Loss of Consciousness Predicts Development of mTBI Symptoms

Subjects: Clinical Neurology | Neurosciences

Contributor: Rina Berman , Haley Spencer , Martin Boese , Sharon Kim , Kennett Radford , Kwang Choi

Traumatic brain injury (TBI) is a condition caused by a blow or jolt to the head. TBI may be classified as mild, moderate, or severe based on several criteria, including the duration of loss of consciousness (LOC), when present. While the majority of mild TBI (mTBI) patients recover without intervention, a subset of patients experience persistent and debilitating symptoms. Therefore, prediction of symptom development in mTBI patients remains an ongoing research goal. LOC is associated with adverse outcomes after mTBI, such as cognitive and memory deficits; psychiatric disorders; physical symptoms; and brain abnormalities associated with the aforementioned impairments.

mild traumatic brain injury | loss of consciousness | symptom development

1. Introduction

Traumatic brain injury (TBI) is a condition caused by a blow or jolt to the head as a result of motor vehicle accidents, falls, blast injuries, or other mechanisms, and is a leading cause of death and disability in the United States [1]. TBI may be classified as mild, moderate, or severe based on the duration of loss of consciousness (LOC), alteration of consciousness (AOC), and post-traumatic amnesia (PTA); structural imaging; and the Glasgow Coma Scale (GCS), which assesses depth of consciousness on a scale of 3–15 whereby 13–15 indicates mild, 9–12 moderate, and 3–8 severe TBI [2]. The vast majority of TBI cases (80–90%) are considered mild; however, the perceived mildness of the condition produces barriers for patients to receive proper treatment [3]. Although mTBI-related symptoms can resolve without intervention, a subset of patients develops persistent symptoms, which is referred to as post-concussive or post-concussion syndrome (PCS) [4][5]. Approximately 10–40% of mTBI cases are accompanied by LOC lasting less than 30 min [6][7], and LOC may be associated with adverse outcomes.

2. Cognitive and Memory Deficits

The presence and duration of loss of consciousness (LOC) are associated with cognitive deficits after mTBI. LOC was associated with cognitive deficits and slow recovery of cognitive function [8]. Among military personnel and civilian contractors, longer duration of LOC was associated with a greater decline in accuracy on the Automated Neuropsychological Assessment Metric (ANAM), which measures reaction time, learning, and memory, between baseline and post-injury tests [9]. Among veterans stratified into reduced or intact executive function subgroups, LOC was more prevalent in the reduced executive function subgroup [10]. Service members and veterans with LOC after combat-related mTBI reported memory problems [11][12]. Longer LOC (1–20 min) was associated with greater impairment rates in declarative memory and executive function tasks compared to mTBI with shorter LOC (<1 min) and control groups [13]. In an earlier study by the same team, longer LOC (1–20 min) was associated with deficits in event-based tasks of prospective memory (PM), defined as remembering the intention to perform a task, compared to the LOC < 1 min group but not the control group, whereas both LOC groups had impairments in time-based PM tasks [14]. Deficits in prospective memory may translate to a worse ability to perform daily tasks. This is consistent with a study reporting that LOC was associated with incomplete functional recovery, defined as the ability to perform activities of daily living, 1 and 3 months after mTBI compared to groups with altered mental state (AMS) and neither LOC nor AMS [15]. AMS is an interchangeable term for AOC, one of the criteria used to diagnose and classify TBI. Altogether, these studies have reported a negative association between mTBI with LOC and cognitive performance as measured by executive function, reaction time, memory, and attention tests, which may have implications for daily functioning.

Interestingly, several studies have reported better cognitive performance associated with LOC following mTBI. For example, LOC duration was inversely correlated with forgetfulness and overall cognitive impairment in the Neurobehavioral Symptom Inventory (NSI) in male veterans [16]. However, no such cognitive correlation existed in female veterans, suggesting sex-specific effects on the relationship between LOC and these outcome variables [16]. In an attention switching task, the difference in reaction time to trials where the placement and direction of arrows on a screen are the same (congruent) or different (incongruent) is referred to as the congruency cost [17]. In this study, mTBI with LOC was associated with lower congruency cost in the attention switching task than mTBI without LOC, which indicated better cognitive performance as less time was needed to complete more difficult tasks [17]. Additionally, LOC was associated with improved visual working memory in students who had sustained mTBI resulting from sports or other causes [18]. One possibility presented by the authors is that LOC may have prompted patients to seek medical care; in contrast, patients not experiencing LOC may have returned to play before recovering fully and thus risked re-injury [18]. These studies indicate that the relationship between LOC and cognitive performance can be inconsistent, and more research needs to be done to reconcile these inconsistencies.

