Traumatic Brain Injury
Case Study and Commentary, Andrew G. Rees, MD

ABSTRACT

- **Objective:** To review the diagnosis and management of traumatic brain injury (TBI) from the psychiatrist’s point of view.
- **Methods:** Review of the literature.
- **Results:** TBI is defined broadly as a physical or mechanical injury to the brain that results in temporary or permanent impairment of brain function. The nature and severity of impairments following TBI depend upon a number of factors, including the patient’s age at the time of the injury, the pattern and severity of injury, and the amount of time that has elapsed since the initial trauma, among others. The consequences of brain injury can be divided broadly into cognitive, physical, and emotional/behavioral manifestations, each of which may have profound psychosocial implications. Treatment of TBI may require a multidisciplinary approach involving physical, occupational, speech, and recreational therapy, as well as cognitive and vocational rehabilitation. Psychiatric care may involve cognitive and behavioral therapies, individual, group, and family therapy, and pharmacotherapy.
- **Conclusion:** TBI is common and imposes a significant burden on individuals, families, and society. Effective treatment often requires a multidisciplinary approach that accounts for the spectrum of physical, emotional, psychological, and social consequences.

An estimated 1.7 million cases of traumatic brain injury (TBI) occur annually in the United States [1]. The great majority (about 75%) of these injuries are classified as mild [2]. Approximately 80,000 to 90,000 patients experience the onset of long-term TBI-related disability each year, and the direct and indirect annual costs of TBI in the United States were an estimated $60 billion in 2000 [2,3]. Nationally, most TBIs occur as the result of falls (35.2%), with the highest rates in this category among the very young (aged 0–4) and the elderly (aged 75 and older) [1]. Other common causes include motor-vehicle trauma (17.3%), unintentionally being struck by or against an object or another person (16.5%), and assaults (10%) [1].

Age-groups most likely overall to sustain a TBI are very young children (aged 0–4), older adolescents (aged 15–19), and the elderly (aged 65 and older) [1]. The highest rates of emergency department visits related to TBI are seen among the very young (aged 0–4) and older adolescents (aged 15–19), while the hospitalization and death rates for TBI-related injuries in the general population are, as might be expected, highest among the elderly (aged 75 and older) [1]. Gender is also an important risk factor, as TBI rates for males are higher than for females among all age-groups [1], although incidence rates among active-duty females serving in the military may approximate rates among civilian males [4].

Military personnel on active duty, even during peacetime, are generally at higher risk than civilians [4]. Among the more than 2 million troops in the U.S. military who have been deployed to Iraq or Afghanistan since 2001, explosions or blast injuries, such as those caused by improvised explosive devices (IEDs), have been the most common cause of wounding [5–7]. Of the blast-exposed patients treated at Walter Reed Army Medical Center as of 2006, nearly 60% were found to have an associated TBI [8]. This predominance of blast injuries, in addition to the use of Kevlar helmets which decrease the likelihood of penetrating head trauma, may help to explain why closed brain injuries have been more common in the Iraq and Afghanistan conflicts [6,9].

Substance abuse is also a major risk factor for TBI. This is particularly true for alcohol, as alcohol intoxication has been reported in up to 50% or more of all TBI patients and is commonly associated with motor-vehicle-related and other types of trauma [10]. Substance use may also be associated with intentional TBI, such as assault [11]. Impulsivity and related risk-taking behaviors that may increase the risk of TBI are common in indi-

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viduals with a variety of psychiatric illnesses, including bipolar disorder, substance use disorders, attention deficit/hyperactivity disorder (ADHD), conduct disorder, and cluster B personality disorders (e.g., borderline and antisocial) [12]. Other mental disorders, including delirium, dementia, depression, and psychosis, are also associated with a variety of symptoms that may increase the likelihood of TBI, such as cognitive deficits, agitation, and impaired judgment [13]. In addition to psychiatric illness, the use of psychotropic medications, such as antipsychotics, anxiolytics, and antidepressants, among others, may be another important risk factor for TBI [13]. Several studies have demonstrated, for example, a higher fall risk among elderly patients taking benzodiazepines [14].

Recent world events, including the armed conflicts in Iraq and Afghanistan, have led to increased emphasis on appropriate diagnosis and treatment of the short- and long-term consequences of TBI, as well as recognition of the difficulties inherent in differentiating TBI-related symptoms from primary psychiatric illness, including posttraumatic stress disorder (PTSD).

