ACLP How To Guide: Traumatic Brain Injury

How to recognize and treat psychiatric symptoms of Traumatic Brain Injury (TBI)

Learning Objectives:

1) Understand clinical presentations of TBI
2) Apply appropriate interview and diagnostic tools for diagnosis of TBI
3) Apply management strategies for patients with neuropsychiatric symptoms of TBI.

Step 1: Recognizing and evaluating clinical presentations of TBI

- DSM-5-TR definition of TBI: An impact to the head or other mechanism of rapid movement/displacement of the brain, with one or more of the following: loss of consciousness, post-traumatic amnesia, disorientation/confusion, or focal neurological deficits. The deficits must also be present immediately after the trauma or after recovery of consciousness.[1]
- Post-concussive syndrome (PCS): symptoms of TBI persisting for more than three months.[2]

Table 1. Categorization of TBI Severity

Categorization of TBI Severity[a,b]

Characteristic	Mild	Moderate	Severe
Structural imaging	Normal[c]	Normal or abnormal	Normal or abnormal
Loss of consciousness	0–30 min	>30 min and <24 h	>24 h
Alteration of consciousness/mental status[d]	Up to 24 h	> 24 h, severity based on other criteria	
Posttraumatic amnesia	0–1 d	>1 d and <7 d	>7 d
Glasgow Coma Scale (best available score in first 24 h)[e]	13–15	9–12	<9

[a]Based on VA/DoD Clinical Practice Guideline for the Management and Rehabilitation of Post-Acute Mild Traumatic Brain Injury, version 3.0, June 2021.[11]
[b]If a patient meets criteria in more than 1 category of severity, the higher level is assigned.
[c]No clinically relevant findings.
[d]Alteration of mental status must be immediately related to head trauma. Typical symptoms include looking and feeling dazed and uncertain about what is happening, confusion, difficulty thinking clearly or responding appropriately to mental status questions, and/or being unable to describe events immediately before or after the traumatic injury.
[e]In April 2015, the DoD released a memorandum against the use of Glasgow Coma Scale scores to diagnose TBI.
Abbreviations: DoD = Department of Defense, TBI = traumatic brain injury, VA = Veterans Administration.

Matta SE, LaCroix C, Walterfang M, et al. Traumatic brain injuries: manifestations, evaluation, management, and outcomes. *Prim Care Companion CNS Disord*. 2024;26(3):23f03667.[2]

Pathophysiology:

- Primary injury is caused by mechanical trauma, which can lead to edema/hemorrhage, resulting in compression of CNS tissue and inhibiting its proper function.[3]
- Secondary injury is due to subsequent intracellular changes that result in widespread degeneration of neurons and glia (taking place over hours or days).[3]

Etiology and epidemiology:

- 40-56% of TBI cases in adults include alcohol as a contributing factor.[4]
- 15 to 25-year-old men and elderly adults are at greatest risk for TBI.[5]
- Those with housing insecurity and minoritized women (particularly African American and Indigenous patients) are at increased risk of TBI from interpersonal violence. Both populations have also been found to experience poorer functional outcomes following TBI.[6,7]
- Service members experience a higher prevalence of blast exposures following deployments to the Middle East.[5]

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- Odds of experiencing a TBI may be higher in individuals with lower educational attainment and low income.[8]
- Black patients are less likely to receive access to appropriate rehabilitation services for TBI compared to White patients.[9]
- Individuals with low income and without health insurance are less likely to receive indicated inpatient rehabilitation services.[10-13]

Table 2. Symptoms/Presentation of TBI

Cognitive	Impaired attention, concentration, and memory
Neuropsychiatric	Anxiety, fear, stress response, PTSD, depression, aggression and irritability, mood swings/lability, impulsivity
Physical Symptoms	Headache, dizziness, vertigo, phonophobia, new visual disturbances, seizures, pain, fatigue out of proportion to sleep quality, tinnitus
Insomnia	Primary or secondary (sleep apnea, RLS, PTSD/nightmares)

Step 2: Formulate a differential diagnosis

- Consider the timeline of the patient's history. If symptom onset is connected in time to a head injury, then they may be secondary to TBI, though if the symptoms predated the injury than they may be due to comorbid disorders.
- Patients with recent TBI may present to the hospital days to weeks later for vague psychiatric/neurologic symptoms without vocalizing concern for TBI or PCS.
- Identify prior treated and untreated head injuries, as TBI can have a multiplicative effect.[4]
- Be aware of potential for misattribution of background symptoms to TBI due to symptom overlap with other physical and psychiatric changes.[14] A clear history and understanding of comorbidities can help minimize this.

Table 3. Differential Diagnosis

Metabolic: hypoglycemia, electrolyte disturbance **Infectious:** encephalitis, neurosyphilis, HIV, prion disease **Structural:** Intracranial hemorrhage, acute TBI, subacute TBI/PCS, stroke **Toxins:** Substance use disorders, substance intoxication or withdrawal, medication overdose, medication side effect (i.e. irritability, affective blunting, akathisia, etc.)	**Psychiatric:** acute stress disorder, PTSD, adjustment disorder, major depression, MDD with psychotic features, anxiety disorders, new personality changes/disorders, new psychosis **Neuropsychiatric:** Mild/major neurocognitive disorder (consider multiple etiologies, including traumatic brain injury) **Sleep disorders:** pre-existing obstructive sleep apnea (OSA), new OSA, central sleep apnea, sleep-related hypoventilation, circadian rhythm sleep-wake d/o

Step 3: Treat acute/subacute psychiatric symptoms of TBI

- "Start low and go slow" when titrating medications. Brain-injured patients are often more sensitive to certain medications and their side effects.[4]

- Consider medication burden that may cloud the clinical picture (e.g., lithium, anticholinergics, opioids, dissociatives such as ketamine, other anesthetic agents, or sedative-hypnotics).[15]
- Treat pre-existing psychiatric illness by restarting medications when medically appropriate.
- Restore high-quality sleep and consider delirium precautions.
- Pharmacologic management varies across published research, yielding imperfect comparisons within the literature. **Table 4** is a summation of treatment options studied for various symptoms of TBI.

