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Neurodegenerative Risks of Professional Sports: A Study on the Potential Linkage Mechanisms Between Alzheimer's Disease, Parkinson's Disease and CTE

Ruixin Li

Department of Semmelweis, University Faculty of Health Sciences, Budapest, Hungary
ruixin.li@stud.semmelweis.hu

Abstract. In recent years, growing attention has been paid to the risk of neurodegenerative diseases triggered by frequent head impacts sustained by professional athletes during long-term training and competitions. Such diseases include dementia, Parkinson's disease and chronic traumatic encephalopathy (CTE), and their onset is closely associated with repetitive concussions and subclinical head impacts. Current research indicates that head impacts can induce common pathological mechanisms such as chronic neuroinflammation, mitochondrial dysfunction and abnormal protein deposition, thereby accelerating the neurodegenerative process. However, many issues remain unsolved in this field, such as undefined safe cumulative impact threshold, unclear genetic and metabolic basis for individual susceptibility differences, and uncertainty over reversibility of early injuries. In addition, existing protective strategies and screening methods still lack sufficient evidence support. Future studies need to rely on large-sample long-term follow-ups, biomarkers and neuroimaging technologies to further clarify the dose-effect relationship among sport types, on-field positions and cumulative impact exposure, and provide evidence for formulating targeted protective measures. This paper reviews pathological mechanisms, clinical manifestations and risk factors of different neurodegenerative diseases, as well as preventive and interventional strategies, and systematically elaborates on the association and underlying mechanisms between head injuries and neurodegenerative diseases in professional sports.

Keywords: Professional Athletes, Neurodegenerative Diseases, Head Impact, Pathological Mechanisms Introduction

1. Introduction

The majority of professional sports require very high rates of physical fitness, speed, and bursts out of athletes, so injuries to the head are virtually unavoidable throughout long-term training and the professional competitions. Examples are the use of the head in soccer, hits and blows in boxing, the rough physical contacts in rugby and ice hockey during training and games. All of this may lead to minor brain injury, although such minor concussions may add up and may result in more significant brain injury. Sports-related brain injury in the earlier times was perceived as something that could be reversed and is a short-lived issue. Nonetheless, studies have established that repetitive or partially

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recovered brain injuries may cause chronic neuroinflammation or neuronal loss, and protein deposition, which increase the susceptibility of developing Alzheimer's disease, Parkinson's disease, and chronic brain injury (CTE) [1]. Such injuries may lead to memory impairments, mood, and impaired firm motor abilities, which critically affect the career life, and the existence of the athletes after retiring.

Neurodegenerative diseases like the Alzheimer disease, Parkinson disease and chronic traumatic encephalopathy severely affect cognition, motor functioning, and daily life. This has become a matter of concern; over the past few years, there has been increased instances of occurrence of these diseases in retired athletes and this has prompted a lot of scrutiny in the role played by professional sports in the development of these progressive neurodegenerative diseases. This paper summarises the risks and mechanisms of neurodegenerative diseases that are potentially encountered by professional athletes.

2. Pathological mechanisms

The onset of the concussions or head trauma during high-intensity or contact sports may trigger one of the series of neuropathological changes. Research indicates that overtrained athletes and neurodegenerative disease patients bear certain pathological similarities especially in the functioning of the mitochondrion [2]. Concussions in sports have a direct effect on mitochondrial structure, the process of energy production (oxidative phosphorylation) and consequently the production of adequate quantities of ATP and the production of vast quantities of reactive oxygen species (ROS). This imbalance in energy metabolism continues to worsen neuronal excitotoxicity and calcium ion imbalance leading to the sustained neuroinflammatory activation.

Repeated traumatic brain injury over the long-term has the potential to progressively change the mitochondrial damages into irreversible, thus eventually leading to the activation of abnormal phosphorylation of Tau protein and neuronal apoptosis [3]. This provides a very essential pathological basis of developing chronic traumatic encephalopathy (CTE) and other neurodegenerative diseases. This cumulative and long-term effect can result over time in acute brain injury slowly progressing into chronic traumatic encephalopathy (CTE), and is in part overlapping with the pathogenesis of other diseases like Alzheimer disease or Parkinson disease.

3. Neurodegenerative diseases caused by sports injuries

3.1. Dementia and/or MCI

Potential risk factors to neurodegenerative diseases, in particular, dementia and mild cognitive impairment (MCI), include professional sports, especially those associated with high frequency of physical contacts and head-bangs. The documented reduction in cognitive functioning and higher rates of dementia among sports players indicate that concussions in sports could be contributing largely.

