Traumatic Brain Injury: Severity, Pathophysiology and Neurobehavioural Outcome

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Summary

At least 1.4 million people die, or receive hospital or emergency care every year in the United States as a result of traumatic brain injury (TBI). Many more are treated in other settings or receive no treatment at all. Thus TBI is often unidentified, with subsequent cognitive, behavioral, emotional and physical sequelae that are not linked to the injury. Yet, over 5.3 million Americans live with TBI-related disabilities that interfere with their overall performance and social roles within the community. Traumatic brain injury is a leading cause of death and disability in developed countries. Damage caused by focal and diffuse lesions produces symptoms involving most major medical systems as well as symptoms of neuro-logical and psychological origin. Recent published articles on emotional and behavioural consequences of traumatic brain injury (TBI) are reviewed. The ranges of clinical problems reviewed include depression and anxiety, post-traumatic stress symptoms, as well as the TBI animal model.

Key words: Traumatic brain injury, behavioural outcome

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Introduction

Traumatic brain injury (TBI) is a leading cause of neurological disability across all age categories. TBI is not an event. It is a life-long disorder, occurring throughout the world in epidemic proportions. TBI is notorious for causing 'hidden disability', as many people who make an excellent physical recovery are left with a spectrum of cognitive or emotional problems that disable them [1]. Personality change, mania, anxiety, depression, sexual dysfunction, impulsivity, aggression, dementia, and schizophrenia-like psychosis can occur following a brain injury [2]. Each year, an estimated 1.5 million peoples sustain a TBI that requires hospitalization. As a result of these injuries, 80,000 to 90,000 patients experience long-term disability [3]. There is consensus that cognitive, emotional, and behavioral problems constitute the major source of disability for TBI patients. Effective interventions following TBI are lacking, and advancing the understanding of neuropathological changes that are triggered by TBI has the potential to reveal new therapeutic targets.

Mild, moderate and severe TBI

Head injuries can be classified into mild, moderate, and severe categories as shown in Table.1. The Glasgow Coma Scale (GCS), the most commonly used system for classifying TBI severity, grades a person's level of consciousness on a scale of 3–15 based on verbal, motor, and eye-opening reactions to stimuli. It is generally agreed that a TBI with a GCS of 13 or above is mild, 9–12 is moderate, and 8 or below is severe [4,5] similar systems exist for young children [5] . However, the GCS grading system has limited ability to predict outcomes. Because of this, other classification systems such as the one shown in the table are also used to help determine severity. A current model developed by the Department of Defense and Department of Veterans Affairs uses all three criteria of GCS after resuscitation, duration of post-traumatic amnesia (PTA), and loss of consciousness (LOC). It is important to stratify the severity of TBI, in order to focus clinical resources on those in greatest need, give more accurate predictions of outcome to patients and families, and make meaningful comparisons between TBI data banks. It is conventional to categorize TBI as mild, moderate, or severe on the basis of clinical data (especially the Glasgow Coma Scale score) and radiological data [6]. In most series, mild TBI accounts for around 80% of cases, with moderate and severe TBI being about 10% each. Even mild TBI can be followed by troublesome cognitive and affective sequelae [7] . The importance of this, of course, is that mild injury accounts for most cases of TBI. These disturbances can be pernicious in their long-term effects, and early intervention is recommended when affective or cognitive problems are identified in people with even a mild TBI.

Table.1. Severity of traumatic brain injury [4,5].

	GCS	PTA	LOC
Mild	13–15	<1 day	0-30 minutes
Moderate	9–12	>1 to <7 days	>30 min to <24 hours
Severe	3–8	>7 days	>24 hours

Symptoms of brain injury

A wide variety of symptoms can occur after "brain injury." The nature of the symptoms depends, in large part, on where the brain has been injured. Below mentioned is a list of possible physical and cognitive symptoms which can arise from damage to specific areas of the brain, as shown in Table.2.[8]

Table.2. TBI symptom specific to various areas of brain.

