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Cannabidiol (CBD) in the Management of Sports-Related Traumatic Brain Injury: Research and Efficacy

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Introduction

The pandemic of sports-related traumatic brain injury and the associated development of chronic traumatic encephalopathy has prompted an interest within the medical community in the role of the endocannabinoid system and the use of Cannabidiol (CBD) to reduce acute and chronic cerebral inflammation among athletes. The purpose of this medical research review is to examine sports-related traumatic brain injury and the preventative and therapeutic use of cannabidiol among athletes. Given the high morbidity and mortality rate associated with post- concussion syndrome and chronic traumatic encephalopathy, and the critical role of the endocannabinoid system in health maintenance and cerebral injury recovery, examination of the administration of Cannabidiol (CBD) is warranted.

The Human Brain

The brain is the core governing structure of the human body. At a weight of over three pounds, the human brain, comprised of eighty-six billion neurons and associated glial cells and blood vessels, is the largest and most complex of all mammalian brains. The human cerebral cortex, a thick layer of neural tissue, is divided into four lobes of the forebrain; the frontal, parietal, temporal, and occipital lobes. Each lobe is comprised of cortical areas associated with particular executive functions, including self control, planning, reasoning, abstract thought, motor control, language, and vision. The two hemispheres of the brain are defined by lateralization processes, such as language, which is associated with left-sided hemispheric dominance, and spatiotemporal reasoning, which is associated with right-sided dominance. The cerebellum, or hindbrain, located at the base of the brain above the brainstem, coordinates voluntary movements such as posture, balance, coordination, speech, and learned motor behaviors. Further, the brainstem, which includes the medulla oblongata, pons, and the midbrain, regulates motor and sensory aspects of the central nervous system, as well as cardiac and respiratory functions. Finally, the endocannabinoid system, comprised of neuromodulator lipids and receptors in the brain, regulates the vast array of physiological processes essential for human life [1,2].

The Human Endocannabinoid System

The human endocannabinoid system is responsible for memory networks in the brain, both excitatory and inhibitory, including the neurogenesis of hippocampal granule cells, which regulate the timing of the endocannabinoids in accordance with the brain's needs, pain perception, mood, synaptic plasticity, motor learning, appetite and taste regulation, and metabolic function, which regulates the storage of energy and transport of cellular nutrition. Cannabinoid receptor binding sites are located in the forebrain areas associated with higher cognitive function, forebrain, midbrain, and hindbrain areas associated with movement control, and hindbrain areas associated with motor and sensory functions attributed to the autonomic nervous system. The endocannabinoid system affects the lipocytes and fat cells, collectively known as adipocytes, hepatocytes, in the gastrointestinal tract, musculoskeletal system, and endocrine system. The endogenous arachidonate-based lipids, anandamide and 2-arachidonoylglycerol (2-AG) are physiological ligands for the cannabinoid receptors.

Cannabinoid receptors CB1 and CB2, two G-protein-coupled receptors, facilitate the responses of the endocannabinoid system in the body, which are critical to maintaining homeostasis. CB1 receptors are located in the central and peripheral nervous systems as well as the lungs, kidneys, and liver. CB2 receptors are predominantly expressed in the immune system and hematopoietic cells.

The direct effect of Endocannabinoid Deficiency (CECD) correlates with multisystem clinical outcomes in such conditions as hyperinsulinemia, diabetes, dementia, cardiovascular disease, multiple sclerosis, and obesity. Three primary categories are herein defined to discuss Endocannabinoid Deficiency (CECD): genetic, acquired, and idiopathic autoimmune. Genetic Endocannabinoid Deficiency (CECD) relates to hereditary acquisition of a disorder; acquired refers to an external impetus or one of traumatic

origination, and idiopathic autoimmune refers to etiologies for Endocannabinoid Deficiencies (CECD) which do not have direct associations. Diseases and disorders are assigned to one or more of these categories because often secondary disorders arise with physiological changes associated with the primary diagnosis. For example, deficiency in human cannabinoids which contribute to ataxia arising from traumatic brain injury is categorized as acquired, originating from an external source. The presentation of ataxia related to CECD in multiple sclerosis, for example, is categorized as idiopathic autoimmune, and ataxia related to CECD in Huntington's Chorea is categorized as hereditary. Because the endocannabinoid system facilitates communication and coordination between various cell types, deficiencies directly affect physiological homeostasis with similar manifestations but unique originations.

Cannabidiol (CBD), a non-psychotropic cannabinoid naturally occurring in human and animal species, occurs as a phytocannabinoid, CBD oil, which is derived from the industrial hemp plant. The restorative effects of Cannabidiol (CBD oil), which increases anandamide and other lipid neurotransmitters, thereby restoring the endocannabinoid system, is of interest in the medical management of traumatic brain injury in athletes. Cannabidiol (CBD), derived from the hemp plant, demonstrates anti-inflammatory and immune-modulating properties. Cannabidiol (CBD) has a low affinity for CB1 and CB2 receptors in the human body, but acts as an indirect antagonist of their agonists. (Antagonists are defined as substances that stop or inhibit the effects of another substance on the cellular surface, producing the same effect as a substance which would normally bind to the receptor. Agonists are chemicals that bind to receptors and illicit a biological response.) Therefore, cannabidiol (CBD) may enhance the therapeutic effects of other cannabinoids, possibly by increasing the density of the CB1 receptors. Cannabidiol (CBD) has been demonstrated to cross the blood-brain barrier and exert antioxidant, antimicrobial, and neuroprotective properties, rendering it valuable in the prevention and treatment of oxidative stress associated with neurological and traumatic cerebral disorders.

The attributes of cannabidiol are critical in the restoration of the brain in traumatic brain injury, which causes acute and chronic disorders of the neurological system. Presently, supportive therapeutic interventions, including rest and physical therapy, remain the medical standard of care. Therefore, the neuroprotective, analgesic, and anti-inflammatory properties associated with cannabidiol, in combination with the ease of oral or aerosolized administration, renders CBD ideal in the medical management of cerebral damage [3-5].

Types of Traumatic Brain Injuries

Diffuse Axonal Injury (DAI)

Diffuse Axonal Injury (DAI) is a traumatic brain injury which causes the formation of extensive lesions in white matter tracts occurs over a widespread area. Diffuse Axonal Injury (DAI) varies in degree from mild to severe, and is one of the most common and devastating types of traumatic brain injury, associated with the primary damage occurring in concussive injury. Severe DAI is associated with coma and a 90% mortality rate. Indeed, those patients who regain consciousness remain significantly impaired and require lifetime care. Concussion is a milder type of diffuse axonal injury. DAI differs from traumatic brain injury secondary to a direct impact to the head which is associated with cerebral deformation. Instead, DAI is associated with repetitive, accelerated and decelerated shear forces and rotational forces which thrust the brain against the skull, similar to shaken baby syndrome. In athletics, examples of forces associated with DAI include repetitive injury to the occipital region of the skull from rebounding in basketball, indirect force to the neck and torso, which causes the head to rotate and move forward and laterally, associated with football and rugby, and head passing associated with soccer, which causes frontal and occipital damage as the brain forcefully impacts with the skull.

