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The Pathophysiological Implications of Mild Traumatic Brain Injury on Diagnosis and Treatment

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THE PATHOPHYSIOLOGICAL IMPLICATIONS OF MILD TRAUMATIC BRAIN INJURY ON DIAGNOSIS AND TREATMENT

by

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ABSTRACT

The Pathophysiological Implications of Mild Traumatic Brain Injury on Diagnosis and Treatment

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A mild traumatic brain injury (mTBI), or concussion, affects millions of athletes on a yearly basis. A mTBI is the result of biomechanical forces, such as acceleration and deceleration, acting on the skull and brain. These forces create acute neurological injuries throughout the brain. The consequences of mTBI are apparent in multiple common medical practices. Sideline assessments and clinical evaluations used in diagnosis are based largely on the signs and symptoms which arise as consequences of mTBI. Treatments, including symptom management and a gradual return to play, are further based on controlling the signs and symptoms of mTBI. The purpose of this article is to display how an understanding of the pathophysiological implications of mTBI is critical to providing an accurate diagnosis and the proper treatment.

KEYWORDS: Mild Traumatic Brain Injury; Concussion; Biomechanical Forces; Diagnosis; Symptoms; Assessments; Treatment; Return to Play

TABLE OF CONTENTS

Topic **Page**

INTRODUCTION

A mild traumatic brain injury (mTBI), commonly known as a concussion, is much more than simply "getting your bell wrung," "feeling foggy," or "seeing stars." A mTBI denotes widespread neurological damage and dysfunction which results from significant trauma to the head. The consequences of this injury are particularly concerning because it is extremely prevalent in high speed contact sports, such as football, ice hockey, and soccer. In fact, it is estimated up to 3.8 million sports related mTBI occur every year in the US alone.[1] The prevalence of mTBI creates a demand to properly understand the implications of this injury. In mTBI, significant trauma to the head creates a multitude of acute neurological injuries. These acute neurological injuries and the biomechanical forces behind them, have serious consequences on proper diagnosis and treatment of mTBI. These consequences have long been over looked. This article will establish the need to understand the pathophysiological implications of mild traumatic brain injury for proper diagnosis and treatment.

This article will present a broad range of information on this topic to assist in the comprehension of the pathophysiological implications behind mTBI. An overview of mTBI, including the basic anatomy of the brain, the biomechanical mechanisms behind the injury, and the acute neurological injuries themselves will first be presented to provide sufficient background information about the pathophysiological implications.

Descriptions of the diagnosis and treatment of mTBI are then provided to demonstrate the need to fully understand the pathophysiological effects of mTBI.

MILD TRAUMATIC BRAIN INJURY

The diagnosis and treatment of mTBI requires an understanding of the implications that arise from the injury. The brain is a complex and delicate structure which is very susceptible to injury. Biomechanical forces create acceleration and deceleration of the skull and brain leading to the acute neurological injuries that make up mTBI. An understanding of the implications of mTBI positively impacts multiple aspects of a diagnosis and treatment.

Basic Brain Anatomy

A proper understanding of mTBI requires the comprehension of the basic anatomy of the brain. The nervous system, including the brain, is made up of billions of neurons and glia.[2] Neurons are the functional unit responsible for transmission of information throughout the nervous system. They consist of cell bodies, axons, and dendrites. Glial cells make up the structural support for neurons. A complex vascular system supports both of these cell types. Together, neurons, glia, and the supporting vasculature create the grey and white matter of the nervous system. The superficial grey matter contains the cell bodies and dendrites of neurons, while the deep white

matter contains long tracts of axons to connect the grey matter.[3] These complex tissues make up the brain.

The brain can be divided into three very basic regions: the cerebrum, brain stem, and cerebellum.[4] First, the cerebrum, is the superior region of the brain. It is the most complex part of the brain and is composed of four lobes including the frontal, parietal, occipital, and temporal lobes.[4] Together, the four lobes of the cerebrum are involved in the central processing of movement, speech, sensory, and memory information. Secondly, the brain stem is located in the middle and inferior portions of the brain. It can be divided into the pons, medulla, and spinal cord. The brain stem is responsible for basic autonomic functions such as breathing, cardiac function, and involuntary muscle movements. Finally, the posterior region of the brain is the cerebellum. Its function is to coordinate muscle movements, posture, and balance. This basic brain anatomy is key to understanding a mTBI.

