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Can we predict how many professional footballers in the UK will develop Alzheimer's?

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Abstract
This paper will be looking be looking at if it is possible to predict how many professional footballers In the UK will develop the neurodegenerative disease called Alzheimer's (AD) which is a progressive disease where symptoms worsen over time affecting brain function. Footballers and other sports where trauma is frequent to the head is known to be linked to AD through chronic traumatic encephalophagy which affects cognitive impairment and behaviour.

Keywords: *Health; Biology; Sport; Football; Neurogenerative disease; Alzheimer's disease*

Introduction
Alzheimer's disease is a brain disorder that can destroy memories and damage thinking skills making even simple tasks difficult to do. Currently over 55.2 million people are living with Alzheimer's globally, and this is predicated to rise to 79 million in 2030 and a staggering 139 million in 2050 [1]. Alzheimer's also is the most common cause of dementia in elderly people. First discovered in 1906 named after Dr. Alois Alzheimer when he noticed abnormalities in brain tissue of a female who had died from mental illnesses with symptoms including memory loss and unpredictable behaviour. Post-mortem he discovered clumps (amyloid plaques) and neurofibrillary tangles which are today considered some of the main identifiers of Alzheimer's along with the loss of connection between neurons in the brain [2].

The causes of Alzheimer's (AD) are still ambiguous but are heavily based on a mixture of factors including genetic and environmental lifestyle factors along with age related changes in the brain [3]. However more recently it has been found that professional footballers are at larger risk of developing Alzheimer's, and this could be related to head impacts that occur during football.

Stages of Alzheimer's and possible causes
Alzheimer's can be classified into two types which are early onset and late onset. Early-onset is common in adults ages 30-60 and is considered very rare making up less that 5% of people with Alzheimer's in total. It is thought to be caused by changes in genes passed down from the parent. Late-onset Alzheimer's is the more common type affecting adults ages 65 plus [4]. The genetic risk factor found with late onset is having an allele of the apolipoprotein E (APOE) gene on chromosome 19 which increases the risk of developing the disease [3]. Other than genetics there are other factors that could contribute to Alzheimer's including heart disease, high blood pressure and metabolic diseases including diabetes and obesity. Having a healthy diet and engaging in physical activity have all been found to reduce the risk of Alzheimer's.

Why would head impacts possible cause Alzheimer's?
An average football player will make head contact with a football on a minimum of 2000 times in a 20-year career which could cause similar effects to high-speed collisions and concussions. A study showed that repeated low-impact head injury was linked to dementia and Alzheimer's in 2017 due to a

relationship between football and CTE [5]. CTE is chronic traumatic encephalophagy which is a brain condition linked to repeated head injuries and blows to the head that can reduce life expectancy to just 51 years (fig. 1) as it causes areas of the brain to waste away (atrophy) [6]. CTE will affect cognitive impairment such as difficulty thinking and memory loss, also aggressive behaviour and mood changes including depression and suicidal thought. However, CTE can't be diagnosed in life and only post-mortem.

In this study researchers looked at the brain tissue of six footballers who had died from Alzheimer's and found that four out of the six had CTE. The researchers also stated that 12% of older people with dementia would be expected to have CTE [5].

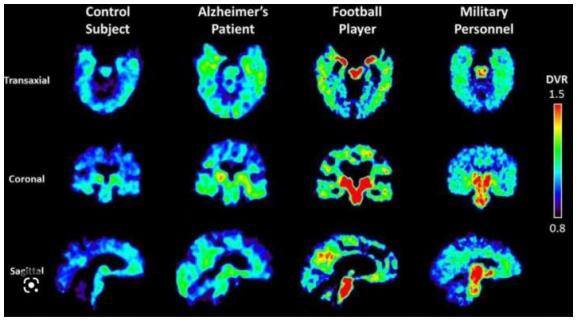

Figure 1 – a PET scan using a radioactive tracer that binds to abnormal proteins in the brain to diagnose CTE in living patients. Warmer colours indicate higher concentrations of tracer highlighting abnormalities [7].

Association of APOE genotypes and CTE

*APOE*ε4 (apolipoprotein E) codes for the primary cholesterol transporter in the brain and has the highest genetic risk for Alzheimer's disease. The ε4 allele has a role in varying the risk for AD and is a risk factor for poor recovery after traumatic brain injury. In a study ran by Boston University Medical Campus took DNA extracts from 364 brain samples were taken from donors with a history of exposure to head trauma from contact sports of military service. Out of the 364 total 294 had neuropathologically confirmed CTE and 70 did not. It was found that *APOE*ε4 was associated with the CTE stage in the dorsolateral frontal lobe in participants aged 65 plus [8]. Among football players the *APOE*ε4 association size for CTE was similar to the results of playing more than 7 years of football meaning that *APOE*ε4 can be linked to increased risk for CTE related neuropathological illnesses including Alzheimer's. A further study conducted by Stern et al found that ε4 homozygotes were overrepresented in 68 individuals with confirmed CTE and no other neurodegenerative diseases. Approximately 15 to 25% of. The population carries the APOE e4 allele which doubles the chances of developing late-onset AD and 2 to 3% will have a copy of the allele which puts them at an 8 to 10% more likely to get AD [9].

What percentage of professional footballers will develop the disease?

A further study conducted on professional footballers from Scotland born before 1977 found that 1.7% of football players died due to neurogenerative disease compared to 0.5% out of the control, ultimately concluding that the risk of dying from a neurogenerative disease such as AD was 3.5 times higher for professional footballers. For AD specifically 0.8% of former players and 0.2% of control group men died from Alzheimer's disease – a risk 4 times greater for the footballers [10]. So, if there are currently there are 5,368 professional footballers in the UK [11], if all of them have a career of 20 years with a minimum of 2000 headers we can predict that 43 out of 5,368 will develop Alzheimer's.

Conclusion

There is not currently a single cause for Alzheimer's disease only lifestyle and genetic factors as of far are related to the likelihood of development of AD. However, if you carry the *APOE*ε4 allele you are significantly more likely to develop late onset-AD and also engaging in contact sports where head trauma is repeatedly experienced over long periods of time will contribute to the development of AD. CTE has been found to be closely linked to the development of AD due to it being caused by repeated blows to the head however CTE can only be diagnosed after death so when looking at someone alive with AD we can't yet link it to CTE and the more post-mortem studies that are completed on this will further add to our knowledge of how the two illnesses relate. The importance of any factors which could increase or decrease the risk of AD will differ from person to person as it is a progressive brain disease and so will the symptoms. When it comes to head trauma in football and other contact sports it is important to try and limit head contact to prevent neurogenerative diseases such as AD and the development of them.

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