Frontal Lobe: Forehead
• Mood changes (Emotionally Labile). • Changes in social behavior. • Difficulty with problem solving.
Parietal Lobe: near the back and top of the head
• Difficulty with drawing objects. • Difficulty in distinguishing left from right. • Inability to focus visual attention. • Difficulties with eye and hand coordination.
Occipital Lobes: most posterior, at the back of the head
• Difficulty with locating objects in environment. • Difficulty with identifying colors (Color Agnosia). • Production of hallucinations. • Word blindness - inability to recognize words.
Temporal Lobes: side of head above ears
• Short term memory loss. • Increased and decreased interest in sexual behavior. • Inability to categorize objects (Categorization). • Increased aggressive behavior.
Brain Stem: deep within the brain
• Difficulty with organization/perception of the environment. • Problems with balance and movement. • Dizziness and nausea (Vertigo). • Sleeping difficulties (Insomnia, sleep apnea).
Cerebellum: base of the skull
• Loss of ability to walk. • Tremors. • Dizziness (Vertigo). • Slurred Speech (Scanning Speech).

Pathology of Traumatic Brain Injury

Primary injuries to the brain, suffered immediately after the injury, are of two major types: contusions/hemorrhages and axonal stretch/shearing. The contusions may be multiple, small, and even microscopic. They are usually immediately below the cortical surface. As the energy of the impact increases, the size and number of such lesions may grow, coalesce and ultimately form an intracerebral hematoma. Vascular injury may also occur at the junction of structures with different mechanical-elastic properties [9]. These types of lesions will give rise to more focal neurologic signs and symptoms. Diffuse axonal injury (DAI) is due to stretching and shearing of the axons. It is a common lesion of the white matter particularly in acceleration/deceleration injuries associated with rotation of the brain on its axis. Although radiographic findings may be limited to small punctate hemorrhages, white matter lesions and diffuse edema, DAI is one of the major causes of severe cognitive and motor deficits following a TBI [10]. DAI within the mesencephalic region is frequently the cause of coma following a TBI. In addition to the primary lesions, secondary processes will produce further damage to the brain. At the cellular level, there will be changes to the basic molecules of metabolism, mechanisms of the cellular response to injury, and to the quantities of certain molecules, such as oxygen free radicals and nitric oxide that may be injurious when in excess. The levels of neurotransmitters may also be changed. Excitatory amino acids such as glutamate and aspartate may occur in huge amounts after a brain injury, leading to over excitation and ultimately the death of neurons. Altered levels of acetylcholine, dopamine and serotonin can affect cognition and behaviour [11].

Behavioural Consequences of TBI

TBI and Depression Neurologic depression that occurs following organic brain insult, such as trauma or infection, differs from endogenous or idiopathic depression. Among human survivors of TBI, neurobehavioral disorders are among the most frequent long-term consequences. Such neurobehavioral changes may include cognitive or memory impairment, apathy, aggressiveness, and mood disorders. Depression has been shown to be a common sequela of TBI in both inpatient and outpatient populations[12].Although most studies have included a majority of patients with moderate to severe injuries, patients with mild injuries also appear to have an increased risk for depression after TBI[13]. Patients with TBI and subsequent depression have greater functional disability and post concussive symptoms and perceive their injury as more severe than do those without depression [14]. Behavioral problems, in particular agitation and aggression, are often comorbid with depression [15] and can occur in up to 70% of patients with TBI [16]. Depression is common after TBI and adversely influences the uptake of rehabilitation, psychosocial adjustment, and return to work. It is estimated that at least half of all people with TBI get depressed at some point during the first year, half of them severely and three-quarters of these are also anxious (which can make the depression last longer). This is twice the incidence of depression after orthopaedic trauma causing similar physical disability [17]. Depression can develop years after injury [18], and the early and late presentations can be different. It can also present in different ways, as other symptoms are also present. Major depression (lasting six months or more) is commoner when there is a history of psychiatric illness, substance abuse, or poor social functioning – factors that also tend to prolong a major depressive episode Although it is well known that anger and aggression are common problems among patients with TBI, they are typically associated with and recognized in patients with more severe injuries [18].

Depression post TBI seems to have its biological basis in altered patterns of release of the peptide transmitters that are important in excitatory brain circuitry, against a backdrop of other pathophysiological changes. Traumatic brain injury selectively affects prefrontal and anterior temporal structures and depression is associated with disruption of neural circuits that involve the prefrontal cortex, amygdala, hippocampus, basal ganglia, and thalamus [17]. It is more common with injuries to the right hemisphere, left basal ganglia, and dorsolateral frontal cortex [19], perhaps because these lesions trigger neurochemical responses that produce depression.

