Traumatic Brain Injury

CHAPTER 17

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Definition and Aetiology

Traumatic brain injury (TBI) is “caused by a bump, blow, or jolt to the head, or penetrating head injury” that disrupts the normal function of the brain[1]. Various systems have been used to classify severity of TBI based on various measures including the duration of the loss of consciousness[2] and initial Glasgow Coma Scores (GCS). Classifications of “mild” to “severe” based on injury characteristics do not necessarily correspond to “mild” or “severe” outcomes and there will be a group of those with “mild” TBI who experience serious and debilitating neuropsychiatric symptoms longer term.

Injury characteristics	Mild TBI	Moderate TBI	Severe TBI
LOC	≤ 30 min	30 min – 24 hrs	≥ 24 hrs
PTA[a]	≤ 24 hrs	24 hrs – 7 days	≥ 7 days
Initial GCS	13 – 15[b]	9 - 12	3 - 8

Table 1: Severity classification of traumatic brain injury (TBI)
a Includes alteration of consciousness (e.g., confusion or disorientation) b Not < 13 at 30 min GCS, Glasgow Coma Scale; LOC, loss of consciousness; PTA, posttraumatic amnesia

Epidemiology

TBI around the world is common, with an estimated lifetime prevalence in the general population of mild TBI of 40% and of moderate-severe TBI of around 3%[3,4]. Around 2% of the UK population present to emergency annually with a head injury[5] and it is the leading cause of death in those under 40 years of age. Risk factors for TBI include male gender, low socioeconomic status, substance use disorder (particularly alcohol), homelessness, and prior TBIs[6,7,8]. The age distribution for TBIs is bimodal with highest rates seen in young children/adolescents and those over the age of 60[6].

Pathophysiology

TBI pathophysiology includes both primary and secondary brain injury. The primary injury happens at the time of the trauma, resulting in damage which may be FOCAL, such as epidural haematoma, subdural haematoma, subarachnoid haemorrhage, brain contusions or intracerebral haemorrhages; or DIFFUSE, such as with diffuse axonal injury (DAI). Direct force to the head (i.e. strikes, penetration or blasts) as well as rapid acceleration/deceleration (coup-contracoup injury) may cause such injuries. The secondary injury occurs in the hours to days and weeks following the injury in the molecular cascade and physical effects (e.g. pressure, infections, seizures) following the injury. The mechanisms involved in this secondary injury include neuroinflammation, mitochondrial dysfunction, oxidative stress, excitotoxicity, and neuronal apoptosis or cell death (Figure 1).

