TRAUMATIC BRAIN INJURY IN ADOLESCENCE

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ABSTRACT

The literature on mild traumatic brain injury (mTBI) is limited in that it does not sufficiently examine the possible connection between concussions experienced in adolescence and later onset neurodegenerative diseases. Research in this area could help to develop our understanding of the brain bases for dementia, Alzheimer's disease, and progressive supranuclear palsy, and provide newly informed treatment plans for affected individuals. It has been strongly suggested that adolescents have prolonged symptoms following mTBI as compared to adults, thus alluding to the hypothesis of concussions experienced in this time frame being more detrimental to brain development. This literature review will (1) use various sources to outline a clear definition of concussion, (2) explain concussion on the cellular level in the context of adolescents, (3) examine behavioral symptoms, and (4) suggest further research to add to the general knowledge of concussion.

Defining Traumatic Brain Injury and Concussion

Traumatic brain injury (TBI) is difficult to define as it includes a wide array of brain injuries, but generally involves an initial head impact and subsequent changes in one's brain that affect cognitive function, memory, motor skills, and behavior (Grady, 2010). In a retrospective, state-wide analysis of high school athletes in Hawaii from 2011-2017, it was found that among 92,966 athletes, there were a total of 5,993 identified concussions (McAlister et al., 2020). As a note, mild traumatic brain injury (mTBI) and concussion are used synonymously in the medical literature. With concussion being a significant concern for many student athletes, understanding the brain bases of concussion will hopefully help to develop effective and reliable treatments that lessen subsequent symptoms. This review aims to first, outline a working definition of concussion, then analyze the relationship between high school athletes (aged 15-19) who have suffered from TBI and the possibility of increased violent behavior later in life as a direct result of the physical changes caused by the sudden head impact.

Upon diagnosis, TBI is categorized as either mild, moderate, or severe, depending on the intensity of the primary collision. Physical changes caused by TBI can include, but are not limited to, diffuse stretching of axons, chronic traumatic encephalopathy, and permanent chemical imbalance in neurons (Grady, 2010). Historically, brain bases for concussion in TBI have been under-studied and therefore remain poorly understood. The importance of understanding brain bases is highlighted by the surge in publicity following headlining news stories regarding uncharacteristically violent tendencies in National Football League (NFL) players with 887 cumulative cases of mTBIs from 1996 to 2001 (Casson, 2010) compared to the 906 total concussions reported by the NFL from the 2017, 2018, 2019, and 2021 seasons together (Battista, 2019; National Football League, 2023; National Football League, 2020; National

Football League, 2018). The 2020 season was excluded because there was no preseason, and therefore the injury data was not complete nor representative of a typical NFL season. This uptick in reported concussions in the 2017-2021 time span may be the result of several factors, including more sensitive diagnostic criteria and higher awareness among players and the league overall. The 4th International Conference on Concussion in Sport, held in Zurich in November of 2012, offered concrete symptoms of concussion, writing:

1. Concussion may be caused by a direct blow to the head, face, neck, or elsewhere on the body with an 'impulsive' force transmitted to the head.
2. Concussion typically results in the rapid onset of short-lived impairment of neurologic function that resolves spontaneously. However, in some cases, symptoms and signs may evolve over a number of minutes to hours.
3. Concussion may result in neuropathologic changes, but the acute clinical symptoms largely reflect a functional disturbance rather than a structural injury, and as such, no abnormality is seen in standard structural neuroimaging studies.
4. Concussion results in a graded set of clinical symptoms that may or may not involve loss of consciousness. Resolution of the clinical and cognitive symptoms typically follows a sequential course. However, it is important to note that in some cases, symptoms may be prolonged. (Grady, 2010)

Concussion on the Cellular Level

In his review of developments in the understanding of concussions in adolescent athletes, Matthew F. Grady (2010) explains the neurological phenomenon of concussion, identifying a two-step process in which the brain (1) rotates, shears, and impacts the skull, causing primary

insult or collision, and (2) subsequent inflammatory response to the site of brain injury. Based on discoveries from rat models, the collision causes the release of excitatory neurotransmitters (glutamate), which decrease cell wall integrity. Since the cell wall is crucial for maintaining the chemical gradients of sodium and potassium for neuronal functioning, its loss of integrity results in increased permeability, allowing influx of sodium into the cell and efflux of potassium to extracellular spaces. This change in chemical composition alters the cell pH, thereby compromising cell functioning and propagation of action potential in neurons. Severely injured cells may undergo apoptosis, releasing cytokines (whose purpose is to control the growth and activity of other immune system cells and blood cells) that recruit resident immune cells to the site of brain injury and clear cell debris, leading to inflammation in the brain. Cell death and consequent inflammatory response form the second step in the two-step process outlined by Grady. Inflammatory response post apoptosis may in turn cause further cell damage, amplifying brain damage and symptom deterioration over the 6-24 hours following the primary insult (Grady, 2010).