The major cause of damage in DAI is the disruption of axons, the neural processes that allow one neuron to communicate with another. White matter is comprised of mylineated tracts of axons. Forces which result in acceleration cause shearing injuries and cellular damage as tissue slides over other tissue. When the brain is accelerated, parts of differing densities and distances from the axis of rotation slide over each other, stretching axons that traverse junctions between areas of different density. Junctions where white and grey matter connect are especially susceptible to the formation of lesions associated with DAI.

In the white matter, lesions associated with DAI range in diameter from one to fifteen millimeters and are characteristically distributed, typically in the brain stem, corpus callosum, and cerebral hemispheres. The frontal and temporal lobes of the brain, the white matter of the cerebral cortex, the superior cerebral, the peduncles, the basal ganglia, the thalamus, and the deep hemispheric nuclei are also probable areas for the formation of lesions because of the difference in density of these structures than that of the remainder of the brain. This finding, which indicates the release of TAU proteins in traumatic brain injury, associated with DAI, is correlated with the development of Chronic Traumatic Encephalopathy (CTE). It is important to note that even mild

forms of DAI are associated with CTE, a finding which explains the development of neurodegenerative disease among athletes who have not experienced a documented concussion or loss of consciousness. A study at Boston University concluded that 91 percent of college football players who sustained TBI developed CTE. It may be argued that this number may be significantly low in light of the exclusion of athletes who have experienced mild diffuse axonal injury.

Assessment has historically involved MRI and/or CAT scan. Treatment protocols recommend abstinence from exercise and athletics, rest, and monitoring of symptoms. Return to competition in most states requires authorization by a physician. Research studies support the use of Cannabidiol (CBD) oil derived from industrial hemp, in the management of DAI. Cannabidiol has anti-inflammatory and neuroprotective properties and is effective in the reduction of pain [6-10].

Concussion

The term concussion, derived from the Latin 'concutere', to shake violently, is the most common type of traumatic brain injury. The medical literature refers to concussive injury as Mild Brain Injury (MBI), Mild Traumatic Brain Injury (MTBI) and Mild Head Injury (MHI) in defining concussion. The traumatic impact of the brain against the skull causes immediate metabolic, structural, and neurocognitive changes. The degree of impact which results in concussion varies between individuals and symptoms may be independent of the degree of concussive injury. Regardless of the impact, concussive injury universally causes a variety of physical, cognitive, and emotional symptoms, which may be subtle and not readily detected using imaging studies.

Symptomatology associated with concussion includes somatic, cognitive, emotional, physical and behavioral characteristics: somatic (headache), cognitive (feeling unclear or as if in a fog and slowed reaction times), emotional (emotional lability), physical signs (loss of consciousness or amnesia and insomnia), and behavioral changes (depression and irritability). Individuals who have sustained a concussion are more susceptible to concussive injuries, particularly if the new injury occurs prior to the resolution of the previous concussion. A negative, progressive process which requires lesser impacts to produce the same level of symptom severity is correlated with concussive injury. Research indicates the chronic traumatic encephalopathy, Parkinson's disease, depression, and neurodegenerative disorders are associated with concussive injury and may emerge throughout the lifespan.

The varying definitions of concussive injury and inaccurate reporting accounts for the inaccuracy in the epidemiology of concussion. In athletics, concussive injury is estimated to exceed 2 per 1000 player hours, or approximately 4 to 5 million per annum. The incidence of concussion in descending order is as follows: men's football, women's soccer, women's basketball, men's basketball, men's boxing and mixed martial arts, women's boxing and mixed martial arts, women's lacrosse, men's lacrosse, men's ice hockey, and men's wrestling. Extreme sports, which include auto racing, snowboarding, competitive skiing, and rock climbing are likewise associated with high incidences of concussion. Indeed, any sport which places the athlete at risk for direct or indirect trauma to the head is significantly considered in the reporting of concussive injury.

The effects of concussion TBI alter the brain's physiology immediately with detrimental effects which last for years. Included in the cascade of events unleashed in the brain by concussion is impaired neurotransmission, loss of regulation of ions, deregulation of energy use and cellular metabolism, as well as a reduction in cerebral blood flow. Excitatory neurotransmitters, biochemical, such as glutamate, serves to stimulate nerve cells, and nitric oxide, which is vital to cerebral blood flow and inflammatory processes, are released in excessive amounts into the white and gray matter. The resulting cellular excitation causes neurons to fire excessively and aberrantly, creating an imbalance of ions such as potassium and calcium across the cell membranes of neurons. Simultaneously, cerebral blood flow is reduced, precipitating a severe reduction in available cerebral energy. The cumulative effects of the acute physiological processes in traumatic brain injury are associated with the expression of TAU proteins within the brain. The dissemination of these proteins is associated with the development of chronic traumatic encephalopathy (CTE), which is epidemic among athletes, especially those who engage in contact sports.

In a 2016 study conducted at Boston University, 91 percent of former college football players who had sustained concussive injury developed Chronic Traumatic Encephalopathy (CTE), a neurodegenerative disorder associated with dementia, erratic behavior, rage, suicide, and demylineation of the central nervous system. Research indicates that concussive injury causes both functional and structural cerebral changes in the human brain. The advent of the use of SPECT scans in the diagnosis of CTE in living patients, which is associated with concussion, clearly supports the presence of neuropathological changes which cause cellular dysfunction with residual neurological, psychological, and structural damage within the cerebellum. Whereas medical research previously supported resolution of the damage associated with concussive injury, current studies indicate that traumatic brain injury initiates an aberrant metabolic and biochemical pathway which is associated with progressive neurocognitive diseases [11-14].

Subdural Hematoma

Subdural hematoma refers to a gathering of blood between the dura mater and the brain and is associated with traumatic brain injuries in such sports as football and soccer. Tears in the bridging veins across the subdural space rupture, causing increased Intracranial Pressure (ICP) causes compression and structural damage to delicate cerebral tissues. Whereas acute subdural hematomas are life-threatening, chronic subdural hematomas are associated with better prognosis with appropriate medical intervention. Permanent structural and functional damage is associated with subdural hematoma and neurocognitive and neurological symptoms may remain for the lifespan of the patient.

Classification of subdural hematomas is relative to onset, and divided acute, subacute, and chronic categories. Acute, traumatic subdural hematomas have the highest mortality rate and require immediate surgical decompression. High speed acceleration or deceleration injuries are associated with expansive hematomas and acute bleeds. Severe cerebral contusions likewise increase the likelihood of death. Whereas chronic subdural bleeds are slower and associated with venous tears, acute subdural bleeds have a high mortality rate which is associated with the degree of force to the brain. Indeed, the mortality rate associated with acute subdural hematoma is 60-80%. Sudden death in football, wrestling, and extreme sports is often associated with acute subdural hematoma.