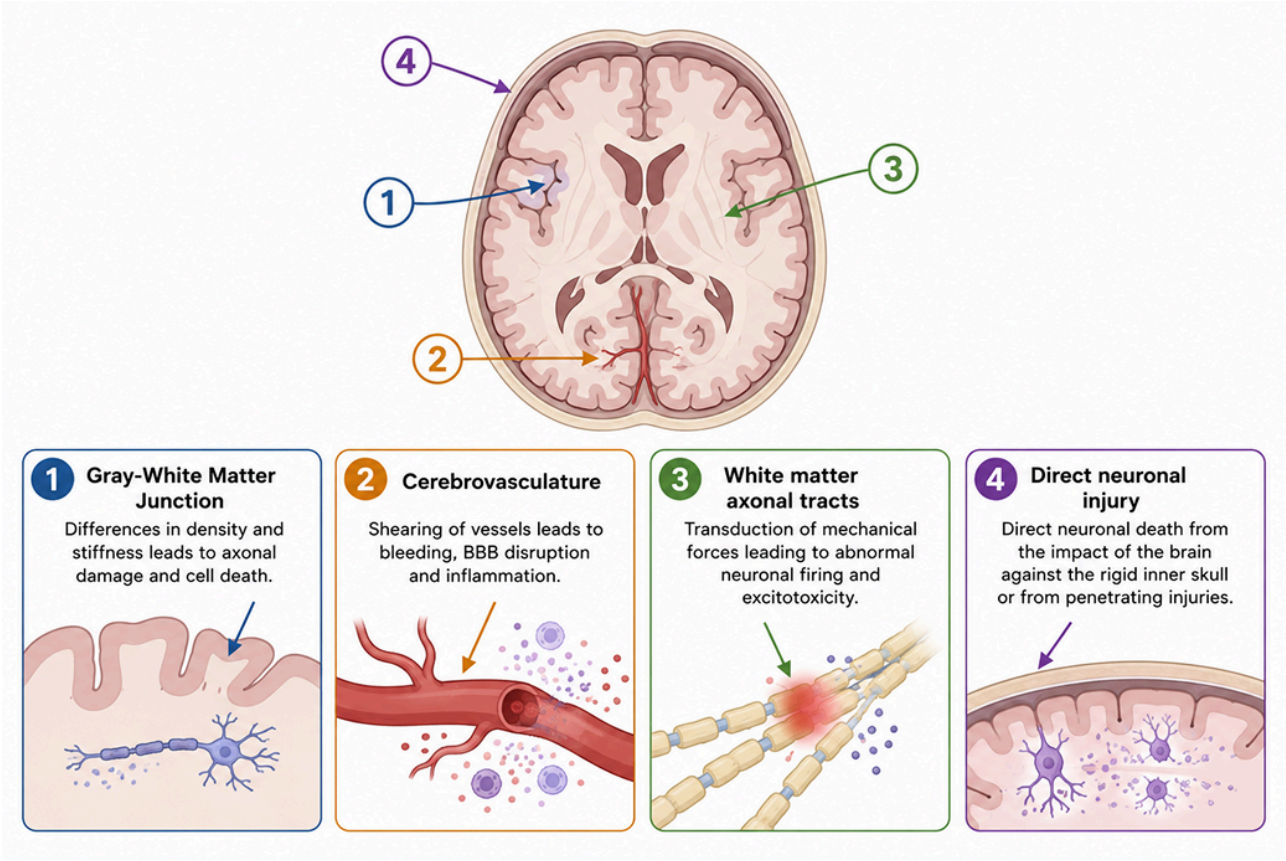


Figure 1: Mechanisms of Traumatic Brain Injury[9]

Presentation and Course of Illness

The most common initial / early presenting symptoms following a TBI include (mnemonic: **HAD A MIS**):

- **H**eadache,
- **A**ffective disturbance,
- **D**izziness,
- **A**pathy,
- **M**emory or attention impairment,
- **I**rritability and
- **S**leep disturbance/fatigue.

Other symptoms can include nausea, blurry vision, and balance difficulties. For the majority of patients with mild TBI these symptoms will resolve rapidly within 7 – 10 days post injury, however symptoms may persist with some functional impairment in 10 - 33% of patients at 3 months and 22% at 1 year[10,11]. For cognitive deficits, once in the chronic post-TBI phase of the illness (i.e. 1 year post-injury) they tend to remain stable or fixed and are not associated with a more rapid rate of decline[3,12–14] (Figure 2).

Other longer-term consequences of TBI include neurological and psychiatric conditions including: seizures (which may be epileptic or non-epileptic), pituitary dysfunction, anxiety disorders, post-traumatic stress disorder, personality changes (aggression, impulsivity and apathy), substance use disorders, post-traumatic psychosis and rarely pseudobulbar affect (PBA) or pathological laughter and crying.

There are a range of pre-injury factors associated with worse outcomes including older age, female sex, developmental factors, poor pre-injury cognitive function, limited coping strategies and low socioeconomic status[15,16]. Perpetuating, post-injury factors linked to worse cognitive function include repetitive TBI, comorbid psychiatric symptoms, difficulties with role adjustments, and legal proceedings (Figure 3).