CASE STUDY

Initial Presentation

J is a 29-year-old male active-duty staff sergeant with no prior history of psychiatric illness and a past medical history of seasonal allergies (on fexofenadine) who presents following exposure to a blast from an improvised explosive device. The patient appears confused and distant but is able to answer questions, with a Glasgow Coma Scale score of 13.

History

The blast occurred approximately 1 hour previously while he was riding in the back seat of an up-armored vehicle; the blast destroyed the vehicle directly in front of him, killing 2 of his close friends, and jolted the vehicle in which he riding, causing his head to whip backward and forward and to strike the window behind him. He was not wearing his Kevlar helmet. A fellow soldier reported that the patient remained unconscious for 3 to 5 minutes after the blast. Upon questioning, the patient reports that he is experiencing occipital headache, nausea, dizziness, and difficulty concentrating.

Physical Examination

Physical examination reveals tachycardia and otherwise normal vital signs, posterior scalp hematoma and contusion and no neurologic deficits (aside from altered mental status). Noncontrast head CT was negative for skull fracture, intracranial hemorrhage, edema, or mass effect.

How is TBI defined and how is severity assessed?

TBI is defined broadly as a physical or mechanical injury to the brain that results in temporary or permanent impairment of brain function [15]. Individual injuries are grossly classified as either closed or open. Closed brain injuries are those that result from blunt-force trauma, the effects of acceleration/deceleration, or a combination of these mechanisms [16]. Open brain injuries involve the penetration of a foreign body into or through the cavity of the skull, thus exposing brain tissue to the external environment [16].

The severity of TBI is commonly graded clinically based upon initial score on the Glasgow Coma Scale (GCS) in concert with other clinical indicators. The GCS allows for rapid assessment of the patient’s level of consciousness and involves observations of eye opening, verbal response, and motor response (Table 1). GCS scores range from 3 to 15, and injury severity is classified as mild, moderate, or severe based upon the composite score (Table 2). In addition to the GCS, other indicators, such as the duration of loss of consciousness (LOC), and the duration of posttraumatic amnesia (PTA), an acute period of confusion following the injury which may involve retrograde as well as anterograde memory loss, have commonly been used to assess the severity of TBI [15,17,18]. Table 2 illustrates one approach to rating TBI severity, although other methods involving alternative indices have been developed for clinical use. For example, TBI that is defined as mild by GCS in the context of neuroimaging abnormalities has been referred to as “complicated mild TBI,” which is associated with cognitive sequelae akin to those experienced by patients with GCS-defined moderate TBI [17].

What is the pathophysiology of TBI?

Gross mechanisms of TBI can include abrupt acceleration or deceleration, blunt force injuries, or penetrating trauma. Specific injuries incurred are characterized as either primary or secondary. Primary injury is that which results
directly from the mechanical impact of the trauma [19]. Examples of primary injury include damage to the scalp or skull, contusions and lacerations, intracranial (eg, epidural, subdural, subarachnoid) and intracerebral (eg, parenchymal) hemorrhage, focal neurologic injury (eg, cranial nerves, hypothalamus, pituitary), and diffuse axonal as well as diffuse vascular injury [19,20].

Focally, the most common type of injury is contusion, which results from what are referred to as coup and contrecoup injuries [19]. Brain injury occurring at the site of cranial impact is referred to as the coup injury, and is typically maximal when a stationary head is struck by a moving object [21]. Contrecoup injury is that which occurs at the site opposite the point of cranial impact, and is usually maximal when a moving head impacts a stationary object [21]. Contusions are most commonly found in the orbitofrontal region and the tips of the temporal lobes, owing to the localization of these areas in relationship to the bony protuberances of the skull [22]. The most common type of diffuse injury is diffuse axonal injury, which results from rotational forces, and involves the twisting and shearing of white matter tracts throughout the brain [19,23].

Secondary injury occurs in the hours and days following the initial trauma and encompasses changes that occur at the molecular and cellular levels [24]. These changes are mediated through a neurochemical cascade of events (eg, formation of free radicals, changes in calcium ion homeostasis) that ultimately leads to further neuronal damage, necrosis, and apoptosis [24]. Raised intracranial pressure, which can result, for example, from intracranial hemorrhage or cerebral edema, may lead to further secondary injury, such as hypoperfusion and hypoxic-ischemic injury, tissue deformation, and herniation, which is often fatal [20].

