association between TBI and potential risk/

protective factors. For initial multivariable analyses, we used logistic regression, whereby key risk/protective factors (e.g., combat exposure, multiple deployments, etc.) were used to estimate the likelihood (i.e., odds ratios, ORs) for mTBI controlling for age, gender, marital status, and other factors that might confound these associations by including these variables in the analyses. We also present descriptive statistics related to vison and concussion symptom scales we used in our study. All the variables shown in the final multivariate models (Tables II–IV) represent the final analysis results after non-significant variables were removed. Analyses were conducted using Stata, version 13.1 and SPSS version 20 software. The Geisinger Health System's, as well as the DoD's Institutional Review Boards (Geisinger IRB #2015-0441; DoD IRB #A-18989) approved the study protocol and all participants provided verbal informed consent.

RESULTS

The 13-item vision scale we used included 5-point scale items (rated "never" to "always"), which resulted in an average vision score of 23.5 (SD = 9.4) and a Cronbach's alpha = 0.85 for the Veterans. The Veterans also reported current symptoms they were experiencing related to their concussion, including headaches, dizziness, and memory problems. The presence of memory problems was minimally screened for in the interview (Appendix A1, TB3c.) to alert for effects on the questionnaire, but no specifically designed neuropsychological tests were administered. The mean concussion symptom count for Veterans was 2.3 (SD = 1.84). Since a goal of our study was to develop a predictive model useful in clinical practice, we used receiver operating curve (ROC) analyses to determine the optimal cut-off point for the vision and concussion symptom scales.[19] Based on these analyses, the optimal cut-point for the vision scale was 24 or higher (ROC area = 0.71); the optimal cut-point for the concussion symptom scale was 3 or higher (ROC area = 0.80). We used these cut-points in our statistical analyses discussed below.

Table IA (Appendix 3) presents the demographic characteristics of the study sample. As can be seen, the mean age of the veterans is 42 (SD = 9.2) and over 58% are less than 45 yr old. The data also suggest that 87.2% of the participants were males, 94.0% were of white race, 84.6% were enlisted military personnel, 75.6% were National Guard/Reserve service members, 39.7% were college graduates, 73.5% were married, and 33.8% had a yearly household income over $100,000. Furthermore, it is noteworthy to add that 54.3% of participants reported multiple warzone tours, and 30.8% had a history of high combat exposure. In addition, 30.6% (95% CI = 25.0–36.9) screened positive for TBI, 10.2% (95% CI = 6.9–14.8) reported a TBI diagnosis during deployment, and 14.9% (95% CI = 10.9–20.1) reported sustaining a TBI during deployment, but that this was not diagnosed (Table IB (Appendix 3). In terms of present TBI symptoms reported, 31.9% (95% CI = 26.2–38.2) of veterans in this study reported presently having greater than or equal to 3 TBI symptoms. Moreover, the prevalence of PTSD in this cohort within the past year was 11.1% (95% CI = 7.7–15.9). Additionally, the prevalence of current depression disorder among the veterans was 14.1% (95% CI = 10.2–19.2) (Table IB (Appendix 3).

Table I presents the associations between sample characteristics and concussion screen results. As seen, the following study variables were found to have a significant association with a positive concussion screen: male sex ($p = 0.008$), difficulty falling asleep during the past 12 mo ($p = 0.040$), multiple warzone tours ($p = 0.005$), high combat exposure ($p < 0.001$), a high BSI-Global Severity Index ($p < 0.001$), multiple current TBI symptoms reported ($p < 0.001$), higher vision dysfunction ($p < 0.001$), current depressive disorder ($p = 0.001$), met criteria for PTSD in the past year ($p = 0.001$), and fair or poor self-rated health ($p < 0.001$).

Following this, multivariate logistic regression analyses were computed to determine the predictive validity of several variables regarding history of concussion during deployment ($n = 72$). Based on the bivariate analyses, the variables investigated were multiple combat tours, high combat exposure, vision score greater than 24, and the presence of three or more current TBI symptoms. Table II lists the results of multivariate analyses conducted for a positive concussion screen. In particular, reporting three or more current TBI symptoms (OR = 5.51, $p < 0.001$), high combat exposure (OR = 2.39, $p = 0.014$), and a vision score greater than 24 (OR = 2.15, $p = 0.025$) all demonstrated significant relationships with deployment concussions. Notwithstanding these results, multiple tours was not statistically associated with concussion in this present veteran sample, when all the variables were included (OR = 1.74, $p = 0.113$).

