Pathophysiology of Traumatic Brain Injury

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KEYWORDS

• Traumatic brain injury • TBI • Pathophysiology • Symptoms • Mild TBI
• Concussion • Blast TBI

KEY POINTS

- Traumatic brain injury (TBI) has become the signature injury of the military conflict in Iraq and Afghanistan and also has a high rate of occurrence in civilian populations in the United States.
- Although the effects of a moderate to severe brain injury have been investigated for decades, the chronic effects of single and repetitive mild TBI are just becoming investigated.
- Data suggest that the different types and severities of TBI have unique long-term outcomes and thus may represent different types of diseases.
- Therefore, this review outlines the causes, incidence, symptoms, and pathophysiology of mild, moderate, and severe TBI.

TRAUMATIC BRAIN INJURY: CAUSES, PREVALENCE, AND DEVELOPMENT OF THE NATIONAL RESEARCH ACTION PLAN

Traumatic brain injury (TBI) may have many different causes, including a blow to the head, penetration of the skull, fast acceleration or deceleration of the head, or exposure to a blast. In the United States, there are more than 5.3 million people living with a disability as a result of a TBI, and each year an additional 1.7 million Americans sustain a TBI.[1,2] These injuries have both short- and long-term effects on health, ranging from symptoms that have a minimal interference on lifestyle, through to physical, emotional, and psychosocial changes that may interfere with daily activities. As well as the burden to the individual, brain injuries also have an annual economic burden of more than US$60 billion, due to both direct and indirect costs, such as loss of productivity.[2] The reasons for the injuries depend on the age of the individual; for example, more than one-third of brain injuries in the United States are due to people falling, which is the leading cause of TBI among the elderly, whereas transportation-related brain injuries are the leading cause for individuals aged 15 to 24 years.[2]

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In recent years, the media have had a strong focus on the long-term outcomes of mild TBI (mTBI) or concussions, such as that which may occur to American football players and military personnel. Pathophysiologic investigations on the brains of these individuals have revealed Alzheimer-like symptoms, termed chronic traumatic encephalopathy (CTE).[3,4] Although this disease has been known to occur in boxers since the 1960s (with numerous names, including dementia pugilistica and punch-drunk syndrome), the recent media attention has highlighted the high prevalence of this disease in other athletic arenas. This attention was followed by the Obama Administration releasing an Executive Order in 2012 to direct the Departments of Defense, Veterans Affairs, Health and Human Services, and Education to develop a National Research Action Plan (NRAP) on TBI, posttraumatic stress disorder (PTSD), and other common comorbidities. The NRAP was released in August 2013 and aims to (1) accelerate the understanding of the causes and mechanisms of TBI, PTSD, and other common comorbidities; (2) develop clinical innovations to detect disorders early and accurately; and (3) develop proven means to prevent and treat the devastating conditions caused by the injuries. To this end, understanding the acute and chronic pathophysiology of TBI is critical to determining the risk factors for individuals to develop symptoms as well as develop therapeutic innovations and interventions.

Given that current clinical imaging techniques do not detect minor changes in the human brain following injury, much of the knowledge on the cellular sequelae in the injured brain is based on rodent studies. To confirm these findings in the injured human brain, on arrival at the emergency department, an individual can be assessed for physical and cognitive functions, have a computed tomographic (CT)/MRI scan performed, have their intracranial pressure and cerebral blood flow measured, and possibly have bio-specimens collected for analysis of protein and messenger RNA expression. Subsequently, on autopsy, brain samples can be collected and analyzed.

MILD TRAUMATIC BRAIN INJURY

Causes, Diagnosis, and Symptoms

A mild brain injury is often caused by a blunt head trauma, and/or acceleration or deceleration forces to the head, and refers to the initial impact of the injury. The diagnosis of an mTBI is the subject of constant debate because no single test is available to definitively confirm the diagnosis. Currently, a combination of tools is used, including history of the injury, patient symptoms, and CT scans. Although most patients with an mTBI recover within weeks to months of the injury without specific intervention, 30% to 53% of affected individuals may still have disabling symptoms at least 1 year after the injury,[5,6] and this is often referred to as postconcussive syndrome. Because by definition mTBI is nonfatal and does not alter life expectancy (0.1% mortality[7]), prolonged symptoms can lead to life-long disabilities. Thus, the term mild brain injury can be misleading, because it does not refer to the severity or time course of injury symptoms.

In the acute period following an mTBI, an individual may experience a brief loss of consciousness (or altered consciousness), transient confusion, disorientation, loss of memory at the time of the injury (amnesia), and other neurologic and neuropsychological dysfunctions, including seizures, headaches, dizziness, irritability, fatigue, and poor concentration. More specifically, diagnosis is based on the Glasgow Coma Scale (GCS) that ranks functional ability from 1 (worst outcome) to 15 (best outcome), with a mild injury defined between 13 and 15.[8,9] Subsequently, these symptoms may evolve into persistent low-grade headaches, pain, poor attention and concentration, fatigue,