According to some studies, the overall mortality rate of American professional soccer players increases, and especially neurological-related mortality, is more than that of the general population [4]. Long-term exposure to high-speed balls and recurrent concussions can be found to present a risk of developing long-term neurological issues even in professional baseball regarded as a low-impact sport. Other than soccer, professional American football, and ice hockey players have been identified to be more susceptible to the onset of dementia much earlier than the rest of the population [5]. In their study to examine particular risk factors in soccer players, Russell et al.

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conducted a retrospective cohort study to investigate the association between on-field positions, career profiles, and the risk of developing neurodegenerative diseases in retired professional male soccer players. Through a link analysis of population health data in Scotland, the study involved 7676 male ex-professional football players aged between 1900 and 1977 and no less than one match 23,028 general males at a ratio of 1:3 as controls [6]. These findings demonstrated that the average risk of neurodegenerative disease occurrence among the former professional football players was 3.66 higher than the control group. The risk differed greatly between playing positions where the defenders were at the highest risk (4.98 times more than the control group) with the increased risk in the goalkeepers being not significant. Moreover, there was a positive association between the risk and the length of the career with players whose career was above 15 years having the highest risk. This indicates that playing position (particularly defensive and midfield positions having high frequency of headers) and higher career are significantly related elements in the risk of the disease.

The other research performed by Pupillo et al. concerned the connection between professional football and amyotrophic lateral sclerosis (ALS) which is a particular neurodegenerative disease. This paper relied on the Italian Football Yearbook archives to determine the sample of 23,586 male professional footballers registered between 1959 and 2000, and verified ALS cases up to the end of 2018 using different public sources. The analysis revealed a significantly higher risk of getting ALS in the whole of the player group compared to the general population (1.91) with that of under-45 years being the greatest risk of getting ALS (4.66 times). In addition, the mean age of players with ALS diagnosis was 45.0 years, which is about 20 years younger than the mean age of onset in the European general population. Interestingly, it is also at the cellular level (abnormal protein (TDP-43) accumulation) that ALS has in common with another disease - frontotemporal lobe degeneration and the evidence inherent in this is that the damage seen in the motor areas of the human brain may be just as likely to be damage to motor-related networks and cognitive-behavioral networks [7].

Overall, chronic neuroinflammation, nerve fiber damage, and distribution of abnormal proteins in the brain caused by long-term and repetitive concussions and comparatively mild head impacts can be the cause of persistent cognitive, executive, and emotional and behavioral abnormalities. The available literature reveals clearly that there is a correlation between involvement in professional sports like football and likelihood of developing neurodegenerative diseases including dementia, memory impairment control and motor neuron diseases. The risk is dependent on positions on the field and relates to the career length. These results provide a strong indication that head impact and exposure related to trauma during sporting activities are critical contributors of this elevated risk and important evidence towards formulating risk reduction strategies that are specifically directed.

3.2. Parkinson's disease

The existence of epidemiological evidence adds to the identification of the relation between professional football and the susceptibility to certain neurodegenerative diseases. One of the fundamental studies revealed that the neurodegenerative disease mortality rate of retired professional football players was significantly higher than in the general population, and the mortality rate of Parkinson and neurodegenerative diseases was largely striking [8]. In this study a population based retrospective cohort design was used which involves the association of the national death registry system and a professional athlete registry database and the study tracked thousands of retired athletes over the long term. Statistical results indicated that the risk of dying from Parkinson's disease among the former professional players was 2.5 times greater compared to the general population (95 percent confidence interval, 1.8 to 3.4) and the risk was known to be dose-responsive in relation to the professional career of the former players. The cause of this risk pattern is largely

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due to the repetitive and long-term head blows on athletes such as recurring heading in games and other forms of physical impact. Such recurrent mild concussions can lead to long-term microscopic damage to important areas of the brain responsible for motor function—particularly the substantia nigra-striatal pathway—and ultimately leading to irreversible neuropathological changes.

In pathophysiological terms, brain trauma may cause cascade reactions: during the acute period, it affects neuroinflammatory processes, activates microglia and secretion of pro-inflammatory cells and factors; concurrently, it causes mitochondrial dysfunction and disorders of cellular energy metabolism, and, as a result, greatly increases the level of oxidative stress. All of these microenvironmental alterations support the progressive deterioration of the dopaminergic neurons and cause the uncharacteristic accumulation and fibrosis of alpha-synuclein thus contributing towards the rapid development of typical Lewy bodies in the Parkinson disease and the progression of the disease [9]. Remarkably, the cumulative loads of brain injury are also more pronounced by the characteristics of position on the field and career: of all positions on the field, non-goalkeeper roles (particularly defenders and attackers) have a significantly higher cumulative loads because of higher rates of aerial duels and incidences of physical contact; and players whose careers span over 15 years exhibit a doubling effect on the rate of neuronal loss in the substantia nigra and pathological load of α-synuclein. These results indicate that an exposure to head impact can also increase the risk of developing Parkinson disease and other related neurodegenerative diseases in a dose dependent manner when exposure to the impact is prolonged and intense [6].