3. Psychiatric Disorders

LOC after mTBI is associated with the development of psychiatric disorders, including post-traumatic stress disorder (PTSD) and major depressive disorder (MDD). One study reported that LOC was associated with MDD and emotional lability, a condition characterized by exaggerated and rapidly fluctuating emotions [8]. Among patients stratified by age, sex, and LOC status, LOC was associated with development of anxiety, suicidal ideation, and MDD within a 180-day period after admission for mTBI [19]. Importantly, all age and sex subgroups with LOC had higher odds of developing MDD [19]. LOC was associated with greater development of MDD compared to AOC/AMS groups and other (non-TBI) injury groups in soldiers studied several months after deployment [11][20]. LOC after mTBI was associated with greater self-reported MDD and somatic symptom disorder (SSD) symptoms compared to the mTBI without LOC group and the non-TBI group in wounded service members [21]. Previous studies suggest that mTBI with LOC is associated with increased development of MDD and other psychiatric disorders.

In addition to MDD, LOC after mTBI is associated with the development of PTSD. In soldiers studied several months after returning from deployment, LOC was associated with greater development of PTSD compared to the AOC/AMS groups and other (non-TBI) injury groups [11][20]. In service members sustaining mTBI after blast injury, LOC was associated with the development of PCS and PTSD after deployment [22]. LOC following blast-related mTBI was associated with acute stress reactions (ASRs), including dissociation, re-experiencing, avoidance, and hyperarousal in veterans [12]. These symptoms resemble those of PTSD, but they have a much more transient time course, typically resolving within a few days after a traumatic incident [12]. Similarly, LOC was associated with avoidance symptomology of PTSD, although not re-experiencing or hyperarousal, and lower psychological quality of life in veterans [23]. In contrast, LOC was associated with higher re-experiencing/intrusion cluster scores compared to head injury without LOC and no head injury groups at 8 months, and elevated PTSD symptom scores at both 10 days and 8 months after a motor vehicle accident [24]. In a longitudinal study following a trajectory of PTSD symptoms over a year after mTBI, LOC was associated with a chronic trajectory marked by consistently high PTSD symptom scores throughout the study [25]. Overall, these clinical studies provide evidence that mTBI with LOC may increase development of psychiatric disorders, including PTSD, compared to mTBI without LOC.

The relationship between LOC and PTSD is controversial, as unconsciousness may theoretically protect against trauma by preventing full awareness and processing of the traumatic event, as discussed in [21]. Interestingly, this study also reported that mTBI with LOC was associated with greater PTSD symptom self-reporting compared to the non-TBI group, but not compared to the mTBI without LOC group, which was unexpected [21]. In contrast, LOC was associated with more PTSD symptoms compared to the head injury groups and no injury groups at 10 days and 8 months after a motor vehicle accident, with elevated re-experiencing/intrusion cluster scores at 8 months post-injury [24]. Interestingly, these patterns emerged despite equal levels of fear and threat perception among groups during the accident [24]. Importantly, these findings remained the same when the data was re-analyzed with the omission of PTSD-related amnesia [24]. The authors suggest several explanations for these findings, such as impaired fear extinction due to psychological disturbances or neuronal damage; cognitive deficits which may impair ability to cope with and process the situation; physical symptoms which may serve as reminders of the event; or the traumatic memory being preserved, as the traumatic memories may be more pronounced with the absence of memories immediately following the incident [24]. Much of the literature on the relationship between LOC, PTSD, and memory is focused on more severe TBI; therefore, more research on these relationships in mTBI patients is warranted.