Biomechanical Mechanisms of Injury

Furthermore, a proper understanding of mTBI also requires the comprehension of the mechanism of injury. A mTBI occurs when an external biomechanical force is transferred to the head resulting in damage to the neurons, glia, and blood vessels of the brain.[5] This external force is called biomechanical loading.[6] The term biomechanical loading is used in mTBI to describe significant force applied to the head. Due to the many physiological articulations of the head and neck, biomechanical loading creates a

considerable amount of head movement, which is similar in the protected, or helmeted, head and the unprotected head. Inertial forces are the primary forces at work in these movements.[6] Inertial forces are often referred to as acceleration forces because they result from violent head motion, regardless of whether the head strikes a surface or is struck itself by an object.[7] In sporting activities, such as football, hockey, and soccer these acceleration forces may result from head contact with a playing surface or with another player.

Acceleration and deceleration are the underlying physical principles of inertial forces. Acceleration and deceleration are defined as the change in velocity over time.[8] From a mechanical point of view, acceleration and the resulting deceleration are the same phenomenon but differ only in direction. For example, accelerating the head in the direction of anterior to posterior is the same as decelerating the head from posterior to anterior. For the sake of simplicity, this article will primarily reference acceleration.

Three types of acceleration and deceleration occur in mTBI: linear, rotational, and angular.[6] Linear acceleration occurs when the brain moves in a straight line without rotation. Linear acceleration alone is rare in clinical situations because of the physiological articulations of the head and neck. An exception to this may occur when linear movements happen for brief periods of time. Rotational acceleration occurs when there is rotation around the center of gravity of the brain, without the center of gravity itself moving. Similar to linear acceleration, purely rotational movements are nearly impossible in clinical situations. The most frequent type of acceleration in mTBI

is angular acceleration. Angular acceleration occurs as a combination of linear and rotational acceleration. The physiologic articulations of the head and neck create complex movements which facilitate angular acceleration. In this situation, the center of gravity moves as the skull and brain rotate about it. As might be expected, angular acceleration is the most destructive force in mTBI.

As a result of biomechanical forces, certain segments of the brain move at a slower rate than others, causing strain on neurological tissue. In general, strain is defined as the deformation the tissue under-goes as a result of biomechanical loading.[7] Three types of strain are common in mTBI: compressive, tensile, and shear strain.[6,7] Compressive strain occurs when the neurological tissue is pressed. This can happen when the brain accelerates into the skull and rapidly decelerates. The rebound effect of this motion also creates tensile strain. Tensile strain in mTBI is when tissue is stretched past its normal limits. The final type of strain, shear strain, is considered the primary cause of neurological tissue damage in mTBI. Shear strain is the rupture of tissue due to multiple forces acting along its surfaces. Some estimates of the biomechanical forces created during high speed contact sporting activities produce levels of shear strain which reach the thresholds for neurological tissue damage and deformation.[9] Many acute injuries can occur when neurological tissue reaches these thresholds for damage and deformation.

Neurological Tissue Damage

Lastly, a proper understanding of mTBI also requires the comprehension of the acute injuries involved. The biomechanical forces and the resulting tissue strain present in mTBI create a cascade of neurological consequences. Neurological injuries vary in severity. Sub-Concussive injuries are injuries which develop after exposure to repeated mechanisms of mTBI without the development of a mTBI.[10] While little is known about Sub-Concussive Injuries, they are less severe than typical mTBI and occur in greater numbers. More severe neurological injuries that make up mTBI can be characterized based on whether they result directly or indirectly from biomechanical loading.[5] A primary injury occurs as a direct result of the mechanism of injury, while a secondary injury materializes as a response to a primary injury. For example, the primary injury would occur when an athlete's brain undergoes strain from biomechanical loading. The secondary injury comes into effect as a result of the original tissue damage.