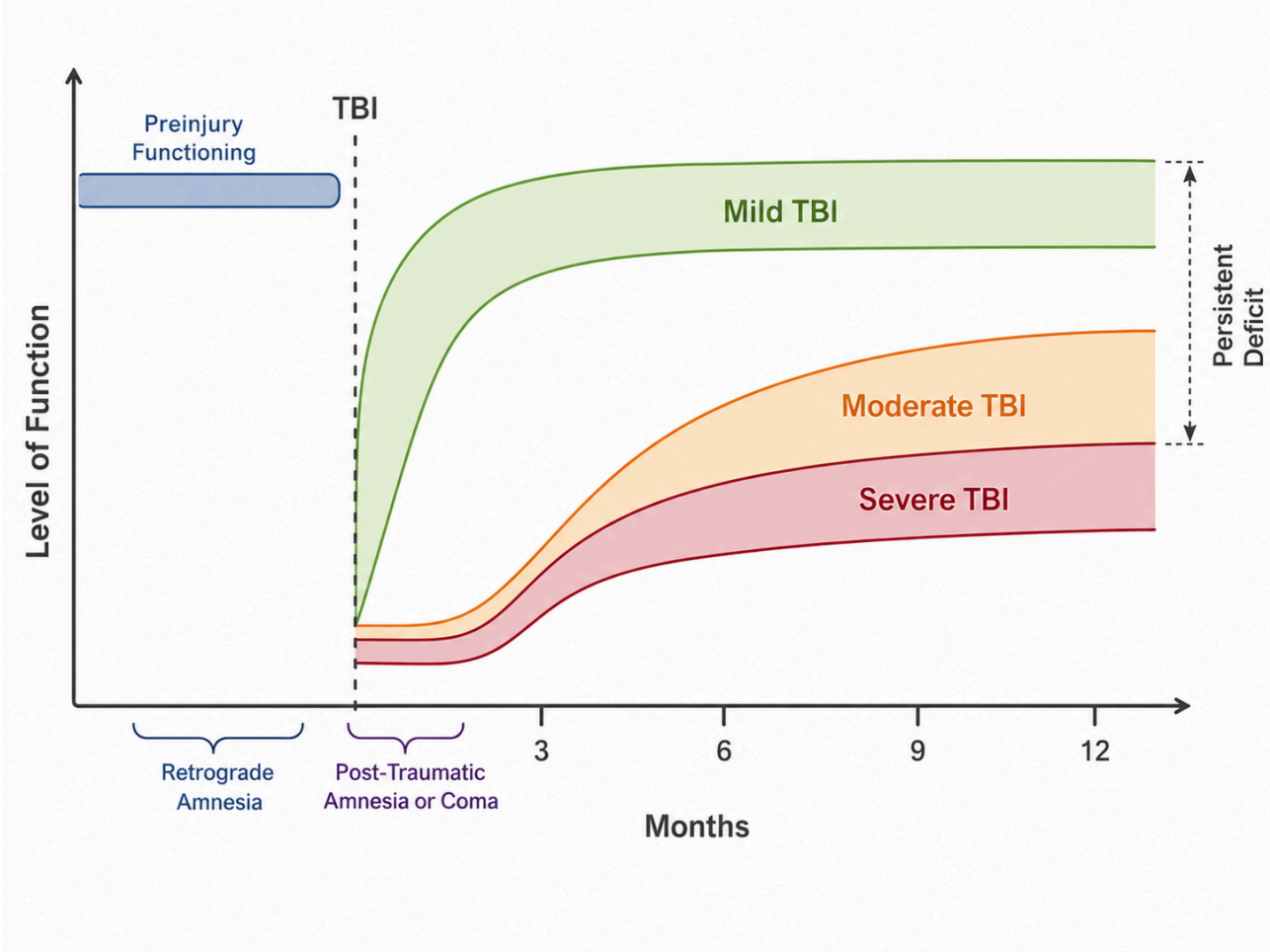


Figure 2: Changes in level of function over time following Traumatic Brain Injury; (TBI). There is an initial severe loss of function followed by a rapid recovery which gradually plateaus generally leaving a degree of persistent deficit.