Table 1. Glasgow Coma Scale

<table>
<thead>
<tr>
<th>Points</th>
<th>Eye Opening Response</th>
<th>Verbal Response</th>
<th>Motor Response</th>
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<tr>
<td>6</td>
<td></td>
<td></td>
<td>Obeys commands for movement</td>
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<tr>
<td>5</td>
<td>Spontaneous—open with blinking at baseline</td>
<td>Oriented</td>
<td>Purposeful movement to painful stimulus</td>
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<tr>
<td>4</td>
<td>To verbal stimuli, command, speech</td>
<td>Confused conversation, but able to answer questions</td>
<td>Withdraws in response to pain</td>
</tr>
<tr>
<td>3</td>
<td>To pain only (not applied to face)</td>
<td>Inappropriate words</td>
<td>Flexion in response to pain (decorticate posturing)</td>
</tr>
<tr>
<td>2</td>
<td>No response</td>
<td>Incomprehensible speech</td>
<td>Extension in response to pain (decerebrate posturing)</td>
</tr>
<tr>
<td>1</td>
<td>No response</td>
<td>No response</td>
<td>No response</td>
</tr>
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Adapted from Centers for Disease Control and Prevention. CDC Emergency Preparedness and Response website. Available at emergency.cdc.gov/masscasualties/pdf/glasgow-coma-scale.pdf.

In cases of moderate to severe injury, the diagnosis of TBI may be clinically or radiographically apparent. In milder cases, however, when medical personnel must rely upon patient history, certain symptoms may be under-reported by patients or missed by examiners (eg, amnesia, disorientation) [25]. Additionally, presenting symptoms may overlap sufficiently with psychiatric symptoms (eg, acute stress disorder) that brain injury may not be considered [25]. In conjunction with history and physical examination, which should include complete neurologic and mental status evaluations, various screening tests, such as the Standardized Assessment of Concussion (SAC) and, in military settings, the Military Acute Concussion Evaluation (MACE), may be useful in cases involving possible or suspected TBI [25].

The initial imaging modality of choice in patients presenting with TBI is a noncontrast computed tomography (CT) scan [26]. This includes patients with penetrating brain injuries in whom a foreign body has penetrated the skull [27]. A head CT, which may reveal intracranial bleeding or skull fracture, allows the treating provider rapidly to determine, for example, whether...
medical or surgical management is the most appropriate course of action [26]. Following stabilization, the preferred method for evaluating the full extent of brain injury is magnetic resonance imaging (MRI), which, in terms of detecting neuronal damage, generally has greater sensitivity than a CT scan, and commonly detects abnormalities missed on CT [27]. MRI is contraindicated, of course, in patients with penetrating trauma in whom ferromagnetic metal may be present [27]. The value and expediency of these studies notwithstanding, it should be noted that CT and MRI in most patients with mild TBI do not show any abnormality, despite clinical evidence of potentially long-term neurocognitive impairments in a subset of these patients [27–29].

In addition to structural imaging, which is paramount in triaging and defining acute care, regular electroencephalography (EEG) should be performed in all cases of suspected seizure activity; in particular, sleep EEG is far more likely than waking EEG to show an abnormality [30]. Functional imaging studies, such as positron emission tomography, single-photon emission computed tomography, functional MRI, and magnetic resonance spectroscopy, have found an important role in identifying the pathophysiologic mechanisms of neuronal injury, as well as in evaluating the effectiveness of various interventions, including experimental therapies [27,31]. Additionally, electrophysiologic studies, such as EEG and the measurement of evoked potentials, may have utility in prognosticating functional outcomes [32].

For the practicing psychiatrist, specific diagnostic challenges encountered clinically may include the differentiation of TBI-related symptoms from primary psychiatric illness, such as depression and PTSD, as well as the assessment of TBI-related symptom severity. Ascertaining symptom etiology may be particularly challenging in cases of mild TBI, which constitute the majority of brain-injured patients. A comprehensive psychiatric evaluation involving sensitive exploration of the traumatic event should include specific questioning to detect comorbid PTSD or other psychiatric illnesses. Data-gathering via self-report questionnaires, such as the Rivermead Post-Concussion Symptoms Questionnaire (RPQ), may be helpful for documenting and tracking the progression of symptoms [33]. Additionally, baseline and subsequent Folstein Mini-Mental State Exams (MMSE) may be useful as an indicator of global cognitive function over time, although, of note, the MMSE is not generally considered to be an adequate screening tool to detect mild TBI-related cognitive impairment [17]. In addition to a thorough psychiatric assessment, referral for neuropsychological testing to evaluate cognitive impairment and functioning in a variety of realms, including attention, concentration, memory, executive functioning, reaction time, and information processing, may be useful in assessing the nature and severity of self-reported symptoms and observed impairments, as well as for monitoring their longitudinal course over time [29,34]. Some authors have recommended formal neuropsychological testing for mild-TBI patients who continue to be symptomatic more than 6 weeks following their injury [35]. There are a variety of tests available, although there are no clear data to demonstrate, in general, which particular test is better or best [35]. Psychological tests, such as the Minnesota Multiphasic Personality Inventory-2 (MMPI-2) and MMPI-2-RF (Restructured Form), may help to assess emotional and personality-related symptoms. In cases where secondary financial or other personal gain might be suspected to impact symptom reporting (eg, pending litigation), there are several neuropsychological tests available which are specifically designed to detect malingering, such as the Test of Memory Malingering (TOMM), the Victoria Symptom Validity Test (VSVT), and the Rey 15-Item Memory Test [36]. Table 3 lists specific diagnoses found in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR), which may be appropriate for brain-injured patients [37].

