

Concussion Management at the NFL, College, High School, and Youth Sports Levels

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Concussion is defined as a complex pathophysiological process affecting the brain that is induced by traumatic biomechanical forces. Sport- and recreation-related concussions are conservatively estimated at 1.6 to 3.8 million cases each year in the United States alone.^{1,2} The wars in both Iraq and Afghanistan have had the distinction of producing the greatest number and percent of mild traumatic brain injuries (TBIs; concussion) that have ever been documented in a major war owing to roadside explosions.³ Whether occurring from sports collisions or bombings, concussion can result in both short-term and long-term impairment of neurological function and the possibility of significant neuropathological changes. A smaller percentage of cases can exhibit signs and symptoms referred to as postconcussive syndrome (PCS), which may be prolonged or permanent.

In sports-related concussion, most physical signs and symptoms such as nausea, visual disturbances, headache, and balance changes will resolve within 2 to 7 days. Longer-lasting complaints such as fatigability, poor concentration, behavior changes, sleep pattern changes, and mood alterations that last beyond this time frame are considered PCS.⁴⁻⁷ Often, PCS will result in significant disruption of school, work, and other activities and in the need for further medical evaluation. The military has seen an increased incidence of depression and other symptoms often referred to as posttraumatic stress disorder in many of the soldiers who have suffered from mild TBIs.

TREATMENTS FOR CONCUSSION: TRADITIONAL AND ALTERNATIVE

Although controversial, treatment for concussion has advanced beyond reassurance and restricted activity. There is currently no Food and Drug Administration–approved pharmacological intervention to treat concussion, but many have been attempted with generally limited success. These treatments include corticosteroids, free radical scavengers and antioxidants, drugs to inhibit arachidonic acid inflammatory

response, and drugs that modify monoamine function. Treatments also used for PCS have included glutamate receptor antagonists, calcium channel blockers, thyrotrophin-releasing hormone, and hyperbaric oxygen therapy.

Alternative nonpharmaceutical treatments appear to be gaining acceptance for the treatment of common neurodegenerative conditions, memory decline, and reduced cognitive function. Substantial animal and human research now suggests that these same natural dietary supplements, vitamins and minerals, and the use of hyperbaric oxygen may be a better first-line choice for the treatment of PCS, which has generally been underreported by both athletes and the military.

Until recently, there have been few therapeutic options beyond pharmacological symptom management. This article reviews the mechanisms, diagnosis, and treatment of concussion and the underlying causes of PCS. There is a greater emphasis on alternative treatments and the emerging research that indicates their potential efficacy for treatment of concussion and PCS.

POSTCONCUSSION SYNDROME

A common disorder, PCS presents after a TBI such as a concussion and describes a variety of symptoms including, but not limited to, headache, dizziness, fatigue, and personality changes. It can occur in up to 80% of people who have had TBI and usually is self-limited.^{8,9} At the present time, the standard treatments for PCS are rest, limiting exposure to possible additional brain injury, and treatment of symptoms as they occur. There is no standard for the diagnosis of this condition; however, agreement is often reported to include at least 3 symptoms associated with the concussive episode. Postconcussive syndrome can be divided into early and late or persistent PCS, with symptoms occurring for > 6 months.

There is believed to be no correlation between the severity of injury and the development of PCS symptoms. The complex of symptoms related to PCS often affects concentration, recent memory, abstract thinking, and the ability to assimilate new information during the recovery period. Additionally, some patients can develop somatic symptoms of dizziness and disequilibrium, among others (Table), which can lead to chronic nausea and anorexia. Most persons with

TABLE. Postconcussive Syndrome Symptoms and Signs

Reported Symptoms	Reported Signs
Anxiety, irritability, depression, sleep disturbance, change in appetite, decreased libido, fatigue, personality change, cognitive impairment, memory impairment, diminished concentration and attention, delayed information processing and reaction time	Dizziness, vertigo, nausea, tinnitus, blurry vision, nystagmus on lateral gaze, hearing loss, diplopia, diminished sense of taste and smell, light and noise sensitivity

PCS report resolution by 3 months, but some studies have shown that up to 33% of patients have some persistent symptoms for > 6 months and 15% of patients complain of problems > 12 months after injury.¹⁰⁻¹²

PCS TESTING

Computed tomography scanning is of very low yield and is unlikely to be positive but is considered standard in the evaluation of acute cases of concussion with associated loss of consciousness. Magnetic resonance imaging (MRI) scanning is often done during the workup of PCS and can occasionally reveal frontotemporal lesions, which seem to correlate with areas of deficit as demonstrated by neuropsychological testing. An MRI obtained several months after the TBI may reveal contusions and loss of discrimination between gray and white matter (shear axonal injury). Experimental MRI scans have demonstrated actual disruptions of the nerve tracts of a TBI subject.¹³⁻¹⁵

NEUROPSYCHOLOGICAL TESTING: IMPACT

The use of neurocognitive testing is essential for the ongoing assessment of PCS. This computer-based neurocognitive test is currently ideally used in subjects with baseline tests, which is now the standard for most organized contact sports in the United States. It provides objective data and prevents athletes who hide their symptoms from returning to play before they are fully recovered. This test can also be useful without an individual baseline because of the enormous database of normal control subjects that has been developed.

