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# A Review of the Co-Occurrence of Posttraumatic Stress Disorder and Mild Traumatic Brain Injury

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***Abstract***

*Posttraumatic stress disorder (PTSD) and traumatic brain injury (TBI) often co-occur. This review describes the overlap between PTSD and TBI with special emphasis on mild TBI (mTBI) by defining these two conditions and their differential diagnosis. The impact of mTBI on PTSD is outlined and vice versa. The various psychotherapeutic and pharmacologic treatment interventions that could provide a symptomatic relief for both conditions are summarized with the hope that by implementing these interventions, individuals afflicted by these potentially very disabling conditions will experience improved functioning and quality of life.*

**Keywords:** Posttraumatic Stress Disorder, Traumatic Brain Injury, Evaluation, Treatment, Psychotherapy, Psychopharmacology, Medications

## Introduction

The link between traumatic brain injury (TBI) and posttraumatic stress disorder (PTSD) is increasingly being recognized by clinicians who are diagnosing and treating these two distinct and yet interacting neuropsychiatric disorders. The severity of a TBI can usually be assessed through brain imaging showing evidence of brain bleeding, bruising, or swelling, the length of loss or alteration of consciousness, the length of memory loss, and the degree of responsiveness following the injury [1]. Most TBIs are considered mild. Mild traumatic brain injury (mTBI) can be more difficult to identify than more severe forms of TBI, due to the absence of observable head injuries, and normal brain imaging. While most individuals recover within hours to weeks and up to three months from an mTBI, some will continue to experience residual symptoms of headaches, dizziness, cognitive difficulties , memory disturbances, and concomitant mental health conditions such as depression and PTSD [2, 3]. The co- occurrence of PTSD and mTBI could lead to marked psychological and physical impairments in many individuals especially in veterans who have sustained traumatic and emotional injuries as a result of their deployment during the Afghanistan and Iraq wars [4] .Exposure to repeated mTBI could also increase the risk of developing neurodegenerative diseases such as chronic traumatic encephalopathy (CTE) and an association between repetitive mTBI and CTE have been found in autopsies of professional athletes and combat Veterans [5]. A comprehensive and integrated treatment of mTBI and PTSD would minimize the complications of both conditions and improve the quality of life of those who are afflicted by these potentially disabling neuropsychiatric disorders.

## Definitions

**Posttraumatic Stress Disorder (PTSD):** This psychiatric disorder develops following a traumatic event that involves physical harm that has been experienced, threated with, or witnessed toward self, loved ones or others. It is characterized by recurrent and intrusive distressing recollections of the traumatic events and is associated with a sense of reliving the experience with intense psychological or physiological distress at exposure to cues that resemble the traumatic event, avoidance of stimuli associated with the trauma, or inability to recall important aspects of the trauma [6]. Individuals with PTSD often experience a cluster of additional symptoms including loss of interest, estrangement from others, sleep disturbances, nightmares, irritability, difficulty concentrating, hypervigilance, exaggerated startle responses, aggressive behaviors, shame and guilt, and some patients develop dissociative flashback episodes [6, 7]. Typical examples of traumatic experiences that may predispose to PTSD include sexual assault, military combat, mass conflict and displacement, and life-threatening physical illness [6].

**Traumatic brain injury (TBI):** The generally accepted definition

of TBI is an injury that occurs following an external force to the head. There are three main types of TBIs: mild TBI or concussion, moderate TBI and severe TBI [1]. Mild traumatic brain injury mTBI is usually described as: (i) an external injury to the brain; resulting in (ii) confusion, disorientation, or loss of consciousness for 30 minutes or less; with (iii) Glasgow Coma Scale score of 13 to 15; and associated with (iv) post-traumatic amnesia for less than 24 hours. Moderate TBI often involves loss of consciousness between 30 minutes and 24 hours, with a Glasgow Coma Scale score of 9 to 12, and post-traumatic amnesia lasting between 1 and 7 days. The Glasgow Coma Scale is depicted in figure1.

