Susceptibility-Weighted Imaging and Magnetic Resonance Spectroscopy in Concussion

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KEYWORDS

• Magnetic resonance spectroscopy (MRS) • Mild traumatic brain injury (mTBI) • Concussion • SWI • Susceptibility-weighted imaging

KEY POINTS

- Despite its exquisite sensitivity in the detection of intracranial blood products, susceptibility-weighted imaging (SWI) does not play a primary role in mild traumatic brain injury/concussion and its clinical utility is currently limited to assessment of diffuse axonal injury.
- Some studies have shown a correlation between the number, volume, and extent of microhemorrhages on SWI and neurologic outcomes, but results have been mixed.
- The most common proton magnetic resonance spectroscopy (MRS) findings in concussion/mild traumatic brain injury are lower concentrations of *N*-acetyl-aspartate (indicating compromised neuronal health) and higher levels of choline (indicating glial abnormalities).
- Correlations with clinical outcome, and the property of the spectroscopic markers to show reversible injury, qualifies proton MRS as a potential tool for monitoring recovery from concussion/mild traumatic brain injury.
- Conflicting results caused by study design factors have impeded widespread applications on an individual patient level, and currently proton MRS has most utility in group-level comparisons designed to reveal the pathophysiologic effects of concussion/mild traumatic brain injury.

INTRODUCTION

The prognosis after a traumatic brain injury (TBI) mainly depends on the classifier of mild, moderate, and severe, which is determined by neurologic assessment. In cases in which minimal or no disturbance of consciousness is present, the patient is assigned a score of 15 to 13 on the Glasgow Coma Scale (GCS)[1] and consequently, a designation of mild TBI (mTBI), the most common and least debilitating TBI type. The term concussion has a broader definition, which includes

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mTBI defined by GCS but also mTBI diagnosed based on retrospective patient report, or based on tools other than the GCS, such as sideline assessment tests used in contact sports.

Despite the overall favorable outcomes after mTBI and concussion (referred to collectively as mTBI henceforth), some patients develop persistent postconcussive symptoms (PCSs) that are not explained by qualitative assessment of conventional MR imaging scans. Given the high incidence of mTBI (>1 million/y in the United States alone),[2] a large body of research has been devoted to developing and testing of techniques sensitive to the subtle MR imaging–occult injury expected in mTBI to address the need for better prognostication through neuroimaging.

Because fractured blood vessels indicate that brain tissue has experienced significant stress/strain, techniques able to detect paramagnetic blood products may be useful for identifying underlying injury.[3,4] One such technique, susceptibility-weighted imaging (SWI), is covered in the first part of this article. SWI is a fully flow-compensated three-dimensional (3D) gradient echo (GRE) sequence that incorporates both magnitude and phase information and that has been shown to be highly sensitive to the signal dephasing caused by paramagnetic blood products (essentially from iron within different states of hemoglobin) and diamagnetic substances (largely calcium).[5] In the setting of moderate and severe TBI, evidence suggests that SWI is significantly more sensitive to hemorrhagic byproducts than its alternative, the T2* GRE sequence.[6] This article reviews the use of SWI in mTBI and discusses its potential added value. Second, it focuses on metabolic imaging by means of magnetic resonance spectroscopy (MRS). Because TBI-associated changes in metabolism can occur even when there are no apparent abnormalities on conventional MR imaging, MRS can provide an additional layer of injury assessment, which, in the case of proton MRS (^{1}H MRS), can be integrated in a standard clinical MR imaging examination. This article therefore reviews the potential clinical utility of ^{1}H MRS, and examines what information its markers have provided about injury mechanisms in mTBI.

PATHOPHYSIOLOGY AND MECHANISMS OF TRAUMATIC BRAIN INJURY

The brain is bathed in cerebrospinal fluid (CSF), which acts like a mechanical cushion and provides a certain degree of motion within the calvarium. During trauma, the brain may be subject to translational, linear, and rotational forces that can generate pressure gradients that result in shearing stress/strain and axonal damage.[7] Depending on the severity of trauma, axonal shearing without intracranial hemorrhage can occur immediately following injury or develop over a longer period of time because of cellular mechanisms that lead to degradation of the cytoskeleton.[8]

Animal Models

Current knowledge of the pathophysiologic mechanisms behind closed head trauma and mTBI are largely derived from animal models that attempt to replicate the injury using low pressure forces. These animal models have generally relied on rodents and with some variations entail the delivery of a force to the intact dura. One of the most extensively used techniques for generating brain trauma in rodent models is via transmission of a fluid pressure pulse (fluid percussion injury).[9] Other techniques involve the use of electromechanically or pneumatically activated rods to deliver a direct force to the brain (controlled cortical impact) or weight drops without the need for a craniectomy.[10]

Neurotransmitter Release, Excitotoxicity, and Ionic Shifts

Cellular distortion with axonal stretching and membrane disruption on impact lead to indiscriminate release of neurotransmitters, efflux of potassium ions, and membrane depolarization.[11] Experimental and clinical studies have shown early release of excitatory neurotransmitters, particularly glutamate, caused by rapid depolarization and also from other potential sources, including extravasation at the site of injury, as well as disruption of the blood-brain barrier.[12] Activation of *N*-methyl-D-aspartate receptors by glutamate further exacerbates ion transport across the membrane, promoting potassium loss and influx of calcium ions, as well as further membrane depolarization.[13] Intracellular accumulation of calcium results in activation of calcium-dependent proteases, mitochondrial dysfunction, and release of oxygen free radicals adding to cellular injury.[8,10,11] Activity of the Na^+/K^+ ATPase pump increases in an attempt to restore the transmembrane ion gradients. The resultant increased glucose metabolism is exacerbated by mitochondrial dysfunction and promotes anaerobic metabolism with increased accumulation of lactate and local acidosis.[14] A second stage of postimpact injury is thought to involve hypometabolism, hypoperfusion, and further disruption of the blood-brain barrier with ensuing edema.[15] However, some data in patients with