Conversely, chronic subdural bleeds develop over a period of days to weeks and often occurs after minor head trauma. Because symptoms of chronic subdural hematoma may be initially subtle, until intracranial pressure increases significantly, clinical diagnosis may require weeks or months after trauma to the head. Shearing forces cause intra and pre-retinal hemorrhages and trauma from rotational and linear forces increases the strain on small bridging veins, causing subtle bleeding into the brain. In athletes, small bleeds, less than one centimeter in diameter, may resolve without intervention. Assessment after head injury is imperative, as a second impact injury in chronic subdural bleeding is associated with high mortality [15-19].

Epidural Hematoma

Epidural or extradural hematoma, also known as an epidural hemorrhage, is a type of traumatic brain injury (TBI) in which a buildup of blood occurs between the dura mater, the resilient outer membrane of the central nervous system, and the skull. Because the spinal cord is also covered by a layer of dura mater, epidural bleeding may also occur within the spinal column. In trauma, the rapid accumulation of blood within the intracranial space compresses delicate brain tissue and causes a shift in cerebral matter. Indeed, at least 15% of all epidural hematomas are fatal.

Epidural hemorrhages, like subdural, and subarachnoid hemorrhages, are categorized as extra-axial bleeds because they occur outside of the brain tissue. Intra-axial hemorrhages, which include intra parenchymal and intraventricular hemorrhages, occur within cerebral tissue. Symptomatology of epidural hematomas are deceiving and relative to the rate and volume of accumulated blood between the dura mater and the skull. A period of lucidity may be followed by weakness of the extremities on the opposite side as the lesion, compression of the crossed pyramid pathways, and loss of the visual field opposite to the lesion site. Intense headache is immediate and may progress to coma within a few minutes. This is associated with the compression of the posterior cerebral artery on the side of the lesion. Athletes involved in traumatic brain injury may emergently present with a fixed and dilated pupil on the side of the injury, with positioning of the eye downward and outward, related to unopposed CNIV and CNVI innervation. Intracranial structures likewise impinge on CN III as the volume of blood accumulates.

In sudden death after a traumatic injury, trans tentorial, or uncal herniation is often suspected, with associated respiratory arrest with the compromise of the medullary structures. As the pons is affected, the trigeminal nerve becomes involved, and is associated with increased mortality. Further, in the event of the presence of an epidural hematoma within the posterior cranial fossa, herniation causes Cushing's triad, defined as hypertension, bradycardia, and irregular respiration.

Intracranial epidural hematoma is most commonly associated with traumatic brain injury which frequently occurs in such sports as football, rugby, wrestling, martial arts, and boxing. Epidural hematomas commonly occur as a result of impact to the side of the head, causing shearing injury to meningeal arteries. Imaging studies reveal the convex shape of the epidural hematoma, as the expansion ceases where the dura mater is firmly attached to the skull. This lens-like shape, or lentiform, confirms the presence of the epidural hematoma and the need for immediate surgical intervention. Because epidural and subdural hematomas can occur simultaneously, earmarked by lucidity with a rapid decline to unconsciousness and sudden return to consciousness, appropriate assessment and emergent medical intervention is imperative. Indeed, the diagnosis of epidural hematoma is often dependent upon accurate assessment during the lucid interval prior to coma, as death is likely to ensue without surgical intervention.

Skull Fracture

Skull fracture is defined as a break in one or more of the eight bones that form the cranial portion of the skull and is usually associated with blunt force trauma. With excessive impact to the skull, fracture may occur at or near the site of the impact and cause damage to physical structures contained within the skull, including membranes, blood vessels, and the cerebellum. A fracture

in the skull of healthy athletes indicates that exceptional force has been applied and always causes concussion, with or without the loss of consciousness. Compound fractures, which lacerate the epidermis and meninges or impede the paranasal sinuses and the middle ear structures allowing the external environment to come into contact with the cranial cavity occur with frequency in competitive sports, including football and lacrosse. Contamination with residue from the playing field increases the likelihood of bacterial infection and encephalopathy.

Skull fractures are categorized as linear, depressed, diastatic, and basilar. Linear fractures occur most frequently and usually require no surgical intervention. Depressed fractures, which are often associated with traumatic injuries in such sports as lacrosse and baseball, are usually comminuted with bone displaced inward, requiring surgical intervention to repair cerebral tissue. Diastic fractures, which widen the sutures of the skull, occur among young children. finally, basilar fractures, which affect the bones at the base of the skull, occur most commonly in contact sports, such as mixed martial arts and boxing.

In the presence of concussion, assessment for compound skull fracture is of critical importance. The complexity of the immediate cascade of cellular inflammatory processes and the possibility of the introduction of bacteria from the external environment places the athlete at exceptional risk for complex neurological and immunological complications. Because athletes are predominantly healthy individuals affected by traumatic brain injury, the impact of sudden loss of neuropsychological function is devastating. The development and implementation of accurate emergent care for the athlete in the arena is imperative and warrants the establishment of universal practices which include neurocognitive and imaging assessments. Rehabilitative interventions, which will be discussed in a subsequent chapter are recommended for universal adaptation as well [20-21].

Second-Impact Syndrome

Second-Impact Syndrome, (SIS), occurs when the cerebellum swells rapidly after an individual sustains a second impact while the brain is inflamed from an initial trauma, resulting in death or catastrophic disability. The second impact, which may be mild or profound, may occur minutes or weeks after an initial impact, causing the cerebral arterioles to become dysregulatory, causing massive cerebral edema. The metabolic dysfunction and rapid increase in intracranial pressure causes uncal and cerebellar brain herniation, a condition in which brain tissue is no longer contained by the skull.

Coup and Contrecoup Injuries

In traumatic brain injury, a coup injury occurs under the site of actual impact and a contrecoup injury occurs on the opposing side from the site of the connecting force. Coup and contrecoup injuries are categorized as focal brain injuries, which produce cerebral contusions. Abrupt deceleration of the head, which causes cerebral impact with the skull, associated with contact sports such as football, rugby, soccer, and basketball, causes metabolic changes, including the release of TAU proteins, and chronic cerebral inflammation. Awareness of the mechanism of focal traumatic brain injuries is imperative in the management of the neurocognitive and neurodegenerative disorders associated with coup and contrecoup injuries.

Chronic Traumatic Encephalopathy (CTE)

Chronic Traumatic Encephalopathy (CTE), a progressive neurodegenerative disease, is associated with repetitive traumatic injury to the brain, including diffuse axonal injury, concussion and coup and contrecoup injuries. Research published in November of 2016 revealed that the inflammatory process which is initiated at the time of injury is progressive, causes immediate metabolic changes in the cerebellum, and the release of hyper phosphorylated TAU proteins which entangle the brain. Symptomatology of CTE includes mood disorders, rage, depression, and dementia. Disorders which mimic Parkinson's and ALS are common with CTE, which affects CB1 and CB2 receptors within the endocannabinoid system, causing aberrant neurotransmitter communication, and augmenting serotonin and dopamine responses. Diagnosis of CTE is now possible with SPECT scan in living patients and intervention with cannabidiol is warranted. CTE has been highlighted as a critical medical condition in football, basketball, boxing, martial arts, kick boxing, wrestling, and soccer, but is likely in any sport after even mild head trauma. The key point in traumatic brain injury is the comprehension of the importance of the continued cascade of metabolic and neurophysiological changes associated with inflammation which progresses over the lifespan. The incidence of CTE among young male and female athletes warrants the need to provide education, phytocannabinoid therapy preventatively as a neuroprotective measure, and post-injury with rehabilitation immediately after a traumatic brain injury to reduce inflammation, restore the function of the endocannabinoid, and reduce pain and the degree of neurological deficits.

