

## **Rethinking Youth Sports**

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*When we consider the health and welfare of our children, few issues are of more concern than the risk and consequences of head trauma in sports. From participation in male-dominated football and hockey to girls soccer and softball, repeated impacts to the head that do not produce recognized concussion is the cutting edge of sports head injury research. Our author, a leading researcher in this field, provides the latest on what we know and don't know on this relatively new frontier of neuroscience.*

In December 1960, President-elect John F. Kennedy (JFK) penned [The Soft American](#) for *Sports Illustrated*, in which he described the importance of physical fitness to brain health: “Physical fitness is not only one of the most important keys to a healthy body; it is the basis of dynamic and creative intellectual activity.” As with many of JFK’s public statements, these prescient words remain spot-on today. Neuroscientists continue to uncover the remarkable connection between physical well-being and brain health on many levels: cognitive, behavioral, social, emotional, and more.

Boxing, JFK noted, was one of the sports the ancient Greek states pursued to enhance national fitness. But the idea that boxing could promote “dynamic and creative intellectual activity” certainly runs counter to current sensibilities, much like the advertisement for Marlboro cigarettes that graced the back cover of *Sports Illustrated* at the time. While JFK did not name other collision sports, it seems reasonable to assume that American football would have also qualified as a rung on his ladder to physical fitness and mental well-being.

From a 2019 vantage point, it seems shocking that JFK was touting the benefits of sport for brain health while ignoring risks of sport-related brain injury. In 1960, however, when he proposed a comprehensive national program to improve physical fitness, the adverse impact of sport-related head trauma on brain development and function was not on anyone’s radar. Even forty-five years later, when “Iron Mike” Webster’s chronic traumatic encephalopathy (CTE) was reported in the journal [Neurosurgery](#), adverse effects of sport-related head trauma were largely unknown to the general public and, at best, widely under-recognized among the medical community. It is worth noting that Mike Webster himself had never been diagnosed with a concussion or other form of brain injury during his time on the gridiron. Attitudes have changed dramatically since, but in what way has our understanding of head trauma and its adverse effects actually evolved? And most importantly, how can our expanding knowledge inform a viable path forward?

### **What is a Sport-Related Head Injury?**

During athletic activity, injury to the brain generally results from its rapid acceleration inside the skull, sometimes referred to as “closed head injury.” Upon impact to the head, forces jolt the brain inside the skull. Following Newton’s third law of motion, the brain moves toward and then away from the point of impact. Even more important, however are the rotational forces that inevitably result from off-center impacts and cause twisting and stretching of the brain. It is important to note that the head impact itself is never delivered directly to the brain tissue. For this reason, helmets and padding that effectively prevent fractures and internal bleeding do not protect the brain from the acceleration that causes injury.

On the field, traumatic injury to the brain is recognized by observed signs of brain dysfunction, rather than any specific diagnostic test. Most commonly, sport-related traumatic brain injury (TBI) causes a transient period in which the player is dazed, disoriented, and confused. Additional symptoms include problems with balance, dizziness, nausea, and headache. With more severe injuries, players may fall unconscious for brief or longer periods of time. Injuries range from subconcussive events that occur without symptoms to mild or, uncommonly, more severe TBI. Repeated injuries may lead to worse outcomes than a single event. Over the long term, neurodegeneration, such as CTE, may result from aggregated damage caused by many hits. CTE is a degenerative brain disease that produces mood, behavior, and cognitive problems years after repetitive head injuries in sports or military combat.

TBI is generally classified based on the duration of unconsciousness it causes. The lion’s share of sport-related TBI in youth falls into the mild TBI category, where unconsciousness either does not occur at all or lasts less than 20 minutes. Concussion is a synonym for mild TBI. Although diagnostic tests are generally not necessary to detect sport-related concussion, research studies have used brain imaging and other tests to demonstrate that sports-related concussion alters both brain structure and function.

The degree of recovery and ultimate outcome following TBI depends on many factors such as age (younger and older age elevate risk) and sex (girls seem to be at higher risk). Risk for poor outcome from severe TBI is elevated in individuals with certain gene variants (e.g., Apolipoprotein E- $\epsilon$ 4) and emerging results suggest that this and other gene variants may adversely impact recovery in concussion as well. Many as yet incompletely understood environmental factors may also modify risk. Higher pre-injury intellectual functioning, for example, is protective. Following a single sport-related concussion, rapid and complete resolution of symptoms is the rule; 95 percent or more of youth athletes will recover within three months. When symptoms persist beyond three months, post-concussion syndrome may be diagnosed. Medications and other therapies are used to treat symptoms of sports-related concussion, but no drug or biological treatment has been shown to prevent the development of symptoms or to shorten time to recovery. As we await the development of effective therapies, a structured recovery program under medical supervision, particularly in regard to when it is safe to return to play, can maximize chances for full recovery.