4. Physical Symptoms

LOC after mTBI is associated with various physical symptoms, including headache, dizziness, and balance problems. The duration of LOC in women, but not men, was positively correlated with loss of balance, poor coordination, fatigue, and overall vestibular impairment score on the NSI in a study comparing male and female veterans [16]. Additionally, LOC was associated with balance problems and fatigue; interestingly, every patient with

LOC in this study reported headache [8]. In military personnel, LOC was associated with greater levels of plasma interleukin (IL)-6, a pro-inflammatory cytokine, and greater self-reported pain levels [26]. In soldiers recently returning from deployment, mTBI with LOC was associated with headache, balance problems, and musculoskeletal pain [11] or headache alone [20] compared to other injuries, with no association between AOC/AMS and physical symptoms [11][20]. Blast-related mTBI with LOC was associated with hearing loss and with difficulty sleeping that persisted at a follow-up visit 48-72 h later [12]. LOC after mTBI was associated with more self-reported somatic symptoms compared to mTBI without LOC and non-TBI groups in wounded service members [21]. Therefore, the presence and duration of LOC following mTBI increased the risk of developing adverse physical symptoms.

Several studies have demonstrated that psychological factors may underlie adverse health outcomes in mTBI patients. For example, adjustment for ASRs nullified the initial associations of LOC with ringing in ears and balance problems after blast-related mTBI in military personnel, and the remaining associations were weakened [12]. In soldiers surveyed several months after returning from deployment, mTBI with LOC was initially associated with almost all health-related outcomes and post-concussive symptoms measured when compared to other injuries [11][20]. However, few associations remained significant when adjusted for PTSD, MDD, and other factors [11][20]. Additionally, the remaining LOC-associated symptoms were more strongly associated with PTSD and MDD than with LOC [11][20]. This confounding effect may be explained by an overlap between adverse symptoms commonly reported after mTBI and those associated with PTSD and MDD, such as sleeping problems [11][20][23]. Taken together, these studies demonstrate that psychological factors partially influence poor physical health outcomes associated with LOC after mTBI.

5. Brain Abnormalities

Variations in LOC after mTBI are associated with structural brain abnormalities which may contribute to functional deficits such as cognitive, psychiatric, and physical symptoms. Magnetic resonance imaging (MRI) demonstrated that LOC was associated with greater thickness of the left and right rostral anterior cingulate cortices (rACC), which itself was predictive of a chronic PTSD somatology trajectory marked by high PTSD symptom scores with minimal improvement [25]. LOC was also associated with a chronic PTSD trajectory, indicating direct a relationship between brain abnormalities, PTSD symptomology, and LOC [25]. A variation of the standard MRI technique is diffusion tensor imaging (DTI), which uses the movement of water molecules to measure white matter integrity. Fractional anisotropy (FA), a measure of directional movement along the axon, is proportional to white matter integrity, while radial diffusivity (RD), which measures diffusion perpendicular to the axon, is inversely related to white matter integrity; in other words, low FA and high RD are indicative of impaired white matter integrity. A DTI study found that lower FA in the internal capsule was associated with greater PTSD symptoms in patients with LOC following blast-related mTBI [27]. Another DTI study revealed that LOC was associated with increased RD in the ventral prefrontal white matter (VPFWM) compared to AOC and control groups [10]. VPFWM FA was decreased in patients with reduced executive functioning, who were significantly more likely to have LOC; therefore, loss of white matter integrity in the ventral prefrontal area may explain the deficits in executive functioning observed in patients with LOC [10]. In summary, associations between LOC after mTBI and outcomes discussed previously have underlying neural correlates, which are themselves associated with LOC. While much of the literature has reported abnormalities in brain function and structure in patients with mTBI, only a handful of papers discuss a direct interaction between brain abnormalities, LOC status, and symptoms; more research on these interactions is warranted.

6. Conclusion on Clinical mTBI and LOC

In patients with mTBI, LOC can be a useful predictor of symptom development and severity. LOC has been associated with adverse effects such as deficits in cognition, learning, and memory; psychiatric disturbances such as PTSD and MDD; physical symptoms such as headache; and brain abnormalities, particularly in white matter areas. As such, one can predict that mTBI patients with LOC are more likely to develop adverse effects. Clinicians should triage mTBI patients with LOC and monitor them to prevent worsening symptoms, particularly in the context of return-to-play decisions in athletes or return to duty in military personnel. Additionally, literature on brain abnormalities has revealed associations with adverse outcomes. In particular, DTI analysis of white matter is a sensitive neuroimaging modality that is gaining popularity among clinicians and clinical researchers. LOC following mTBI may be a useful indication for this advanced imaging technique, allowing for more accurate detection of mTBI-related abnormalities that traditional techniques may miss.

