Sports-related concussions & sub-concussive impacts in athletes: Incidence, diagnosis, and the emerging role of EPA & DHA

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| Novelty bullets: points that summarize the key findings in the work: | • SRC have garnered widespread attention due to the growing body of reported prevalence in youth and professional sports., • Current definitions and protocol(s) for diagnosing SRC and SCI have improved, but still require further evaluation., • n-3, EPA and DHA, reduce inflammation and promote recovery following brain injuries in experimental models. |
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Sports-related concussions & sub-concussive impacts in athletes: Incidence, diagnosis, and the emerging role of EPA & DHA

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Abstract

Sports-related concussions (SRC) are a traumatic brain injury induced as the result of a biomechanical force to the body which temporarily impairs neurological functions. Not all traumatic impacts reach the threshold necessary to produce concussive symptoms, however, the culmination of these events are known as sub-concussive impact(s) (SCI). Athletes who have been diagnosed with a SRC, or those who accumulate multiple SCI have exhibited structural damage to the brain, impairments to learning and memory, and an increase in depressive symptoms. This area is rapidly evolving and current clinical definitions of injury, diagnosis and treatment of SRC and SCI are reviewed. In tandem, there is also growing research examining the role of nutrition in brain injuries focused primarily on n-3 polyunsaturated fatty acids (PUFA). The potential role of which eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) reduce inflammation and promote recovery following brain injury are also reviewed. Overall, advancements in the evaluation of SRC and SCI coupled with n-3 PUFA supplementation shows promise in the management of brain injuries leading to better long-term health outcomes for athletes.

Bullet Points:

- SRC have garnered widespread attention due to the growing body of reported prevalence in youth and professional sports.
- Current definitions and protocol(s) for diagnosing SRC and SCI have improved, but still require further evaluation.
- n-3, EPA and DHA, reduce inflammation and promote recovery following brain injuries in experimental models.
Keywords: n-3 fatty acids, nutrition, brain, sports, athletes, concussion, sub-concussive

Introduction:

The prevalence of sports-related concussions (SRC), also referred to as mild traumatic brain injuries (mTBI), at the collegiate and professional levels has been at the forefront of research and media in recent years. Growing attention surrounding the increased incidence and negative long-term side effects of SRC has been coupled with increased interest in ways to prevent SRC occurrence and severity. Reported incidences of SRC are on the rise which may be in part due to advancements in medical technology and improved assessment protocols for identifying a concussed athlete. Governing bodies of various professional leagues are taking SRC seriously by implementing changes to equipment and rule changes designed to reduce the severity head impacts. Nutritional interventions are beginning to garner increased interest as n-3 polyunsaturated fatty acids (PUFA) have shown promise to promote protection from head injuries (Kim 2014). However, current n-3 PUFA status in a large number of athletes is far below recommended values (Anzalone et al. 2019).

As of 2006 it is estimated that 1.6 to 3.8 million SRC occur annually in the United States (Langlois et al. 2006). A systematic review by Prien et al. (2018) examining head injuries in adult team sports ranked rugby, football and ice hockey as the 3 sports with the highest concussion incidence per 1000 exposures. The National Collegiate Athletic Association (NCAA) also compiled data from 2009-2014 which parallels the findings of Prien et al. (2018) ranking men’s wrestling, men’s ice hockey, women’s ice hockey and men’s football as the sports with the highest incidence of SRC (Zuckerman et al. 2015). Rugby is cited in many studies as a high-risk sport globally, but in North America the National Football League (NFL) is most often
heavily associated with SRC. As of the 2012 season, the NFL began to publicly release data on concussions to reveal that preseason and regular season total number of concussions peaked in 2017 (281) with the lowest incidence occurring in 2014 (206) (NFL 2019). The second major North American sport closely associated with SRC is ice hockey. Unlike the NFL however, the National Hockey League (NHL) does not currently release their SRC data to the public. Adams et al. (2018) examined SRC during the 2013-2017 NHL seasons based on publicly available online injury data released by FOX Sports. The lowest incidence of reported SRC occurred during the 2014-2015 season with 27, and the highest during the 2016-2017 season with 46 (Adams et al. 2018). Based on roster size estimates in the NHL and NFL, the lowest incidence of SRC in a season for each league represents approximately 4%, and 12% of players being impacted respectively. SRC are not only a concern at the professional level, athletes at any age who have previously been diagnosed with a SRC are more likely to experience a 2nd SRC and slower recovery time between each occurrence (Guskiewicz et al. 2003). Putting emphasis on decreasing the likelihood of the initial concussion in youth athletes could help reduce the severity of symptoms later on in life.