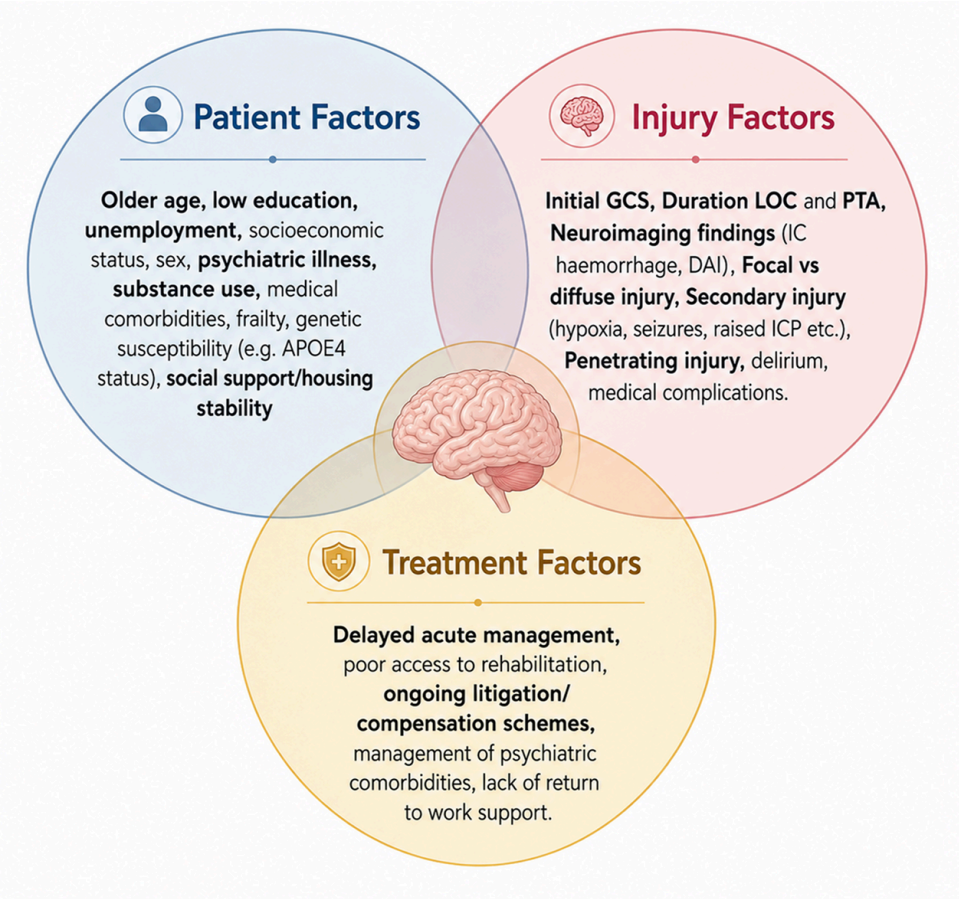


Figure 3: Patient factors, injury factors, and treatment factors that predict worse outcomes following a TBI. More important or significant factors are in bold. GCS – Glasgow Coma Scale; LOC – Loss of Consciousness; PTA – Post-Traumatic Amnesia; DAI – Diffuse Axonal Injury; ICP – Intracranial Pressure.

Assessment and Diagnosis

The core of the assessment of a post-TBI patient is a through history and neurological examination, paying attention to the pre-injury risk factors, pre-TBI events and severity, and early post TBI course. Neurological examination findings may include vision changes like reduced visual acuity, unexplained numbness, weakness, or tremors, and difficulty with speech or balance. Other red flags for TBI complications are seizures, gait disturbance, and abnormal
reflexes. More commonly however, patients will report ongoing cognitive and psychiatric problems which need to be well characterised and given targeted treatment.

Table 2: DSM-V Criteria for Major and Mild Neurocognitive disorder Following TBI

DSM-V Criteria for Neurocognitive Disorder Following TBI
1. **Criterion A** - The criteria are met for major or mild neurocognitive disorder

Criterion B - There is evidence of a traumatic brain injury—that is, an impact to the head or other mechanisms of rapid movement or displacement of the brain within the skull, with one or more of the following:

1. Loss of consciousness.
2. Posttraumatic amnesia.
3. Disorientation and confusion.
4. Neurological signs (e.g. - neuroimaging demonstrating injury; a new onset of seizures; a marked worsening of a preexisting seizure disorder; visual field cuts; anosmia (loss of smell); hemiparesis).

