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Traumatic brain injury, collision sports participation, and neurodegenerative disorders : narrative power, scientific evidence, and litigationd

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2022

Batty, G D & Kaprio, J 2022, 'Traumatic brain injury, collision sports participation, and neurodegenerative disorders : narrative power, scientific evidence, and litigationd ', Journal of Epidemiology and Community Health, vol. 76, no. 11, pp. 905-908. https://doi.org/10.1136/jech-2022-219061

http://hdl.handle.net/10138/355860 https://doi.org/10.1136/jech-2022-219061

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Editorial – Journal of Epidemiology and Community Health
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3	Traumatic brain injury, collision sports participation, and neurodegenerative disorders: narrative power,
4	scientific evidence, and litigation
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15	Manuscript characteristics: 1990 words; no displayable items
16	
17	Conflicts of Interest: David Batty is a Deputy Editor for the Journal of Epidemiology and Community Health
18	
19	Acknowledgements: GDB is supported by the UK Medical Research Council (MR/P023444/1) and the US
20	National Institute on Aging (1R56AG052519-01; 1R01AG052519-01A1), and JK by the Academy of Finland
21	Centre of Excellence in Complex Disease Genetics (336823).
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24 The present and future burden of neurodegenerative disorder, particularly dementia, for individuals, 25 society, and health care systems has been extremely well documented. Dementia currently directly affects 26 around 50 million people globally and, owing to demographic expansion, its prevalence is expected to triple 27 over the following three decades.¹ The disappointing results of trials of drug treatments for dementia, 28 motor neuron disease (amyotrophic lateral sclerosis), and Parkinson's disease – particularly curative 29 therapies – brings into sharp focus the need to identify modifiable risk factors. Head injury has been 30 advanced in this regard,² is common³ and, in principle, has the potential for amelioration via advances in 31 safety legislation and protective technologies.

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33 Operationalising head impact

34 Head injury severity might be operationalised as a continuum. The traumatic insults occurring at the higher 35 end of this spectrum result from vehicular accidents, assaults, and falls in civilian populations and bomb 36 blasts in the military. Direct trauma to the head is not, however, a pre-requisite for a significant brain 37 injury; it can also result from rapid acceleration-deceleration as seen as in whiplash-type episodes. Severe 38 head injury may also occur in selected sports, most obviously boxing, mixed martial arts (so called 'cage fighting'), and professional wrestling,^{4 5} where the infliction of head trauma is a key objective. In other 39 40 sports such as soccer, while trauma to the head may also occur, typically in elbow-on-head collisions,⁶ head 41 impact – as it is perhaps most usefully termed – is most likely to result from contact with equipment. 42 Typically, this would be the seemingly innocuous sub-concussive 'heading' of the ball for its redirection. Of 43 the non-sport activities, similar low intensity neurological insults might be the product of the percussive 44 movement of the head in accompaniment to contemporary music – so called 'head banging'.⁷

45

46 Traumatic head injury and dementia

47 While the influential 2020 report of the Lancet Commission on dementia – an asystematic, selective,

48 narrative overview of the field – lists traumatic brain injury as one of twelve modifiable risk factors,²

49 position statements from prominent organisations such as the World Health Organization⁸ and the US

50 National Academies of Sciences⁹ make no mention of it. This may be a reflection of the discordant

51 literature. There is evidence, for instance, from large scale, retrospective and prospective cohort studies of 52 the general population of an approximate doubling in the rate of dementia in people who experienced 53 head trauma severe enough to warrant hospitalisation relative to the unaffected.¹⁰⁻¹³ In selected analyses, 54 there is also a suggestion that risk is elevated in the months immediately following exposure but wanes thereafter.¹² These studies, generated from linkages of administrative datasets, seem to reveal stronger 55 56 effects than conventional, field-based cohort studies.^{14,15} This may be explained by the greater availability 57 of confounding factors in the field-based studies. Equally likely, physician-corroborated head injury 58 assessment in data linkages studies may be less subject to misclassification than when captured by self-59 report in the field-based investigations.¹⁶

60

61 Collison sports participation and dementia: 'consistent' anecdotal evidence

62 Media coverage is a powerful force in forming public opinion and behaviours in a variety of areas, including health and disease prevention.¹⁷ Press reports of the consequences for brain health of participation in 63 64 collision-heavy sports often comprise a mix of heart-rendering accounts of understandably distressed 65 relatives of retired athletes who live(d) with the condition, who are convinced of the very singular dementia-causing effect of such activities,¹⁸⁻²⁰ sometimes interwoven with mention of film dramatisation.²¹ 66 67 Indeed, the recently convened UK Parliament cross-party Committee on Concussion in Sport was notable 68 for its focus on anecdotal accounts of the affected patients, carers, relatives, or treating physicians but light on scientific representation.²² While any disease entity is under the control of a multitude of genetic and 69 70 environmental risk indices rather than a single factor,²³ for the lay population, these anecdotal accounts 71 make for a powerful and often definitive narrative, and one that is typically more persuasive than the 72 inevitably less consistent picture drawn using empirical data.