In brief the existing epidemiological and pathological data sets a rapidly growing point that repetitive head impacts in professional football are a meaningful environmental risk factor in the acquisition of Parkinson disease. These effects can be involved in progressive neurodegenerative mechanisms as a result of cumulative subclinical damage and chronic neural stress. The upcoming studies need to focus on large, longitudinal cohort designs that would include prospective measures of the biomarkers and the next-generation neuroimaging follow-up to establish the dynamic nature of the relationship between the occurrence and severity of the head impacts and the time-based development of the Parkinsonian pathology better. The objective is to establish robust dose-response relationships and provide evidence-based guidance, thereby laying the foundation for formulating targeted preventive measures, such as limiting leaping exposure during training and optimizing the design of protective equipment.

3.3. Chronic Traumatic Encephalopathy (CTE)

One of the most prevalent neurodegenerative diseases, a characteristic of chronic traumatic encephalopathy (CTE), is the result of the repeatedly occurring head impacts, and it shows high epidemiological convergence in selected professional sports populations. The recent systematic reviews and meta-analyses have indicated that post-mortem brain tissue pathology investigations of athletes who sustained recurrent head hits over an elongated period reveal an excessively high prevalence of CTE in comparison to general population with American football, boxing, ice hockey, and soccer players under significant danger.

The neuropathology research on various sports has also shown differences in risks associated with each sport. A sequential examination of more than 200 former professional athletes found that former American football players had an unusually high level of detection of chronic traumatic encephalopathy pathology with typical topographical phosphorylated tau protein deposition patterns in their cerebral cortex and deep brain nuclei [10]. Equally, neuropathology studies of retired boxers showed that the neurofibrillary tangles distribution in the samples were diagnostic, CTE-wise; a similar percentage of tau protein pathology was found in ice hockey players. It is important to note

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that, in spite of these players actually experiencing less-intense single head collisions in general, the additive subconcussive injuries caused by repetitive heading, as well as competitive contact headers, over a lengthy career in soccer, have been proved to be directly linked to the typical tau protein deposition, which occurs in the temporal region and hippocampus.

These studies all indicate that repeated head impacts are a core pathogenic factor in the pathogenesis of chronic traumatic encephalopathy (CTE), and the risk of developing typical CTE pathological changes directly depends on the impact dose, namely the frequency of head impacts during exercise, the increase in years of professional experience, and the cumulative impact energy load [11]. The factors that are most closely associated with this risk pattern include the playing field of the athlete, the intensity of the training, and protection, and this provides a neuropathological foundation to how head injury prevention measures can be developed with regard to various sports.

Table 1. Comparison of clinical features, risk and prevention measures of sport injury induced neurodegenerative diseases

Type of disease	Major risk factors	Main clinical manifestations	Long-term effects	Prevention and intervention strategies
Dementia and/orMCI	Repetitive concussion, subclinical head impact, career extension	Memory decline, executive dysfunction, emotional instability	early-onset dementia, impaired social function	limiting head impact frequency, improving competition rules, early screening of cognitive function, long-term follow-up after retirement.
Parkinson's disease	Long-term head impact, repeated mild traumatic brain injury	Tremor, bradykinesia, gait abnormalities	persistent decline in motor function, limited ability to perform daily activities	enhanced head protection equipment; adequate post-concussion recovery period; early motor and neurological assessmen
Chronic traumatic encephalopathy (CTE)	High-intensity, long-term repetitive head impact	Cognitive impairment, impulsive behavior, emotional dysregulation	progressive neurodegeneration, severe mental and behavioral disorders	monitoring cumulative head impact exposure, limiting high-risk training in adolescents, career management and retirement assessment

Table 1 summarizes the primary risk factors, clinical presentation, long-term outcomes, prevention and intervention measures to sports injury-associated neurodegenerative diseases. It has been demonstrated that repetitive concussions and chronic exposure to head impacts are closely associated with cognitive, motor, and neuropsychiatric deficits. Most of the preventative strategies currently applied consist of impact reduction, enhanced early screening, as well as career-long-term management; they are, however, yet to be investigated and their ideal implementation routes to be validated by research.

4. Conclusion

Current literature suggests that sport-related injuries exhibited by athletes during their professional careers, especially frequent concussions and persistent head traumas, are directly connected with the onset of a range of neurodegenerative illnesses, and the latter tend to be characterized by a continuous form of manifestation.