Many impacts to the head occur during collision sports in the apparent absence of signs or symptoms of brain injury. These “subconcussive” impacts still apply force to the brain and may induce subclinical pathologic changes similar to what occurs in overt concussion. We have found, in fact, that [subconcussive events may be associated with brain symptoms](#) that most athletes do not notice, but are elicited by careful questioning. Subconcussive impacts are also associated with objective alterations in brain function and microscopic structure as assessed by electroencephalography (EEG), magnetic resonance imaging (MRI), and formal cognitive and balance tests. The importance of repeated subconcussive head impacts, accumulated over an athlete’s lifespan, is currently a focus of intense interest.

Studies have shown, for example, that among former NFL players, beginning tackle football before age 12 is associated with [worse cognitive function in later adulthood](#). This and other studies note that tackle football, similar to soccer, rugby, hockey, lacrosse, and other collision sports, exposes players to hundreds or thousands of impacts of which only a small number result in recognized concussion. It seems likely that these impacts are consequential and may

be more important, in aggregate, than a few isolated concussive injuries. However, the full picture is just beginning to take shape.

Impact to the head may result in dramatic acute injury, such as skull fracture and hematoma—either epidural (bleeding between the skull and the membranes covering the brain or subdural (bleeding between these covering membranes and the brain surface). Bleeding within the brain tissue may result from tearing of tissue or blood vessels. Fatality due to these more severe types of injury was a major problem in early American football (before the introduction of helmets) but is exceedingly uncommon in modern collision sports. Helmets, padded headgear, and padded goalposts reduce the risk of skull fracture and complications such as epidural or subdural hematoma by distributing the impact force over a larger surface area to attenuate its severity. But protective headgear does not mitigate brain injury that results from acceleration of brain tissue inside the skull.

### **Deepening Our Understanding of Brain Damage**

The human brain is an exquisitely delicate and complex information processing powerhouse. Within its soft, gelatinous 1,400 or so grams ([see a fresh brain at autopsy](#)), are 100 billion neurons, each projecting an axon, a filamentous projection up to a meter in length that sends electrochemical messages to nearby neurons and the spinal cord. An axon measures one-tenth the diameter of a single red blood cell. Axons form the brain's network wiring and transmit information through as many as a quadrillion network connections, termed synapses, that allow neurons to process information together. Notably, the brain cannot switch to Wi-Fi; we are fully reliant on its physical networks for simple functions like movement and especially for the complex behaviors that embody our humanity, such as memory, imagining, planning for the future, and controlling behavioral impulses. These latter functions require information to be processed across widely distributed brain networks. When networks are disrupted, functions, simple and complex, are adversely impacted.

The brain's structural and functional complexity is unique among the body's organs and tissues and makes it particularly vulnerable to injury. When the head undergoes rapid acceleration following impact, the soft brain moves within the skull and is compressed,

stretched, and twisted. In some respects, the brain is remarkably resilient to these forces. It is uncommon, for example, for bleeding to result. Nonetheless, linear and rotational forces propagate through the brain, causing injury to axons, termed traumatic axonal injury. This type of injury is the pathology underlying transient and permanent brain network dysfunction and consequent functional problems following head trauma.

When the brain sloshes about inside the skull following an impact, we might expect delicate axons to be torn asunder, leading to immediate disruption of network traffic and loss of function. And we might expect the injury to exhibit maximum functional effect at the time of trauma. Remarkably, this is not the case. The level of head trauma that occurs during sports, due to collisions, falls, or heading a soccer ball, is not likely to involve frank tearing of tissue or axons. For this reason, sports-related head trauma, including sports-related concussion, is rarely associated with gross clinical imaging signs like bleeding in the brain. Rather, strain on axons instigates a cascade of molecular and cellular events that may lead to their dysfunction and ultimate degeneration. Ultimately, the resultant pathology impairs brain function.

