Association between *MAPT* polymorphism but not *APOE* promoter and elite rugby athlete status.

Antrobus, M.R.[1, 5], Brazier, J.[1, 7], Herbert, A.J.[1], Stebbings, G.K.[1], Day, S.H.[1], Heffernan, S.[2], Erskine, R.M.[3, 6], Kilduff, L.P.[4] & Williams, A.G.[1, 6]

[1]Sports Genomics Laboratory, Manchester Metropolitan University, Crewe, UK, [2]University College Dublin, School of Public Health, Physiotherapy and Sports Science, Dublin, ie, [3]Research Institute for Sport & Exercise Sciences, Liverpool John Moores University, Liverpool, UK, [4]College of Engineering, Swansea University, Swansea, UK, [5]University of Northampton, Department of Life Sciences, Northampton, UK, [6]Institute of Sport, Exercise and Health, University College London, London, UK, [7]University of Hertfordshire, Department of Psychology and Sports Science, School of Life and Medical Science, Hatfield, UK

Introduction

Incidence and outcomes of concussions have been hypothesised to be genetically influenced. Within rugby, the primary mechanical stress injury to neurons is often a result of a collision and can initiate the secondary (delayed) injury of a neurometabolic cascade, resulting in neuropathologic events. The *APOE* promoter G219T (rs405509) polymorphism has been associated with differential promoter activity and unfavourable outcomes after traumatic brain injury. The TT genotype has been associated with a 3-fold greater risk of multiple concussions[3]. The TT genotype of *MAPT* (rs10445337) has also been associated with poorer outcomes after concussion[2], potentially due to the formation of neurotoxic neurofibrillary tangles[1]. Rugby has one of the highest incidences of concussion in sport, so it was hypothesised that *APOE* promoter TT and *MAPT* TT genotypes would be less prevalent in elite rugby athletes because those genotypes, previously associated with increased risk, would be less compatible with achieving elite athlete status.

Method

Participants were from the RugbyGene project, comprising elite Caucasian male rugby athletes (n = 528; mean (standard deviation) height 1.85 (0.07) m, mass 101 (14) kg, age 29 (7) yr), including 420 rugby union (RU) athletes that for some analyses were divided into forwards and backs and 108 rugby league (RL) athletes. Non-athletes were 592 Caucasian men and women (57% male, height 1.72 (0.10) m, mass 74 (14) kg, age 31 (7) yr). PCR of genomic DNA was used to determine genotypes using TaqMan probes, then groups were compared using $\chi 2$ and odds ratio (OR) statistics.

Results

All genotype data were in Hardy-Weinberg equilibrium. For *MAPT* (rs10445337), the risk genotype (TT) was underrepresented in rugby athletes (60%) compared to non-athletes (66%), CT more common in rugby athletes (34%) than non-athletes (29%) and little difference in CC genotype frequencies ($\chi 2 = 7.092$, P = 0.029; TT genotype frequency OR = 0.80, 95% confidence intervals (CI) = 0.62-1.02). There were no differences in *MAPT* (rs10445337) genotype frequencies between RU forwards and backs (Fig 1). For *APOE* promoter G219T (rs405509), there were no differences in genotype frequencies between all athletes (RU and RL) and non-athletes (27% TT genotype in players and non-athletes), nor between RU forwards and backs (Fig 2).