**Figure1: The Glasgow Coma Scale**

| BEHAVIOUR | RESPONSE | SCORE |
|---|---|---|
| Best Eye Response | Spontaneously | 4 |
| | To speech | 3 |
| | To pain | 2 |
| | No response | 1 |
| Best Verbal Response | Oriented to time, place, person | 5 |
| | Confused | 4 |
| | Inappropriate words | 3 |
| | Inappropriate sounds | 2 |
| | No response | 1 |
| Best Motor Response | Obeys commands | 6 |
| | Moves to localized pain | 5 |
| | Flexion withdrawal from pain | 4 |
| | Abnormal flexion(decorticate) | 3 |
| | Abnormal extension(decerebrate) | 2 |
| | No response | 1 |
| Total Score | Best response | 15 |
| | Comatose client | 8 or less |
| | Totally unresponsive | 3 |

Severe TBI involves more extended loss of consciousness and post-traumatic amnesia, which typically results in more severe cognitive impairment. These differences in TBI severity are important because they appear to interact differentially with PTSD. At least 75% of all TBIs are considered mTBIs[8]. Although there is a tendency to distinguish mTBI from concussion, there is no clear distinction in the pathological findings, between these two conditions and these terms are usually used interchangeably. As is the case in PTSD, TBIs could occur due to motor vehicle accidents, sports injuries, assault, or injuries during military training or combat [4].The complications of PTSD and TBI are illustrated in [Table1].

**Table 1: Complications of posttraumatic stress disorder and traumatic brain injury**

| Complications | Posttraumatic stress disorder | Traumatic brain injury |
|---|---|---|
| **Dissociation** | | |
| Emotional numbing | Present | Present |
| Reduced awareness | Present | Present |
| Depersonalization | Present | Present |
| Derealization | Present | Present |
| Amnesia | Present | Present |
| **Re-experiencing** | | |
| Recurrent images | Present | Present |
| Nightmares | Present | Not Present |
| Distress on reminders | Present | Not Present |
| **Avoidance** | | |
| Avoid reminders | Present | Not Present |
| Social detachment | Present | Present |
| Diminished interest | Present | Present |
| Foreshortened future | Present | Not Present |
| **Increased Arousal** | | |
| Insomnia | Present | Present |
| Irritability | Present | Present |
| Hypervigilance | Present | Not Present |
| Increased startle response | Present | Not Present |
| Cognitive difficulties | Present | Present |
| Sleep disturbances | Present | Present |
| Social isolation & coworkers | Self-imposed | Loss of friends |
| Substance Abuse effects | Self medications | Magnified |
| Suicide civilians | Increased risk in veterans | Uncommon in |

## The effects of TBI on the development of PTSD

Some of the leading causes of TBI involve the experience of a traumatic and potentially life-threatening event, such as a motor vehicle accident, fall, serious physical assault or combat related injuries[9].During a TBI recovery process the individual will under-

go several medical procedures, with possibility of extended hospitalization, and the prospect of adjusting to multiple physical and/or emotional difficulties [10],as a result TBI and its sequalae are considered a potential risk for the development of PTSD [11]. The impaired consciousness and amnesia for the injury-related event associated with TBI was once considered a factor that precluded the development of PTSD [12].However it is now widely recognized that PTSD may develop following TBI due to several factors [13].These factors include the implicit or unconscious encoding of feeling and sensory experiences such as visual and olfactory stimulation associated with the traumatic event, the conscious encoding of some aspects of the event, and the reconstruction of the trauma related memories from collateral sources such as family, and onsite observers [13].The memory of the specific circumstances surrounding the traumatic event could also be triggered by similar aspects such as the sights and sounds that were present at the scene of an accident after consciousness was regained [13]. When psychological traumas are repeated during military combat, or in domestic violence incidents then, PTSD may develop in response to the broader series of events, even if the specific event leading to TBI was not remembered [13].It has also been proposed that the individuals who lack conscious memory of the traumatic even may still recall some elements of the traumatic experience, which could later be manifested in the form of PTSD symptoms of intrusive recollections [14]. Studies have also documented higher rates of PTSD associated with mTBI in veterans compared to the civilian populations which was attributed to the occurrence of TBI in the context of deployment to intensive combat theaters and its association with exposure to psychological traumas[15]. Other findings pointed to the development of PTSD among women veterans who experience intimate partner violence that resulted in high rates of both mTBI and PTSD [16]. Sports related mTBI, although stressful, are often not associated with PTSD [13]. In both civilian and military populations, the risk of developing PTSD as a consequence of TBI would vary in its occurrence depending on the psychological attributes and the context of the TBI event especially in individuals with history of psychological trauma exposures and preexisting PTSD symptoms related to repeated traumas such as in veterans with multiple intense combat deployments and in victims of reoccurring domestic violence events [13].