Table III depicts the findings of the multivariate prediction analysis that evaluated the variables described in predicting having a concussion diagnosis during deployment ($n = 24$). The results of this revealed slightly different predicative findings. Consistent with the first model, reporting of greater than or equal to three current TBI symptoms was found to be positively associated with reporting a concussion diagnosis (OR = 4.93, $p = 0.006$). In line with this, high combat exposure demonstrated another significant variable in predicting concussion diagnosis (OR = 4.05, $p = 0.010$). Multiple combat tours also exhibited analogous results relative to the previous model, as it was found to be not significantly associated with concussion diagnosis (OR = 2.37, $p = 0.128$). Having a concussion diagnosis was found to be unrelated to vision scores greater than 24 within this cohort (OR = 1.87, $p = 0.226$), which also varied from its previous association with concussion (Table II).

To assess which variables were sensitive in predicting the presence of a concussion with no diagnosis reported ($n = 35$), a subsequent multivariate analysis was conducted using the same variables. Table IV displays the results of this predictive model, which evidenced some differences from previous analyses. The only variable found to be significant for predicting concussion with no diagnosis reported was having

TABLE I. Sample Characteristics Related to Concussion Symptoms (N = 234–235)

Sample Characteristics	Concussion Positive N (%)	Not Concussion Positive N (%)	Odds Ratio (95% CI)	X^2 (p-Value)
Age				
18–44	43 (59.7)	94 (58.0)	0.93 (0.53–1.64)	0.059 (0.808)
45+	29 (40.3)	68 (42.0)		
Total	72 (100)	162 (100)		
Sex				
Male	69 (95.8)	135 (83.3)	4.60 (1.35–15.7)	6.968 (0.008)
Female	3 (4.2)	27 (16.7)		
Total	72 (100)	162 (100)		
Race				
Non-White	3 (4.2)	11 (6.8)	1.68 (0.45–6.20)	0.610 (0.435)
White	69 (95.8)	151 (93.2)		
Total	72 (100)	162 (100)		
Education				
Non-college graduate	44 (61.1)	97 (59.9)	0.95 (0.54–1.68)	0.032 (0.859)
College graduate	28 (39.9)	65 (40.1)		
Total	72 (100)	162 (100)		
Difficulty falling asleep past 12 mo				
No	30 (41.7)	91 (56.2)	1.79 (1.02–3.15)	4.201 (0.040)
Yes	42 (58.3)	71 (43.8)		
Total	72 (100)	162 (100)		
Multiple Warzone Tours				
No	23 (31.9)	84 (51.9)	2.29 (1.28–4.11)	7.960 (0.005)
Yes	49 (68.1)	78 (48.1)		
Total	72 (100)	162 (100)		
High combat exposure				
No	33 (45.8)	129 (79.6)	4.26 (2.53–8.43)	26.727 (<0.001)
Yes	39 (54.2)	33 (20.4)		
Total	72 (100)	162 (100)		
BSI-Global Severity Index				
Not High	47 (65.3)	145 (90.1)	4.82 (2.37–9.79)	21.076 (<0.001)
High	25 (34.7)	16 (9.9)		
Total	72 (100)	162 (100)		
Multiple current TBI symptoms reported (≥3)				
Less than 3	25 (34.7)	135 (82.8)	9.06 (4.81–17.08)	53.173 (<0.001)
3 or more	47 (65.3)	28 (17.2)		
Total	72 (100)	163 (100)		
High vision dysfunction symptom score				
Less than 24	29 (40.3)	112 (68.7)	3.26 (1.83–5.79)	16.823 (<0.001)
24 or higher	43 (59.7)	51 (31.3)		
Total	72 (100)	163 (100)		
Current depression disorder				
No	54 (75.0)	147 (90.7)	3.27 (1.54–6.94)	10.195 (0.001)
Yes	18 (25.0)	15 (9.3)		
Total	72 (100)	162 (100)		
Met criteria for PTSD with impairment past year				
No	53 (73.6)	147 (90.7)	3.51 (1.67–7.41)	11.777 (0.001)
Yes	19 (26.4)	15 (9.3)		
Total	72 (100)	162 (100)		
Self-rated health fair/poor				
No	39 (54.2)	127 (78.4)	3.07 (1.69–5.57)	14.194 (<0.001)
Yes	33 (45.8)	35 (21.6)		
Total	72 (100)	162 (100)		

