

Warm up

A cause for concern?

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Just to add to the recent concern over heading soccer balls and the risk of chronic brain injury¹, another study has just appeared that raises new fears. In a paper published in *Brain*², Chio and his colleagues from Italy reported that there was an increased risk of developing motor neurone disease (MND) amongst Italian soccer players. In this retrospective cohort study, there were five diagnosed MND cases in a subpopulation of 7435 soccer players of the top two Italian divisions who played in the period from 1970 to 2001. Although only small numbers of MND patients were identified, this exceeded the statistical likelihood of developing MND in this population.

This paper adds to the growing body of concern in regard to the risk of developing this condition from sport. Previously a judicial report from the Italian soccer leagues raised similar concerns. A 4 year study commissioned by a local magistrate looked at every player in Serie A and B between 1960 and 1997. Of the total of 24 000 calciatori, eight were found to have died from MND. A further follow up of those who were dead or who had fallen ill since 1997 found a further 32 cases.³

The Guardian has reported that MND has claimed a number of former players in England in recent years including Don Revie, Rob Hindmarch of Derby and Sunderland, Middlesbrough's Willie Maddren, and the former Celtic winger Jimmy Johnstone.³ As a result long term follow up studies of English footballers have been mooted.

DOES NEUROTRAUMA CAUSE MND?

Trauma has long been hypothesised but never proven to be a risk factor for MND.

Environmental risk factors of neurodegeneration in MND have also been suspected. Cycad nuts were found to be a chronic neurotoxic risk for the Guam population who develop a different condition that shares a number of clinical features with MND; other putative environmental risk factors for

amyotrophic lateral sclerosis (ALS) include a history of nervous system trauma, exposure to heavy metals, radiation, electrical shocks, welding or soldering materials, and employment in paint, petroleum, or dairy industries.⁴

Could the effect of repetitive heading soccer balls be somehow related to the development of MND in the presence of a genetic predisposition? An association between MND and head trauma has never been clearly demonstrated nor has the association between skeletal fracture of head, neck, or spine and pathogenesis of MND.⁵

A Medline survey of the medical literature found only retrospective studies on this topic with just one cohort study of ALS after head injury.⁶ In this cohort of 821 individuals who had suffered a head trauma between 1935 and 1974, and were older than 40 years in June 1988, there was one case of ALS—unexpected in a small population of 821. All of the other reports^{7–11} retrospectively evaluate the frequency of previous head trauma in small groups of ALS patients, with the severity of head injury being clearly defined in only one of the references.¹²

Compared to individuals with other neurological disease, patients with ALS are more likely to have a history of being athletic and slim, according to Scarmeas *et al.*¹³ Such a somatotypic linkage has been suggested by the development of MND in athletes. In the US, boxer Ezzard Charles, baseball player Catfish Hunter and, of course, baseball icon Lou Gehrig all died of MND. Three players from the San Francisco 49ers were diagnosed with MND in the 1980s, and Glenn Montgomery of the Seattle Seahawks lost his life to MND in 1998.¹³

It is likely that the pathogenesis of MND reflects a complex interaction between environmental factors and specific susceptibility genes.⁴ To date, only some of these genes have been identified.⁴

Approximately 1–2% of the cases of sporadic ALS and 15–20% of familial ALS are caused by mutations of superoxide dismutase 1 (SOD1), which

belongs to the endogenous antioxidative system. The fact that transgenic expression of a human SOD1 mutation (SODG93A) leads to an MND-like disease in mice underlines the pathophysiological significance of this mutation.⁴

Apart from a single major gene responsible for the disease, MND may also be caused by certain polygenic combinations that may in part explain the so-called sporadic cases that require co-factors to occur. Among these co-factors, neurotrauma may play a prominent role. Athleticism or an athletic body type is also linked in at least one study.

SO WHAT NOW?

It would appear that we have some epidemiological evidence of a link between neurotrauma and the development of MND based on a small number of retrospective studies. To date, this evidence is inconclusive and a prospective cohort study is desperately needed to provide an answer to this controversy. Given the low frequency of MND in the population, it is likely that this study will not give a definitive answer for many years.

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REFERENCES

- 1 McCrory P. Brain injury and heading in soccer. *Br Med J* 2003;**327**:352–352.
- 2 Chio A, Benzi G, Dossena M, Mutani R, Mora G. Severely increased risk of amyotrophic lateral sclerosis among Italian professional football players. *Brain* 2005;**128**:472–6.
- 3 Fotheringham W. Club doctor fears Italian study could lead to a legal nightmare. *The Guardian*, 16 January 2003.
- 4 Majoor-Krakauer D, Willems P, Hofman A. Genetic epidemiology of amyotrophic lateral sclerosis. *Clin Genet* 2003;**63**:83–101.
- 5 Riggs J. Amyotrophic lateral sclerosis, heterogeneous susceptibility, trauma, and epidemiology. *Arch Neurol* 1996;**53**:225–7.
- 6 Williams D, Annegers J, Kokmen E, *et al.* Brain injury and neurologic sequelae: a cohort study of dementia, parkinsonism, and amyotrophic lateral sclerosis. *Neurology* 1991;**41**:1554–7.
- 7 Mandrioli J, Faglini P, Merelli E, *et al.* The epidemiology of ALS in Modena, Italy. *Neurology* 2003;**60**:683–9.
- 8 Kondo K, Tsubaki T. Case-control studies of motor neuron disease: association with mechanical injuries. *Arch Neurol* 1981;**38**:220–6.
- 9 Gawel M, Zaiwalla Z, Rose F. Antecedent events in motor neuron disease. *J Neurol Neurosurg Psychiatry* 1983;**46**:1041–3.
- 10 Gallagher J, Sanders M. Trauma and amyotrophic lateral sclerosis: a report of 78 patients. *Acta Neurol Scand* 1987;**75**:145–50.
- 11 Jelliffe S. The amyotrophic lateral sclerosis syndrome and trauma. *J Nerv Ment Dis* 1935;**82**:415–35.
- 12 Strickland D, Smith S, Dollif G, *et al.* Physical activity, trauma, and ALS: a case-control study. *Acta Neurol Scand* 1996;**94**:45–50.
- 13 Scarmeas N, Shih T, Stern Y, *et al.* Premorbid weight, body mass, and varsity athletics in ALS. *Neurology* 2002;**59**:773–5.