The predominant primary and secondary injuries in mTBI develop in a diffuse pattern.[11] Diffuse brain injuries are, as the name implies, structural damage widely distributed throughout the brain. This distribution helps contribute to widespread dysfunction and confusion which is characteristic of mTBI. Diffuse brain injury entails damage to neurons, glia, and the vascular structures of the brain.

The most frequent diffuse brain injury is diffuse axonal injury.[11] Diffuse axonal injury occurs when the brain experiences strain and axons, the long connecting nerve fibers of neurons, are stretched, damaged, or broken. Axons in the white matter are

especially susceptible to damage because of their highly organized, highly directional structure.[11] In fact, severe tensile and shear strain is able to stretch an axon to more than twice its resting length and produce a complete transection of the axon.[5,11] When axons are stretched and damaged, neurons experience increased membrane permeability, disruption of microtubules, and changes in membranous organelles.[5] Another diffuse brain injury in mTBI is diffuse vascular injury.[13] Microscopic vascular structures are often in close proximity to axons. As expected, these vascular structures experience the same shear forces as axons and may be stretched, broken, or damaged themselves. This leads to acute intracerebral hemorrhaging at the site of the rupture.

Diffuse brain injuries are often associated with secondary changes that contribute to further neurodegeneration and neurologic dysfunction.[5] The secondary injuries common in mTBI are cerebral edema and ischemia. Often developed first is cerebral edema. Cerebral edema is the excess accumulation of water in the intracellular and extracellular spaces of the brain.[15] As neurons, glia, and vascular structures are damaged by strain, water accumulates and creates swelling. Severe cerebral edema can lead to distortion, shift, and herniation of the brain due to the increase in intracranial pressure produced from swelling.[5] In response to cerebral edema, and the previously mentioned disruptions in vascular structure, neurological tissue is subject to cerebral ischemia. Cerebral ischemia is a condition characterized by a lack of blood flow to the brain.[16] This limited oxygen and nutrient supply as well as damage to axons and vascular tissue create a metabolic crisis within neurological tissue.

Immediately after biomechanical injuries, neurological tissue undergoes a cascade of metabolic changes.[17] As neurons and glial cells are damaged, there is a disruption of cell membranes. This comes in the form of increased membrane permeability and changes in gated membrane channels within the cell membrane. A marked increase in extracellular potassium leads to an uncontrolled release of neurotransmitters and amino acids such as dopamine and glutamate. This chain of events creates deficits in cellular functioning and further neuronal cell damage and death. Further complications arise when chemicals, including potent vasoconstrictors, are released during neurological damage.[14] These chemicals can contribute to changes in vascular tone and acute intracerebral hemorrhaging which ultimately leads to further neurodegeneration. This metabolic cascade of events causes rapid neurodegeneration and exacerbates neurological damage during mTBI.[12,13]

The common consequence of the metabolic cascade associated with mTBI is neurodegeneration.[14] Neuronal cell death is present in the sub-concussive injuries, primary injuries such as diffuse axonal and vascular injuries, as well as in secondary injuries like cerebral edema and ischemia. These neurological injuries and the biomechanical forces that create them are some of the main sources of cerebral damage and dysfunction, making them major implications of mTBI. These implications are critical to understanding the diagnosis and treatment of mTBI.

DIAGNOSIS

The numerous pathophysiological implications of mTBI, including acute neurological injuries and the biomechanical forces behind them, are apparent in diagnosis. The acute neurological injuries involved in mTBI create a multitude of signs and symptoms which are the basis for proper diagnosis. Sideline assessments and clinical evaluations used in diagnosis, are dependent on signs and symptoms to determine the severity of the injury. A complete understanding of the implications of mTBI positively impact multiple aspects of a diagnosis, including the recognition of frequent signs and symptoms, as well as the sideline assessments and clinical evaluations.

Signs and Symptoms

The diagnosis of mTBI is primarily influenced by the proper recognition of signs and symptoms. If an athlete has experienced a significant mechanism of injury, the athlete may begin to show the signs and symptoms of mTBI. Signs are the visible consequences of an injury and may include possible loss of consciousness and posttraumatic amnesia.[18] Other signs of mTBI are loss of orientation and changes in mood.[18] These common signs are accompanied by many symptoms and are characteristic of mTBI.