Traumatic Brain Injury

Traumatic Brain Injury (TBI), also known as intracranial injury, is caused by external force on the skull (closed) or via perforation of the skull (penetrating). TBI can occur as a consequence of a sudden acceleration or deceleration within the cranium or via a complex combination of movement and sudden impact upon the skull. Brain trauma causes an immediate inflammatory response, regardless of the severity of the impact. Metabolic changes include changes in cerebral blood flow and intracranial pressure, metabolic fluctuations, including a burst

of nitric oxide followed by a rapid intracellular decline, and the expression of TAU proteins into the cerebellum. The release of the TAU proteins is directly associated with the development of chronic traumatic encephalopathy (CTE), a neurodegenerative and neurocognitive disease. The key point of research completed in November of 2016 is that the inflammatory response following cerebral injury is progressive and has extensive detrimental effects upon the individual's cognitive, social, emotional, and behavioral patterns. Less than ten percent of structural changes are visible on MRI and SPECT scan has recently been employed to visual CTE in living patients. However, inflammatory processes negatively impact the brain prior to visibility on imaging scans. In athletics, diffuse axonal injury, concussion, and coup-contra coup injuries initiate the progressive inflammatory responses which are associated with depression, rage, headache, confusion, memory loss, Parkinson's disease, and ALS.

Traumatic brain injury is classified based upon the severity of the anatomical features of the injury and the causative force, or mechanism. Mechanism-related classification divides TBI into closed and penetrating head injury. Severity of the injury may be cited as mild, moderate, or severe. The Glascow Coma Scale (GCS) is the most commonly utilized system for tracking the severity of TBI. The scale grades a person's level of consciousness on a scale of 3 to 15 based upon verbal, motor, and reactionary ocular testing. A GCS of 13 or greater is noted as mild, 9-12 as moderate, and 8 or below as severe. GCS is useful as an assessment instrument, but has no predictive outcome value. A current model developed by the Department of Defense employs three systems of assessment, the Glascow Coma Scale (GCS), the Posttraumatic Amnesia Scale (PTA), and the Loss of Consciousness Scale (LOC). Additional assessments are based upon imaging studies and physiological markers such as Intracranial Pressure (ICP).

Additional systems classify TBI according to pathological features. For example, a cerebral assessment may determine the presence and location of lesions, whether extra-axial, which occur within the skull but external to the brain, or intra-axial, which occur within the brain tissue. Damage from TBI may be described as focal or diffuse and located within specific or generally, across various regions of the brain. Concomitant use of these classifications allows the clinician to thoroughly document the traumatic brain injury.

While diffuse injury manifests with little apparent damage in neuroimaging studies, inflammatory processes can be detected in serum and spinal fluid studies which assess the presence of cytokines and TAU proteins. In 2016, researchers at Boston University confirmed that SPECT scans are useful in determining the presence of CTE as well as diffuse axonal injury, inflammatory processes secondary to mild concussion, and widespread damage to the white matter and cerebral hemispheres. Whereas cerebral edema and profound lesions and hemorrhages are visible on CAT and MRI, the determination of inflammation secondary to mild traumatic brain injury is critical, since cumulative injuries increase the likelihood of CTE.

Symptoms of traumatic brain injury vary according to the functions of the affected area. Focal injuries, for example, most frequently occur in the orbitofrontal cortex and the anterior temporal lobes of the brain. These regions are involved in social behavior, regulation of emotions, olfaction, and decision-making. Hence, manifestations of TBI such as rage, depression, diminished impulse control, and poor judgement are common among athletes who sustain focal injuries. Cerebral laceration and hematomas also affect language and motor centers, producing aphasia and hemiparesis respectively. And, while the severity of symptoms varies according to the degree of injury, traumatic brain injury symptomatology includes unconsciousness, inability to remember the cause of the injury or events that occurred immediately before or up to 24 hours after the event, confusion and disorientation, difficulty remembering new information, headache, dizziness, blurry vision, nausea and vomiting, tinnitus, default with speech, and mood fluctuations. And, where it was previously understood that concussive injury resolves completely without intervention, research now indicates that even mild brain trauma initiates a sustained inflammatory process which may culminate in the development of permanent neurological impairment.

One of the most significant complications of traumatic brain injury is the pattern of sleep disruption or somnipathy. This manifestation of traumatic brain injury interferes with physical, mental, emotional, and social function. Dyssomnias, parasomnias, circadian rhythm sleep disorders, sleep apnea, narcolepsy, hypersomnia, cataplexy, and sleeping sickness from subclinical infection and structural damage are frequent manifestations of traumatic brain injury. In traumatic brain injury, the allostatic load associated with sleep disorders increases mortality significantly from cerebral ischemia, diabetes, and myocardial infarction. The allostatic load is defined as the cumulative effect of physiological stress on the body related to chronic exposure to fluctuating and heightened neuronal and neuroendocrine responses. In athletes, the immunological, cardiovascular, and neurological systems are affected by continuously elevated levels of epinephrine and cortisol levels. Homeostasis is maintained in the short-term when these systems are fully functional [1]. However, longitudinal reactive oxidative stressors cause chemical imbalances in the autonomic nervous system and central nervous

system, diminishing circulating cannabinoids and affecting CB1 and CB2 receptors. The cascade effect of the immunological response to mild traumatic brain injury facilitates the early development of chronic traumatic encephalopathy in athletes. Indeed, the illusion of health among athletes masks the significance

of underlying inflammatory processes which often culminate in severe or rapidly progressive neurological deterioration following cessation of participation in such sports a football, basketball, soccer, boxing, and martial arts.

Cognitive and Psychiatric Effects of Traumatic Brain Injury

Regions of The Brain and Their Function

The responsibility for all human thought and movement lies within the cerebellum. The ability to interact with the environment, communicate with others, and discern sensory information and language is contingent on the level of cerebral intracellular and extracellular function. The endocannabinoid system provides the circuitry via the CB1 and CB2 receptors to facilitate synaptic communication between cerebral centers and the spinal cord, maintain homeostasis, and neurochemical balance. Inadequate levels of cannabinoids affect hormonal and biochemical processes which directly affect regions of the brain, causing aberrant emotional, social, behavioral, and physical responses. Indeed, traumatic brain injury, is a primary source of endocannabinoid imbalance in athletes, causing inflammatory processes which affect circulating cannabinoid levels and cause a subtle and progressive decline in cerebral function. Comprehension of the regions of the brain and their respective function is imperative in the assessment of the traumatically brain injured athlete and in the development of an effective plan for remediation.