A summary of the referenced studies is provided in **Table 1**.

Table 1. A summary of clinical studies. mTBI = mild traumatic brain injury; LOC = loss of consciousness; AMS = altered mental status/altered mental state; MDD = major depressive disorder; PTSD = post-traumatic stress disorder; ANAM = Automated Neuropsychological Assessment Metric; AOC = alteration of consciousness; EMED = Expeditionary Medical Encounter Database; PCS = post-concussive/post-concussion syndrome; ASR = acute stress reaction; FA= fractional anisotropy; QoL = quality of life; CLSA = Canadian Longitudinal Study on Aging; PM = prospective memory; IL-6 = interleukin 6; PTA = post-traumatic amnesia; NSI = neurobehavioral symptom inventory; HeadSMART = Head injury Serum Markers for Assessing Response to Trauma; AST = attention switching task; rACC = rostral anterior cingulate cortex; MS-TBI = moderate-to-severe TBI; SSD = somatic symptom disorder.

Author, Year	Patient Population	Nature/Cause of Injury	Timing of Assessment	Groups	Outcomes
Vanier et al., 2020 [8]	mTBI patients in litigation for brain injury	Motor vehicle accidents, fall, assault, other	Variable	mTBI with LOC mTBI without LOC	LOC associated with balance problems, MDD, fatigue, emotional lability, cognitive deficits with slow recovery
Luethcke et al., 2011 [9]	Military personnel and civilian	Blast injury, non-blast injury (blunt object,	Within 72 h of injury	Blast mTBI Non-blast mTBI	LOC duration correlated with greater decline in

Author, Year	Patient Population	Nature/Cause of Injury	Timing of Assessment	Groups	Outcomes
	contractors in Iraq	sport/recreation, falls, motor vehicle accident)		No LOC LOC <1 min LOC 1–20 min LOC >20 min	ANAM accuracy scores between baseline and post-injury tests
Sorg et al., 2014 [10]	Afghanistan and Iraq war veterans	Blunt or blast injury	Variable	mTBI with LOC mTBI with AOC Controls	LOC associated with reduced executive functioning, reduced ventral prefrontal white matter integrity
Wilk et al., 2012 [11]	Soldiers returning from Afghanistan and Iraq	Blast/explosion, bullet, fragment/shrapnel, fall, vehicle crash, or other	4–6 months after deployment	Single AOC Single LOC Multiple AOC Multiple (1+) LOC Other injuries No injury	LOC associated with MDD, PTSD, headache, memory problems, balance problems, musculoskeletal pain
Norris et al., 2014 [12]	Military personnel in Afghanistan	Blast-related injury	mTBI diagnosis within 72 h of injury; follow-up 48–72 h later	mTBI with LOC mTBI without LOC	LOC associated with ASRs, memory problems, hearing loss, difficulty sleeping, increased symptom reporting
Bedard et al., 2020 [13]	mTBI patients from CLSA cohort	Not specified	1 year or more after mTBI	LOC <1 min LOC 1–20 min Controls	LOC 1–20 min associated with higher impairment rates in declarative memory and executive functioning tasks
Bedard et al., 2018 [14]	mTBI patients from CLSA cohort	Not specified	1 year or more after mTBI	LOC <1 min LOC 1–20 min Controls	LOC 1–20 min associated with worse performance on event-based PM tasks compared to LOC <1 min, but not compared to controls; both LOC groups had