Criterion C - The neurocognitive disorder presents immediately after the occurrence of the traumatic brain injury or immediately after recovery of consciousness and persists past the acute post-injury period.

Investigations

Specific blood tests including serum GFAP, S100B, and nerve specific enolase, are approved in some jurisdictions to guide further imaging investigations and prognosis but are not routine in most parts of the world[17]. In the acute phase of the injury Brain computed tomography (CT) is normally used to assess for any intracranial bleeds or skull fractures (See Figure 4). However, for the neuropsychiatrist Magnetic Resonance Imaging (MRI) will be more sensitive to detecting subtler changes associated with poor TBI outcomes, including cerebral contusions, diffuse axonal injury (Figure 5) and changes to the white matter that may suggest deeper axonal damage. Imaging findings suggestive of repetitive or severe neurotrauma include generalised atrophy (particularly in the frontal and temporal lobes), reduced volumes in the hippocampi and thalami, enlarged ventricles (particularly 3rd ventricle) and cavum septum pellucidum (Figure 6)[18]. For the majority of cases (mild to moderate TBI), brain imaging findings are either non-specific or absent, and serve only to rule out a focal lesion.

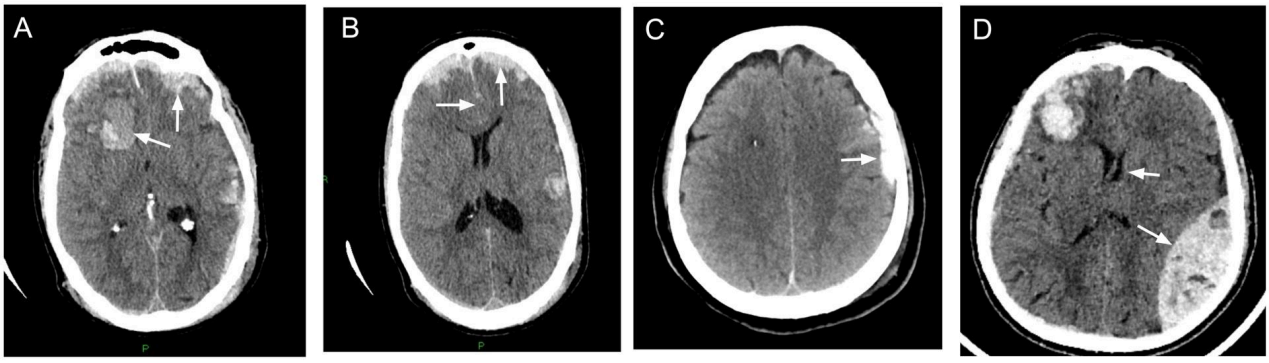


Figure 4: Non-contrast CT scans showing types of intracranial bleeds following Traumatic Brain Injury (TBI). Images taken with permission from Radiopaedia.org. **A** – 60 yo M post TBI with arrows showing R frontal lobe intracerebral bleed and mixture of subdural and subarachnoid bleeding **B** – Same case as A with arrows showing midline shift and again the subdural and subarachnoid blood. (Case courtesy of Derek Smith – Full scan at radiopaedia.org/cases/multiple-cerebral-contusions-and-temporal-bone-fracture) **C** – 75 yo F post-TBI with stable L subdural haematoma. (Case courtesy of Henry Knipe – Full scan at radiopaedia.org/cases/traumatic-intracranial-haemorrhage-with-intracranial-pressure-monitor) **D** - 75 yo F with extradural haematoma, midline shift and evident countracoup cerebral contusion in the R frontal/temporal lobe (Case courtesy of Emma Gevorgyan – Full scan at radiopaedia.org/cases/traumatic-brain-injury-8)