In the United States, there were 1.1 million football players, 36,000 ice hockey players and a total of over 7.8 million high school sport athletes in 2014-2015 (NFHS 2016). Bryan et al. (2016) estimated between 1.1-1.9 million sport-related and recreation-related concussions occur annually in those ≤18 years of age. This large range is due to the majority of US youth who likely sustained a concussion but were not examined by a qualified professional and thus, were not accurately diagnosed (Bryan et al. 2016). From 2001-2012 a reported 3.42 million SRC were treated in emergency departments of US youth ≤19 years of age (Coronado et al. 2015). On an annual basis, 285,000 were treated in emergency departments, which is significantly lower than
the estimate reported by Bryan et al. (2016) and provides credence to their claims that SRC are often not properly assessed. Recent emphasis on enhancing safety in both the NFL (NFLPA 2018), NHL (NHL Public Relations 2016) and other professional organizations alike have been implemented to improve diagnosis of SRC during games to ensure players can safely return to competition. However, even at the professional level there is still no current method of ensuring 100% accuracy in their reporting of SRC (Adams et al. 2018). Being able to reduce the prevalence of SRC and provide accurate diagnosis are key elements in the safety of athletes as they progress throughout their career and beyond.

Concussions:

The exact definition of a concussion continues to evolve (McCrory et al. 2017a). The 5th International Conference on Concussion in Sport (McCrory et al. 2017b) led to a review identifying the most commonly used definition of concussion developed by the Concussion in Sport Group (CISG) (McCrory et al. 2017a). In the simplest terms, a SRC is a brain injury traumatically induced by a biomechanical force to the body, most often directly to the head resulting in temporary impairment of normal neurological functions (McCrory et al. 2017b). The pathophysiological response following a SRC is a complex, multi-faceted interaction which can present itself immediately or often as a delayed response (McCrory et al. 2017b). Less contested are the common symptoms that athletes exhibit following a SRC.

A traumatic impact rendering an individual unconscious is a symptom typically associated with a SRC (McCrory et al. 2017b). Surprisingly, it has been shown that the majority of diagnosed concussions are associated with no reported consciousness disturbance (Hill 2014). Other common physical symptoms may include headache, issues related to balance, nausea and
vomiting, and blurred vision with more intense symptoms including tingling of the extremities and convulsions/seizures (Public Health Agency of Canada 2019). Along with the physical symptoms there is a diverse spectrum of non-physical symptoms following a SRC such as memory impairment or ‘foggy’ thinking, feeling sleepy or lethargic, slowed movement/reaction time, sleep disturbances, and drastic emotional swings (Public Health Agency of Canada 2019). Depression and depressive-like symptoms have frequently been reported by athletes following their career and are strongly associated with a history of SRC diagnosis (Manley et al. 2017). Questionnaires completed by former professional athletes reported strong correlations between athletes who have suffered multiple SRC and the severity of their depressive symptoms (Gouttebarge et al. 2017). The visible and ‘invisible’ presentation of various SRC symptoms is where the difficulty of an accurate diagnosis protocol becomes evident.

Currently, there is no diagnostic test to immediately and without fail diagnose a SRC in a competitive setting (McCrory et al. 2017b). The Sport Concussion Assessment Tool 5th Edition (SCAT5) is presently the most well-established standardized SRC assessment tool suited for sideline diagnosis by licensed healthcare professionals (McCrory et al. 2017b; Echemendia et al. 2017). The SCAT has gone through many revisions, including adding a Child-SCAT in 2012, specifically for youth athletes under the age of 13, and a Concussion Recognition Tool 5 (CRT5) for use by non-medically trained individuals (Echemendia et al. 2017). On-field and off-field assessments are used in the SCAT5 as the entire protocol takes >10 minutes to fully evaluate an injured athlete (Echemendia et al. 2017). The on-field assessment makes use of Maddocks Questions (Maddocks and Saling 1995), evaluating the injured athletes immediate sport-specific recall, along with the Glasgow Coma Scale (GCS) which assesses verbal, motor, and eye movement responses (Jennett and Bond 1975) amongst other measures. The off-field assessment
is more intensive as it includes a cognitive screening consisting of the Standardised Assessment of Concussions (SAC) (McCrea 2001) which an abridged version of the protocol is provided as Supplementary Table S1. As SRC are unable to be diagnosed on any modern imaging scan (Public Health Agency of Canada 2019) and evidence supporting SRC effects compounding (Guskiewicz et al. 2003), further validating sideline assessment tools to determine when to remove an athlete from play is important for their long-term recovery.