Results

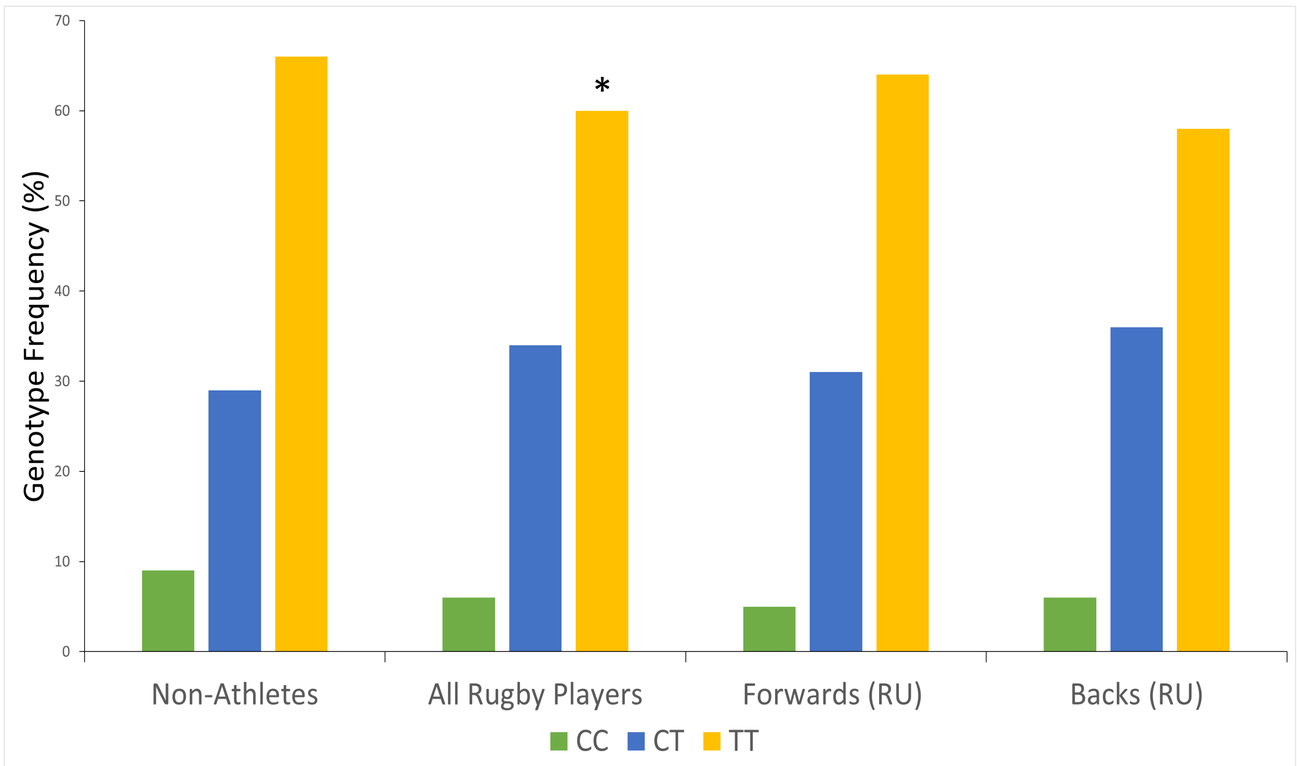

Fig. 1 *MAPT* (rs10445337) genotype frequencies. * Different from Non-athletes (P = 0.029)

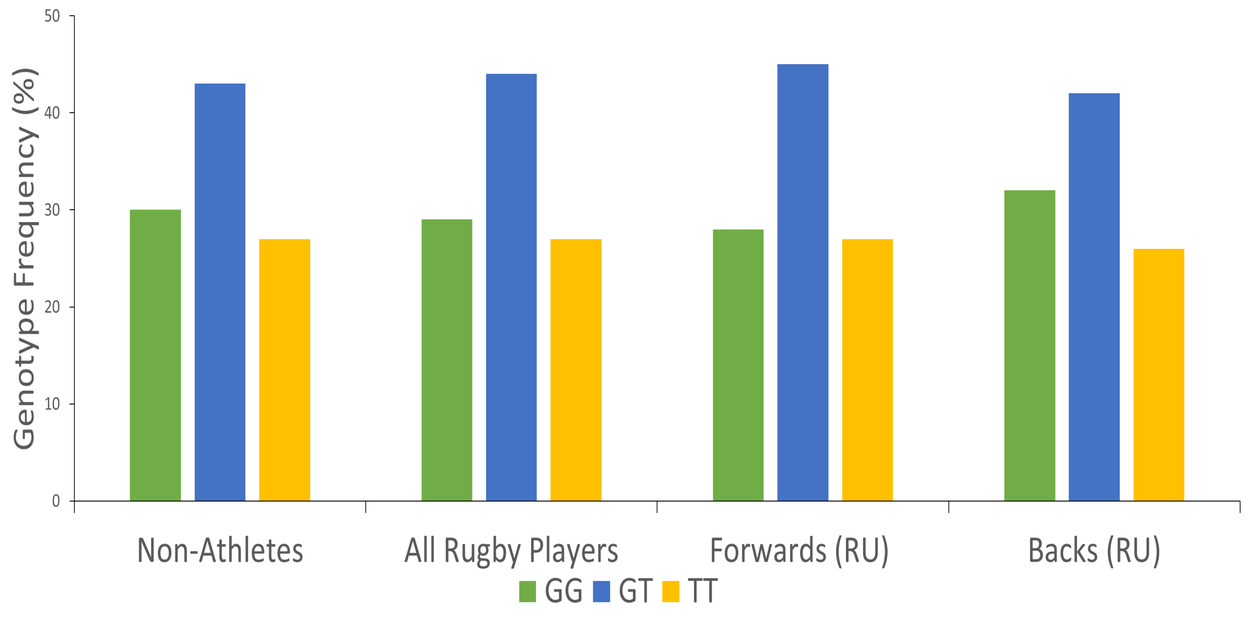

Fig. 2 *APOE* promoter G219T (rs405509) genotype frequencies

Conclusion

The *MAPT* (rs10445337) TT genotype is 6% less common in elite rugby athletes than non-athletes. Therefore, carrying at least one rs10445337 C allele appears to increase the probability of sustained career success in the high-risk concussion environment of elite rugby, perhaps via a greater ability to recover from concussions.

References

1. Liraz, O., Boehm-Cagan, A. and Michaelson, D.M. (2013) ApoE4 induces Aβ42, tau, and neuronal pathology in the hippocampus of young targeted replacement apoE4 mice. *Molecular Neurodegeneration*, 8 pp. 16.
2. Terrell TR, Bostick RM, Abramson R, Bostick, R. M., Abramson, R., Xie, D., MD, Barfield, W., Cantu, R., Stanek, M. and Ewing, T. (2008) APOE, APOE promoter, and Tau genotypes and risk for concussion in college athletes. *Clinical Journal of Sports Medicine*, 18 pp. 10–17.
3. Tierney, R., Mansell, J. L., Higgins, M., McDevitt, J. K., Toone, N., Gaughan, J. P., Mishra, A. and Krynetskiy, E. (2010) APOE genotype and concussion in college athletes. *Clinical Journal of Sports Medicine*, 20 pp. 464-468.

Contact details

mark.antrobus@northampton.ac.uk