73

74 Collison sports participation and dementia: inconsistent empirical evidence

75 In the scientific literature also, case reports, often of a solitary athlete,^{24,25} can be misrepresented as

76 evidence of cause and effect, even by scientists. While case series have historically provided important

descriptive medical insights – most obviously for past²⁶ and present²⁷ pandemics – in failing to offer cross-

group comparisons of disease rates in exposed and unexposed, they do little to advance understanding of disease causation. The counter-factual, such as accounts of sprightly centenarians who have consumed cigarettes, cake, and soap opera reruns on a daily basis since kindergarten²⁸ are rarely advanced as evidence for the health-enhancing effects of tobacco, saturated fat, and a dedication to sedentarism.

Despite estimates of the occurrence of head trauma in Ivy League college football,²⁹ and debates over its 83 84 links with dementia in boxers (so called *dementia pugilistica*³⁰) first appearing a century ago, the long term 85 impact on brain health of membership of athletic groups has been relatively little-scrutinised in an 86 epidemiological context. Most studies have examined the association between participation in American 87 football and dementia in samples which, unsurprisingly, are exclusively based on retired athletes from that 88 country. Similarly, with the exception of one study,³¹ former Italian soccer players comprise the other large 89 body of work linking engagement in that sport with amyotrophic lateral sclerosis^{32,33} (the origins of this focus stem from an judicial investigation of illicit drug use in these athletes).³⁴ In these studies, 90 91 membership of professional athletic groups is used as a proxy for exposure to brain trauma. Rates of death 92 ascribed to neurodegenerative disease in aggregate have been reported as being higher in American football players relative to comparison groups comprising baseball players³⁵ and the general population,³⁶ 93 94 both of whom are likely to have a much lower period prevalence of brain injury. These results are not 95 universal however – in long-term follow-up of football-playing University students, for instance, the occurrence of degenerative disorders as alumni was essentially the same as the general population.^{37 38} A 96 97 major methodological shortcoming of these studies is their extremely low statistical power: in a recent 98 review, a single report aside,³¹ the frequency of neurodegenerative disease cases across studies ranged 99 between 17 and 55, while for dementia/Alzheimer's disease it was 7 and 26. As such, these studies may 100 simply not have the capacity to detect a relationship should one exist, nor rebut one if it does not.

101

In studies of soccer, although no better powered, results are more consistent: quantitative aggregation of
 studies featuring retired soccer players suggest around a 6-fold increase in risk relative of amyotrophic
 lateral sclerosis versus less exposed groups.³² The magnitude of this association is unusually high by the

105 standards of modern epidemiology, potentially elevating soccer participation, and its cumulative head

106 trauma, to risk factor status.

107

108	In other sports, investigators have also used cognitive function as a quasi-dementia endpoint. ³⁹⁻⁴² In these
109	studies, a single baseline measure, as opposed to serial measurement which captures cognitive decline,
110	may in fact provide more insights into intelligence differences between sporting and non-collision
111	sporting/general population groups as opposed to cognitive impairment. Thus, where cognition is higher in
112	non-collision sports participants, ⁴¹ it may be that these individuals had sufficiently high perception of risk to
113	simply avoid potentially injurious activities.

114

115 Confounding in studies of collision sports and dementia

116 While the results suggesting higher rates of degenerative disorders in retired American football and soccer 117 athletes are intriguing and provide the highest level of epidemiological evidence to date, instinctively, 118 concerns are raised about the limited array of confounding factors in the published studies. With most 119 studies relying on employment or pension records, beyond age, gender, and career duration, very little else 120 is known about the study members. As is rarely the case, however, confounding may have minimal impact 121 in this context. Putting aside the key exposure of head injury and also specific athletes whom, for instance, 122 high body weight – and all its negative consequences for health – is prized (e.g., linemen in American football,⁴³ professional wrestlers⁴⁴), retired athlete groups, relative to general population controls, typically 123 124 have a more favourable risk factor profile for dementia. This includes a lower prevalence of hypertension, diabetes, and other co-morbidities, smoking, and overweight.⁴⁵ Accordingly, rates of total mortality and 125 126 cardiovascular disease in former elite sports participants are typically lower than the general population^{31,46,47} – an exemplar of the so called 'healthy worker' effect.⁴⁸ Thus, dementia rates in the 127 128 general population are more likely to be higher than athletic groups. Adjustment for these factors in 129 analyses of collision sports participation would then increase any group difference in dementia risk 130 (positive confounding), not attenuate it.