The NFL and NHL have their own league-specific concussion protocols in place which differs from the widely used SCAT5, but still incorporates aspects of it in their assessment (Ellenbogen et al. 2018; NHLPA 2016). One prominent limitation to the SCAT5 is the prominence of self-reporting and the time it takes to complete a full assessment (>10 minutes). Some athletes have limited knowledge when it comes to the specifics of concussions and their related symptoms (Robbins et al. 2014), which can negatively impact the reliability of self-reporting tests. Due to the pressure that athletes feel to perform at a high level, not wanting to lose playing time, or let their team down, it is likely those who are aware they have suffered a SRC could withhold their injury in an attempt to keep playing (Wallace et al. 2017). Collegiate level athletes were found to experience extrinsic pressure from coaches, other members of the team, parental figures and even fans which may further compel an athlete to withhold their injury status (Kroshus et al. 2015). To avoid this type of bias alternative sideline diagnostic tools which do not rely on self-reporting have been examined. The King-Devick (K-D) test has standardized instructions and requires the injured athlete to rapidly name numbers while tracking eye movements which takes <2 minutes to administer (Galetta et al. 2016). A meta-analysis and review by Galetta et al. (2016) found an 86% sensitivity and 90% specificity in detecting SRC at sideline using the K-D test. Although not perfect, it does help eliminate the bias of self-reporting
with a relatively high accuracy rate. However, amongst 171 sports medicine clinicians only 12% reported to utilizing eye tracking technology and 77% did not use eye assessment tools for concussion diagnosis, indicating these procedures are still uncommon in regular practice (Snegireva et al. 2019). Future diagnostic tools look to improve accuracy, and practicality of sideline testing for identifying SRC in athletes during any type of competition scenario.

**Sub-Concussive Impacts:**

Not all traumatic blows to the head result in a SRC and the result of these sub-concussive impact(s) (SCI) still pose a prominent threat to health. A SCI, similar to a SRC, is a traumatic biomechanical force most commonly applied to the head/upper body, but the impact does not reach the necessary threshold to elicit SRC symptoms (Johnson et al. 2014). A systematic review by Mainwaring et al. (2018) found that there is currently no consensus definition used for a SCI. SCI are often simply defined as an impact that doesn’t cause a SRC, which is limited in scope, as it does not provide any clarification of whether an injury or mechanism is being described (Mainwaring et al. 2018). Each individual impact does not impart any discernible damage, but the cumulative effect of repetitive injury over time results in a rather dramatic result. Scenarios resulting in a SCI are common place in most contact and even non-contact sports such as heading a ball in soccer, diving for a catch in baseball, amongst numerous others. The primary concern involving SCI are their long-term effects on the brain and mental health of athletes.

Brains of former NFL players exhibited abnormalities in their white matter (WM) tracts coupled with decreased executive functioning which associated positively with those who had accumulated more SCI (Alosco et al. 2018). Injury to the (WM) is significant because it
comprises 50% of the human brain and acts as a “subway” that connects various regions, with its dysfunction being linked with cognitive impairments as well as numerous psychological disorders (Fields 2008). Data from high school football players has shown that after only a single season there was indication of WM tract abnormalities (Kuzminski et al. 2018). Davenport et al. (2016) found a single season of American football results in negative changes of brain MRI results independent of any clinical concussion diagnosis. The most commonly noted symptoms exhibited by SRC and SCI over time are cognitive declines, adverse emotional states, and depressive symptoms (Slobounov et al. 2017). In a majority of these studies, increased accumulation of SCI over the course of a season/career correlated positively with the severity of symptoms later on in life (Slobounov et al. 2017). Thus, due to the increased exposure of physical contact, athletes who compete in contact sports are likely to experience more severe symptoms compared to those who compete in non-contact sports. As these are “invisible” symptoms it is nearly impossible that an athlete would have any indication of these changes thus, practical methods of diagnosis become critical to protect athletes in the long-term.