Author, Year	Patient Population	Nature/Cause of Injury	Timing of Assessment	Groups	Outcomes
					impairments in time-based PM tasks
Roy et al., 2020 [15]	mTBI patients from HeadSMART cohort	Blunt head trauma by pedestrian struck, motor vehicle collision, fall, assault, struck by or against and object, bicycle collision, other	Medically evaluated within 24 h of mTBI; functional recovery assessed 1, 3, 6 months after TBI	AMS only LOC only LOC and AMS Neither LOC nor AMS	LOC associated with incomplete functional recovery 1 and 3 months after injury
Gray et al., 2020 [16]	Retrospective study of veterans from Polytrauma Network Site	Blasts, motor vehicle accidents, falls, blunt trauma	Variable	Men or women mTBI with LOC mTBI with AOC mTBI with PTA	-LOC duration correlated with loss of balance, poor coordination, fatigue, worse vestibular score on NSI in women -LOC duration correlated with less forgetfulness and better cognitive score on NSI in men
Karlsen et al., 2021 [17]	mTBI patients in Trondheim mTBI follow-up study	Fall, violence, bicycle, sport motor vehicle accident, struck object, other	Approximately 2 weeks following mTBI	mTBI with LOC mTBI without LOC Community controls Trauma controls	LOC associated with lower congruence cost (better performance) on AST
Arciniega et al., 2020 [18]	Undergraduate students with mTBI	Closed-head injury from non-sport causes or individual, high-impact, or team sports	Average of 4 years after injury	mTBI with LOC mTBI without LOC Controls	LOC associated with better visual working memory
Shahrestani et al., 2022 [19]	Retrospective cohort analysis of mTBI patients from Nationwide Readmission Database	Not specified	Followed until readmission within 180 days after primary admission	mTBI with LOC mTBI without LOC Male or female	LOC patients had higher rates of MDD in all groups, age- and sex-dependent increases in anxiety and suicidal ideation

Author, Year	Patient Population	Nature/Cause of Injury	Timing of Assessment	Groups	Outcomes
				Age <26, 26–50, 51–75, >75 years old	
Hoge et al., 2008 [20]	Soldiers returning from Iraq	Blast or explosion, bullet, fragment or shrapnel, fall, vehicle accident, other	3–4 months after deployment	mTBI with LOC mTBI with AMS Other injury No injury	LOC associated with headache, MDD, PTSD
Kim et al., 2023 [21]	mTBI or MS-TBI service members in Iraq and Afghanistan	Not specified	Initial intake within a few days of injury, initial assessment up to 72 h later, follow-ups 0–75 days (AP1) and 90–365 days (AP2) post-injury	mTBI with LOC mTBI without LOC MS-TBI Non-TBI	mTBI with LOC associated with: -higher MDD and SSD vs. mTBI without LOC -higher PTSD, MDD, and SSD vs. non-TBI
Eskridge et al., 2013 [22]	Retrospective study of male service members in Iraq from the EMED	Blast-related injury	mTBI diagnosed within 48 h of injury; variable follow-up	mTBI with LOC mTBI without LOC	LOC associated with PTSD and PCS
Sofko et al., 2016 [23]	Afghanistan and Iraq war veterans	Fragments, bullets, vehicular accidents, falls or blasts	Shortly following intake for PTSD treatment	mTBI with LOC mTBI without LOC	LOC associated with avoidance, lower psychological QoL, and more post-concussive symptoms
Roitman et al., 2013 [24]	Motor vehicle accident survivors	Motor vehicle accident	Admission average of 1.5 h after the accident; PTSD evaluation 10 days and 8 months later	LOC Head injury No head injury	LOC associated with elevated PTSD scores at 10 days and 8 months vs. head injury and no head injury groups; elevated PTSD prevalence and re-experiencing/intrusion cluster scores 8 months post-injury

Author, Year	Patient Population	Nature/Cause of Injury	Timing of Assessment	Groups	Outcomes
Kosaraju et al., 2022 [25]	mTBI patients from trauma center study of serum biomarkers and PTSD	Interpersonal, motor vehicle accident, other	Enrolled at initial ED visit; PTSD symptom evaluation 1, 3, 6, 12 months after enrollment	mTBI with LOC mTBI without LOC	LOC associated with chronic PTSD profile, thickness in left and right rACC
Kanefsky et al., 2019 [26]	Active duty military personnel recruited from sleep study cohort	Not specified	3–18 months after returning from deployment	mTBI with LOC mTBI without LOC Controls	LOC associated with higher pain self-reporting and higher levels of plasma IL-6
Hayes et al., 2015 [27]	Afghanistan and Iraq war veterans	Blast-related injury	Variable	mTBI with LOC mTBI without LOC Controls	Lower internal capsule FA associated with greater PTSD symptom severity in LOC group

References

1. CDC. Traumatic Brain Injury in the United States: Epidemiology and Rehabilitation; National Center for Injury Prevention and Control, Division of Unintentional Injury Prevention: Atlanta, GA, USA, 2015.