## The Effects of PTSD on mTBI

The occurrence of PTSD could impede mTBI recovery in the context of negative feedback loop of anxiety and sensitivity to threat. Specifically, the hypervigilance to perceived threat associated with PTSD may disproportionately extend to the distress associated with mTBI somatic symptoms, which then further strengthens the sensitivity to threat [16].The psychosocial burden of PTSD symptoms could also affect the ability to cope with the sequelae of mTBI, especially in individuals with a history of trauma exposure or PTSD prior to the TBI event thus preventing the process of positive adaptation to adversity and the development of resilience [17].The presence of resilience has been shown to predict better functional outcomes with fewer symptoms in individuals with mTBI and this potential for recovery could be hampered due to PTSD [18].

## Differential Diagnosis

The mTBI nonspecific symptoms of concentration problems, cognitive difficulties, mood lability and uncontrolled anger are difficult to differentiate from PTSD [13]. In clinical settings it is challenging to determine if the symptoms of confusion and disorientation are due to the neurophysiologic disruptions inherent to the mTBI or if they are components of the emotional and psychophysiological responses that are a manifestation of PTSD particularly in persistent cases of mTBI[11-13].Symptoms of dysphoric mood, anxiety, sleep disturbance, irritability, anger, poor concentration, fatigue, dysregulated arousal, memory deficits are frequently present in both PTSD and mTBI [19,20]. Additionally some of the overlapping symptoms between PTSD and mTBI could be due to the co-occurrence of other psychiatric disorders especially anxiety and depression [11, 13, 21]. Another compounding factor in the differential diagnosis in related to the fact that mTBI, PTSD, anxiety and depression commonly also occur in the context of chronic pain, which results in symptoms that overlap with each of these conditions and further complicating their clinicals presentation [13, 22].It is also important to rule out several medical conditions in the differential diagnosis of mTBI as outlined in [Table 2].

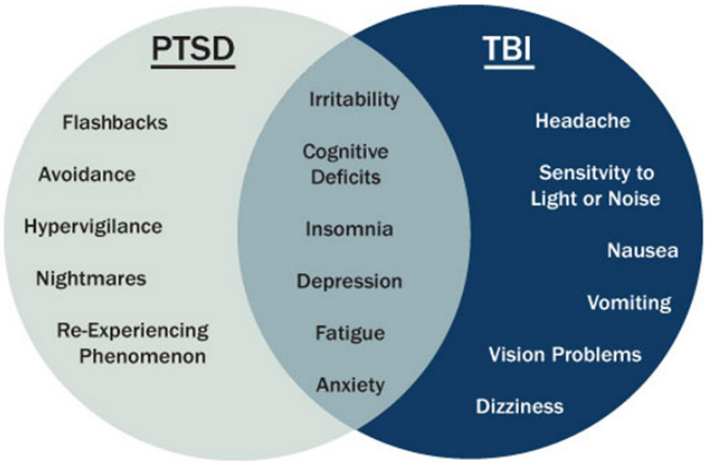
**Table 2: The differential diagnosis of mild traumatic brain injury.**

| Diagnosis | Diagnostic Studies |
|---|---|
| Intracranial hemorrhage | Head CT |
| Cerebral edema | Brain MRI, head CT |
| Skull fracture | Head CT, skull X-Rays |
| Cerebrovascular accidents/Strokes | History and physical examination ,head CT, echocardiogram, carotid ultrasound, cerebral angiogram |
| Seizures | History, electrolytes, EEG, brain MRI |
| Infections -meningitis, encephalitis | History and physical examination, lumbar puncture (spinal tap) for CSF evaluation |
| Hyperthermia | History , basic metabolic panel, response to cooling and fluid resuscitation |
| Diabetic ketoacidosis | History and physical examination, basic metabolic panel, blood gas analysis |
| Migraine headache | History, physical and neurological examination. |
| Substance induced | History, urine and serum drug screen |