Table 2. Severity of Traumatic Brain Injury with Respect to Glasgow Coma Scale (GCS), Loss of Consciousness (LOC), and Posttraumatic Amnesia (PTA)

<table>
<thead>
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<th>Severity</th>
<th>Initial GCS</th>
<th>LOC</th>
<th>PTA</th>
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<tr>
<td>Mild</td>
<td>13–15</td>
<td>≥ 30 min</td>
<td>0–1 day</td>
</tr>
<tr>
<td>Moderate</td>
<td>9–12</td>
<td>&gt; 30 min</td>
<td>&gt; 1 and &lt; 7 days</td>
</tr>
<tr>
<td>Severe</td>
<td>3–8</td>
<td>&gt; 24 hr</td>
<td>&gt; 7 days</td>
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The patient is closely monitored for any changes in his mental state, which improves over the next several hours, and for any new or worsening symptoms that could suggest deterioration in his clinical status. He is diagnosed with mild TBI, and receives standard medical care, including rest from all activities, and is prescribed acetaminophen for headaches. Both the patient and his military commander are educated verbally and in written format regarding his condition and also the need for continued rest and duty restrictions until cleared by medical personnel. The patient reluctantly agrees to speak with the chaplain for supportive counseling regarding the deaths of his friends.

FOLLOW-UP

A few weeks later, the patient reports that his prior symptoms of headache, nausea, and dizziness have resolved. He reports that mild difficulty concentrating has persisted since the recent incident. Physical exam reveals no neurologic abnormalities. His physician queries him regarding his emotional adjustment in the wake of recent events, though the patient insists that he is doing “fine” and has no other complaints.

Four months after the incident, at the urging of his wife, who states he has been irritable, “jumpy,” and aloof, the patient presents to a psychiatrist and reports trouble focusing at work and difficulty sleeping due to nightmares. Clinical interviewing, including exploration of other possible posttraumatic or postconcussive symptoms and collateral history obtained from the patient’s spouse, reveals persistent intrusive (albeit piecemeal) memories of the period of time surrounding the trauma, including nightmares and nighttime awakenings, hypervigilance, avoidance of trauma-related stimuli, and profound feelings of guilt and self-blame regarding the deaths of his friends, as well as memory difficulty. Score on Mini-Mental State Exam was 28/30 (2/3 on 3-object recall, and difficulty spelling WORLD backwards). Neuropsychological testing revealed mild impairment in attention and concentration and no other cognitive deficits.

The nature and severity of impairments following TBI depend upon a number of factors, including the patient’s age at the time of the injury, the pattern and severity of injury, and the amount of time that has elapsed since the initial trauma, among others [38]. The complex of symptoms commonly reported following mild TBI has been referred to as the postconcussive syndrome (PCS), although similar symptoms can also occur with moderate and severe TBI [17]. The consequences of brain injury often manifest in a variety of realms (Table 4); post-TBI impairments can be divided broadly into cognitive, physical, and emotional/behavioral manifestations, each of which may have profound psychosocial implications [22,39].

COGNITIVE SYMPTOMS

Subsequent to the initial period of coma or LOC that may follow brain trauma, patients may experience both cognitive and behavioral abnormalities, including disorientation and confusion, as well as agitation or other changes in psychomotor activity; both retrograde and anterograde amnesia may be associated with this period, which has been referred to as a form of posttraumatic delirium [22]. Following the acute confusional state, or PTA, a number of cognitive deficits have been noted to persist following TBI, including impairments in memory, attention, concentration, and executive function [40]. Among these deficits, memory loss is the most commonly reported by patients, and may be verbal as well as nonverbal [19]. Neuropsychological testing tends to reveal impairment of episodic or declarative memory and relative sparing of procedural memory [19]. Executive dysfunction, which may, in particular, be overlooked by clinicians, is common and may include deficits in...
routine tasks such as planning, organizing, sequencing, and abstraction [19]. Cognitive changes are most prominent immediately following the injury, and, in cases of mild TBI, will generally resolve over a period of 3 to 6 months, although in some cases may persist for much longer [39,40]. Both focal and diffuse cortical damage may produce cognitive impairment, the severity of which depends upon the location, size, and degree of injury and the duration of PTA, among other variables [19].