2. VA/DoD Clinical Practice Guideline for the Management and Rehabilitation of Post-Acute Mild Traumatic Brain Injury. Washington, DC, USA, 2021. Available online: https://pubmed.ncbi.nlm.nih.gov/20108447/ (accessed on 25 March 2023).

3. McCrea, M.A.; Nelson, L.D.; Guskiewicz, K. Diagnosis and Management of Acute Concussion. Phys. Med. Rehabil. Clin. N. Am. 2017, 28, 271–286.

4. Cnossen, M.C.; Winkler, E.A.; Yue, J.K.; Okonkwo, D.O.; Valadka, A.B.; Steyerberg, E.W.; Lingsma, H.F.; Manley, G.T.; Investigators, T.-T. Development of a Prediction Model for Post-Concussive Symptoms following Mild Traumatic Brain Injury: A TRACK-TBI Pilot Study. J. Neurotrauma 2017, 34, 2396–2409.

5. McInnes, K.; Friesen, C.L.; MacKenzie, D.E.; Westwood, D.A.; Boe, S.G. Mild Traumatic Brain Injury (mTBI) and chronic cognitive impairment: A scoping review. PLoS ONE 2017, 12,

e0174847.

6. Cassidy, J.D.; Boyle, E.; Carroll, L.J. Population-based, inception cohort study of the incidence, course, and prognosis of mild traumatic brain injury after motor vehicle collisions. Arch. Phys. Med. Rehabil. 2014, 95, S278–S285.
7. Hobbs, J.G.; Young, J.S.; Bailes, J.E. Sports-related concussions: Diagnosis, complications, and current management strategies. Neurosurg. Focus. 2016, 40, E5.
8. Vanier, C.; Pandey, T.; Parikh, S.; Rodriguez, A.; Knoblauch, T.; Peralta, J.; Hertzler, A.; Ma, L.; Nam, R.; Musallam, S.; et al. Interval-censored survival analysis of mild traumatic brain injury with outcome based neuroimaging clinical applications. J. Concussion 2020, 4, 2059700220947194.
9. Luethcke, C.A.; Bryan, C.J.; Morrow, C.E.; Isler, W.C. Comparison of concussive symptoms, cognitive performance, and psychological symptoms between acute blast-versus nonblast-induced mild traumatic brain injury. J. Int. Neuropsychol. Soc. 2011, 17, 36–45.
10. Sorg, S.F.; Delano-Wood, L.; Luc, N.; Schiehser, D.M.; Hanson, K.L.; Nation, D.A.; Lanni, E.; Jak, A.J.; Lu, K.; Meloy, M.J.; et al. White matter integrity in veterans with mild traumatic brain injury: Associations with executive function and loss of consciousness. J. Head. Trauma. Rehabil. 2014, 29, 21–32.
11. Wilk, J.E.; Herrell, R.K.; Wynn, G.H.; Riviere, L.A.; Hoge, C.W. Mild traumatic brain injury (concussion), posttraumatic stress disorder, and depression in U.S. soldiers involved in combat deployments: Association with postdeployment symptoms. Psychosom. Med. 2012, 74, 249–257.
12. Norris, J.N.; Sams, R.; Lundblad, P.; Frantz, E.; Harris, E. Blast-related mild traumatic brain injury in the acute phase: Acute stress reactions partially mediate the relationship between loss of consciousness and symptoms. Brain Inj. 2014, 28, 1052–1062.
13. Bedard, M.; Steffener, J.; Taler, V. Long-term cognitive impairment following single mild traumatic brain injury with loss of consciousness: Findings from the Canadian Longitudinal Study on Aging. J. Clin. Exp. Neuropsychol. 2020, 42, 344–351.
14. Bedard, M.; Taler, V.; Steffener, J. Long-term prospective memory impairment following mild traumatic brain injury with loss of consciousness: Findings from the Canadian Longitudinal Study on Aging. Clin. Neuropsychol. 2018, 32, 1002–1018.
15. Roy, D.; Peters, M.E.; Everett, A.D.; Leoutsakos, J.M.S.; Yan, H.; Rao, V.; Bechtold, K.T.; Sair, H.I.; Van Meter, T.; Falk, H.; et al. Loss of Consciousness and Altered Mental State as Predictors of Functional Recovery Within 6 Months Following Mild Traumatic Brain Injury. J. Neuropsychiatry Clin. Neurosci. 2020, 32, 132–138.
16. Gray, M.; Adamson, M.M.; Thompson, R.C.; Kapphahn, K.I.; Han, S.; Chung, J.S.; Harris, O.A. Sex differences in symptom presentation and functional outcomes: A pilot study in a matched sample of veterans with mild TBI. Brain Inj. 2020, 34, 535–547.