Generally, the PCS disappears before the neurocognitive findings return to normal, although occasionally this can be reversed. For this reason, symptom evaluation cannot be used as the sole criterion for recovery of PCS.

ImPACT (Immediate Post-Concussion Assessment and Cognitive Testing) is the first, most widely used, and most scientifically validated computerized concussion evaluation system. Developed in the early 1990s by Drs Mark Lovell and Joseph Maroon, ImPACT is a 20-minute test that has become a standard tool used in the comprehensive clinical management of concussions for athletes of all ages.¹⁶ ImPACT testing for concussion management allows individualized assessment at baseline, before the sport or combat, and comparison of postinjury neurocognitive testing results with the baseline

testing. This type of concussion assessment can provide objective data of the concussed individual's postinjury condition and track recovery for safe return to play, thus preventing the cumulative effects of concussion. Neurocognitive testing is now considered the "cornerstone" of proper concussion management by an international panel of sports medicine experts.

ImPACT is the most widely used computer-based testing program in the world. It is the standard for concussion testing for the National Football League (NFL), Major League Baseball (MLB), most professional and collegiate teams in the United States, and > 3000 high schools. ImPACT can be administered by an athletic trainer, school nurse, athletic director, team coach, team doctor, or anyone trained to administer baseline testing.

TRADITIONAL TREATMENTS

Treatment for PCS is supportive and focused primarily on ameliorating symptoms. Unfortunately, PCS can occasionally be devastating and may lead to job loss and chronic impairment. Medical, social, and family support is critical to those suffering from PCS.

Beside headaches, sleep-related issues tend to be the most reported. Initially, many PCS subjects are fatigued after even simple activities and sleep more than usual. Later, they may have difficulty falling asleep and sleep less than usual. Lack of sleep can often worsen other symptoms that the subjects are experiencing; therefore, sleep disorders can be treated with sedative-hypnotic medications.

In adolescents and some adults, the stimulant Ritalin (methylphenidate) is sometimes effective for treating the inability to concentrate and poor memory, often associated with increased PCS headaches during school or work. Depressive symptoms are also common with PCS and are believed to be directly related to reduced or altered production of brain neurotransmitters such as serotonin, norepinephrine, and dopamine as a result of TBI. Additionally, the persistence of PCS and the inability to resume normal life activities may cause depression. Psychotherapy and antidepressant medication may be warranted. Studies using amitriptyline, which inhibits serotonin and noradrenaline reuptake, have shown up to 90% efficacy at 75 to 250 mg/d to relieve PCS headaches.¹⁷ Biofeedback also is moderately helpful in 80% of patients.^{18,19}

ETIOLOGY THEORIES OF PCS

There is no consensus as to the exact physiological mechanisms occurring in the concussed brain that cause the symptom complex known as PCS. Occasionally, MRI scans can demonstrate small contusions and other structural abnormalities. There is general consensus in the treatment of acute TBI that the brain insult will result in areas of localized edema and inflammation. Treatments to reduce inflammation have been shown to be effective in managing acute TBI in the hospital setting with high-dose steroids, hypothermia, and fluid management to reduce brain edema and swelling.

Other causes that have been suggested for PCS include injury to the upper brainstem, affecting serotonin production, abnormal brain electrical activity, cerebral blood flow abnormality with loss of autoregulation, and ischemic damage.

THE CASE FOR CHRONIC TRAUMATIC ENCEPHALOPATHY

A certain number of individuals suffering from mild TBIs, especially repetitive mild concussions, are known to develop a slowly progressive encephalopathy, referred to as chronic traumatic encephalopathy (CTE). The postmortem neuropathological elements of CTE are characterized as being similar to both Alzheimer disease and Parkinson disease. The pathological mechanism explaining the development of neurodegeneration in this subset of individuals has not been elucidated. Yet, a considerable number of studies indicate that a process called immunoexcitotoxicity may be playing a central role in both neurodegenerative disease and CTE.^{20,21}

The term immunoexcitotoxicity was first coined to explain the evolving pathological and neurodevelopmental changes in autism and the Gulf War Syndrome but can be applied to a number of neurodegenerative disorders. The interaction between immune receptors within the central nervous system and excitatory glutamate receptors triggers a series of events such as extensive reactive oxygen or nitrogen species generation, accumulation of lipid peroxidation products, and prostaglandin activation, which then leads to dendritic retraction, synaptic injury, damage to microtubules, and mitochondrial suppression.²² The mechanism of immunoexcitotoxicity and its link to each of the pathophysiological and neurochemical events previously described with CTE are currently being investigated.