TBI and Anxiety Anxiety disorders occur in a significant proportion of patients with a TBI and frequently coexist with depressive disorders [20]. There is a significant degree of comorbidity between mood and anxiety disorders among patients with a TBI. For example, about two-thirds of patients in whom major depression develops also meet diagnostic criteria for generalized anxiety disorder. Posttraumatic stress disorder (PTSD) is another frequent psychiatric complication in patients with traumatic injuries [21]. Whether unconsciousness and posttraumatic amnesia associated with a TBI would preclude the onset of PTSD in patients who have had a life-threatening experience, such as a motor vehicle accident or physical assault, has been widely debated. In fact, PTSD has been described in patients with a TBI of different degrees of severity, even among those patients who have partial or fragmentary recollection of the contingencies of the traumatic episode [22,23] . Recently, Glaesser and colleagues [24] assessed the occurrence of PTSD in a group of 46 patients with a TBI who were admitted to an acute neuro-rehabilitation clinic. They concluded that a TBI and PTSD are not mutually exclusive. However, PTSD was unlikely to develop in victims of accidents if trauma had resulted in a prolonged period of unconsciousness. Bryant and colleagues [25] analyzed the relationship between resting heart rates at 1 week and 1 month following a severe TBI and a PTSD diagnosis assessed 6 months after the injury. In these trials, PTSD developed in 16 of 68 (23%) severely injured patients. Compared with patients in whom PTSD did not develop, the patients had significantly higher heart rates at 1 week but not at 1 month after trauma. These findings suggest that fear conditioning can occur independently of the level of awareness and contribute to the onset of PTSD. These investigators also reported that patients who had PTSD at 6 months following a severe TBI had significantly poorer functional and vocational outcomes than did patients who did not have PTSD [26].

TBI and Mania The spectrum of mood disorders attributable to traumatic brain injury (TBI) spans almost the entire spectrum of psychiatric disorders. Mania and hypomania have been reported in a number of medical conditions. Mania is uncommon after TBI. It may be due to the involvement of the aminergic limbic pathways, perhaps with aberrant regeneration patterns [27]. Diagnosis of mania following brain injury is based on DSM-IV criteria for mood disorder due to TBI with manic features or with mixed features. Predisposing factors for development of mania after TBI include damage to the basal region of right temporal lobe and right orbitofrontal cortex in patients who have family history of bipolar disorder [17].

TBI and Sleep disorders One of the very significant problems arising from TBI is that the biological rhythm of sleep is disrupted. A majority of victims of TBI express difficulty in sleeping, altered sleep pattern or need to sleep for an unusually long duration following injury. A recent study published in Chest [28] found that almost half of the TBI population can be expected to have a sleep disorder, with obstructive sleep apnea being the leading cause. A study by Merskey [29] found that 68% of TBI patients had disturbances of night time sleep. There was no relationship between the severity of initial injury and the prevalence of sleep disorder.

People suffering from Sleep Awake Cycle Disturbance (SWCD) have longer stays in both acute and rehabilitative settings and this may be a marker for more severe injury [28].

The problem with sleep deprivation is that it causes a decrease in cognitive ability and increase in irritability and in many other ways can give symptoms similar to those from TBI itself. If those TBI symptoms are already present, it can tend to aggravate them [6]. Therefore, patients who suspect problems in sleep need to get those problems addressed by referral to a specialist. This type of disorder needs to be determined and then a treatment plan enacted [27]. Lack of sleep is known to depress scores of neuropsychological tests batteries. Thus, someone in the grips of a terrible sleep pattern is going to show having possibly of more severe cognitive deficits than they actually have. Sleep depravation effects on other common psychological disturbances from TBI including depression and anxiety are known as well [28].

Animal models of Traumatic Brain Injury

Types of Animal Models TBI may be produced by the head impacting or coming into contact with an object (contact phenomena) or acceleration/deceleration forces producing vigorous movement of the brain (acceleration/deceleration or inertial phenomena), or varying combinations of these mechanical forces (Fig.3).

