Peer-review

Tompkins, Claiborne. 2025. “Analyzing Sports-Related Concussions and Traumatic Brain Injuries and Their Effects on Adolescents and Athletes.” *Journal of High School Science* 9 (3): 50–67. https://doi.org/10.64336/001c.142146.

As writtten, the review does not meet the Journal’s expectations for a review paper as seen here: https://jhss.scholasticahq.com/for-authors, types of manuscripts, review papers. However, addressing the points below will allow the manuscript to do so. Please therefore, address and include the following three points of concern in the revised manuscript. I look forward to your revised manuscript.

1.This review leaves out much current information. For example, hydraulic liquid shock absorbing helmets need mention and discussion, as do ncRNA saliva methods for TBI detection (see some references and patents below). Please perform an exhaustive search of the literature.

2.Please discuss possible mechanisms of bio-compensation to TBI (biomarkers present in sputum post injury) from the KEGG enrichment pathway results; including those in Table 4 of reference https://doi.org/10.1002/ctm2.197

3.Discuss in the manuscript: if increased levels of ncRNA (post trauma) imply compensatory increased protein production by the cRNA of the corresponding gene, then agonists of those genes/pathways/enzymes can be used to “prime” the brain BEFORE a game or practice, so that immediate relief is available as soon as a concussion occurs. For example, Adenosine is a V-ATPase agonist (ATP6V1G2), GABA-a agonists (GABRG2) (unfortunately most anxiolytic drugs are also sedative), Thrombospondin-1 agonists (or angiogenesis inhibitors) (THBS1) such as specific soy products and mushrooms, SNARE protein agonists, such as Lithium (GOSR1). Therefore, put forward the speculation that a sports drink that contains Lithium, soy and mushroom extract, and adenosine may be beneficial to attenuating concussion injury and should be investigated further in controlled trials as being mandatory for all contact sport athletes before a game or practice. This - as yet previously unexplored content in the published literature - will allow your manuscript to meet the Journal’s review paper expectations. Please provide a detailed discussion and analysis in the manuscript. You are of course - free to think of your own differentiating content/idea.

https://doi.org/10.3389/fbioe.2023.1160387
https://doi.org/10.1177/1045389X211023578
https://doi.org/10.1055/a-2342-3604
https://doi.org/10.1016/j.ijpsycho.2018.01.007
https://doi.org/10.1002/ctm2.197
https://doi.org/10.1136/bjsports-2020-103274
https://patents.google.com/patent/US20200385808A1/en
https://doi.org/10.1016/j.expneurol.2016.12.006

Discussion of Revisions for “Analyzing Sports-Related Concussions and Traumatic Brain Injuries and their Effects on Adolescents and Athletes”

Claiborne Tompkins 7/12/2025

In the revised manuscript, I have addressed the reviewer’s comments in several key ways:

1) In **Section 2.1 - Definition of a Concussion,** I added an extensive discussion of subconcussive impacts and repetitive subconcussive head impacts (RSHIs), with a primary focus on changes in brain structure and function. This included defining an RSHI as a cranial impact that did not result in overt symptoms such such as dizziness, headaches, or short term memory loss. I also used

research from Hack et al. (2024) and Mainwaring et al. (2018) to focus on the fact that structural alterations from these
subconcussive impacts were typically found within the white matter of the brain. Additionally, I discussed how the authors of these studies identified a dose-response relationship between white matter abnormalities and the sustained cumulative number of RSHIs, implying that the cumulative number of head impacts causes structural brain damage.

2) In **Section 2.5 - Concussion and TBI Assessment and Diagnosis** (previously named Section 2.5 - Prevention and Assessment, which I broke down into two smaller sections)**,** I added an extensive discussion of saliva RNA and the possibility of utilizing ncRNA in the saliva as a biomarker in the diagnosis of a TBI. I focus on two papers (Hicks et al.
(2020) and Di Pietro et al. (2021)) which utilize slightly different methods to identify noncoding RNA (ncRNA) biomarkers in saliva that may allow differentiation between individuals with mTBI from peers without mTBI. I spend time discussing the Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways and the activation of key responses in the human brain in the aftermath of a TBI that could lead to an altered saliva RNA profile. Ultimately, using the research of the two papers, I concluded that these
saliva RNA biomarker advancements are promising and should be researched further with possible future implementation.

3) In **Section 2.6 - Concussion and TBI Prevention** (previously named Section 2.5 - Prevention and Assessment which I broke down into two subsections), I focused on football helmet technology, discussing the current helmet tech paradigm, including viscoelastic foams, buckling beams and structures, gas chambers, and 3D printed lattices. I pay special attention to Cecchi et al. (2023) to discuss liquid shock absorption technology which may provide avenues for future advancements in helmet technology.
To that end, I discuss how liquid shock absorption technology has outperformed traditional helmet technology. I also briefly discuss collapsible fluid-filled fabric shock absorbers and their possible applications in football helmets.

4) In **Section 3.1 - Recommendations for Further Study,** I make a key suggestion surrounding unexplored content in the published literature, focusing on the possibility of a pre-activity sports drink which may be utilized to limit concussions and head injuries
for athletes by priming key brain pathways. I include in-depth discussions about several ingredient options such as adenosine, lithium, theanine, mushroom extract, and certain soy products. For each ingredient, I focus on the potential benefits while also discussing possible limitations to their inclusion. For adenosine, I discuss its role as a V-ATPase agonist and its anti-inflammatory qualities. I also mention that exogenous adenosine administered after ischemia has been shown to improve hippocampal neuron survival, neuroprotection, and functional recovery in rodents. For theanine, I discuss its possible ability to activate the GABA modulator, suppressing overexcitation and potentially protecting neurons from acute damage in the aftermath of TBI. For soy products, I discuss their ability to support THBS1 function, possibly helping to prevent vascular
leakage and secondary injury after head trauma. I specifically discuss how lunasin, which is found in soy, leads to epigenetic upregulation of THBS1 expression. I also discuss how certain types of mushrooms can act as angiogenesis inhibitors, mimicking THBS1 expression. Finally, I discuss lithium and its ability to increase SNARE protein and

SNARE complex abundance after TBI which can offset TBI's ability to limit the SNARE complex. I conclude by recommending further examination and possible controlled trials for the development of the pre-activity drink.

5) In the **Abstract,** the topics of discussion were updated, reflecting the additional examinations in the body of the paper:

   (1) the effects of subconcussive impacts on brain structure and function
   (2) the emerging literature surrounding traumatic brain injuries diagnosed with the use of miRNA biomarkers in saliva samples
   (3) shock-absorption and impact reduction helmet technology
   (4) possible future development of a pre-activity sports drink designed to prime the brain of an athlete prior to a competition or practice

6) Finally, I made various grammatical improvements throughout the body of the paper and added additional citations as needed.

Thank you for addressing my comments. Accepted.