There is no scientific consensus on the actual existence of CTE in athletes or what the association is between those in whom CTE changes have been found and their underlying cause. However, because of the potential long-term concerns of how chronic concussions might play a role, major contact sports teams, including those in the NFL, are investigating this phenomenon. Both postmortem and longitudinal studies are

now being funded to investigate CTE by sporting organizations and government agencies.

ALTERNATIVE TREATMENT FOR PCS

Because the “watchful-waiting” treatment currently advocated for those with PCS is not a treatment and does not address the underlying organ involved, the brain, there are many who advocate alternative methods to address brain healing and recovery after TBI and concussion. The brain itself is made up mostly of fatty acids; the most predominant, making up 40% of these fatty acids, is docosahexaenoic acid (DHA).²³⁻²⁵ Eicosapentaenoic acid (EPA) and DHA are referred to as omega-3 essential fatty acids (EFAs).

Omega-3s are called EFAs because our body cannot produce them and must extract them from the food we eat. α -Linolenic acid is also an important part of the omega-3 EFAs because it, along with DHA and EPA, is used as a structural component in every organ of the body. Fish, walnuts, flaxseeds, and certain other vegetables have these EFAs that we must consume. Besides being part of the bilipid membrane in every cell of our body, in the brain, they allow and enhance neuronal cell fluidity and stability and act as part of the neurotransmitter system.²⁶⁻²⁸

Omega-3 EFAs have been found to have significant health benefits in disease prevention and treatment, especially for the brain.^{29,30} Their major benefits in this area are as both an essential cellular component and, once converted, antiinflammatory prostaglandins.³¹ By countering inflammation, the adequate consumption of omega-3 EFAs can help to decrease the production of inflammatory prostaglandins and potentially decrease brain trauma-related inflammation.^{32,33}

OMEGA-3 EFAS AND BRAIN FUNCTION

Brain omega-3 EFAs are the most extensively studied fatty acids in the body. Omega-3 EFA deficiency alters the structure and functions of our cell membranes and can induce brain dysfunctions, as demonstrated in both animal models and human infants.²⁴ Specifically, omega-3 EFA deficiency alters brain development and disturbs the normal composition and chemical properties of brain cell membranes, neurons, oligodendrocytes, and astrocytes.²⁹ This leads to altered brain cell function and results in neurosensory and behavioral abnormalities. Omega-3 supplementation for milk formula for infants is now required and has been shown to support visual and cognitive abilities, including intellect.

Age-related impairment of hearing, vision, and smell is due to both decreased efficacy of the parts of the brain concerned and disorders of sensory receptors, particularly of the inner ear or retina. The latest research now shows that those with omega-3 EFA deficiency have more difficulty distinguishing the tastes of sweet and salty.³⁴

RESEARCH ON BRAIN INJURY AND OMEGA-3 EFAS

Investigators have shown that administration of EPA, an omega-3 EFA, has a favorable effect on blood flow and metabolism in the brains of rats suffering from brain cell death caused by an interruption in blood flow.³² Other studies have reported that long-term treatment of EPA improved an age-related reduction in blood flow in the brain and increased glucose metabolism.^{30,35}

In other studies, researchers have found that omega-3 EFAs can decrease the toxic effects of glutamate, which is released in large amounts after TBI and can lead to the death of still-surviving brain cells within the area of the injury.^{27,32,36} Typical in TBI, excessive excitatory activity caused by neurotransmitter glutamate increases overall intracellular calcium ion concentrations. It is believed that omega-3 EFAs may have a suppressive effect on ion channels and prevent cell death.³⁵

Additionally, omega-3 EFAs have been found to stabilize cell membranes by inhibiting the release of arachidonic acid.^{27,32,37} Inhibition of arachidonic acid release from cell membranes may stabilize the cell and protect it from damage because arachidonic acid can be converted to inflammatory prostaglandins, which can induce the inflammatory response.

CASE REPORT

The sole survivor of the 2006 Sago Coal Mine disaster in West Virginia suffered from extreme carbon monoxide exposure, which can result in severe brain damage.³⁶ Neurosurgeons at the West Virginia University initiated standard interventions, including hyperbaric oxygen treatment, and then made the unprecedented decision to administer very high doses of omega-3 EFAs. The physicians believed that, to begin to heal, the survivor's brain would require large amounts of omega-3 EFAs to reconstruct the damaged brain cell membranes. As the membranes began to heal, the patient improved clinically and is now essentially normal. Although this is currently just a dramatic case report, there are now investigations into large-scale trials for the treatment of TBI with omega-3 EFAs.