greater than or equal to three current TBI symptoms (OR = 3.94, p = 0.002). Across all three multivariate models, greater than or equal to three current TBI symptoms was found associated with predicting concussion in an array of diagnostic presentations. As such, this variable was the best predictor of concussion among this sample of veterans. Despite prior relationships with concussion prediction, high combat exposure was not associated with having a concussion with no diagnosis reported (OR = 2.12, p = 0.082). Multiple combat tours were also not associated with predicting concussion with no diagnosis as well (OR = 0.88, p = 0.770). In addition, having a vision score greater than 24 was also not significantly associated to concussion with no diagnosis (OR = 2.14, p = 0.070).

TABLE II. Multivariate Logistic Regression Predicting Positive Concussion Screen ($n = 72$)[a]

Variables	B	SE	Wald Statistic	p-Value	Odds Ratio (95% CI)
Multiple Combat Tours	0.552	0.349	2.506	0.113	1.74 (0.877–3.443)
High combat exposure	0.872	0.355	6.028	0.014	2.39 (1.192–4.798)
Vision score >24	0.763	0.341	4.999	0.025	2.15 (1.099–4.188)
Current TBI symptoms ≥3	1.706	0.349	23.890	<0.001	5.51 (2.778–10.908)
Constant	−2.458	0.352	48.725	<0.001	—

[a]$N = 235$.

TABLE III. Multivariate Logistic Regression Predicting Concussion Diagnosis ($n = 24$)[a]

Variables	B	SE	Wald Statistic	p-Value	Odds Ratio (95% CI)
Multiple Combat Tours	0.864	0.568	2.312	0.128	2.37 (0.779–7.232)
High combat exposure	1.398	0.541	6.680	0.010	4.05 (1.402–11.692)
Vision score >24	0.627	0.518	1.467	0.226	1.87 (0.679–5.168)
Current TBI symptoms ≥3	1.596	0.579	7.593	0.006	4.93 (1.585–15.339)
Constant	−4.630	0.692	44.814	<0.001	—

[a]$N = 235$.

TABLE IV. Multivariate Logistic Regression Predicting Concussion with No Diagnosis ($n = 35$)[a]

Variables	B	SE	Wald Statistic	p-Value	Odds Ratio (95% CI)
Multiple Combat Tours	−0.123	0.419	0.086	0.770	0.88 (0.389–2.010)
High combat exposure	0.750	0.431	3.028	0.082	2.12 (0.910–4.928)
Vision score >24	0.760	0.420	3.282	0.070	2.14 (0.940–4.869)
Current TBI symptoms ≥3	1.382	0.446	9.615	0.002	3.94 (1.663–9.541)
Constant	−3.001	0.429	48.838	<0.001	—

[a]$N = 235$.

DISCUSSION

TBI and PTSD are understood as the signature injuries of the Iraq and Afghanistan conflicts. With the extensive use of IED by the enemy, the concussive effects from blast can cause mTBI in Military Service Members. However, mTBI and the associated co-morbidities can go unrecognized, particularly when service members are seen outside of military or VA medical facilities that have less familiarity with this condition.[20] Mild TBI can also go undiagnosed due to the clinical attention given to other more obvious injuries. In addition, the ocular and visual processing dysfunctions manifest in mTBI can be subclinical, highlighting the need for more detailed evaluation in the ocular and visual processing examinations.

Visual processing and eye movements are frequently affected by mTBI. Common problems among patients presenting with mTBI include pupillary response deficit, visual processing delays (poor attention to detail, poor visual attention, and poor visual memory), photosensitivity, impaired oculomotor convergence (difficulty focusing on nearby objects or images), and related oculomotor-based reading dysfunctions.[21] Nearly 70% of sensory processing in the brain is vision related[22] and 7 of the 12 cranial nerves are utilized by the visual system. Brain structures most vulnerable to mTBI that are vision related include the frontal, occipital, temporal, and parietal lobes as well as the long axonal fibers connecting the midbrain to the cortex. It has been established that autonomic nervous system dysfunctions can occur in those with mTBI/concussion-type injuries,[23] including the pupillary light reflex.[24] Given that certain neurological deficits might lead to impairment of the oculomotor system, accommodation, and pupillary light reflex, it is not surprising that patients with a brain trauma typically present with a myriad of visual dysfunctions.