The TBI cascade is instigated by mechanical stress on subcellular components of the axon, such as its membrane, the axolemma, and ultimately produces a toxic microenvironment that causes further injury. Mechanical stressors lead to aberrant function, depolarization of neurons (a shift in the electronic charge at the surface of the cell), excess release of the excitatory neurotransmitter glutamate, and dysregulation of the balance of sodium (Na) and potassium (K) ions within the neuron. Excess release of glutamate activates n-methyl d-aspartate (NMDA) receptors on brain cells, which adversely impacts cellular pumps that maintain intracellular Na/K balance. Excitotoxicity, the overactivation of these receptors in response to excess glutamate, NMDA and other toxic substances, results in further ionic dysregulation of neurons and the accumulation of metabolites, in particular sequestration of calcium, that further contributes to the toxic microenvironment.

The toxic microenvironment leads to multiple secondary cellular effects that propagate injury. One example of “secondary injury” is the activation of brain immune cells such as microglia and astrocytes. In laboratory mice, controlled cortical impact, a model of severe TBI,

induces release of the amino acid D-serine. D-serine binds NMDA receptors, causing damage to synapses, the communication junctions between brain cells. Blocking release of D-serine confers a protective effect in this animal model. Another injury mechanism is thought to arise from longer-term persistence of adverse cellular responses and diminished axonal transport. Decreased clearance of metabolites by routes such as the glymphatic system of the brain contributes to toxicity of the microenvironment and accumulation of toxins such as hyperphosphorylated tau protein (pTau). Neurofibrillary tangles formed by pTau, particularly around small blood vessels in the brain, are found in CTE and other neurodegenerative diseases in which they are thought to lead to cell death.

Knowledge regarding molecular and cellular mechanisms of brain injury has expanded dramatically over recent years, based largely on experimental studies. These studies, however, have relied upon models of rather severe injuries that are quite different from those that typically occur in sports. Another important limitation on our understanding of clinical phenomena is that mechanisms of human brain injury are not directly observable *in vivo*. Recently, however, radioactively labeled antibodies to pTau have opened the door to its detection *in vivo* with positron emission tomography (PET). pTau-PET holds much promise for directly detecting long-term damage from repetitive head impacts *in vivo* but is currently in early stages of development and not yet in clinical use. The true incidence and impact of injury phenomena such as pTau deposition cannot be known until clinical testing has been validated and become widely available.

The degree to which excitotoxicity, neuroinflammation, and the resultant toxic microenvironment develop following head trauma, the timeframe over which they evolve, and the extent to which they regress or persist, determines whether an individual will sustain lasting adverse effects. In this regard, the cascade of injury mechanisms that evolves over time may hold the key to effective treatment of brain injury. Methods that target and suppress injury mechanisms could be utilized to turn off adverse molecular processes before they have caused damage. Achieving this goal will require recognition of the injury, understanding of its time course, and timely intervention with precisely targeted interventions.

Drawing a contrast between TBI and other common injuries is instructive. A bone fracture or muscle tear occurs and is complete at the moment of trauma. Subsequently, the body begins to repair the injury. When the liver is damaged during a motor vehicle crash, regeneration of new functioning liver tissue ensues. But brain injury, as described above, is a process, set in motion by trauma that evolves over time. Proceeding unchecked, the resulting pathology can be irreversible. Fortunately for the vast majority of head-injured athletes, rapid resolution of symptoms occurs within minutes to weeks following a single episode of head trauma. This resolution is possible when the cascade of adverse molecular and cellular responses described above subsides before causing permanent injury to axons. Once axons degenerate, however, they cannot repair and are not regrown or replaced. The [context of the injury as well as innate and environmental factors](#) are likely to hold important keys to understanding the great variability in timing and completeness of recovery from head injury. The details, however, are only beginning to emerge and are a current focus of intense research.

### **Diversity is the Rule**

Two lacrosse players moving at similar speed collide on the field and hit head-to-head. Both experience immediate symptoms of confusion and imbalance. Neither is knocked unconscious. Both are diagnosed with sports-related concussion and removed from the game. One player is feeling back to normal within a week and gradually returns, under medical supervision, to physical activity. His teammate remains symptomatic three months later, sitting out lacrosse and having trouble with schoolwork.

Those who care for concussion patients are familiar with this conundrum: two similar individuals seem to experience a similar injury but diverge greatly in terms of symptoms and the it takes to make a complete recovery. Although full recovery from concussion is the rule, a sizable minority of patients remain with symptoms and dysfunction, some permanently. In our lacrosse scenario, each player's brain may have experienced a similar biomechanical insult, but severity, time course, and persistence of molecular and cellular consequences of their injuries diverge leading to disparity in the rate and completeness of each player's recovery. The parents of the player who experiences persistent symptoms express concerns



to their son's physician about the longer-term outlook; not just recovery from his current dysfunction, but his risk for later neurodegeneration such as CTE.