Cognitively, professional athletes are at a much higher risk to develop dementia and mild thinking impairments as compared to the general population. The most typical symptoms are

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memory loss, problems with executive functions and emotional control. In the case with the motor system, the rate of mortality due to neurodegenerative diseases is higher in former professional soccer players and such groups and can be connected to the long-term damages to the brain regions related to Parkinson disease (substantia nigra dopaminergic neurons) and the abnormality of accumulation of α-synuclein. The chronic traumatic encephalopathy (CTE) is known to be one of the diseases with the best-known pathological characteristics and is considered a direct consequence of numerous head blows. The disease is characterized by deposition of abnormally phosphorylated Tau in the brain and in most cases the patients tend to have a progressive experience of cognitive impairment, behavioral defects and psychiatric disorders.

Although the diseases have different forms of manifestation, some common pathways are common in the pathogenesis of the diseases, such as chronic neuroinflammation, mitochondrial dysfunction and the proliferation of abnormal brain proteins. This indicates that sports related brain injury does not occur as a single event as an isolated phenomenon, but may trigger a chain of neurodegenerative processes that has far reaching effects on the life time of an athlete in terms of career duration and subsequent quality of life after retirement.

Although the extent of current research has successfully presented a correlation between sports injuries and several neurodegenerative diseases, several questions are yet to be answered. Subsequent studies need to be conducted at large-scale, long-term follow-up to determine the causal association among different sports, different positions as a player, accumulation of head hits, and the ultimate occurrence of neurodegenerative diseases. To prevent this, we must work on better head protection equipment, better training and competition regulations, and early screening procedures, which are biomarker and neuroimaging-based.

Moreover, there are some more basic questions that are not clear such as: which is the level of cumulative head impact which is safe? Why do certain individuals succumb to injury more than others (this can be associated to the issue of genetics and metabolic conditions)? Are early stages of the pathological process that follow the brain injury reversible? It is upon knowing these mechanisms that we are able to formulate indeed specialized paths of prevention and treatment in helping athletes postpone or even prevent the onset of such neurodegenerative diseases.

References

[1] Bellomo, G., Piscopo, P., Corbo, M., Pupillo, E., Stipa, G., Beghi, E., Vanacore, N. and Lacorte, E. (2022) A systematic review on the risk of neurodegenerative diseases and neurocognitive disorders in professional and varsity athletes. Neurological Sciences, 43(12), 6667-6691.

[2] Ostojic, S.M., Ratgeber, L., Olah, A., Betlehem, J. and Pongras, A. (2021) What do over-trained athletes and patients with neurodegenerative diseases have in common? Mitochondrial dysfunction. Experimental Biology and Medicine (Maywood), 246(11), 1241-1243.

[3] Hakiminia, B., Alikiaii, B. and Khorvash, F. (2022) Oxidative stress and mitochondrial dysfunction following traumatic brain injury: From mechanistic view to targeted therapeutic opportunities. Fundamental & Clinical Pharmacology, 36(4), 612-662.

[4] Nguyen, V.T., Zafonte, R.D. and Chen, J.T. (2019) Mortality among professional American-style football players and professional American baseball players. JAMA Network Open, 2(5), e194223-e194223.

[5] Willer, B.S., Zivadinov, R. and Haider, M.N. (2018) A preliminary study of early-onset dementia of former professional football and hockey players. The Journal of Head Trauma Rehabilitation, 33(5), E1-E8.

[6] Russell, E.R., Mackay, D.F. and Stewart, K. (2021) Association of field position and career length with risk of neurodegenerative disease in male former professional soccer players. JAMA Neurology, 78(9), 1057-1063.

[7] Pupillo, E., Bianchi, E. and Vanacore, N. (2020) Increased risk and early onset of ALS in professional players from Italian Soccer Teams. Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 21(5-6), 403-409.

[8] Mackay, D.F., Russell, E.R. and Stewart, K. (2019) Neurodegenerative disease mortality among former professional soccer players. New England Journal of Medicine, 381(19), 1801-1808.

DOI: 10.54254/2753-7048/2026.ZJU31596

[9] Tofaris, G.K. (2022) Initiation and progression of α-synuclein pathology in Parkinson's disease. Cellular and Molecular Life Sciences, 79(4), 210.
[10] Mez, J., Daneshvar, D.H. and Kiernan, P.T. (2017) Clinicopathological evaluation of chronic traumatic encephalopathy in players of American football. JAMA, 318(4), 360-370.
[11] Qi, B., Tan, J. and Feng, D. (2025) Prevalence of Chronic Traumatic Encephalopathy in Athletes With Repetitive Head Impacts: A Systematic Review and Meta-Analysis. Scandinavian Journal of Medicine & Science in Sports, 35(4), e70047.