131

132 **Potential mechanisms**

133 The mechanisms linking brain insults to neurodegenerative disorders is likely to vary according to the 134 disease endpoint in question. Of the collision sports, most mechanistically-orientated research has again 135 been conducted in American football and soccer, in former participants of which there are autopsy reports of chronic traumatic encephalopathy-type neuropathological change.⁴⁹ There is also evidence that heading 136 137 of a soccer ball produces a measurable if temporary lowering of cognitive function,⁵⁰ while potentially more permanent structural changes to the brain are evident upon imaging.⁵¹ Head impact, particularly when 138 139 severe, has been implicated in the occurrence of stroke,⁵² and stroke is itself related to the development of 140 dementia.53

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142 Future research directions in collision sports

143 Aside from the generally trivial number of events in existing studies, methodological advances might 144 include a version of the randomised controlled trial. Clearly, the notion of an experiment where head 145 injury was administered to one group and not to another, and then both groups were followed for 146 ascertainment of neurodegenerative outcomes is as ridiculous as it is unethical. The converse may be 147 plausible, however, whereby, for instance, collision sports participants are randomised to the wearing of 148 head gear in training and competition versus none, and then followed for an array of intermediary markers 149 for dementia (e.g., cognitive decline) or proxies (e.g., brain atrophy from computerised tomography 150 scanning). Rather like amateur boxing, the assumption is that the deleterious impact – acute and long-term 151 - would be mitigated by the wearing of such gear - a point not shared by the International Boxing 152 Association.⁵⁴ An alternative study would be a quasi-experimental investigation whereby cognition is 153 assessed pre- and post-issuance of legislation designed to protect the players, such as this withdrawal of 154 head protection in boxing and also recent World Rugby guidance to limit full-contact training, and, in 155 soccer, the restriction of heading in certain levels of the sport.²⁰

156

Lastly, notion of sensitive or critical periods may have relevance to the study of the implications for brain
health of a history of sports-acquired head impacts. Defined as a narrow period of time in which an

exposure can have positive or negative effects on brain development and disease outcome, on the one hand, earlier life exposure to head impact may be plausibly compensated by neurological plasticity.⁵⁵ The opposite is also conceivable: exposure in early life could lead to 'programming', whereby an insult during a specific period has long-standing effects on brain architecture and physiology. Well characterised cohort studies with data captured across the life course are required for examination of critical and sensitive periods.

165

166 Epidemiology and workplace injury litigation

167 Alongside other scientific evidence, epidemiological data have long been cited in industrial litigation.^{56,57} 168 On both sides of the argument, epidemiological findings have been central to legal action for: asbestos 169 exposure and the risk of mesothelioma;⁵⁸ specific tampons brands ('Rely') and toxic shock syndrome;⁵⁹ 170 silicone gel breast implants and connective tissue disease;⁶⁰ and passive smoking and lung cancer,⁶¹ 171 amongst others. In 2011, multiple class (group) and individuals law suits were brought against the National 172 Football League by retired American football players and a no-liability (no-guilt) settlement was reached in 173 2013⁶² (a dedicated website to process the claims of affected former players was subsequently established⁶³). Media reports in the UK⁶⁴ indicate that claims of negligence have been made by former 174 175 rugby union and soccer players against their respective governing bodies.

176

177 Conclusions

Taken together, the low quality, paucity, and inconsistency of the evidence base for engagement in collision sports as a potential risk factor for specific neurodegenerative disorders does not facilitate the formulation of many clear conclusions. One exception might be the strong suggestion of an elevated risk of amyotrophic lateral sclerosis in former soccer athletes. These findings suggest that concussion is not a prerequisite for there to be a deleterious influence on brain health. Moreover, while data are generally sparse, they also exclusively comprise men. The population impact of head injury may in fact be greater in women given its apparent higher prevalence relative to males in the same sports.⁶⁵

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