The complexity of TBI is now widely recognized, but we are only beginning to sort out how circumstances align and interact to yield a final outcome. The myriad factors involved can be crudely divided into (a) injury characteristics; (b) player characteristics; and (c) environmental factors before or after the injury. Injury characteristics such as the direction and magnitude of the impact as well as the timing or absence of earlier impacts are a factor in determining the magnitude of the biomechanical trauma to the brain. Player characteristics and environmental factors, on the other hand, may play a role in determining the brain response at the time of impact as well as during the period of evolution of molecular and cellular responses to and recovery following head trauma.

Girls, for example, sustain fewer head impacts, but report more concussion symptoms and take longer to recover from sports-related concussion than boys. Girls' neck muscles are less developed than boys', limiting capacity for stabilization of the head at the time of an impact, with consequently greater head and, ultimately, brain acceleration. Are these biomechanical features the sole key to sex-based difference in risk? Or, do sex hormone effects, such as progesterone withdrawal during the menstrual cycle, create a vulnerable period in girls? More generally, gene variants, IQ, nutrition, personality, and many other factors have been suggested to explain individual differences in response to and recovery from head injury, including sports-related concussion. Scientists are just beginning to understand how factors such as genes and sex might synergize to exacerbate or mitigate the adverse effects of sports-related concussion and repetitive head impacts.

### **Multiple Hits – Intentional and Not**

In popular sports such as football, soccer, hockey, and lacrosse, player-to-player collision is a feature of play. In football, collisions may, for certain player positions, be an intended feature of every single play. Even if players are instructed not to "lead with the head," they will nonetheless regularly collide with one another, with the ground, goalpost, or other equipment. Such collisions and falls are the source of numerous direct blows to the head.

Even in the absence of direct impact, however, a body hit or fall will induce rapid brain acceleration. The forces thereby generated are transmitted to the brain in much the same way as in whiplash injury.

Soccer provides an additional, unique source of exposure to repetitive head impacts, beyond trauma from unintended collisions and falls. Soccer players intentionally and repeatedly head the ball in competition and practice, as a technique for directing its course. In our [work with adult amateur soccer players](#), we found that the range of exposure to heading is enormous. While some players do not head the ball at all, many others do so thousands of times per year. Although these ball-to-head impacts generally produce lesser degrees of head acceleration than player-to-player contact and are commonly subconcussive, they may be repeated very closely together over short periods of time. If a second or subsequent impact occurs while the molecular and cellular brain response to the first impact is still evolving, the effect of the second impact may be magnified, essentially hitting the brain while it is already down and vulnerable.

Closely spaced impacts, whether multiple sports-related concussion or subconcussive repetitive head impacts, may become “superadditive,” with an aggregate adverse effect greater than that of a similar number of individual hits separated sufficiently in time to allow complete recovery from each. For this reason, one of the most important recommendations following sports-related concussion should be avoiding any additional head injury until symptoms have fully resolved.

### **How Much is Too Much for Whom?**

We find repetitive head impacts in all collision sports, although those exposed to them are not universally symptomatic or impaired. Studies have shown that in the long term, repetitive head impacts are associated with worse cognitive function and with structural brain changes. Moreover, the duration of exposure to and number of these repetitive head impacts may affect risk.

In our own studies of soccer players and others' investigations of American football, repetitive head impacts are associated with adverse effects. However, this relationship appears to be nonlinear. That is, relatively few such impacts seem to be generally well tolerated whereas greater numbers of impacts are strongly associated with adverse effects. Our findings indicate a threshold below where risk is acceptably low. Defining such a threshold could make it possible to protect players by monitoring exposure to repetitive head impacts and curtailing exposure when the threshold approaches. A similar approach has been implemented successfully for the [Pitch Smart](#) program, which monitors pitching activity in youth baseball players to mitigate upper extremity injuries. In order to realize the promise of a threshold-based intervention, however, we will need to know how to correctly characterize risk thresholds. Such a program must also incorporate individual risk factors (as described above); a one-size-fits-all approach is unlikely to protect vulnerable individuals.

#### **For Now, and the Future – Long-Term Delayed Effects**

The detection of neurodegenerative [CTE in professional collision athletes](#) catapulted repetitive head impacts into the spotlight. Players diagnosed when their brains were examined under the microscope after death had often begun to exhibit CTE symptoms only long after their active playing days were over and exposure to repetitive head impacts had ended. Also, the brains of players who did not exhibit behavioral signs of CTE have been found to harbor its pathologic hallmarks at autopsy. While the mechanisms underlying the development of CTE remain to be elucidated, one hypothesis is that repetitive head impacts induce an ongoing injury process and accumulation of subclinical brain pathology, in the form of poorly cleared pTau, which continues even after impacts have ceased. Overt symptoms only manifest if and when brain pathology builds to a sufficient level.