RECOMMENDATION FOR OMEGA-3 EFA SUPPLEMENTATION FOR PCS

Postconcussive syndrome is a complex condition owing to its varied constellation of symptoms and signs. Although related to TBI, its pathophysiological origin is difficult to define. Cellular inflammation of brain tissue, however, clearly plays a role in this condition.

Lack of effective treatments has traditionally meant that patients with PCS were generally relegated to suffer in silence until their symptoms resolved. The use of omega-3 EFA supplementation has been shown to improve a wide range of

brain-related conditions with similar underlying etiologies that are inflammatory and require cellular repair using the EFA substrate (omega-3 EFAs) to rebuild. Providing omega-3 EFA supplementation to subjects with PCS will supply the needed fatty acids required for brain cell healing and help reduce the inflammatory response activated by TBI.³²

Long-term placebo-controlled trials using various doses of omega-3 supplementation are now being planned to compare recovery time for those seeking treatment of PCS. In the short term, I have observed many case reports that indicate a significant and dramatic improvement in symptoms with the use of high-dose fish oil in the 2- to 4-g/d range. Because of the limitations of the current research, however, no clear dosage recommendations can be made. Omega-3 fish oils should be used with caution in those on prescription anticoagulants because of a potential to increase bleeding.²⁴

OTHER ALTERNATIVE TREATMENTS OF PCS

Because one of the central mechanisms for PCS is thought to be trauma-induced brain inflammation, natural supplements that have been shown to reduce cellular inflammation are also being tested to treat PCS. One of the most exciting areas of alternative treatment research designed both to improve cellular health and to reduce cellular inflammation involves the plant-based molecule called resveratrol.³⁷⁻³⁹

Resveratrol is a polyphenol that is found in various concentrations in many different plant sources. Polyphenols are the molecules in plants that provide color to the skin of fruit such as the red in raspberries and the blue in blueberries, and as a group, they provide much of the nutritional benefits we obtain from eating fruits and vegetables. The plant called Japanese Knot weed or *polygonum cuspidatum* and the skins of red wine grapes are believed to have the most concentrated amounts of resveratrol.⁴⁰ In plants, resveratrol, like other polyphenols, is generally found in the plant skin and acts to protect the plant from infection and excessive ultraviolet radiation and to aid in general plant defense. In addition, like other polyphenols, resveratrol has significant anticancer, antiinflammatory, antioxidant, and DNA-protective actions when consumed by animals and humans.⁴⁰

In animal research done at the University of Pittsburgh, researchers found that 100 mg/kg resveratrol administered intraperitoneally after controlled brain injury provided significant behavioral protection in the rats tested.³⁷ Specifically, rodents treated with 100 mg/kg resveratrol showed improvements in motor performance (beam balance and beam walking) and testing of visuospatial memory. Behavioral protection was correlated with significantly reduced contusion volumes and the preservation of neurons in the resveratrol-treated animals. They concluded that their study added to the growing literature identifying resveratrol as a potential therapy for human brain injury.

Hyperbaric oxygen has been used for many decades to treat healing wounds and to help reverse the potentially life-threatening effects of the “bends” associated with deep-sea diving. In a sealed chamber, the patient breathes 100% oxygen, which is set to a pressure greater than sea level (1 atm absolute). In several published studies, mostly from the military, long-term PCSs (≥ 6 months) have been successfully treated.⁴¹ Additionally, treatment durations have been reported to be very short (≤ 35 days) with 5 d/wk, 1.5 atm absolute/60-minute hyperbaric oxygen therapy treatments, with 100% recovery.⁴¹

These reports have attracted significant attention both inside and outside the military. Larger randomized studies are being planned.

CONCLUSION

On the basis of a review of the pertinent literature and physiological mechanisms associated with concussion management and PCS, supplementation with omega-3 EFAs in the form of fish oil supplements may offer a viable alternative to the current watchful-waiting techniques currently used. Additional research is needed in this area, however, before standard use can be recommended in all cases. Preliminary research in animal studies indicates that the supplement resveratrol and other natural antiinflammatory supplements may also offer a safe, low- to no-risk recommendation for those who have suffered a TBI and resultant PCS. Additionally, early studies indicate that hyperbaric oxygen may have a significant role in the treatment of protracted symptoms related to PCS.

Disclosure

Dr Joseph Maroon is a shareholder in and Jeffrey Bost is a consultant for ImPACT Applications, LLC.

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