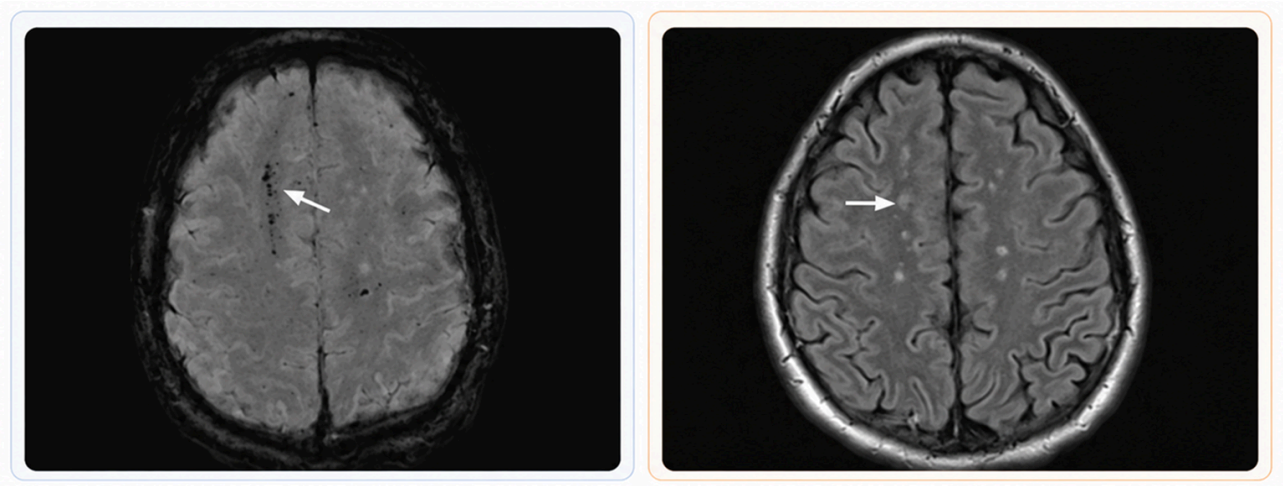


Figure 5: MRI scan of 25-year-old male with 2 weeks of post-traumatic amnesia and mixed neurological symptoms. **A** – Susceptibility Weighted Image (SWI) showing blooming associated with microhaemorrhages from Diffuse Axonal Injury (DAI) **B** – Same case with T2-FLAIR showing White Matter Hyperintensities corresponding with the DAI associated microhaemorrhages evident on SWI.(Case courtesy of Henry Knipe – Full scan available at radiopaedia.org/cases/diffuse-axonal-injury-grade-2-1)

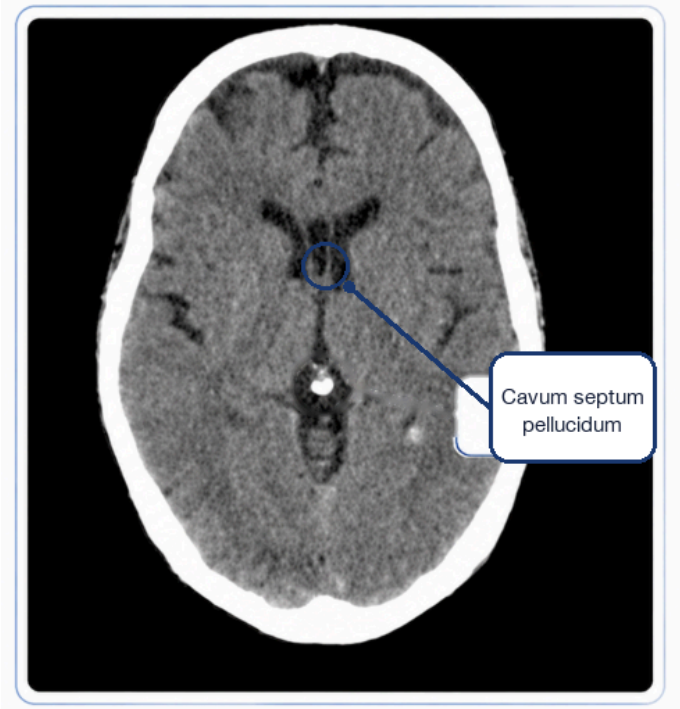


Figure 6: Cavum Septum pellucidum (Septum pellucidum with a cave) also sometimes referred to as the 5th Ventricle. This image is taken with permission from Radiopaedia.org Case courtesy of David Puyó Vera - Full scan at https://radiopaedia.org/cases/cavum-septum-pellucidum-2.