17. Karlsen, R.H.; Saksvik, S.B.; Stenberg, J.; Lundervold, A.J.; Olsen, A.; Rautio, I.; Folvik, L.; Haberg, A.K.; Vik, A.; Karr, J.E.; et al. Examining the Subacute Effects of Mild Traumatic Brain Injury Using a Traditional and Computerized Neuropsychological Test Battery. J. Neurotrauma 2021, 38, 74–85.
18. Arciniega, H.; Kilgore-Gomez, A.; McNerney, M.W.; Lane, S.; Berryhill, M.E. Loss of consciousness, but not etiology, predicts better working memory performance years after concussion. J. Clin. Transl. Res. 2020, 5, 169–177.
19. Shahrestani, S.; Ballatori, A.M.; Ton, A.; Chen, X.T.; Zargarian, A.; Chan, A.K.; Strickland, B.A.; Brunswick, A.; Micko, A.; Zada, G. Demographic-Dependent Risk of Developing Severe Novel Psychiatric Disorders after Concussion. J. Neurotrauma 2022, 39, 131–137.
20. Hoge, C.W.; McGurk, D.; Thomas, J.L.; Cox, A.L.; Engel, C.C.; Castro, C.A. Mild traumatic brain injury in U.S. Soldiers returning from Iraq. N. Engl. J. Med. 2008, 358, 453–463.
21. Kim, S.Y.; Soumoff, A.A.; Raiciulescu, S.; Kemezis, P.A.; Spinks, E.A.; Brody, D.L.; Capaldi, V.F.; Ursano, R.J.; Benedek, D.M.; Choi, K.H. Association of Traumatic Brain Injury Severity and Self-Reported Neuropsychiatric Symptoms in Wounded Military Service Members. Neurotrauma Rep. 2023, 4, 14–24.
22. Eskridge, S.L.; Macera, C.A.; Galarneau, M.R.; Holbrook, T.L.; Woodruff, S.I.; MacGregor, A.J.; Morton, D.J.; Shaffer, R.A. Influence of combat blast-related mild traumatic brain injury acute symptoms on mental health and service discharge outcomes. J. Neurotrauma 2013, 30, 1391–1397.
23. Sofko, C.A.; Currier, J.M.; Hill, B.D.; Drescher, K.D. History of loss of consciousness with mild traumatic brain injury affects PTSD symptom presentation in treatment-seeking Iraq/Afghanistan veterans. Brain Inj. 2016, 30, 1561–1569.
24. Roitman, P.; Gilad, M.; Ankri, Y.L.; Shalev, A.Y. Head injury and loss of consciousness raise the likelihood of developing and maintaining PTSD symptoms. J. Trauma. Stress. 2013, 26, 727–734.
25. Kosaraju, S.; Galatzer-Levy, I.; Schultebraucks, K.; Winters, S.; Hinrichs, R.; Reddi, P.J.; Maples-Keller, J.L.; Hudak, L.; Michopoulos, V.; Jovanovic, T.; et al. Associations among civilian mild traumatic brain injury with loss of consciousness, posttraumatic stress disorder symptom trajectories, and structural brain volumetric data. J. Trauma. Stress. 2022, 35, 1521–1534.
26. Kanefsky, R.; Motamedi, V.; Mithani, S.; Mysliwiec, V.; Gill, J.M.; Pattinson, C.L. Mild traumatic brain injuries with loss of consciousness are associated with increased inflammation and pain in military personnel. Psychiatry Res. 2019, 279, 34–39.
27. Hayes, J.P.; Miller, D.R.; Lafleche, G.; Salat, D.H.; Verfaellie, M. The nature of white matter abnormalities in blast-related mild traumatic brain injury. Neuroimage Clin. 2015, 8, 148–156.