Analysis of the composition of the human brain reveals a complex array of systems which are intricately balanced to optimize function of the body. Traumatic brain injury, therefore, disrupts the equilibrium of this delicate system, causing an inflammatory effect which adversely affects cognition, emotional balance, and social function. In greater than 35% of individuals who have sustained concussion or mild TBI, persistent symptoms can permanently impact an individual's ability to return to daily functioning. Physical symptoms, including headache, nausea, fatigue and dizziness, cognitive symptoms, including memory, attention and executive function impairments, and mental health concerns, including depression, anxiety and post-traumatic stress disorder, are commonly observed among athletes who sustain mild to moderate head injury.

Cognitive impairments secondary to Traumatic Brain Injury (TBI) are substantial sources of morbidity for affected individuals, their family members, and society. Neurocognitive consequences of all levels of TBI include disturbances of attention, memory, and executive functioning. The disturbances of attention and memory are particularly problematic for patients because disruption of these relatively basic cognitive functions exacerbate additional disturbances in executive function, communication, and other relatively more complex cognitive functions. The increased incidence of psychiatric syndromes associated with TBI requires a through neuropsychiatric assessment to minimize the potential for progressive neurocognitive manifestations associated with TBI. Research indicates that mild inflammatory processes impede cognitive and neuropsychiatric function in traumatic brain injury. Manifestations may include memory impairments, difficulty with new learning, difficulty with attention and concentration, reduced speed and flexibility of thought processing, impaired problem solving skills, problems with planning, organization, and decision-making, expressive and receptive aphasia, impaired judgement pertaining to safety, impaired writing skills, amnesia, difficulty with multi-tasking, and anomia (can't name).

Psychiatric manifestations of traumatic brain injury include an array of clinical presentations including major depression, anxiety, schizophrenia, bipolar disorder, and psychosis. Athletes with a history of TBI are at increased risk for rage, suicidal ideation, homicidal ideation, and disconnectedness. Interventions include cannabidiol to facilitate cerebral plausticity, reduce inflammation, and correct neuronal malfunction.

Assessment of Traumatic Brain Injury in Athletes

Traumatic brain injury in athletes is of paramount importance. In 2016, the ability to discern chronic Traumatic Encephalopathy (CTE) in living individuals using SPECT scanning and TAU serum and cerebrospinal fluid specimens provided insight into the epidemic of CTE among athletes of all ages and skill levels. Whereas CT scan and MRI were used in the past, research indicated that less than 10 percent of all concussive injuries were evident upon these types of imaging studies. Post-mortem examinations have revealed the extensive damage among young male athletes who participated in football and correlations have been made pertaining to behavior patterns and these post mortem examinations. It is currently understood that even mild injury to the brain causes an inflammatory response with progressive deterioration. The concept of resolution of concussive injury without intervention has been reassessed in current medical research. Interventions which employ hyperbaric oxygen therapy, cannabidiol, and rehabilitation are outlined in a subsequent chapter and are imperative in light of the reality of chronic cerebral inflammation following traumatic brain injury.

The assessment of the type of cerebral injury and symptoms as well as the comprehension of the type of micro-traumatic injury affecting the brain is critical in the management of the athlete with TBI. The following chart outlines specific injuries and correlating activities which cumulatively affect the individual, increasing inflammation and contributing to TAU protein expression. Because CT and MRI scans are inaccurate and SPECT scans are not readily available, the use of serum TAU protein levels and psychometric assessments are necessary in the determination of traumatic brain injury. Baseline psychometric and color vision testing is recommended with repeated testing following injury

and/or post-game to detect subtle inflammatory processes with the intent of providing early intervention prior to the development of neurodegenerative disease processes which often manifest as depression, rage, cognitive impairment, and poor decision-making.

Athlete Assessment Chart

Athlete Injury Assessment Chart	Clinically Defined Symptoms per Literature	Specific Claimant's Symptoms	Micro-Traumatic Activities which Directly Contribute or Cause the Diagnosis	Specific Athlete's Micro-Traumatic Activities
Non-Specific Encephalopathy (Global brain damage)	Permanent (or degenerative) brain injury with common neurological symptoms including loss of cognitive function, subtle personality changes, inability to concentrate, lethargy, and depressed consciousness.	Loss of cognitive function, schizophrenia, bipolar disorder, depression, inability to concentrate	Repetitive closed head injuries, concussive injuries, internal cerebral impact against skull, repetitive impact against occipital area radiating to frontal lobe	Repetitive impact with opponents elbows to head, rebounding, impact with opponents causing internal cerebral shift against skull, impact against floor, ball, and inanimate objects
Secondary Infection	Suspected or confirmed infection, such as staph or strep	Fatigue, fever	Contact with playing surface, contaminated equipment	Immune suppression, immune dysfunction
Epileptogenicity (Micro and macro abnormal brain activity and seizures)	A chronic condition in which brain neurons fire in a hyper-synchronous manner, also referred to as a seizure.	Headaches, tremor, changes in level of consciousness	Repetitive closed head injuries, concussive injuries, internal cerebral impact against skull, repetitive impact against occipital area radiating to frontal lobe	Repetitive impact with opponents elbows to head, rebounding, impact with opponents causing internal cerebral shift against skull, impact against floor, ball, and inanimate objects
Sleep Disruption (Insomnia, daytime sleepiness, cessation of breathing during sleep)	Dyssomnias are a broad classification of sleep disorders that result from problems in initiating or maintaining sleep or of excessive sleepiness, and are characterized by a disturbance in the amount, quality, or timing of sleep.	Interrupted sleep, minimal sleeping time, poor quality of sleep	Repetitive closed and concussive injuries to the brain with and without loss of consciousness causing diffuse neuronal damage in region of repetitive impact with dissemination throughout the brain	Repetitive impact with opponents elbows to head, rebounding, impact with opponents causing internal cerebral shift against skull, impact against floor, ball, and inanimate objects
Dysfunction of Corticospinal Pathway (Pain and numbness in limbs, limited range of motion in limbs, back and neck)	Dysfunction resulting from damage to the white matter motor pathway starting at the cortex that terminates on motor neurons in the spinal cord which controls the movements of the limbs and trunk.	Pain, numbness, and weakness in the limbs, spine, neck, hands, and feet	Repetitive closed head injuries, concussive injuries, internal cerebral impact against skull, repetitive impact against occipital area radiating to frontal lobe, and repetitive impact in cervical, spinal, and lumbar regions	Repetitive impact with opponents elbows to head, rebounding, impact with opponents causing internal cerebral shift against skull, impact against floor, ball, and inanimate objects, direct impact to cervical, spinal, and lumbar regions during play