There are a variety of symptoms associated with mTBI. The most prevalent symptoms of mTBI generally fall into one of three categories: somatic, cognitive, and

affective.[18] Somatic symptoms are often the first symptoms an athlete with a mTBI experiences. These symptoms can be physical or sensory in nature and often include, headache, dizziness, nausea, blurry vision, fatigue, and sensitivity to light and sound.[19] Cognitive and affective symptoms appear alongside somatic symptoms, but may be less distinct. Cognitive symptoms are recognized as deficits in general functioning. These symptoms include difficulty thinking clearly, as well as deficits in attention, memory, and thought processing.[18] The last type of symptoms in mTBI, affective symptoms, are defined as symptoms which affect emotion and mood. Affective symptoms involve increases in irritability, anxiety, and depression.[10] Following a mTBI, somatic, cognitive, and affective symptoms may interact and exacerbate each other.[18] For example, as somatic symptoms like headaches and nausea develop, athletes with mTBI may experience intensifying cognitive and affective symptoms like difficulty thinking clearly and irritability. Together, somatic, cognitive, and affective symptoms provide a broad spectrum of mTBI symptoms.

The signs and symptoms experienced with a mTBI continue to vary based on multiple clinical considerations. This makes each case of mTBI unique. Signs, symptoms, and the likelihood of being diagnosed with a mTBI differ by age, sex, and past mTBI history. Research has found that adolescents between the ages of 14 and 19 display the most symptoms and have the highest rates of mTBI.[20] This may be because of improper techniques used in sporting events, like leading with the head during hitting and tackling, or anatomic differences in the head and neck which may create greater inertial forces during impact. Differences in sex contribute to more somatic and

affective symptoms in females and more cognitive symptoms in males.[10] Additionally, females are reported to have higher rates of mTBI than males in comparable sports.[20] The final aspect of mTBI diagnosis to consider is past mTBI history. A recent diagnosis of a mTBI contributes to a higher likelihood of displaying more mTBI symptoms after a significant mechanism of injury and a higher risk of obtaining another mTBI.[19,20] Regardless of age, sex, or past mTBI history, athletes experiencing any signs and symptoms of mTBI should be referred to an athletic trainer or physician for further evaluations.

Sideline Assessments & Clinical Evaluations

The diagnosis of mTBI is dependent on the use of sideline assessments and clinical evaluations. Because mTBI can produce various neurological deficits, a wide range of assessments and evaluations are necessary to recognize mTBI. Once an athlete shows the signs and symptoms of mTBI, sideline assessments and clinical evaluations are necessary for proper diagnosis. Basic sideline assessments are completed in order to determine the initial existence of neurologic deficits in the form of signs and symptoms. Clinical evaluations are then used to confirm the presence of signs and symptoms as well as any persistent neurological deficits.

Sideline assessments are the first tests given following a significant mechanism of injury. The purpose of a sideline assessment is to test for neurologic deficits in memory, vision, and general degree of cognitive impairment.[10] Sideline assessments

are relatively simple tasks or observations which take between two and five minutes to complete. The first assessment usually done is the Glasgow Coma Scale (GCS). This observation measures the degree of cognitive impairment, via scores for eye, verbal, and motor responses. The assessment is scored out of a possible 15 points. The Glasgow Coma score usually associated with mTBI is between 13 and 15.[21] Common sideline assessments to further evaluate athletes with a possible mTBI are the Standardized Assessment of Concussion (SAC), Sport Concussion Assessment Tool (SCAT), and the King-Devick Test. The SAC and SCAT assessments are a simple set of questions which assesses an athlete's orientation, immediate memory, and concentration.[10] This test has good sensitivity and specificity for mTBI when used with a pre-injury baseline score.[22] Because vision is often impacted by the presence of mTBI, the King-Devick Test is utilized to test rapid eye movements and concentration. The King-Devick Test is a timed trial which involves reading a series of numbers on multiple test cards. Like the SAC, the King-Devick Test most accurately assesses mTBI when used with a pre-injury baseline time and score. The GCS, SAC, SCAT, and the King-Devick Test assessments may be able to determine the initial presence of mTBI, but further evaluation is necessary for proper diagnosis.