Concussion causes the head to move rapidly back and forth, thereby jostling the brain inside the skull (CDC, 2019). Jostling rotates and shears the brain, causing diffuse axonal stretch injuries, and the stretch of the axon causes deterioration of the cytoskeleton of the cell, leading to cell death. Additionally, axonal stretch can lead to injurious shearing of the cerebral vasculature (Knutsen et al., 2021), damaging the highly specialized capillaries in the cerebral vasculature that ensure constant brain perfusion, which reduces the ability of the vasculature to meet the neurons' and glial cells' need for oxygen and glucose (Agarwal, 2021). A study from Yuen et al. (2009) suggests a lack of obvious pathological change following minimal axonal stretch (5% of its breaking point) but points to subtle physiological changes (e.g., increased expression of sodium

channels on the axonal membrane surface; Grady, 2010). These subtle changes allow higher amounts of sodium to pass through the membrane and cause the cell to become depolarized. Cell depolarization results in temporary atypical cell function that increases cellular demands for glucose and metabolism, thus increasing the cerebral blood flow during healing (Grady, 2010). Adolescence is a crucial period for brain development and prior studies have shown that adolescents may take longer to recover from concussions than professional NFL players, who take 3-5 days to recover (Pellman et al., 2006) while adolescents take 7-14 days to be completely free from performance deficits (McClincy et al., 2009).

Behavioral Symptoms

The symptoms associated with mTBI have been shown to cause mental health challenges and persistent affective-related symptoms despite the affected individuals having returned to previous cognitive and functional performance levels (Grady, 2010). In a study using orthopedic trauma control subjects, mTBI patients were shown to have higher levels of psychological stress (Howlett et al., 2022). Because both groups experienced trauma with their respective injuries, and the orthopedic patients had significantly lower levels of psychological stress, the concussed individuals are likely not experiencing prolonged stress due to the trauma of the injury but rather persisting brain injuries from diffuse axonal stretch injury. Specifically, some affective symptoms of mTBI reported by victims and caregivers include increased impulsivity, irritability, affective instability, apathy, and a general lack of awareness of these changes (McAllister, 2008). Affective symptoms have been hypothesized as a result of impaired functioning of certain frontal-subcortical circuits that are at a particularly high risk for damage from TBI (Howlett, 2022). Because these symptoms have considerable overlap with mood disorders (e.g. major

depressive disorder and generalized anxiety disorder), analyzing these disorders and their connection with violent behavior later in life may deepen our understanding of which areas of the brain are linked to violent behavior.

Relationship between Concussion and Neurodegenerative Diseases

There have not been sufficient longitudinally designed studies to deduce the effect of mTBI in adolescence on those impacted individuals in their adult years, but post-mortem studies of professional athletes have hinted at a relationship between mood and behavioral difficulties and chronic traumatic encephalopathy (CTE). CTE is the buildup of the tau protein in the brain's sulci, suspected to be caused by microscopic injuries to the brain's surface (Grady, 2010). Although the definite cause of CTE is unclear, the disease has been linked to repeated head injuries (National Health Service 2022), and has higher prevalence among former professional football players. CTE could be a predictor for late onset neurodegenerative disease as the tau protein buildup has also been found in neurodegenerative diseases such as Alzheimer's disease, variations of dementia, and progressive supranuclear palsy (Manley et al., 2017). Traumatic encephalopathy syndrome (TES) refers to the symptoms of CTE, its definition expanding in the early 2000s to include mood and behavioral problems with cognitive impairment (Howlett, 2022). TES symptoms include but are not limited to depression, substance abuse, disinhibition, aggression, and paranoia. As issued by the National Institute of Neurological Disorders and Stroke, consensus criteria are: substantial exposure to repetitive head impacts, cognitive impairment and/or behavioral dysregulation, a progressive course, and lack of explanation for the clinical features based on another condition (Katz et al., 2021). This expanded criterion stems

from post-mortem brain examinations of American football players and the reports from their loved ones explaining the athlete's psychological and behavioral problems during their lifetime.

Future Research

The proposed relationship between concussion and neurodegenerative diseases such as dementia, chronic traumatic encephalopathy, and Alzheimer's disease requires further research aimed at better understanding the brain bases of concussion. By establishing a solid foundation on which to build upon, researchers will hopefully be able to better identify and treat neurodegenerative diseases. Therefore, my research will explore how concussion and repeated head impacts affect brain metabolism in high school football players and contribute a greater understanding of post-concussion cerebral blood flow to the literature. In addition to this research, more longitudinal studies regularly examining brain development following athletes through their high school, collegiate, and professional athletic careers are needed. Ultimately, our knowledge of concussion, TBI, CTE, and the brain is insufficient to accurately and reliably draw conclusions and relate aspects of these conditions to each other, but there is potential to make impactful discoveries with further study in this field.

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