Association between *COMT* polymorphism but not *BDNF-AS* or *NOS3* and elite rugby athlete status.

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Introduction

Incidence of and recovery from concussion have a substantial genetic component that probably involves the interaction of multiple genes. *COMT* (rs4680) AA carriers in youth and professional South African rugby athletes (RA) were ~3-fold more likely to have a history of concussion (McFie et al., 2018). Similarly, *BDNF-AS* (rs6265) AA genotype has been associated with a higher risk of sustaining a concussion and associated with poorer outcomes post-concussion (Dretsch et al., 2016; Narayanan et al., 2016). Lower cerebral blood flow has been reported in *NOS3* (rs2070744) C-allele carriers with traumatic brain injury, postulated to negatively affect a concussed individual during recovery (Robertson et al., 2011). As rugby has one of the highest incidences of concussion in sport (Williams et al., 2013), it was hypothesised that *COMT* AA, *BDNF-AS* AA and *NOS3* CC genotypes would be less prevalent in elite rugby athletes because, previously associated with increased risk, they would be less compatible with achieving elite athlete status.

Method

Participants were from the RugbyGene project, comprising elite Caucasian RA (648 men; mean (SD) height 1.85 (0.07) m, mass 101 (12) kg, age 28 (7) yr) competing at an elite level in rugby union (n = 550) and rugby league (n = 98) in the UK, Ireland, Italy and South Africa. Non-athlete participants (NA) were 803 Caucasian men and women (58% female, height 1.69 (0.10) m, mass 72 (14) kg, age 41 (23) yr). PCR of genomic DNA was used to determine genotypes using TaqMan probes, then groups were compared using χ^2 and odds ratio (OR) statistics. Alpha was set at 0.05.

Results

All genotype data were in Hardy-Weinberg equilibrium. For *COMT*, the risk genotype (AA) was underrepresented in RA (25%) compared to NA (30%) and GG more common in RA (26%) than NA (22%) (χ^2 = 6.129, P = 0.047; GG genotype frequency OR 2.43, 95% confidence intervals (CI) = 1.88-3.22) (Fig. 1). For *BDNF-AS*, there were no differences in genotype frequencies between RA and NA (4% AA genotype in both cohorts, χ^2 = .311, P = 0.856) (Fig. 2). There were also no differences in *NOS3* genotype frequencies (16% CC genotype in RA and 17% in NA, χ^2 = 1.040, P = 0.595) (Fig 3).

Results

Fig. 1 *COMT* (rs4680) genotype frequencies. * Difference between Non-athletes and all Rugby Athletes (P = 0.047)

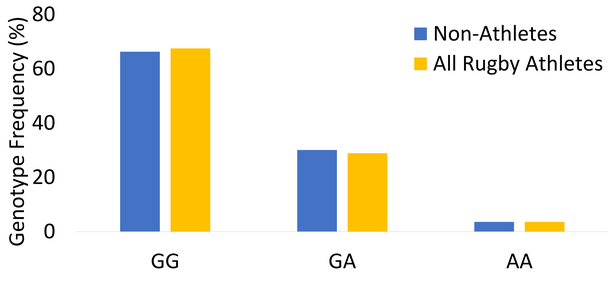

Fig. 2 *BDNF-AS* (rs4680) genotype frequencies.

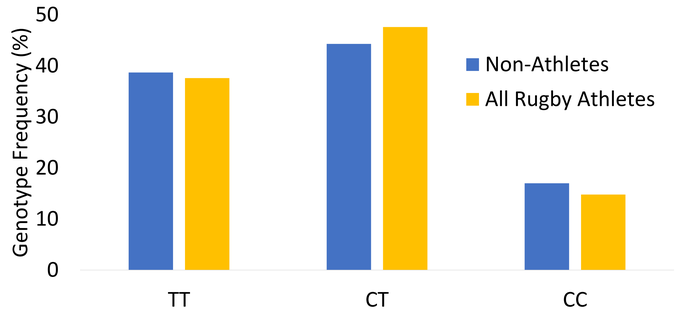

Fig. 3 *NOS3* (rs2070744) genotype frequencies.

Conclusion

The *COMT* AA genotype is 5% less common in elite rugby athletes than non-athletes. There was over twice the odds of Rugby Athletes possessing the GG genotype than Non-athletes. Therefore, carrying at least one rs4680 G allele, perhaps via a lower risk of experiencing concussion, a greater ability to recover from concussions or altered impulsivity and risk-taking behaviour, appears to increase the probability of reaching elite level in a sport with a high risk of concussion.

References

Dretsch et al. (2016) *Brain and Behav.* 6, 1–12; Narayanan et al. (2016) *PLoS ONE.* 11, e0158838; Mc Fie et al. (2018) *J Sports Sci.* 36, 920–933; Robertson et al. (2011) *J Neurotrauma*. 28, 727–737; Williams et al. (2013) *Sports Med*. 43, 1043–1055.

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