Cognitive Dysfunction (Changes in mood, behavior, memory and decision making)	A category of mental health disorders that primarily affect learning, memory, perception, and problem solving, and include amnesia, dementia, and delirium. Causes vary between the different types of disorders but most include damage to the memory portions of the brain.	Loss of cognitive function, schizophrenia, bipolar disorder, depression, inability to concentrate	Repetitive closed head injuries, concussive injuries, internal cerebral impact against skull, repetitive impact against occipital area radiating to frontal lobe	Repetitive impact with opponents elbows to head, rebounding, impact with opponents causing internal cerebral shift against skull, impact against floor, ball, and inanimate objects
Alloplasticity (Changes in brain effecting systems that control hormones causing medical issues, such as diabetes, stroke, eating disorders and obesity) -allostasis and allostatic load -central nervous system -neuroendocrine -immune system Activity	Neuroplastic changes in the brain that may involve individual neurons, or at whole-brain scales in response to an injury or prolonged stress.	Loss of cognitive function, schizophrenia, bipolar disorder, depression, inability to concentrate	Repetitive closed head injuries, concussive injuries, internal cerebral impact against skull, repetitive impact against occipital area radiating to frontal lobe	Repetitive impact with opponents elbows to head, rebounding, impact with opponents causing internal cerebral shift against skull, impact against floor, ball, fixed objects
Cervical Spine Injuries (Damage to the spine causing problems with movement and numbness)	Damage to the cervical region of the spinal cord that causes changes in its function. These changes may translate into loss of muscle function, sensation, or autonomic function in parts of the body controlled by the cervical spinal cord.	Pain in neck and upper back, headaches, loss of motor function in hands, numbness and tingling in hands and digits, loss of range of motion in neck	Repetitive closed head injuries, concussive injuries, internal cerebral impact against skull, repetitive impact against occipital area radiating to frontal lobe. cervical spine injuries	Repetitive impact with opponents elbows to head and neck, rebounding, impact with opponents causing internal cerebral shift against skull, impact against floor, ball, fixed objects
Oral-Maxillofacial Injuries (Injuries to face, teeth, head and jaw causing difficulty in chewing, speech impairment and pain) -fracture/dislocation -nerve damage	Injuries to the head, neck, face, jaw and the hard and soft tissues of these areas.	Headaches, pain in the face, loss of teeth, chewing difficulties, pain in jaw and sinuses	Repetitive facial injuries related to impact to face, jaw, teeth, and head	Repetitive impact with opponents elbows to head and neck, rebounding, impact with opponents causing internal cerebral shift against skull, impact against floor, ball, fixed objects
Rotator Cuff and Brachial Plexus Injuries	Injuries and damage to the muscles, ligaments, nerves and/or tendons of the arm and shoulder.	Pain, loss strength in arms and torso, muscle wasting and diminished motor control	Repetitive impact to shoulders and upper torso, neck, repetitive execution of movements including throwing and catching.	Repetitive throwing, rebounding, impact with players, inanimate objects, strain and minimal recovery time after injury

Orthopedic Injuries (Injuries to joints and ligaments of the hips, knees, ankles, feet, wrists and hands that cause pain, limited range of motion and loss of use)	Injuries and damage to the musculoskeletal system including bones, joints, ligament and nerves.	Pain in limbs, hips, ankles, hands, arms, and legs and loss of motor function, fatigue with exertion	Repetitive injuries to the spinal column and muscles secondary to throwing, rebounding, player impact	Repetitive throwing, rebounding, impact with players, inanimate objects, strain and minimal recovery time after injury
Auditory Injury (Damage to the anatomical components of the ear, loss of hearing, ringing in the ears)	Injuries and damage to the ear and the process of hearing	Loss of hearing, ringing in the ears, difficulty understanding language	Repetitive closed head injuries, concussive injuries, internal cerebral impact against skull, repetitive impact against occipital area radiating to frontal lobe. cervical spine injuries	Repetitive impact with opponents elbows to head and neck, rebounding, impact with opponents causing internal cerebral shift against skull, impact against floor, ball, fixed objects
Ocular Injuries (Damage and injury to the eye(s), loss of vision, cataracts, macular degeneration)	Injury, damage, and disorders affecting the eye and the process of vision.	Changes in visual acuity and low vision. Predisposition to cataracts and macular degeneration in later life	Repetitive closed head injuries, concussive injuries, internal cerebral impact against skull, repetitive impact against occipital area radiating to frontal lobe. cervical spine injuries. Exposure to UV and arena lighting.	Repetitive impact with opponents elbows to head and neck, rebounding, impact with opponents causing internal cerebral shift against skull, impact against floor, ball, and fixed objects. Exposure to UV and arena lighting.

Concussion and Traumatic Brain Injury in Football

American football poses the greatest risk for concussive injury for athletes. Indeed, the chance of experiencing a traumatic brain injury exceeds 75%. The physiology of impact between players of the game and players and the playing field account for the high incidence of concussive injury. Comprehension of the mechanical aspects of brain injuries associated with football is vital in the assessment of the athlete.

The adult brain is a three-pound organ, surrounded by cerebral spinal fluid, located inside the skull. The cerebral spinal fluid is intended to act as a shock absorber for minor impact to the "floating" brain: not buffer severe blows to the head associated with football. A concussion occurs, for example, when the brain moves rapidly inside and against the skull. A direct impact to the head or whiplash effect to the body causes the brain to accelerate and strike the inner skull, called the coup. When the head decelerates, and the motion ceases, the brain then hits the opposite side of the inner skull, called the contrecoup. In football, rotational concussion, in which the head rapidly rotates from one side to another side, causing shearing and straining of brain tissues, likewise causes damage to delicate neuronal pathways within the cerebellum, progressive inflammation, and residual neurological disturbances.

In professional football, the vast majority of concussions are associated with "T-bone" hits, which occur at the entrance to the ear canal or between the eyes. These hits disrupt the brain's center of gravity, causing a rocking effect, backward and forward with repetitive internal impacts against the skull. Whereas the brain is more flush with the skull in adolescence, the space between the skull and the adult brain increases to one-eighth to one-quarter inches, permitting the opportunity for a ricochet effect off of the skull upon impact and increased cerebral trauma. As a point of reference, the G-force associated with T=bone hits and helmet-to helmet hits range between 100-150 G's. A rolling F-16 fighter jet produces a G-force of 9 to the pilot. Hence, the traumatic brain injuries associated with parietal and temporal lobe impacts are extremely dangerous, and are associated with CTE. The Boston University study indicated a 91% incidence of CTE in deceased college football players. Currently, as SPECT scanning becomes standard practice to identify CTE in living athletes, the statistic is expected to exceed 95% in active players.

Criticism of the NCAA and the NFL regarding the assessment and treatment of concussion in athletes is a critical issue. As the number of traumatic brain injuries increases, exceeding 11 per 1000 exposures, including diffusal axonal injury, concussive injuries, and coup-contracoup injuries, the challenge to assess and intervene immediately is imperative. Because young athletes are being diagnosed with CTE in their twenties and thirties, the need

for education of athletic trainers, coaches, physicians, and health care practitioners has increased dramatically. Inflammation of the brain leads to progressively debilitating physical and emotional disorders, attention disorders, depression, headache, amnesia and motor diseases. The presence of inflammatory processes in the developing brain, which continues until age 25, is of utmost important to preserve optimal neurological and cognitive development. Comprehension of the full spectrum of injury from field or court through rehabilitation and medical management is imperative for the physician, nurse, athletic trainer, and coach who are in positions of critical decision-making which inevitably affects the well-being of the athlete. Liability for treatment of the injured player is associated with proper medical attention, reinforcing the need for understanding of all of the aspects of injury and intervention. While concussion is not particular to anyone sport, the model of concussive injury in American football will be herein presented to highlight the scope of medical intervention from initial incident through medical rehabilitation.

