Pathophysiology of Sports-Related Concussion

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KEYWORDS

• Concussion • Traumatic brain injury • TBI • Trauma

KEY POINTS

- Concussion pathophysiology is complex and still under investigation.
- Concussion pathophysiology involves excessive neurotransmitter release, excitotoxicity, neuroinflammation, and axonal disruption.
- It remains unclear how these mechanisms are affected by genetics, premorbid conditions, and environmental factors.

INTRODUCTION

Sports concussion is a public health epidemic with 1.6 to 3.8 million sports-related concussions occurring annually.[1] Our current recommendations for treatment include rest, symptomatic treatment, and a gradual return to mental and physical activity. At this time, we do not have specific treatment options for the treatment of an acute concussion or to prevent prolonged or permanent symptoms. To develop more targeted management and treatment options, the underlying pathophysiology needs to be better defined.

In addition, a concussion is not the same as a moderate or severe traumatic brain injury. There is currently a large body of evidence demonstrating the mechanisms underlying moderate to severe traumatic brain injury; however, the pathophysiology underlying concussion and mild traumatic brain injury remains under investigation. Sports concussion is complicated and its pathophysiology will likely vary depending on the mechanism and characteristics of the impact, susceptibility of the individual including genetics and premorbid risk factors, and environmental factors. Thus, it is not surprising that numerous mechanisms have been demonstrated in both animal models and in vivo advanced neuroimaging studies. These mechanisms are likely

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not mutually exclusive and are most likely occurring concurrently in varying degrees in different individuals affected by a sports concussion. This evidence-based article reviews the current understanding in the diverse pathophysiology of sports concussion in efforts to educate and inspire additional research.

DEFINITION OF CONCUSSION

The definition of concussion is widely debated, but the most accepted definition by McCrory et al[2] states that a concussion is a complex pathophysiological process affecting the brain, induced by biomechanical forces with alteration in mental status with or without loss of consciousness.[3] A concussion is a subset of mild traumatic brain injury and is commonly used interchangeably. More recently, it has been recommended to use the diagnosis of concussion for injuries with more complete recovery and the diagnosis of mild traumatic brain injury for the injuries that are associated with more persistent symptoms.[2] Several prognostic risk factors have been identified for prolonged recovery after concussion, including younger age, female gender, premorbid migraine history and psychiatric history, prior concussion, and history of migraine, higher symptom severity score acutely, and duration of posttraumatic amnesia.[4–6]

Concussion symptomatology can be divided into 4 domains: physical (headache and dizziness), cognitive (concentration and memory), emotional (depression, anxiety, and mood lability), and sleep (hypersomnia and insomnia). Although the most commonly reported symptoms are typically headache, dizziness, and difficulties with concentration and memory, oftentimes the most bothersome symptoms fall within the emotional and sleep domains.

Despite the presence of significant symptomatology and acute disability, routine neuroimaging is typically unhelpful at demonstrating evidence of neuropathologic changes. These symptoms are likely caused by functional, metabolic, and microstructural abnormalities as opposed to gross macrostructural damage. A better understanding of concussion pathophysiology and its associated functional and microstructural abnormalities will improve the management and treatment of concussion. It may also be helpful to determine preventive or at least protective measures.

Pathophysiology in Sports Concussion

It is a common misconception that a mechanical injury to the brain results in direct structural damage; however, these biomechanical forces result in abnormal function at the level of the individual cell. Abnormal cellular function is what results in functional impairment and may lead to microstructural and even eventually macrostructural damage.

NEUROTRANSMITTER DYSREGULATION

Massive unregulated, unchecked excitatory neurotransmitter release results in functional impairment, excitotoxicity, and possibly permanent damage. Mechanical injury disrupts cellular membranes causing an efflux of intracellular potassium through voltage-gated channels, resulting in neuronal depolarization.[7] With open voltage-gated channels, a feedback loop is created resulting in increased extracellular potassium, depolarization, and further neurotransmitter release. One excitatory neurotransmitter clearly implicated is glutamate.[8] Glutamate has been identified as not only promoting potassium efflux, stimulating receptors, and inducing ligand-gated potassium channels, but also in binding *N*-methyl-D-aspartate receptors allowing for unrestricted cortical depolarization and increased hyperexcitability.[9] In addition, the increased release of excitatory neurotransmitters results in the accumulation of