Table 4. Treatment Options for TBI

<table>
<tr>
<td>Agitation/impulsivity/aggression (acute)
Avoid benzodiazepines and HPAs if possible[16]
LPA alternatives can be considered[16]
Methylphenidate[17]
Olanzapine: can consider low doses (5-10mg PO/IV PRN)</td>
<td>Agitation/impulsivity/aggression (subacute)
Amantadine, propranolol or pindolol, antidepressants, buspirone, or beta-blockers[16,17,23]
Valproic acid[18]
Quetiapine[23] (or other LPAs)</td>
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<tr>
<td rowspan="2">Mood/depression
Citalopram, fluoxetine, sertraline[2,4]
Methylphenidate: 10-40 mg PO daily (consider split dosing); 60mg/day max dosing.[4,17,21]
S-Adenosylmethionine (SAMe): 400-800mg PO BID; over-the-counter supplement. Improvements in depression, treatment resistant depression, pain, fatigue, attention, and cognition.[22]</td>
<td>Short-term memory
Donepezil
Citicoline (CDP-choline)[25]</td>
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<tr>
<td>Comorbid Acute Stress or Post Traumatic Stress Disorder (PTSD)
Paroxetine, sertraline, venlafaxine[29]
CPT, EMDR, PE[29]</td>
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<td rowspan="4">Reduced attention, concentration, processing speed
Methylphenidate[4,21,26]
Vortioxetine[18,27]
Donepezil: 5-10 mg PO daily. In small trial for moderate to severe TBI, has shown benefit in improving short term memory and sustained attention.[18]
Amantadine: Improvements included decreased fatigue, decreased distractibility, increased arousal level, increased attention and concentration, sequencing skill, processing time.[28]
SAMe[22]
Citicoline (CDP-choline): Potential benefit for memory and brain function after TBI. Accelerated cerebral edema reabsorption, contributing to shorter hospital length of stay.[25]</td>
<td>Fatigue (out of proportion to sleep quality)
Methylphenidate[4,21]
Amantadine[28]
SAMe[22]</td>
</tr>
<tr>
<td>Sleep disturbance
Melatonin[18], Ramelteon. Melatonin associated with improved sleep efficiency and decreased anxiety and fatigue.[18]
CBT[30], CBTi[31]</td>
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<tr>
<td>Pain
Maximize non-pharm interventions
Minimize opiates when possible
SAMe[22]</td>
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<tr>
<td>Pathological laughter/crying (pseudobulbar affect)
Dextromethorphan and quinidine[18]</td>
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Table 4: LPA: low potency antipsychotic (D_2 antagonism); HPA: high potency antipsychotic (D_2 antagonism); CPT: cognitive processing therapy; EMDR: Eye Movement Desensitization and Reprocessing; PE: prolonged exposure

Medications to use with caution or with no evidence-based benefit in TBI:

- Benzodiazepines can contribute to patient confusion.[15]

- Haloperidol (High potency D_2 receptor antagonist): A systematic review recommends AGAINST using haloperidol and benzodiazepines in acute agitation following TBI due to observed negative outcomes and reduced recovery of TBI-induced deficits.[16]
- Lithium: Neurotoxicity may develop at higher rates in patients with TBI.[4]
- Methylphenidate (pre-synaptic dopamine and norepinephrine re-uptake inhibition): Studied for attention, fatigue, and depression in mild TBI (mTBI).[21] Consider hx of HTN, cigarette smoking, obesity, other cardiac risk factors, family hx of MI.[18] May lower seizure threshold.[18] Paradoxical dysphoria, agitation, and paranoia may be seen in a brain-injured patient.[4] Consider potential for misuse.

Step 4: Provide education and follow-up

- Prognosis:
  - Most patients who experience mTBI recover without sequelae, though a significant minority report symptoms for months to years.[2]
  - Survivors of moderate-severe TBI will likely experience long-term deficits. However, many resume work and activities of independence, such as driving.[2]
  - Total deficits more strongly correlate with the duration of post-traumatic amnesia (including time in coma) than with initial Glasgow Coma Scale scoring.[5]
- Establish outpatient psychiatry follow-up, if indicated.
  - Individuals with TBI and comorbid psychiatric symptoms have worse cognitive outcomes compared to those without psychiatric symptoms.[2]
  - Preexisting and post-injury depression are predictors of poorer functional and health-related quality of life.[19,20,32]
- Neuropsychiatric assessment may differentiate cognitive deficits related to TBI from those associated with preexisting psychiatric conditions. Not recommended within 30 days of TBI.[2,4]
- Complications and sequelae:
  - Survivors of severe TBI are 18 times more likely to experience complications due to binge drinking.[5]
  - History of mild, moderate, or severe TBI is associated with higher risk of hypertension, stroke, and diabetes.[33]
  - Quality of life can be optimized by utilizing physical and occupational therapies, yoga, meditation, and mindfulness.[34]
- Psychoeducation is invaluable to patients and families because people with TBI can often look normal. However, they may develop changes in their personality and/or cognitive function that could be difficult for others to understand.[35]
- Support groups, such as The Brain Injury Association for America, can be beneficial for civilians. Resources through the Veterans Affairs and the Department of Defense are available for military veterans.

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