Impact acceleration models involve direct head impacts using a piston, humane stunner or captive bolt pistol, calibrated pendulum, or weight drop onto the skull. This focal mechanical loading causes deformation of the brain which, being almost incompressible, is particularly vulnerable to strain injury. These models resemble closed head injury in motor vehicle accidents or falls where there is rapid acceleration/deceleration of the head after impact to an intact skull, which sometimes fail to produce a highly repeatable injury [30-33] . *Inertial acceleration* models involve acceleration of the head without impact, unlike most human motor vehicle accident situations (Fig.2). Inertial acceleration devices generate a repeatable pathologic response, especially when the direction and distance of head movement is constrained. Angular acceleration, especially in the coronal plane, has been shown to be particularly injurious in nonhuman primates, and cats. In these models, the acceleration required to produce injury experimentally is found only in human TBI when head impact occurs [34,35] . *Direct brain deformation* models include both fluid percussion and rigid indentation types and uses either a fluid pulse or mechanically driven piston, respectively, to rapidly compress the exposed dura or cortex through a craniotomy site. These models produce well-controlled levels of localized injury rather than diffuse damage [36]. The complexity and diversity of TBI pathology will ensure a continuing role for animal models to define more accurately the cascade of morphologic and biochemical events occurring after a traumatic insult.

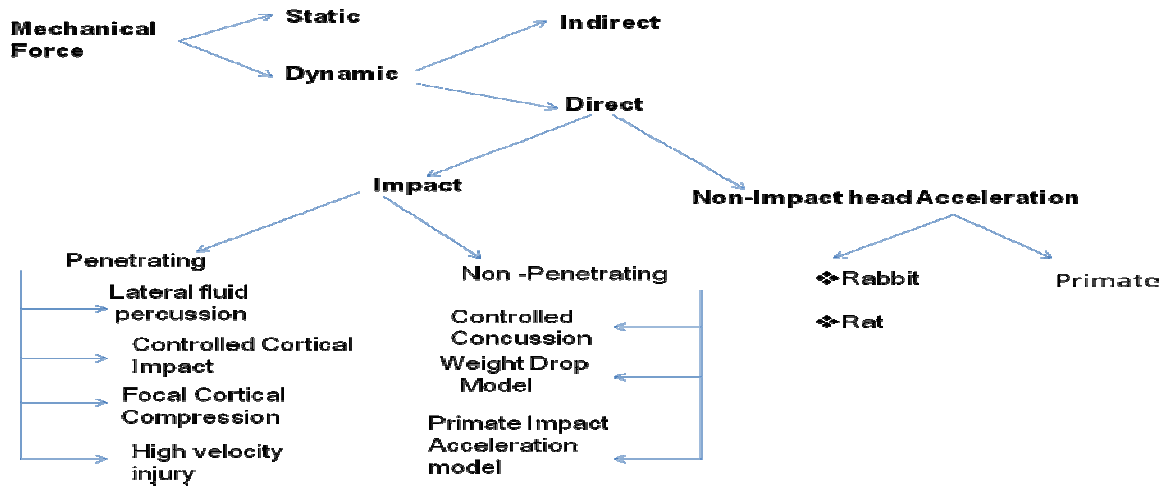

Fig.1. Schematic representation of in vivo experimental models of traumatic brain injury [37].