The force of head-to-head impact is a common source of concussive injury, and subclinical traumatic brain injury, which are associated with progressive cerebral inflammation and the development of chronic traumatic encephalopathy. In head-to-head collision, the G-force increases with speed and weight of the individual players, but can easily exceed 1600 pounds when two 250 pound athletes collide running at a speed of 4.56 seconds. In such incidents, the immediate impact causes a rapid frontal-to-occipital cerebral shift, with internal rebound of the brain within the skull. The athletic trainer, coach, and medical practitioner observe that two players collide with the frontal portion of the helmet, immediately alerting them to the possibility of a concussive injury. The importance of recognizing the type of impact and estimating the relative degree of force is important on the field. For example, if two players are abutting helmets without significant force, the possibility of concussive injury is diminished. Conversely, if two players are moving with acceleration and collide, the potential for concussive injury of one or both players is dramatically increased. In situations where an increased degree of G-force is observed and estimated, concussion may occur and include symptoms such as the immediate loss of consciousness or vertigo, disorientation, headache, tinnitus, nystagmus, nausea and vomiting, and impaired memory. The athlete may remain ambulatory, but experience impaired motor coordination, or become obtunded on the court or field. First responders, which include athletic trainers, assistant and head coaches, and ancillary personnel, must secure stabilization of the player, including maintaining prone position on the field with neck stabilization. Assessment of acute head injury, which includes eye movement, level of consciousness using the Glasgow Coma Scale and the Balance Error Scoring System, which assesses vertigo and the ability to maintain motor function is readily employed. Regardless of the degree of potential head injury, removal from the field is imperative. Immediate placement of a phone call for paramedic and physician assessment, if available, is mandated for the player with acutely symptomatic head injury and transport to the local emergency room by ground or air, when necessary is warranted.

At this junction, it is critical that the athletic trainer, coach, and medical practitioner comprehend the importance of their actions. Failure to secure medical care for the injured payer or recommendation to allow the athlete to return to play may increase the morbidity and mortality of the athlete.

Second Impact Syndrome (SIS), for example, is an increasingly common phenomenon with devastating consequences. The likelihood of the incidence of Second Impact Syndrome (SIS) increases when return to play erroneously occurs after the occurrence of either a concussive injury or subclinical concussive injury. Second Impact Syndrome (SIS) is characterized by rapid and severe cerebral swelling with a catastrophic outcome. This medical emergency occurs when a second concussive injury is sustained before the resolution of a previous concussion. Because inflammatory processes remain after concussive injury, dysregulation of intracranial pressure and cerebral perfusion ensue, leading to diffuse cerebral edema and possible cerebral herniation. On the field, the athletic trainer, coach, and medical practitioner may observe a direct or indirect impact of varying degree of force. The injured player immediately losses consciousness and emergent care is critical, given the high fatality percentage associated with SIS. First responders on the field may observe dilated pupils, loss of eye movement, loss of consciousness, acute respiratory failure, and/or death of the injured player. Team medical personnel and coaches must be prepared to administer cardiopulmonary resuscitation and facilitate ground or medevac transport of the athlete. In the vast majority of cases, SIS causes death within minutes. In instances where SIS is not fatal, neurosurgery is considered to alleviate the cerebral edema and herniation. The long-term effects in the survivor include loss of motor function, dependency upon mechanical ventilation, loss of cognitive function, loss of memory, paralysis, and seizure disorders. Administration of cannabidiol, which has antispasmodic, antiepileptic, and anti-inflammatory properties, enhances recovery of cognitive and motor function. The key points for the athlete and athletic staff are prevention of SIS incorporation of preventative use of cannabidiol, and the adoption of policies which prevent admission to play when head trauma is suspected or observed.

Traumatic brain injury, which varies with the severity of impact and the individual's immune response, is always medically critical. Cerebral edema and contusion occur immediately and rapidly accelerate. Because athletic trainers and coaches are often unaware of the progression of the cerebral inflammatory response following concussion, education is paramount to both reinforce

the critical need for appropriate intervention for the athlete and reduce the likelihood of morbidity and mortality. In the emergency room or trauma center, immediate efforts are initiated to attempt stabilization, including insertion of intravenous access for fluid administration, linkage for cardiac monitoring, application of cervical spine and head braces, and conduction of imaging studies, including CAT and MRI. Severe concussion may interfere with respiratory status, warranting the application of oxygen via mask or nasal cannula, or intubation for mechanical ventilation when respiratory decompensation has occurred. If cerebral edema is rapidly compromising the neurological and cardiopulmonary status of the injured player, craniotomy is performed to reduce intracranial pressure. In concussive injury where these emergent measures are employed, transport to the intensive care unit follows stabilization in the emergency area. Concussive injuries which are less severe are treated according to the results of the CAT and MRI and symptomatology of the athlete. Discharge of the individual to home, however, following a concussive injury, requires continuous monitoring by the family or support system who is in physical attendance to the injured player. Because progressive cerebral edema or vascular changes may lead to loss of consciousness, seizure activity, disorientation, and death if left untreated, immediate transport to the hospital is warranted if changes occur in the athlete who has experienced head injury.

Concussion in the hospital is treated supportively and includes continuous monitoring and assessment until rehabilitation is possible. It should be noted that chronic progressive inflammation occurs after any degree of traumatic brain injury and is causatively associated with the development of chronic traumatic encephalopathy (CTE). Whereas standard rehabilitation for post-concussion includes rest and abstinence from athletic training and competition, and physical and occupational therapy in severe cases, the use of cannabidiol is herein suggested for remedial intervention. Recent research indicates that the progression of cerebral inflammatory processes and the release of TAU proteins continues after head injury. Recent research indicates that cannabidiol reduces cerebral inflammation, increases cerebral plausticity, and promotes neurogenesis and revascularization of damaged brain tissue. Restoration of cognitive function, motor coordination, memory, verbal expression, and visual acuity accompany reduction in cerebral inflammation. Headache, concentration difficulty, and disorientation are improved and research indicates that athletes who have been administered CBD experience a reduction in pain, anxiety, depression, mood instability, and dissociative behavior [22,23].

Because subclinical brain injury is associated with the development of Chronic Traumatic Encephalopathy (CTE), use of cannabidiol is warranted as a preventative measure to address chronic cerebral inflammation in athletes. Whereas phytocannabinoids may be administered to maintain ideal nitric oxide levels in the non-injured athlete, cannabidiol therapy may be administered routinely to athletes to reduce cerebral inflammation post-competition, even in the absence of concussive injury. The development of CTE, for example, increases with the incidence of subclinical cerebral injuries, which cause the release of TAU proteins and illicit a chronic inflammatory response. Cannabidiol reduces cerebral inflammation and reduces reactive oxidative stress, which is associated with cellular dysfunction. Because the endocannabinoid system is critical in the regulation of immunological and inflammatory responses in the brain, maintenance of the endocannabinoid system is imperative to reduce devastating cellular responses to traumatic brain injury. Administration of cannabidiol is suggested as remediation in the management of post-concussion syndrome, chronic traumatic encephalopathy, and as preventative therapy to thwart chronic progressive inflammatory process in the cerebellum.