*Abbreviations: CSF: cerebrospinal fluid; CT: computed tomography; EEG: electroencephalogram; MRI: magnetic resonance imaging*

While PTSD and mTBI are separate clinical entities with each diagnosis having distinguishing characteristics, there is an observable overlap and interplay among their different and common symptoms. A comprehensive treatment approach should focus on identifying the origin of the chief presenting symptoms while recognizing mTBI, PTSD, anxiety, depression and chronic pain each on their own merits [23]. The overlap in symptoms presentation between PTSD and TBI are illustrated in (figure 2).

**Figure2: Overlap between PTSD and TBI symptoms presentation**




## Navigating Treatment

Due to the effects of mTBI, treatment of PTSD may need to be modified to accommodate the overlap and the interplay between these two conditions. Treatment usually combine psychotherapies with psychopharmacology.

## Psychotherapy

The most evidence based psychotherapy for PTSD is Cognitive Behavioral Therapy (CBT) which is effective in treating both acute and chronic PTSD following a range of traumatic experiences in adults, children and adolescents, across many cultures [24]. Particular types of CBT that are indicated for PTSD are Prolonged Exposure Therapy (PE) [25] and Cognitive Processing Therapy (CPT) [26]. Supportive psychotherapy and Eye Movement Desensitization and Reprocessing (EMDR),have also benefited some individuals who do not wish to pursue CBT,PE or CPT[27]. Significant benefits could also be attained from trauma-focused psychotherapy which include components of CPT, PE, and imaginal exposure [28]. Non-trauma-focused treatments aim to reduce PTSD symptoms, but not by directly targeting thoughts, memories and feelings related to the traumatic event. Examples of non-trauma-focused treatments include relaxation, stress inoculation training (SIT) and interpersonal therapy [28]. Some beneficial effects in reducing the intensity of PTSD although not evidence based could also be achieved from patient education, psychodynamic therapy, acceptance and commitment therapy, dialectical behavior therapy ,hypnosis, group therapy and family therapy[29] .The cognitive deficits that are secondary to TBI can impede optimal response to PTSD recommended psychotherapies thus requiring the introduction and implementation of additional techniques that minimizes reliance on executive cognitive processes. Modifications may include the provision of detailed homework exercises, assisting with focused attention during exposure exercises, simplifying cognitive therapy techniques, and ensuring that all therapy tasks are written in a format that can enhance adherence to treatment tasks between sessions[30].

## Psychopharmacology

The evidence base for pharmacological interventions in co-occurring PTSD and TBI still remains scarce [31]. Until more randomized controlled trials are conducted to determine the most effective interventions in providing symptomatic relief , general treatment principles have been recommended and include : (1) To conduct a comprehensive treatment approach with special consideration of the immediate presenting psychosocial needs; (2) To obtain and confirm diagnostic accuracy and initiate one pharmacological intervention at a time; (3)Always starting with the lowest doses due to side-effects sensitivity in patients with TBI; and (4) Considering longer treatment duration to determine efficacy , prior to switching to other pharmacological agents [32]. Based on clinical experience, the following pharmacotherapeutic approaches may be beneficial: (1) standard approaches in using antidepressants; (2) anticonvulsants for treating mood disorders, impulsive anger, irritability and aggression, although they may exacerbate cognitive deficits; (3) very low dose antipsychotics in the treatment of psychotic symptoms; and (4) anxiolytics could be used with the exception of benzodiazepines which should be avoided due to their adverse cognitive effects, potential for addiction and risk of accidental or intentional overdose especially when combined with other sedative hypnotics, opioids or alcohol [32,33]. The selective serotonin reuptake inhibitors (SSRIs) are recommended as first-line medications for the treatment of PTSD and may have additional beneficial effects on treating the co-occurrence of PTSD with depression, anxiety and panic disorders [13]. The SSRIs are also recommended as first-line choice in treating depression associated with TBI [34].The serotonin norepinephrine reuptake inhibitors (SNRIs) such as venlafaxine or duloxetine can also be considered for treatment of PTSD and mTBI [35].If patients do not respond to either SSRIs or SNRIs, other pharmacological agents that can be used for the treatment of PTSD and mTBI as suggested by the Veterans Affairs and Defense Departments (VA/DOD) and are summarized in table 3 [36].