While it is the physical symptoms of TBI that may be the most troubling immediately following the injury, cognitive deficits can be among the most persistent and disabling, and may be of such severity as to limit basic functioning, including the patient’s ability to care for themselves, drive a vehicle, or maintain employment [38]. In milder cases involving more subtle cognitive changes, certain circumstances, such as a very demanding vocation, may lead some patients to be more aware of their impairments, and, hence, more likely to report them [40].

As similar types of cognitive deficits are commonly observed with multiple psychiatric and physical conditions which are frequently comorbid with TBI, including anxiety, depression, chronic pain (eg, headaches), and sleep disturbances, care should be taken in identifying the appropriate etiology [40]. Depressed individuals, for example, often manifest impairments in concentration, memory, and executive function [40]. In this regard, even neuropsychological testing, though useful in assessing and monitoring the nature and severity of symptoms, generally lacks diagnostic specificity, and should be considered in the context of the overall clinical picture [40].

**PHYSICAL SYMPTOMS**

Physical symptoms most commonly reported following mild TBI include fatigue, headaches, sleep disturbance, and dizziness or vertigo [41]. In more severe cases, significant neurologic impairment may be present, including motor or sensory abnormalities, difficulties with speech, language, or swallowing, gait disturbance, and sexual dysfunction [42,43]. Cranial nerve injuries associated with TBI may result in a range of deficits, such as loss of or alteration in olfaction or, less commonly, hearing or vision [15]. Physical complications of TBI may also include gastrointestinal (eg, hepatic dysfunction), genitourinary (eg, incontinence), cardiovascular (eg, hypertension), neuro-endocrine (eg, hypopituitarism, SIADH, serum glucose changes), and other types of abnormalities [42].

Seizures, which may occur at the time of or up to years following the initial injury, are an important potential physical complication of TBI, and their occurrence has been shown to have a significantly negative impact on functional outcome [44]. Following a closed brain injury, the incidence of posttraumatic seizures is an estimated 5%; following open brain injuries, they are extremely common, occurring in up to half of this group.
Affective/Behavioral Symptoms

Neurologically mediated emotional, behavioral, and cognitive changes that occur in the wake of TBI might be described by family and friends as “personality changes.” Irritability, anger, verbal or physical aggressiveness, disinhibition, and emotional lability are common, and, in association with various cognitive impairments, may result from damage to frontotemporal regions (e.g., in cases of moderate to severe brain injury) in a pattern of symptoms sometimes therefore referred to as a “frontal or temporal lobe” syndrome [19]. Apathy is also commonly observed, may occur with or without depressive symptoms, and can significantly impact the outcome of rehabilitation [45]. Psychiatric illness in general, including mood and anxiety-spectrum as well as psychotic disorders, plays a central role in the morbidity of TBI [19].

Mood disorders occur more often following TBI than in the general population, with an estimated frequency of major depression at around 25% to 50%, 15% to 30% for dysthymia, and an estimated 9% for mania [46]. Affective lability in general is common, with an approximate prevalence of 11% during the first year following the injury [17]. A past history of psychiatric illness has been shown to be a risk factor for depression following TBI, although the physiologic mechanism of depression in the injured brain may be related to neuronal disruption in the frontal-subcortical white matter or basal ganglia [22]. Patients with left-hemispheric lesions of the dorsolateral frontal lobe and basal ganglia are more likely to develop major depression [22]. Mania, with its associated alterations in sleep, mood, and activation, occurs less commonly than depression, although far more frequently following TBI than in the general population, and is often observed in patients with limbic lesions of the right hemisphere [22].