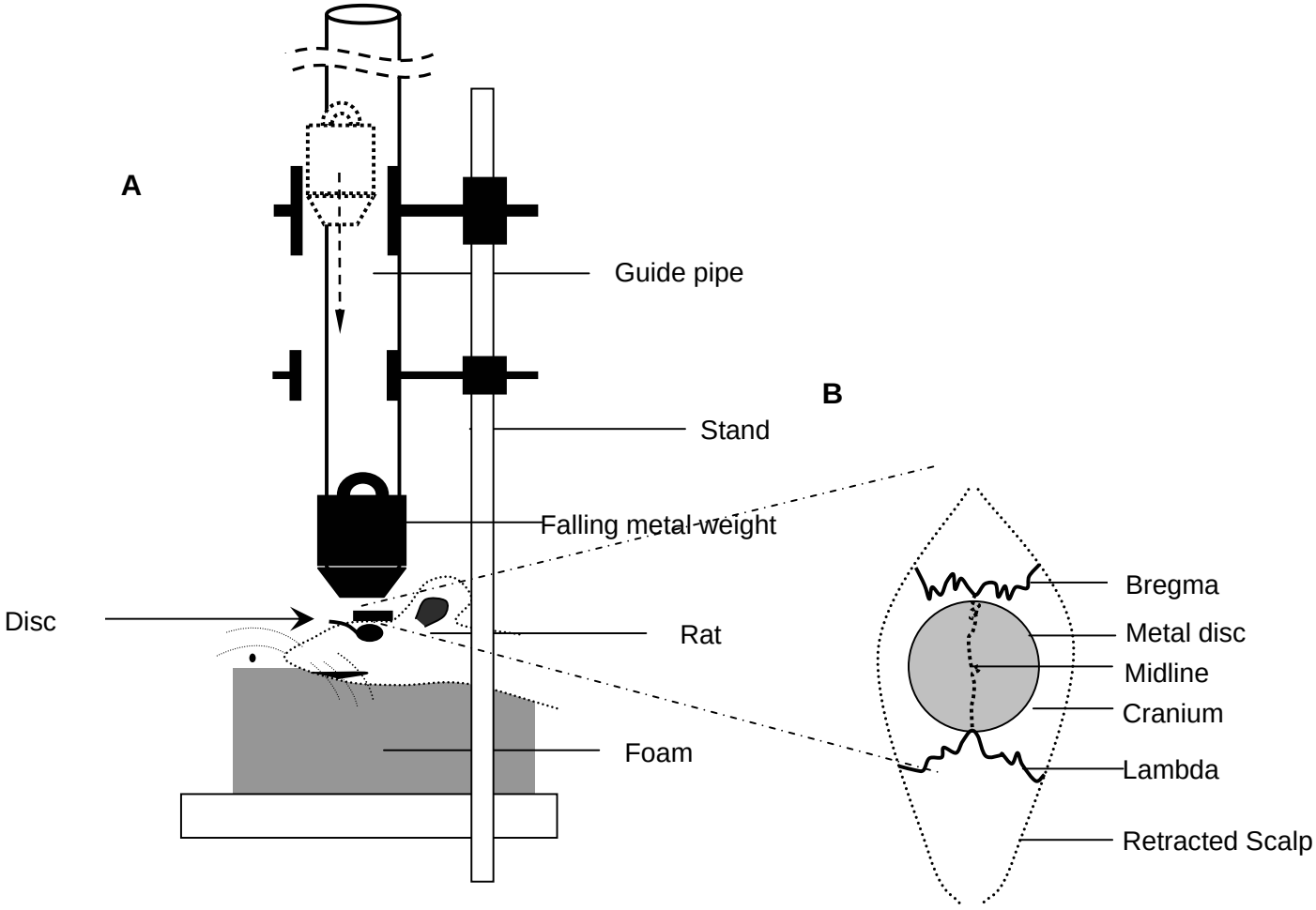

Fig. 2. A. Schematic representation of the method employed to induce traumatic brain injury in rats. B. Dorsal view of the rat cranium showing the positioning of the metallic disc.

Conclusion

In summary, neurobehavioural consequences following TBI is associated with multiple biological and psychosocial factors, including major depression, substance abuse, and impaired social function as well as the presence of brain injury involving the frontal lobe and prefrontal cortex. Providing care to psychiatric patients requires keen assessment, documentation of symptoms that could be attributed to TBI, implementation of interventions directed at overcoming deficits, and evaluation of functional outcomes. Attention to the diagnosis and management of the neurobehavioral sequelae of TBI can serve a critical role in advancing the rehabilitative process. It requires a knowledge and understanding of the profile of regional structural and neurochemical injury associated with the typical TBI and how that profile predicts the common neurobehavioral sequelae. Careful assessment requires an accurate description of the individual's functional and neurobehavioral status prior to the injury and how that has changed subsequent to the injury. It is helpful to be aware of the problems in diagnosis in individuals who have a fluctuating behavioural baseline, who may have significant cognitive deficits or in whom the usual connection between internal feeling state and external behaviors may be uncoupled. Treatment should follow from a clearly articulated diagnostic scheme and should be time-limited and re-evaluated in the presence of poor or incomplete response.

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