Clinical evaluations are used to confirm the continued signs and symptoms, as well as the sideline assessment. Common comprehensive evaluations involve symptom scores, measures of balance, and neurocognitive testing. Neuroimaging and biomarkers are being developed and may eventually be utilized to assess mTBI. A complete

evaluation, using multiple tests, is generally able to properly diagnose each unique mTBI.

A symptom evaluation is often the first information gathered in comprehensive mTBI assessments.[18] A post injury symptom survey is used to develop a subjective view of the severity of the symptoms present. A symptom scale survey is a Likert style survey over a broad range of symptoms common in sports-related mTBI. A comprehensive symptom scale survey usually contains somatic, cognitive, and affective symptoms to provide the best diagnosis possible. The symptom scale survey alone, however, is not the best measure of a mTBI. Athletes eager to get back into play may minimize the symptoms and avoid management advice.[19] Nonetheless, when used with other assessment measures, the survey method is an effective way to begin a diagnosis.

Balance tests are also commonly used in the comprehensive assessment of mTBI.[18] Evaluations of balance are necessary to determine disturbances in bodily orientation after an impact. Tests such as the Balance Error Scoring System (BESS) and the Sensory Organization Test (SOT) are standard clinical balance evaluations.[23] They involve testing postural stability, vision, and vestibular systems. BESS has athletes stand in multiple stances on stable and unstable surfaces to test postural stability and balance. SOT places athletes in different sensory conditions to identify abnormalities in somatosensory, visual, and vestibular systems used to maintain postural control. The sensitivity of balance assessments is dramatically improved when there is an established baseline for each athlete, as well as when used in conjunction with symptom scores and neurocognitive testing.

The last evaluation frequently completed in comprehensive mTBI assessments is neurocognitive testing.[18] Neurocognitive tests are used to detect cognitive changes in athletes following injury. Computerized neurocognitive assessment tools like CogSport, Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT), and the Automated Neuropsychological Assessment Metrics (ANAM) identify common cognitive deficits following a significant mechanism of injury.[10] These assessments consist of a series of questions and tasks which assess speed of processing, visual attention, vigilance, and verbal and visual learning and memory. The scores from each examination are compared to pre-injury baseline scores for deficits in neurologic functioning. Computerized neurocognitive assessments, together with symptom scales and balance testing, generally produce an accurate diagnosis.

Additionally, neuroimaging and biomarkers may eventually be used to assess mTBI. Conventional neuroimaging systems, like computed tomography (CT) scans and magnetic resonance imaging (MRI), are unable to show mTBI. More advanced imaging techniques, such as Diffusion Tensor Imaging (DTI) and Functional Magnetic Resonance Imaging (fMRI), may provide the future for mTBI diagnosis.[24] These advanced imaging techniques are able to look at the microscopic structures and blood flow patterns of the brain to see damage from mTBI. Likewise, biomarkers for mTBI have the potential to provide diagnoses. Biomarkers for mTBI are proteins, metabolites, or other precursor molecules that arise after injury.[5] Neuroimaging and biomarkers, if improved, would provide a definitive way to diagnose and monitor mTBI. The pathophysiological implications of mTBI are evident in a quick and proper diagnosis.

TREATMENT

The pathophysiological implications of mTBI, such as acute neurological injuries and the biomechanical forces which create them, are further apparent in the treatment of mTBI. The implications behind mTBI complicate treatment. The acute neurological injuries and biomechanical forces involved limit treatment to symptom management followed by a gradual return to activity. An understanding of the implications of mTBI positively impacts multiple aspects of treatment, including the management of symptoms and return to involvement in activities.

Symptom Management

The treatment of mTBI is more often thought of as the management of signs and symptoms. The signs and symptoms that arise from mTBI may dissipate relatively quickly, or persist for a period of time. In most cases of mTBI, the consequences of injury resolve automatically within one to two weeks of the injury.[10] In fact, studies show most athletes diagnosed with mTBI fully recover within seven to ten days.[25] There are currently no targeted pharmaceutical treatments for mTBI, so drugs such as acetaminophen and ibuprofen are utilized to assist in the management of symptoms, rather than treat injuries.[26] Immediate rest and symptom management are the only proven treatments of mTBI.