Every type of anxiety-spectrum disorder has been observed following TBI, including PTSD, generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, and phobic disorders [22]. Anxiety disorders are more commonly associated with right-hemispheric lesions [22]. PTSD, a frequent psychiatric complication of traumatic injury in general, and its precursor, acute stress disorder (ASD), may present with symptoms similar to those of TBI, such as difficulty concentrating, sleep problems, dissociative symptoms, and irritability, and differentiating symptom etiology may be challenging, particularly when the history is ambiguous [47,48]. Certain physical symptoms, such as nausea, vomiting, balance problems, and the immediate onset of headache, are more commonly associated with TBI, while nightmares and flashbacks may suggest ASD or PTSD, although the diagnoses are not mutually exclusive [25,49].

While relatively rare, psychosis has been observed following TBI, occurring at a rate higher than that observed in the general population [50]. Psychotic symptoms can occur early or late after the injury, and may manifest as a schizophrenia-like psychosis, with hallucinations, frank delusions, and illogical thinking [22,50]. The differential diagnosis of psychotic symptoms such as hallucinations and delusions should, of course, include the possibility of substance abuse, as well as various organic etiologies, including posttraumatic seizures [50]. In terms of the pathophysiology of psychosis, both hemispheres have been implicated [22]. Other psychiatric illnesses associated with TBI may include adjustment reactions, pain disorders, sleep disorders, and, as noted, personality changes, among others. Clinicians should also be aware that while the emotional sequelae of TBI may be the result of neuronal and glial-cell injury, they may also represent the individual's response to the psychosocial or other consequences of their injury, such as loss of functioning or pain.

• What are some important management considerations in TBI?

The initial management of TBI patients is focused on the preservation of vital cardiopulmonary and neurologic functions as well as identifying patients at risk for further deterioration. In addition to standard medical care (e.g., avoiding drugs known to be associated with bleeding risk, such as NSAIDs), which should include appropriate pain management, treatment of TBI may require a multidisciplinary approach involving physical, occupational, speech, and recreational therapy, as well as cognitive and vocational rehabilitation [22]. Psychiatric care may involve cognitive and behavioral therapies, individual, group, and family therapy, and pharmacotherapy [22].
Family Support and Education
For families and caregivers, there may be significant stressors associated with adapting to the changes in their loved one and providing care, including possible financial difficulties, social isolation, adjusting to role changes, and family relational difficulties [19]. Psychiatric illness, including depression and anxiety, is common among those providing care for TBI patients [19]. Families should receive the needed emotional support and should be provided with resources, such as contact information for national and local brain injury association centers, and access to psychiatric care [19].

Families and caregivers should also be educated about the symptoms and natural course of the illness, as well as necessary follow-up measures and safety precautions, which the patient may not accurately understand or retain, such as medication instructions, or the need to abstain from high-risk activities for a period of time.

Return to Activity
Fatal outcomes have occurred when even minor head trauma is experienced following the initial TBI [21]. This has been referred to as a “second-impact syndrome,” which may occur when a second or subsequent episode of head trauma is sustained prior to complete recovery from the previous head injury, resulting in an uncontrollable elevation in intracranial pressure secondary to diffuse cerebral edema, with consequent brain herniation and death [21]. For this reason, athletes, for example, should be completely asymptomatic for a period of time, in some cases weeks to months, before returning to play [21]. Neuropsychological testing may be helpful in this regard, as athletes may minimize their symptoms in order to return to the game [34]. While there are no universally agreed-upon criteria for determining when to allow patients to return to potentially higher-risk activities, such as certain sports, published guidelines from the American Academy of Neurology and other organizations are available [21]. Physical and cognitive activity should be limited in the recovery period, and patients with any persistent postconcussive symptoms or whose cognitive testing reveals persistent deficits should abstain from high-risk, high-speed activities [34]. Neuropsychological testing may be required for assessing potential risks prior to reengaging in activities for which cognitive abilities are paramount, such as independent living, work, school, and other activities [38]. For example, caution should be exercised in deciding when to allow a return to driving, particularly for patients with deficits in attention, reaction time, or processing speed [34].

Rehabilitation Training
Specific training techniques designed to help patients either restore or compensate for impaired cognitive function may be employed in the process of neurologic rehabilitation. Support exists for various forms of cognitive rehabilitation therapy (CRT) in addressing specific deficits following TBI in areas such as attention, memory, and functional communication [51]. For patients with postconcussive symptomatology, several cognitive techniques have been employed with varying degrees of success, including biofeedback, progressive muscle relaxation, and cognitive restructuring [52]. With regard to the latter, the maintenance of postconcussive symptoms has been associated with symptom attribution by patients, who may, at times, erroneously ascribe normally occurring symptoms to their brain injury as a result of a selective attention bias and heightened awareness of normal somatic events, which may arise from beliefs about the consequences of their injury [52]. Identifying and challenging specific dysfunctional thought patterns, as well as stress management techniques, behavioral training, and concrete goal-setting, have all been shown to be of benefit [52].