Following a head impact there is an acute inflammatory response that occurs with certain biomarkers reflective of injury to specific areas of the brain (Zetterberg et al. 2013). The composition of cerebrospinal fluid (CSF) reflects these acute biochemical changes in the brain (Zetterberg et al. Blennow 2013). Neurofilament light (NF-L) is an integral structural component of neuronal axons, primarily the myelinated axons of WM, which upon head impact releases NF-L into the blood and CSF (Kawata et al. 2018a). As previous studies have noted links between SCI and WM abnormalities in athletes (Alosco et al. 2018; Kuzminski et al. 2018) this provides a link for NF-L as a potential biomarker. When examining division 1 football players over the course of a full season Oliver et al. (2016a) discovered there was a substantial increase in levels
of serum NF-L in starting players (high accumulation group) compared to non-starting players (low accumulation group). Amateur boxers were found to have increased levels of CSF NF-L 1-6 days post-match, yet there was no indication of impairment in memory tests, processing speed, or executive functioning compared to controls (Neselius et al. 2014). This implies NF-L levels can be an effective tool at monitoring the severity of SCI accumulation in research settings going forward. A comprehensive study by Rubin et al. (2019) compared NF-L with other biomarkers in division 1 football players and found a positive relationship between blood levels of NF-L and frequency of head impacts. Although this study and others use blood serum or plasma to measure NF-L rather than CSF, a strong correlation between the two has been noted (Kawata et al. 2018b), further increasing the validity and reliability of NF-L.

Unlike SRC, there are currently no officially recognized tools or scales that are used for the diagnosis of SCI. As symptoms are commonly invisible not only to medical personnel and athletes, many diagnostic approaches are currently being investigated. Research examining postural sway velocities has been mixed, with some reporting increased sway following head impacts (Miyashita et al. 2018) and others finding no relation (Dierijck et al. 2018). A more sensitive physical diagnostic tool may be the assessment of ocular-motor function. Examination of Division 1 football players found those who sustained a greater frequency of head impacts, which did not result in a SRC, performed worse on a near point of convergence (NPC) test (Kawata et al. 2016). Similarly, high school football players after a full season who had increased amounts of SCI had decreased NPC values similar to that of college athletes (Zonner et al. 2019). Examination of university aged lacrosse players found a decline in a visuomotor tracking task performance following SCI (Brokaw et al. 2018). However, the sensitivity of this test is not currently known and may not be applicable for sideline use. With the reported number
of brain injuries in sport rising, finding practical and effective methods of attenuating long-term
damage is vital to benefitting the overall well-being of athletes.

**Biology of EPA and DHA**

Nutritional interventions, including n-3 PUFA, have shown promise in decreasing the
likelihood of SRC and improving recovery following a traumatic head impact (Wu et al. 2013).
Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are both n-3 PUFA
endogenously derived from α-linolenic acid (ALA) (Lauritzen et al. 2016). Although EPA and
DHA are not classified as essential dietary fatty acids, they are products in the downstream
metabolism of ALA (as seen in Figure 1), which is an essential fatty acid obtained through diet
(Richard and Calder 2016). The overall process of synthesizing ALA to EPA and DHA however
is quite inefficient in humans (Richard and Calder 2016; Echeverria et al. 2017). Recent research
finds conversion rates of ALA to DHA typically fall below 1% with EPA conversion rates also
being quite low but, are often greater than that of DHA (Hussein et al. 2005). Due to ALA
conversion rates being quite inefficient, consuming EPA and DHA from marine-based food
sources and fish-oil supplements is the most effective route for increasing circulating levels
(Richard and Calder 2016; Wiktorowska-owczarek and Nowak 2015).

DHA is one of the main structural components of the neuronal cell membrane and
accounts for approximately 10% of the total lipid content in the brain (Kitson et al. 2016). With
such a large quantity of DHA present, compared to ALA or EPA, it is a more common target in
research in relation to brain health. Sufficient amounts of DHA over a lifespan leads to overall
better development, and maintenance of the central nervous system and thus, improved cognition
(Weiser et al. 2016). More specifically, DHA has shown to play a role in neurogenesis (Innis
2007) and hippocampus-related cognitive functions such as memory and learning (Cao et al. 2009). Due to the brain's poor capacity to convert DHA on its own, almost all DHA must first pass through the blood brain barrier (BBB) (Lacombe et al. 2018). The BBB is highly selective and contains specialized tight junctions for increased protection (Lo Van et al. 2016). Transport of DHA is mediated by the Major Facilitator Superfamily Domain containing 2a (Mfsd2a) which is found to be expressed exclusively in the endothelium of the BBB (Nguyen et al. 2014). The two plasma pools of DHA which are the most common source of uptake into the brain are the non-esterified fatty acid (NEFA) pool bound to albumin and DHA esterified to lysophosphatidylcholine (LPC-DHA) (Lacombe et al. 2018). Mfsd2a is only able to transport DHA into the brain as the LPC-DHA form and not as the NEFA form (Nguyen et al. 2014). Studies examining the different plasma pools efficacy in increasing brain DHA content have typically found, due to the preference of the Mfsd2a transporter, LPC-DHA to be more effective (Nguyen et al. 2014). Chen et al. (2015) found NEFA DHA uptake to be nearly 10-fold greater to that of LPC-DHA in certain conditions but, are one of very few studies to make this claim in favour of NEFA DHA. As DHA entry into the brain is complex, examination of specific transporters and pathways have also begun as possible therapeutic targets for brain injuries (Lacombe et al. 2018).