The general consensus on treatment is athletes should receive sufficient rest and manage the severity of their symptoms. Complete physical and mental rest are recommended for at least one to two days or until the immediate signs and symptoms of mTBI are resolved.[10] The purpose of physical and mental rest is to minimize the energy demands of neurological tissue. Any activities that increase the energy demands of neurological tissue may worsen symptoms and prolong recovery time.[26] The amount of rest required is dependent on the severity of the injury. Physical rest may range from bed rest to simply avoiding contact athletic activities. Mental rest generally includes avoiding anything that requires prolonged periods of concentration, including schoolwork and other mentally stimulating activities. The proper management of symptoms, including physical and mental rest, generally results in the gradual improvement of symptoms in the days and weeks following injury.

In 10 to 20 percent of individuals, however, mTBI symptoms may persist for a number of weeks, months, and even years. This condition is called Post-Concussion Syndrome (PCS).[10] PCS is defined as the persistence of somatic, cognitive, and affective symptoms beyond the usual recovery period after a mTBI. The development of PCS can be difficult to predict. Some studies have shown a greater than normal mechanism of injury is commonly associated with the development of PCS.[10] Once diagnosed, individuals with PCS are given acetaminophen and ibuprofen for the management of their somatic symptoms and are also prescribed antidepressants and antianxiety medications for the management of their long-term cognitive and affective symptoms.

Although the symptom management for individuals with PCS is different than the management of normal mTBI symptoms, the return to activity is similar in each case.

Return to Activity

As symptoms improve, athletes are slowly allowed to return to various activities. Return to activity involves the gradual resumption of physical, as well as mental activities that may have been avoided during the management process. The involvement in an activity is determined by the presence of symptoms.[10] If an activity produces or worsens a common symptom of mTBI, it is suggested the activity is postponed until no symptoms appear. The same clinical evaluations that are utilized to form a diagnosis, are also implemented in the management of mTBI. Symptom scales, balance testing, and neurocognitive assessments are important to monitor the severity of physical and mental impairments during an athlete's return to activity.

A gradual return to activity generally starts with the return to mentally stimulating activities before a return to physical activity.[26] Steps involved in a progressive return to mental activity include: light and moderate cognitive activity, combinations of cognitive activities, and full return to cognitive processes.[10] The return to physical activity follows a similar outline. Steps involved in the return to physical activity include: light aerobic exercise, sport specific exercise with no contact, full contact practices, and the full return to game play of a sport.[27] A step-by-step return to mental and physical activity allows the brain to acclimate to greater demands of

cognitive functioning. In some cases, early exercise is thought to improve symptoms and shorten the duration of return to activity protocols. Early exercise therapy includes moderate exercise in the beginning of the recovery and treatment processes. This generally improves the outcomes of mTBI cases by managing symptoms while continuing healthy activity and exercise.[28] The gradual and early return to activity is largely in place for the prevention of further neurological injuries because, as previously stated, one mTBI may put an athlete at a significantly higher risk for developing a second mTBI.[19,20] The proper treatment of mTBI, including symptom management and the return to activities, is positively impacted by a complete understanding of the pathophysiological implications behind the injury.

CONCLUSION

Ultimately, this article has established the need for a complete understanding of the pathophysiological implications of mTBI which impact diagnosis and treatment. A proper diagnosis and treatment plan for mTBI is heavily reliant on this complete understanding of the injury. A mTBI stems from biomechanical forces such as acceleration and deceleration. These forces create numerous acute neurological injuries throughout the brain. Through this article, it is evident that the consequences resulting from mTBI are apparent in common clinical practices. A complete understanding of the pathophysiological implications is extremely important. The millions of athletes estimated to have sustained a mTBI are highly dependent on a quick

and accurate diagnosis followed by the proper treatment.[1] This article reiterates the demand for precise diagnosis and treatment; however, a complete understanding of the pathophysiological implications of mTBI is necessary to ensure precision.

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