Pharmacotherapy Considerations
There is a dearth of randomized, double-blind, controlled medication trials in TBI patients [17]. While there are currently no FDA-approved pharmacologic treatments for managing the neuropsychiatric sequelae of TBI, several medications have been employed off-label for this purpose, based largely upon anecdotal or limited observational evidence or studies limited by small sample size and other variables [17]. For example, various treatments have been utilized off-label to address TBI-related cognitive impairments, such as decreased attention, memory, information processing speed and executive functioning, as well as the symptom of apathy [17,45,53]. Of course, the potential for adverse effects, such as propensity to alter the seizure threshold—a common theme among psychotropic medications in general—should be carefully considered prior to initiating any pharmacologic intervention. It is also important to note that much of the available evidence (which is limited) supporting pharmacologic options for TBI-related symptomatology is based upon patients with moderate to severe injury [53].
Benefits should outweigh risks, particularly as medication side effects in this population may worsen TBI-related symptoms or impede rehabilitation, and as some concerns may remit without intervention.

In terms of selecting appropriate antidepressant medication in this group of patients, important considerations include minimizing anticholinergic and sedative effects as well as lowering of the seizure threshold [54]. Selective serotonin reuptake inhibitors (SSRIs), which are likely to be better tolerated than tricyclic antidepressants (TCAs) or monoamine oxidase (MAO) inhibitors, may be useful in treating depression, affective lability, and irritability, as well as anxiety-spectrum disorders [17,55]. Due to their anticholinergic side effects, TCAs are generally not preferred in TBI, and have been associated with an increased incidence of seizures [17,22]. Bupropion is well known to be associated with a dose-related seizure risk, and, hence, may increase the likelihood of posttraumatic seizures. MAO inhibitors, with their propensity for severe drug-food interactions (e.g., hypertensive crisis), are also not preferred treatments, particularly in this population which may have cognitive impairments that undermine adherence to dietary restrictions [22]. While TBI is not considered an absolute contraindication for electroconvulsive therapy (ECT) and this modality may be considered if other treatment methods are unsuccessful, the propensity for cognitive toxicity must be considered; furthermore, relative contraindications associated with TBI which may substantially increase risks may be present and warrant medical consultation (e.g., with neurology or neuro-surgery) [53,54].

Valproate, lithium, and carbamazepine have all been employed in the management of secondary mania, although each is associated with specific risks [54]. For example, lithium, in addition to lowering the seizure threshold, has been associated with impairment of cognitive performance in this group of patients [54]; moreover, patients with preexisting brain injury are also more predisposed to lithium toxicity at a given dose [54,56]. Various pharmacotherapies, including β-blockers, SSRIs, buspirone, and mood stabilizers, are potentially useful in the management of aggression after TBI, and trazadone may be helpful for insomnia and agitation [22,53].

Antipsychotic use, if deemed necessary, should be undertaken with particular caution, as there are several potential problems with these medications in the brain-injured population [50]. TBI patients commonly have impairments in motor function and gait that may be worsened (even fatally) by the psychomotor slowing and extrapyramidal symptoms (e.g., parkinsonism) associated with antipsychotic agents; additionally, the sedative, anticholinergic, and antihistaminic properties of these drugs can exacerbate cognitive deficits [50]. The use of highly anticholinergic agents (e.g., chlorpromazine, thioridizine) should be avoided [57]. Typical neuroleptics (e.g., haloperidol) may decrease synaptic plasticity, and have been found to inhibit recovery following TBI [43,50]. Furthermore, brain-injured patients may be particularly sensitive to sedation, orthostasis, and extrapyramidal effects, and may be more likely to develop tardive dyskinesia [50,58]. TBI has also been suggested as a risk factor for the development of neuroleptic malignant syndrome [57]. Clozapine, in addition to being highly anticholinergic, poses a well-known and significant seizure risk. Benzodiazepines, which can impair memory, concentration, and motor skills, in addition to their potential to worsen disinhibition, have also been shown to inhibit recovery and, like antipsychotics, should be avoided [19,43].

Finally, it is worth noting that several studies have demonstrated an association between SSRIs and bleeding risk, particularly gastrointestinal bleeding [59]. A recent case-control study found that antidepressants as well as antipsychotic medications may increase the risk of intracranial bleeding [59]. A recent case-crossover study suggested that antidepressants may be associated with increased risk of stroke, noting also that antidepressants with high inhibition of the serotonin transporter were associated with greater risk than other types of antidepressants [60]. Further research may help to clarify the clinical significance of these types of findings in the management of patients with TBI.

