Advanced Neuroimaging of Mild Traumatic Brain Injury

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KEYWORDS

- Mild traumatic brain injury • Concussion • Diffuse axonal injury
- Diffusion tensor imaging • Susceptibility-weighted imaging
- Magnetic resonance spectroscopy

KEY POINTS

- Traumatic brain injury (TBI) is an important cause of death and disability in the United States, with annual incidence of approximately 1.7 million and overall annual costs estimated to be $76.5 billion.
- 75% of all TBIs can be classified as mild TBI (mTBI), defined as Glasgow Coma Scale score of 13 or more. Concussion, a term commonly used in sports-related injuries, is a form of mTBI.
- The goals of neuroimaging in TBI are to identify treatable injuries, assist in the prevention of secondary damage, and provide useful prognostic information on a patient's long-term clinical condition.
- Advanced neuroimaging of mTBI includes anatomic/structural imaging techniques, such as diffusion tensor imaging and susceptibility-weighted imaging, and functional imaging techniques such as functional MRI, perfusion-weighted imaging, MR spectroscopy, and positron emission tomography.

INTRODUCTION

Traumatic brain injury (TBI), a major public health concern at the beginning of the 21st century, has been called a "silent epidemic"[1] because it is underreported, often remains undiagnosed, and its long-term consequences are generally underrecognized. However, owing to growing experience with combat-related TBI among military personnel, media focus on TBI-related long-term disability in professional athletes,

The authors have no financial conflicts to disclose.
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Neurol Clin 32 (2014) 31–58
http://dx.doi.org/10.1016/j.ncl.2013.08.002 neurologic.theclinics.com
0733-8619/14/$ – see front matter

educational initiatives, such as the "Heads Up" program of the Centers for Disease Control and Prevention,[2] and the voices of patients and affected families, the silence is beginning to be broken.

Approximately 75% of all reported TBIs can be classified as mild TBI (mTBI).[3] Although most patients with mTBI become asymptomatic within days to weeks, some develop persistent troubling symptoms that have been referred to as "persistent postconcussive syndrome."[4,5] One of the inherent challenges in applying neuroimaging to predict clinical outcome in mTBI is that patients who develop persistent symptoms typically have no detectable abnormalities on conventional neuroimaging, such as computed tomography (CT) and magnetic resonance imaging (MRI) of the brain. Novel structural and functional neuroimaging techniques have emerged that have the sensitivity to identify hitherto undetected brain abnormalities in mTBI. This article focuses on advancements in neuroimaging techniques, compares the advantages of each of the modalities in the evaluation of mTBI, and discusses their contribution to our understanding of the pathophysiology as it relates to prognosis.

MTBI: BRIEF OVERVIEW

Terminology

"Traumatic brain injury" refers to an alteration in brain function or other evidence of brain pathology caused by external force[6] and traditionally is classified as mild, moderate, and severe based on the Glasgow Coma Scale (GCS).[7] TBI with GCS score of 13 or more is classified as mild, 9 to 12 as moderate, and 8 and lower as severe.[8] mTBI is defined as a traumatically induced physiologic disruption of brain function as manifested by at least 1 of the following: (1) any period of loss of consciousness up to 30 minutes, (2) any loss of memory for events before or after the accident not exceeding 24 hours, (3) any alteration in mental state at the time of the accident, and (4) focal neurologic deficits that may or may not be transient.[9,10] Concussion is a form of mTBI, and "concussion" is a term commonly used in sports, whereas "mTBI" is used more often in the medical context.[11]

Pathophysiology

Pathophysiologically, TBI involves 2 phases of tissue injury: primary and secondary. Whereas primary injuries are almost immediate and generally irreversible, secondary injuries are delayed and can continue for an extended period of time and thereby provide an opportunity for therapy.[12] The primary injury phase involves direct and indirect mechanical damage from impact and acceleration/deceleration that could result in cortical contusions, subdural or epidural hematomas, axonal shearing, and microvascular injury. Secondary injury is the nonmechanical damage that results from a complex metabolic cascade set off by neuronal cell membrane disruption and axonal stretch.[13] Neuronal membrane deformity leads to ionic flux and release of excitatory neurotransmitters. Attempts to restore homeostasis lead to a cellular energy crisis. Depletion of cellular energy stores leads to initiation of apoptosis and neuronal death. Impaired cerebrovascular autoregulation that leads to decreased cerebral blood flow (CBF), inflammatory response with activation of microglia,[14] and release of free radicals are additional mechanisms of tissue damage during the secondary injury phase of TBI.

Diffuse axonal injury (DAI) is best described after severe TBI and is characterized by axonal stretching leading to axolemmal disruption, ionic flux, neurofilament compaction, and microtubule disassembly. The effect of these pathophysiologic processes is axonal swelling and eventual disconnection.[15,16] Although best described in severe TBI, DAI occurs in mTBI as well and is recognized as an important determinant of