**Table 3: Pharmacotherapy of PTSD and mTBI**

| Medications | Initial dose | Dose range | Clinical considerations |
|---|---|---|---|
| **Monotherapy** | | | |
| Sertraline1,2 | 25–50 mg daily | 50–200 mg daily | Start low, go slow. |
| Paroxetine1,2 | 10–20 mg daily | 20–50 mg daily | Use: prazosin – nightmares; trazodone/ mirtazapine – insomnia;<br>buspirone/hydroxyzine – anxiety; bupropion – lack of motivation or concentration |
| Fluoxetine2 | 10–20 mg daily | 20–80 mg daily | Stimulants are not recommended for mTBI and can worsen arousal<br>symptoms of PTSD |
| Venlafaxine3 | SA (XR):37.5 mg daily | SA (XR): 75–225 mg daily | Combining TCAs with other serotonergic agents (SSRIs, SNRIs,<br>trazodone, triptans) can precipitate serotonin syndrome |
| Augmentation4 | | | High dose trazodone or hydroxyzine can worsen fatigue and/or concentration. |
| Prazosin | 1 mg bedtime | 1–15 mg bedtime | Titrate prazosin slowly; can cause dizziness |
| Trazodone | 25–50 mg bedtime | 50–100 mg bedtime | Bupropion increases risk of seizure |
| Mirtazapine | 7.5–15 mg bedtime | 15–45 mg bedtime | Antidepressants and stimulants can precipitate mania in bipolar disorder |
| Buspirone | 5 mg BID | 30–60 mg in 2 or 3 divided doses | VA/DOD Evidence-based guidelines recommend against benzodiazepines |
| Hydroxyzine | 25 mg 1–4 times a day PRN anxiety | 50–100 mg 1–4 times a day PRN anxiety | Caution is advised for use of medications in pregnancy and lactation. |
| Bupropion | 150 mg daily | IR: 150–450 mg in 2 or 3 divided doses<br>SR: 150 mg BID<br>XR: 300 mg daily | Side Effects of SSRIs and SNRIs: Nausea, headache, diarrhea, anxiety,<br>nervousness, sexual dysfunction, agitation, dizziness, and hyponatremia<br>or SIADH. High dosage of venlafaxine can increase blood pressure |

*Abbreviations:1 .FDA approved for PTSD ,2.SSRI,3.SNRI,4.If lack or partial response after 6 weeks of treatment adherence with adequate dosing ,then augmentation would be recommended.*

Current available evidence suggests that the pharmacological treatment of PTSD in patients with mTBI could be implemented by using the same medications that are recommended for PTSD alone. Many of the medication side effects relevant to TBI are also relevant to PTSD, although the risk of certain side effects may be especially concerning in patients with co-occurring PTSD and TBI, and thus requiring vigilant and consistent monitoring by clinicians due to the potential of medication side effects in increasing risk of TBI-associated problems, such as cognitive deficits, sensory and balance issues, and seizures [13, 37, 38].

## Summary

The co-occurrence of PTSD with TBI and especially mTBI pause a clinical challenge in the context of accurately diagnose and effectively treat both conditions due to the overlap of their symptoms spectrum .It is important for clinicians caring for these individuals to identify the effects of PTSD on TBI and vice versa. The implementation of a comprehensive integrated treatment that combine psychotherapy and psychopharmacology to address PTSD and mTBI each on its own merits while focusing on the uniqueness of their similar clinical presentations could eventually lead to improvement and symptomatic relief for patients who are afflicted by these potentially disabling conditions. This review attempted to clarify the different and yet similar aspects of PTSD and mTBI and summarized some of the effective treatments that would decrease and reverse PTSD and mTBI multiple overlapping and interacting symptoms.. Research is still needed to determine the clinical effectiveness of treatments that were designed for either PTSD or mTBI but not particularly evidence based or recommended for individuals with co-occurring PTSD and mTBI.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## Conflicts of Interests

No conflicts of interests. The materials described in this article are

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