After assessment for those who had a history of service related concussion using the 3-Question TBI Screen, our study examined thirteen self-reported questions relative to changes or loss in vision, diplopia, light or glare sensitivity, balance and dizziness, and visual changes with computer and hand held device usage. The vision score was derived from Likert scale responses to 13 specific questions, (ranging from 1 to 5, coded "Never" to "Always"). Based on ROC analyses, a vision score greater than 24 demonstrated a significant capability in predicting deployment concussions, based on the TBI screener (ROC area = 0.71). For example, data in Table II suggest that in a logistic regression model that included number of combat tours, high combat exposure, and current TBI symptoms >3, a vision score >24 still significantly predicted deployment TBIs (OR = 2.15, $p = 0.025$). However, a vision score >24 is neither significant in predicting self-report of having a medical diagnosis of TBI nor is this significant in predicting self-report of TBI without a medical diagnosis of TBI (Tables III and IV).

Several studies imply that most of the symptoms of mTBI will resolve or become subclinical within 6 mo of the trauma.[25–27] Our results did suggest that the visual symptoms were significant for a positive mTBI screen among the subjects surveyed, even though all had experienced an mTBI event greater than five years ago. Considering that the self-reporting of visual symptoms does not equate with a more detailed assessment of the visual system, a full ocular structural and visual functional assessment is warranted for deployed veterans, with specific attention directed to any afferent visual dysfunction, efferent visual defects and/or higher order deficits, as outlined by Barnett and Singman.[28]

Although we did find an association with concussion and visual symptoms, the association for concussion was strongest with having greater than or equal to three current TBI symptoms. By far, this variable was the best predictor of concussion among this sample of veterans. Surprisingly, experiencing multiple combat tours was not a predictor of concussion in the current study (Tables II–IV). By contrast, reporting >3 TBI symptoms was significant in all the models assessed (p-values < 0.01).

The limitations for this study include the accuracy of the patients in reporting visual symptoms relative to recall due to the time elapsed since the concussive event, as well as the unrecognized presence of subclinical symptoms. Additionally, the study included only previously deployed U.S. veterans who were predominantly white, male, and outpatients in a large, multihospital health care system located in Pennsylvania. Thus, it may not be possible to generalize these finding to other clinical populations in different regions and among different demographic groups. Another limitation is that the sample size in this study was limited to 235 veterans. Consequently, the statistical power to detect statistical differences was limited.

CONCLUSION

Although many visual dysfunctions associated with mTBI can resolve in time, chronic or subclinical visual problems can go unrecognized by the patient. Eye care providers, especially outside of a VA or military facility, need to be vigilant with combat veterans for underlying structural and functional visual issues related to mTBI. A complete patient history, to include military service, deployments, TBI or exposure to blast should be accomplished prior to the visual examination. A dilated fundus examination, including full binocular and oculomotor assessments should be the standard of care for this patient population. In addition, awareness of and recognition for the co-morbidities of mTBI is essential for this group, especially if the veteran reports a history of high combat exposure, TBI, and reports the presence of current TBI symptoms. Communication with the patient's primary care provider or specialist with the findings of the visual examination will help facilitate further evaluation and appropriate referral for any co-morbidities associated with these veterans.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *Military Medicine* online.

ACKNOWLEDGMENTS

The study team wishes to acknowledge the input and effort of the veterans who volunteered to take part in this project.

CONFLICTS OF INTEREST

None of the authors have any potential conflicts of interest or financial interests in the topic covered by this manuscript.

FUNDING

Support for this research was provided by: Geisinger Auxiliary Fund, the Kline & Ditty Health Fund, the National Institute of Mental Health (Grant No. R21-MH-086317), the Wounded Warrior Project, and the Department of Defense (Contract No. W81XWH-15-1-0506) to Dr Joseph A. Boscarino

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