Despite the paucity of well-designed pharmacologic studies in this population, evidence-based guidelines are available, such as those proposed by the Neurobehavioral Guidelines Working Group [53]. Furthermore, certain general principles of pharmacotherapy have been observed in patients with TBI. This population has been noted, for example, to be more sensitive in general to medication side effects, and particularly so with psychotropic medications, suggesting the prudence of “starting low and going slow,” as well as close and careful monitoring [43]. Also implied is the prudence of minimizing polypharmacy and targeting as many symptoms as possible with the fewest medications. As the symptoms of TBI are generally expected to improve with time and treatment, the tapering off of psychotropic medications to determine therapeutic necessity should be considered [43].
Indications, risks, and benefits of medication use should be clearly explained and discussed with the patient, family members, and caregivers. Patients should also be counseled to abstain from alcohol during the recovery period.

The high incidence of TBI in troops returning from overseas combat in recent years has prompted further research into additional management options, including nonpharmacologic interventions such as hyperbaric oxygen and acupuncture. For instance, the Department of Defense is currently conducting clinical research on hyperbaric oxygen in the treatment of persistent post-concussive symptoms following mild TBI. A toll-free hotline (1-877-445-3199) is available for those seeking further information [61].

CASE CONTINUED

The patient was diagnosed with PTSD and started on sertraline and a low dose of prazosin for nightmares, which was subsequently discontinued due to dizziness and changed to trazodone for insomnia. He and his spouse were educated regarding his diagnosis and the patient was referred to a psychologist for weekly individual and group therapies, with significant reduction in his symptoms as reflected by self-report and a 36-point decrease on the PTSD Checklist (military version) over the next 6 months. He also reported gradual resolution of concentration and memory problems, excellent functioning in his job as a vehicle mechanic, and improvement in his marital relationship.

• What is the prognosis in patients with TBI?

Multiple studies have demonstrated that the majority of patients with mild TBI report complete recovery at 3 months following their injury [62]. Nevertheless, 1 year after the injury, up to 15% continue to report symptoms [39]. Several variables, such as comorbid psychiatric conditions, substance use, social support (or lack thereof), potential for secondary gain, and others, may impact symptom recovery and prognosis. Among other factors, recurrent concussions may be linked to slower recovery of neurologic function, and in some cases repetitive trauma may result in a chronic encephalopathy termed dementia pugilistica [63,64]. Other variables influencing outcome following TBI in general include severity and mechanism of injury, with penetrating injuries typically portending a worse prognosis, as well as the patient’s age and gender, with elderly patients and females tending to fare less well [65]. Several studies have, with some limitations, demonstrated GCS scores to have a degree of predictive value in terms of early morbidity and mortality as well as subsequent functional outcomes, such as return to employment [18]. Nevertheless, LOC and PTA have been found by multiple investigations to be superior to GCS in terms of predicting functional status [18]. Data obtained through the use of MRI may also have potential in terms of predicting long-term neurologic outcomes [66]. One MRI technique in particular, diffusion tensor imaging, is able to reveal damage to long white-matter tracts, and relates to prognosis [67].

Genetics may also play a role in terms of prognosis [65]. The ε4 allele of apolipoprotein E, which is associated with Alzheimer’s disease, may predispose to poor outcome following TBI [65]. An increase in the deposition of beta-amyloid peptides after TBI has been observed, and an increased risk for developing dementia, including Alzheimer’s disease, has been suggested, even many years after the initial trauma [54,68,69].

Patients, parents, and caregivers should be educated regarding appropriate prevention strategies to minimize the likelihood of TBI occurring. The reader is referred to the Centers for Disease Control and Prevention’s (CDC) informational booklet entitled, Heads Up: Facts for Physicians About Mild Traumatic Brain Injury, which reviews age-appropriate primary prevention strategies, and is available online at the CDC’s website (www.cdc.gov) [34].

CONCLUSION

TBI is common and imposes a significant burden on individuals, families, and society. Effective treatment often requires a multidisciplinary approach that accounts for the spectrum of physical, emotional, psychological, and social consequences. There is a need for researchers and clinicians to continue to work collaboratively toward the development of improved algorithms for understanding and treating TBI. Familiarity with basic diagnostic and therapeutic strategies will assist the practicing psychiatrist in effectively caring for civilian as well as military patients and families whose lives have been impacted by this condition.

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REFERENCES