Concussion and Traumatic Brain Injury in Basketball

Basketball has historically been considered a non-contact sport. The rate of concussion and traumatic brain injuries among basketball players has increased over 100% over the past two decades. Women's basketball is second to American football in the number of traumatic brain injuries, followed in the rankings by men's basketball. The degree of brain injury and increased incidence among women is also associated with hormonal fluctuations which alter prothrombin and clotting times in women, permitting prolonged microcirculatory hemorrhages in the brain. Among both genders, traumatic brain injury in basketball is related not only to player-to-player and player to environment contact, but to repetitive rebounding, which forces the spinal column upward, forcing the brain against the frontal portion of the skull. This repetitive, mild to moderate trauma increases the likelihood for the development of frontal lobe cognitive and emotional disorders and, of course, chronic traumatic encephalopathy. Further, the evolution of the game itself permits players to aggressively use their physical body to fight for position, draw contact in the air with other players, and land onto the court with G-forces similar to those experienced in football.

Research published in 2010 in Pediatrics indicated that over 375,000 youths are sent to the emergency room each year due to basketball-related injuries, with 70 percent related to head injury. Collisions with the floor, ball, and player are routinely assessed and reported, especially in youth league competition. However, the diffuse axonal injuries, which occur as a part of the vertical movement associated with the game, are not typically evaluated until cognitive or emotional issues present in the athlete. The symptoms of depression, cognition, rage, confusion, and short term memory loss indicate frontal lobe damage. In light of the use of SPECT scanning for detection of CTE among football players,

employment of the same technology for evaluation of basketball players is warranted. Although the total number of injuries declined over a 10-year period, the report highlighted a 70 percent increase in traumatic brain injuries on the court.

Concussion and Traumatic Brain Injury in Boxing and Martial Arts

Boxing and martial arts serve as exemplars for how repetitive head trauma affects cerebral brain function and structure in the athlete. While the negative effects of boxing were medically recognized in 1928, the identification of Chronic Traumatic Encephalopathy (CTE) on post-mortem examination of athletes within the past five years, provided the data necessary to fully capture the severity of repetitive traumatic brain injury. Boxing and martial arts, including kick-boxing, engages athletes in receptive contact with thousands of cerebral impacts of varying degrees. Radiological findings support the development of CTE among living boxers and martial arts participants and long-term consequences of cumulative head trauma have received attention after the deaths of high-profile athletes such as boxing legend Mohammad Ali, who developed Parkinson's disease, secondary to CTE, and professional wrestler Brian "Axl Rotten" Knighton, who developed CTE. Clinical manifestations of CTE include various symptoms affecting the pyramidal and extrapyramidal systems, which manifest most often as disturbed gait and coordination, slurred speech and tremors. Cerebral dysfunction also ensues, causing cognitive impairment and neurobehavioral disturbances, including memory loss and rage. Cumulative head trauma alters brain structure, plausticity, and functionality. Elevated scores on the Fight Exposure Score (FES) have indicated decreased brain volumes among boxing and martial art athletes, especially in the areas of the thalamus and caudate. This scale includes information pertaining to the length of time engaged in the sport and the number of competitions. Further, research indicates that greater exposure to repetitive head trauma is associated with lower brain volumes and lower processing speed among active professional fighters. Post-mortem examinations of boxers have shown structural changes in the subcortical and cortical regions. With the advent of the use of SPECT among professional football players, medical evidence warrants the employment of such imaging among boxers and martial arts athletes as well. The clear correlation between neurodegenerative and neurocognitive decline among athletes who sustain repetitive head injury is attributable to the expression of TAU proteins within the brain and progressive inflammatory responses which accompany traumatic brain injury.

Traumatic Brain Injury in Soccer

Traumatic brain injury among soccer players includes Diffuse Axonal Injury (DAI) and concussive injury comparable in incidence to that of American football players. Among collegiate athletes, concussion had been experienced by 40% of football and soccer players at the time of entrance into NCAA. Whereas the head is shielded in American football by a hard helmet, the head is unprotected in soccer. The concussive injuries in soccer, are directly related to player-to-player contact, player-to field contact, and player to ball contact. Indeed, the technique of using the head to pass the ball places the soccer player for frontal lobe damage via repetitive cerebral injury, which is associated with the development of chronic inflammation. Memory loss, behavioral and emotional changes, insomnia, and cognitive dysfunction are indicative of brain injury among soccer players. Research indicates that those players who frequently employ the head pass experience significant decrease in verbal, visual tracking, and visual learning abilities. Fine visual discrimination and visuospatial organization abilities were also affected, indicating damage to the occipital portion of the brain, secondary to the rebounding effect after a frontal head impact. In light of recent research pertaining to CTE in American football, several professional soccer players have indicated that they will donate their brains post-mortem for CTE research. The use of SPECT scan imaging is also warranted to assess CTE in soccer players given the comparable rates of concussive injury between the two sports.

Concussion and Traumatic Brain Injury in Hockey

Concussive injury in ice hockey is associated with impact routinely sustained throughout the course of the game: blindsiding (checking from the player's blind side with primary contact to the head), checking to the head, checking to the body, fighting, collision with a teammate, hit by a stick or hit by a puck. Imaging research indicates that microstructural alterations occur among players who have sustained TBI secondary to ice hockey, including decreased extracellular space and decreased diffusivities in white matter tissue. These MRI findings suggest axonal injury and increased cellularity of glia cells. Accompanying symptoms include headache, confusion, memory loss, aggressive behavior, depression, and diminished neurocognitive responses.

Recent research indicates that players with a history of sustained concussion showed significant changes in their white matter microstructure in comparison with those players who had no documented history of concussive injury. However, recent use of SPECT scans has indicated that chronic inflammatory changes evolve into CTE in athletes with histories of diffuse axonal injury or mild traumatic brain injury. The incorporation of SPECT scanning in the assessment of living ice hockey players is now being advocated and the use of cannabidiol may reduce the incidence progressive neurocognitive degeneration in ice hockey players.

Conclusion

Traumatic brain injury defines a vast array of neuroinflammatory processes related to impact to the brain. The direct effect of acquired Clinical Endocannabinoid Deficiency (CECD) in traumatic brain injury affects cerebral intracellular and microvascular function. The progressive development of Chronic Traumatic Encephalopathy (CTE) after concussive injury, a form of traumatic brain injury, is of paramount concern among athletes, who face disability and economic loss as neurological health declines with the progression of the disease. Research supports the efficacy of administering Cannabidiol (CBD) preventatively and therapeutically in head injury. The decrease in human cannabinoids is associated with neurological inflammation, and, because the endocannabinoid system regulates the vast array of physiological processes essential for human life, the pathology of cerebral disorders affects all facets of the brain's function. Administration of phytocannabinoids is essential in restoring neurological function which affects pain perception, mood, synaptic plausticity, motor learning, appetite and taste regulation, and metabolic function. Cannabidiol is therefore recommended as both a preventative and therapeutic intervention in the management of traumatic brain injury, providing the anti-inflammatory and neuroregenerative mechanisms necessary for cerebral homeostasis.

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