One of the primary beneficial effects of n-3 PUFA is their capability to exert anti-inflammatory properties via lipid mediators throughout the body. Oxylipins are lipid mediators formed from PUFA precursors via cyclooxygenase (COX) and lipoxygenase (LOX) pathways (Gabbs et al. 2015). The most well-known oxylipins are the eicosanoids produced via the n-6 PUFA arachidonic acid (AA), which have shown to exhibit proinflammatory effects (Gabbs et al. 2015). EPA is also converted to eicosanoids known as E-series resolvins but, compared to
AA, results in beneficial anti-inflammatory effects (Gabbs et al. 2015). DHA is converted to
docosanoids which includes D-series resolvins along with additional mediators than that of EPA
known as protectins, and maresins (Weiser et al. 2016; Calder 2015). Protectins are also known
as neuroprotectin(s) when they are found in the central nervous system and are induced by
oxidative stress which in return protects neuronal cells (Bradbury 2011). The pro-resolving
mediators of n-3 PUFA overall have found to inhibit migration of neutrophils, exhibit anti-
inflammatory properties, and can downregulate NF-κB (Bradbury 2011). In one of the few
human studies examining CSF content following brain injury, increased AA levels correlated
with decreased health outcomes of patients (Pilitsis et al. 2003). Due to n-3 and n-6 PUFA
competing for similar enzymes needed to produce docosanoids and eicosanoids (Gabbs et al.
2015), shifting ratios of n-3:n-6 consumption can alter the production of either pro or anti-
inflammatory oxylipins (Broughton and Wade 2002). Schuchardt et al. (2017) found 12-weeks of
DHA supplementation can shift oxylipin profiles by increasing DHA and EPA-derived oxylipins
and causing a decrease of AA-derived oxylipins. Increasing DHA-derived oxylipins promotes
neuroprotective effects in rats following brain injury (Bisicchia et al. 2018). There are
similarities in the anti-inflammatory properties of n-3 PUFA but, EPA and DHA do exhibit
distinct differences. Even though E-series resolvins have shown to be reduce depression-like
behaviours (Deyama et al. 2018) and decrease inflammation of microglial cells (Rey et al. 2016),
a direct comparison showed that DHA was more effective at decreasing markers of inflammation
(Allaire et al. 2016). In the future, examining the capabilities of n-3 PUFA to impact gene
transcription and protein expression in the brain could provide novel insight into their beneficial
effect long-term.
EPA and DHA Intervention for Brain Health

Regular consumption of n-3 PUFA has been compared to providing the brain with its very own “nutritional armour” by suppressing injury responses such as neuronal cell death via promoting neurogenesis and restoring synaptic function (Kim 2014). Guo et al. (2017) using mass spectrometry imaging found DHA and DHA-containing lipids to flood the injured area of the brain less than 24 hours following injury. Male rats consuming DHA leading up to a mTBI had improved neurological function, improved learning and memory and decreased oxidative stress following injury compared to placebo-fed rats (Zhu et al. 2018). ER Stress is a complication which can occur during brain injuries and has been linked to neurodegenerative disorders such as Alzheimer’s, and Parkinson’s (Begum et al. 2014). Post-mortem human brain analysis found neural degradation was linked to ER stress pathways which was attenuated in rats supplemented with DHA (Lucke-wold et al. 2016). Other rodent brain injury models found DHA supplementation to not only reduce ER stress marker proteins (Begum et al. 2014; Harvey et al. 2015) but, decrease abnormal brain protein accumulation which can be the result of ER stress (Begum et al. 2014). Initiating supplementation following a brain injury upregulates proteins to counteract oxidative damage that could lead to cognitive decay (Wu et al. 2011). Conversely, brains of experimental models depleted of DHA have impaired recovery following brain injuries specifically in regard to cognitive (Desai et al. 2014) and sensorimotor outcomes (Russell et al. 2013). Following a brain injury, it is interesting to note aerobic exercise in mice was found to facilitate the action of DHA in recovery from traumatic brain injury (Wu et al. 2013). Oliver et al. (2016b) did find college football players that supplemented with high levels of DHA (2-6 grams) over the course of a season resulted in decreased NF-L levels, one of the prominent biomarker reflecting SCI accumulation, suggesting that DHA was able to attenuate neural
damage associated with multiple SCI. These few studies highlight the potential benefits of DHA, but limitations of the current literature include the overall lack of studies on EPA and DHA in athletes. Nevertheless, insight can still be applied from the broader literature examining the role of EPA and DHA in the aging brain of athletes.