In many ways, the evolving consequences of repetitive head impact follows a script familiar in other contexts. Toxic effects of environmental exposures, such as lead poisoning, cause clinical disease in a similar manner: subclinical pathology accumulates in the brain before symptoms manifest. By monitoring lead levels, overt clinical disease and irreversible damage can be averted by avoiding exposure when subclinical changes are detected using a blood test. If the exposure persists too long, however, pathological changes may not recover. By

determining the point at which accumulated brain injury becomes irreversible and devising means to identify those approaching hazardous levels, lasting brain dysfunction due to repetitive head impacts might be prevented. A blood test that can identify abnormal proteins (e.g., pTau or neurofilament light chains) could allow screening for accumulating brain pathology in at-risk athletes even before symptoms are present. Recently, the Food and Drug Administration approved such a blood biomarker to assess risk of intracranial bleeding after a head injury. Several other potential biomarkers are currently under development or investigation to detect brain injury pathology from a blood test.

CTE has become the subject of books, film, and news stories. However, the number of affected players is quite small compared to the hundreds of millions of youth and adult amateur athletes worldwide. If newer techniques such as neuroimaging and blood biomarkers confirm that repetitive head impacts adversely affect brain structure and function in this population and leads to overt brain dysfunction in the long term, a much greater challenge to the health of society will need to be addressed.

### **Maximizing the Yield of Sport Participation – Risk vs. Benefit**

What then of JFK's exhortation to pursue physical fitness as the "basis of dynamic and creative intellectual activity?" We have extensively explored the risk for adverse effects of head trauma, but at the same time evidence strongly supports the notion that physical activity improves cognitive function, mood regulation, sleep, and a host of other positive outcomes. [Students who are physically fit perform better on standardized academic tests.](#) Participation in team sports—many of which may involve exposure to repetitive head impacts confers [additional benefits in the realms of social development, leadership, and more.](#) Beyond that, mental activity positively influences physical well-being and may delay and attenuate the decline of old age.

How do we weigh such benefits against the risk of sports-related concussion and repetitive head impacts? Consider the following thought experiment: assume the benefits of varsity football are effectively offset by the adverse effects of repetitive head impacts from blocking and tackling. At the end of the day (or season or school year) football players would perform

in school as if they had sat out sports altogether. At the same time, for varsity swimmers, the benefits of fitness training and teamwork might improve academic performance more than time spent in the library. Should youth athletes be directed toward non-collision sports or should these risky sports be modified? No one has the answer to these questions, which are particularly gnarly because individuals and their responses to head trauma are so varied and complex. Much more enters the equation than simply sports and grades.

### **Putting It Together and Forging Ahead**

Athletic activity provides a popular avenue to enhanced fitness, which is extremely important to health and wellbeing over the short- and long-term. The potential for repetitive head impacts to adversely affect brain development and function, on the other hand, is a scary prospect for parents and athletes and may negate fitness benefits of collision sports. The complexity of the range of factors affecting damage from repetitive head impacts, including sports-related concussion and subconcussive impacts, and their varied manifestations in individual athletes, combined with a dearth of clear evidence to inform risk-benefit assessment, only adds uncertainty to this concern. Yet, salient features of existing knowledge suggest factors that predispose to adverse effects could be identified and characterized sufficiently to design interventions to minimize risk and maximize the benefit of athletics.

As a society, we need to define priorities and future goals. Physical activity must be promoted: its benefits for education and intellectual development, unimpeded by brain dysfunction, are clear. Can we diminish the intensity of collision sports? Does a youth athlete, who is unlikely to ultimately go pro, actually stand to lose if they monitor and control exposure to repetitive head impacts through an evidence-based risk assessment or, especially for those at highest risk, opt for non-collision sports like running or swimming?

Collision sports are entrenched cultural institutions and many of their advocates, including organizations that govern sports, find a broad receptive audience when they downplay risk. In the lay press as well as the scientific literature, research findings on repetitive head impacts are commonly minimized or attributed to methodological limitations. Parents and educators should therefore strongly advocate for the large-scale studies necessary to identify and

characterize relevant risk factors and develop and implement preventive interventions. Only then will young athletes be able to realize JFK's dream of the "dynamic and creative intellectual" potential of sports.

**Bio**

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