Neuropsychological findings

Formal neuropsychological testing will not be required for the majority of post-TBI patients given that most will recover within days to weeks of the injury. For those with ongoing symptoms (> 4 weeks) neuropsychological testing can help characterise and document the cognitive deficit severity and domains affected. The most common domains affected include episodic memory, executive function, processing speed, attention, and working memory[19–21], whereas procedural memory and

language tend to be more preserved. Memory deficits are more pronounced in recall rather than recognition tasks, indicating that the memory deficits are secondary to the executive problems in memory acquisition and retrieval[22]. The key domain deficits generally relate to the location and pattern of injury (e.g. DAI, affecting white matter tracts, associated with executive dysfunction and processing speed).

Generally, non-specialist clinicians will start with a neuropsychological screening test (e.g. Montreal Cognitive Assessment (MOCA), Frontal Assessment Battery (FAB), or Addenbrookes Cognitive Examination (ACE)). If needed specialised neuropsychological testing will explore each relevant domain in more detail[23], also providing tests for symptom validity (e.g. the Test of Memory Malingering (TOMM))[24] and ratings for depression and anxiety as possible confounders (e.g. Depression, Anxiety and Stress Scale (DASS)). Importantly, the findings of the neuropsychological testing can assist in the development of patient-specific cognitive retraining, behavioural techniques, family and patient psychoeducation, as well as psychotherapy that are all important parts of remedial therapy. Ultimately if a medico-legal claim is included in the outcome, testing will support this too.

Neuropsychiatric aspects of post-TBI treatment

Post-TBI or postconcussive syndrome (PCS) includes a range of neuropsychiatric symptoms including behavioural, affective, cognitive and somatic[25]**.** Treatment targets need to be individually defined based on the patient symptom profiles. First-line treatments for the management of TBI symptoms are non-pharmacological. In the first instance supported active recovery, that is graded physical exercise and cognitive activation in the acute post TBI phase, has been shown to reduce recovery times and improve longer term outcomes superseding previous guidelines recommending “brain rest”[26]. In the acute phase, reassurance is important, emphasising that most symptoms resolve within the first three months. For those with longer standing TBI symptoms (>3 months), treatment should be given early and with a multidisciplinary, rehabilitative approach. The non-pharmacological strategies include psychoeducation, patient and family support groups, psychobehavioural interventions (e.g. mindfulness-based stress reduction, behavioural activation and problem solving therapy), cognitive remediation training, compensatory strategies (e.g. carrying a notebook or regularly diarising) and metacognitive training (e.g. self-prediction and evaluation). Psychotherapies including Cognitive Behavioural Therapy and Acceptance and Commitment therapy have both been adapted to treat depression in those with TBI[27].

Where non-pharmacological treatments are ineffective or insufficient to manage the severity of the post-TBI symptoms, symptom-targeted medications can be considered. All treatments should be considered with the caveat that there are no approved treatments for neuropsychiatric disorders in TBI and there are only few randomised clinical trials to help guide pharmacological treatment. Treatments with supporting evidence are summarised in Table 3. There have been three small trials (n = 29, 51 and 32)[26] of methylphenidate in patients with post-TBI symptoms (in the cognitive / behavioural domains) that have variously found that it significantly improved fatigue, attention, cognitive processing speed, post-concussive symptoms and social functioning generally.

For those with depression, the most evidence has accumulated for sertraline and citalopram, with small trials finding that over 10-weeks the treatment groups had significantly higher response and remission rates compared to placebo groups[28]. Given the lack of evidence for management of

neuropsychiatric symptoms in those post-TBI, clinical practice generally follows guidelines for management of those symptoms in the general population (i.e. pharmacological guidelines for depression, agitation, mood lability, psychosis, epilepsy etc.)