The role of EPA in attenuating factors of brain injury has not been found to be as robust compared to that of DHA (Dyall 2015). Due to relatively high DHA levels in the brain, it stands to reason that DHA would play a larger role in neuronal health compared to EPA (Russell et al. 2013). Levels of EPA have been shown to be quite low as it is either rapidly oxidized or converted to DHA (Weiser et al. 2016) resulting in difficulties studying its overall effects on the brain. However, there is some evidence of EPA providing a specific benefit to mental health. A meta-analysis by Martins (2009) found EPA, not DHA, to be more effective at reducing symptoms of depression which is common in both SRC and SCI accumulation. The E-series resolvins derived from EPA have shown to improve mood disorders, specifically depression, more effectively than the D-series resolvins of DHA (Deyama et al. 2018). Both n-3 PUFA provide benefits but, DHA is more effective overall at improving structural integrity and EPA appears to impact mood disorders to a larger degree (Devassy et al. 2016). With emerging evidence in animal models showcasing n-3 PUFA being effective at attenuating damage and promoting recovery from a brain injury, it is relevant to recognize other benefits to athletes, such as improved cardiovascular health (Langlois and Ratnayake 2015). Additionally, EPA has shown to be biologically active in skeletal muscle, augmenting protein synthesis and anabolic signalling (Kamolrat and Gray 2013). Omega-3 Index values have long been a general surrogate for assessing n-3 PUFA status (Langlois and Ratnayake 2015) and recent literature has found these values to be quite low in athletes (Anzalone et al. 2019; Heikkinen et al. 2011).
Health Organization (WHO) has the acceptable macronutrient distribution range (AMDR) for EPA+DHA at 250mg to 2g a day, with the upper-end typically reserved for those requiring secondary prevention (Elmadfa and Kornsteiner 2009). However, few studies have examined requirements for n-3 PUFA in athletes with concussions and further research is necessary to determine appropriate dosage and duration of any interventions.

Conclusion:

In conclusion, protocols for concussion diagnosis continue to evolve as they currently rely on observational measures which may be biased by information passed on by the athlete. In order to optimize treatment of SRC and SCI, future research should aim to unify clinical definitions and continue to identify the gold-standard for sideline diagnosis. n-3 PUFA (specifically EPA and DHA) have exhibited promising results in rodent models at attenuating factors of neurological damage and promoting recovery following brain injuries. Longitudinal human studies examining the impacts of SRC and SCI are needed in order to substantiate the benefits of EPA and DHA. Overall, the emerging evidence for EPA and DHA in SRC and SCI may provide a simple, nutritional strategy to mitigate the effects of such injuries, thus warranting further investigation.

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Conflict of Interest
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**Figure 1:**

Interconversion pathway of n-6 and n-3 polyunsaturated fatty acids and their resulting oxylipins. Those bolded/italicized in grey exhibit anti-inflammatory and/or neuronal health benefits for promoting recovery from a concussion.

ALA, α-Linolenic acid; ARA, Arachidonic Acid; COX, Cyclooxygenase; DHA, Docosahexaenoic Acid; EPA, Eicosapentaenoic Acid; HETE, Hydroxyeicosatetraenoic acid; HpDHA, Hydroperoxy docosahexaenoic acid; HPETE, Hydroperoxyeicosatetraenoic acid; LA, Linoleic Acid; LOX, Lipoxygenase; PD, Protectin; PG, Prostaglandin; PUFA, Polyunsaturated fatty acids; RvD, D-Series Resolvins; RvE, E-Series Resolvins; Tx, Thromboxane.