Medication	Class	Target Symptom	Usual dosages (adult)
Methylphenidate	Stimulant	Cognitive Deficits, mental fog and fatigue	5–20 mg, 2–3 times/day
Amantadine	Dopamine Agonist	Cognitive Deficits	100–300 mg, 2 times/day
Galantamine	AchE inhibitor	Cognitive Deficits	4–8 mg, 2 times/day
Donepezil	AchE inhibitor	Cognitive Deficits inc. memory and attention	5–10 mg daily
Sertraline	SSRI	Depression/Anxiety	50–200 mg daily
Citalopram	SSRI	Depression/Anxiety	20–40 mg daily
Bupropion	NDRI	Depression/Anxiety	200–300 mg daily
Venlafaxine	SNRI	Depression/Anxiety	75–225 mg daily, divided into 2 or 3 doses
Valproate	Mood Stabilisers	Aggression/Agitation	200 – 1000 mg, divided into 2 doses
Propranolol	Beta/Alpha Blocker	Aggression/Agitation	40 – 240 mg, divided in 3 doses
Olanzapine	Antipsychotic	Aggression/Agitation	2.5 – 20 mg daily or divided into 2 doses

Table 3: Pharmacological management of the neuropsychiatric aspects of post-TBI syndrome. AchE – Acetylcholineserase; SSRI – Selective Serotonin Reuptake Inhibitor; NDRI – Noradrenaline-Dopamine Reuptake Inhibitor; SNRI – Serotonin-Noradrenaline Reuptake Inhibitor. [26,29]

Chapter Summary

Definition & Classification: TBI is caused by an external force to the head; severity is classified using duration of loss of consciousness, post-traumatic amnesia, and initial Glasgow Coma Scale scores.

Epidemiology: Mild TBI has a lifetime prevalence of ~40% and moderate–severe TBI ~3%; highest incidence occurs in young people and older adults, with risk factors including male sex, low SES, substance use, homelessness, and prior TBIs.

Primary vs Secondary Injury: Primary injury occurs at impact and includes haematomas, contusions, and diffuse axonal injury; secondary injury evolves over hours to weeks through mechanisms such as neuroinflammation, oxidative stress, mitochondrial dysfunction, excitotoxicity, and apoptosis.

Clinical Presentation: Common acute symptoms (HAD A MIS) include headache, affective changes, dizziness, apathy, memory/attention problems, irritability, and sleep disruption; most mild TBI symptoms resolve within 7–10 days, though 10–33% persist at 3 months.

Long-term Sequelae: Chronic effects may include cognitive deficits, post-traumatic seizures, psychiatric disorders (anxiety, PTSD, personality change), substance use, pituitary dysfunction, and rarely pathological laughter/crying.

Prognostic Factors: Worse outcomes are associated with older age, female sex, developmental and cognitive vulnerabilities, low SES, repetitive TBIs, comorbid psychiatric symptoms, poor coping, and legal/role adjustment difficulties.

Assessment & Diagnosis: Evaluation relies on detailed history and neurological exam; DSM-5 criteria identify major/mild neurocognitive disorder due to TBI when cognitive decline follows documented injury and persists beyond the acute phase.

Neuroimaging: CT is used acutely to detect bleeds or fractures; MRI is more sensitive for subtle findings like contusions, diffuse axonal injury, white-matter microstructural changes, and signs of repetitive trauma (atrophy, hippocampal/thalami volume loss, cavum septum pellucidum).

Neuropsychological Profile: Persistent symptoms (>4 weeks) warrant testing, which commonly reveals deficits in episodic memory, attention, executive function, processing speed, and working memory, while procedural memory and language are relatively preserved.

Management: First-line therapy is non-pharmacological—graded physical and cognitive activity, psychoeducation, psychotherapy (CBT, ACT), cognitive remediation, and compensatory strategies; medications may help specific symptoms (e.g., methylphenidate for fatigue/processing speed, SSRIs for depression), though no drugs are formally approved for TBI.

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