# Concussion-associated gene variants and history of concussion in elite male rugby athletes.

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## Introduction

Occurrence of and outcomes following a concussion are probably affected by the interaction of multiple genes in a polygenic manner [1,2]. This study investigated whether suspected concussion-associated polygenic profiles of elite rugby athletes with a history of previous concussion (RAC) differed from rugby athletes with no history of previous concussion (RANC). We hypothesised that concussion-associated risk genotypes would be underrepresented in RANC compared to RAC.

## Method

Participants were from the RugbyGene project, comprising elite male rugby athletes (RA) (185 white males; mean (standard deviation) height 1.86 (0.07) m, mass 102 (12.6) kg, age 26.4 (5.1) yr) competing at an elite level in rugby union (n = 165) and league (n = 20) in the UK, Ireland, Italy and South Africa. Concussion history was collected using a self-reported concussion history questionnaire. PCR of genomic DNA was used to determine genotypes using TaqMan probes, and total genotype scores (TGS) were calculated, then groups were compared using $\chi^2$ and odds ratio (OR) statistics. In addition, multifactor dimensionality reduction (MDR) was used to identify genetic interactions.

## Results

Seventy-eight percent of RA reported a history of sustaining at least one concussion and 54% of RA reported sustaining multiple (≥2) concussions from rugby.

For *BDNF-AS* rs6265, the GG genotype was more common in RAC compared to RANC (69.7% vs 61.0%, $P$ = 0.006, OR = 9.90, 95% CI = 01.81-54.06) (Fig. 1). The GG genotype of *BDNF-AS* rs6265 was more common in RAC compared to RANC (70.7% vs. 61.0%, $P$ = 0.041, OR 4.44, 95% CI = 1.04-120.97) (Fig. 1). However, TGS did not differ between RANC and RAC (Fig. 2A) recovery duration and family history of neurological conditions ($P$ > 0.05).

Receiver operating characteristic curve (ROC) and area under the curve (AUC) analysis confirmed the TGS algorithm could not identify concussion history (AUC = 0.436; 95% CI = 0.338-0.534; $P$ = 0.218; Fig. 2B). MDR could not identify a model to predict concussion history, recovery duration and family history of neurological conditions with a sufficiently powerful cross-validation statistic ($P \leq 0.05$).

## Results

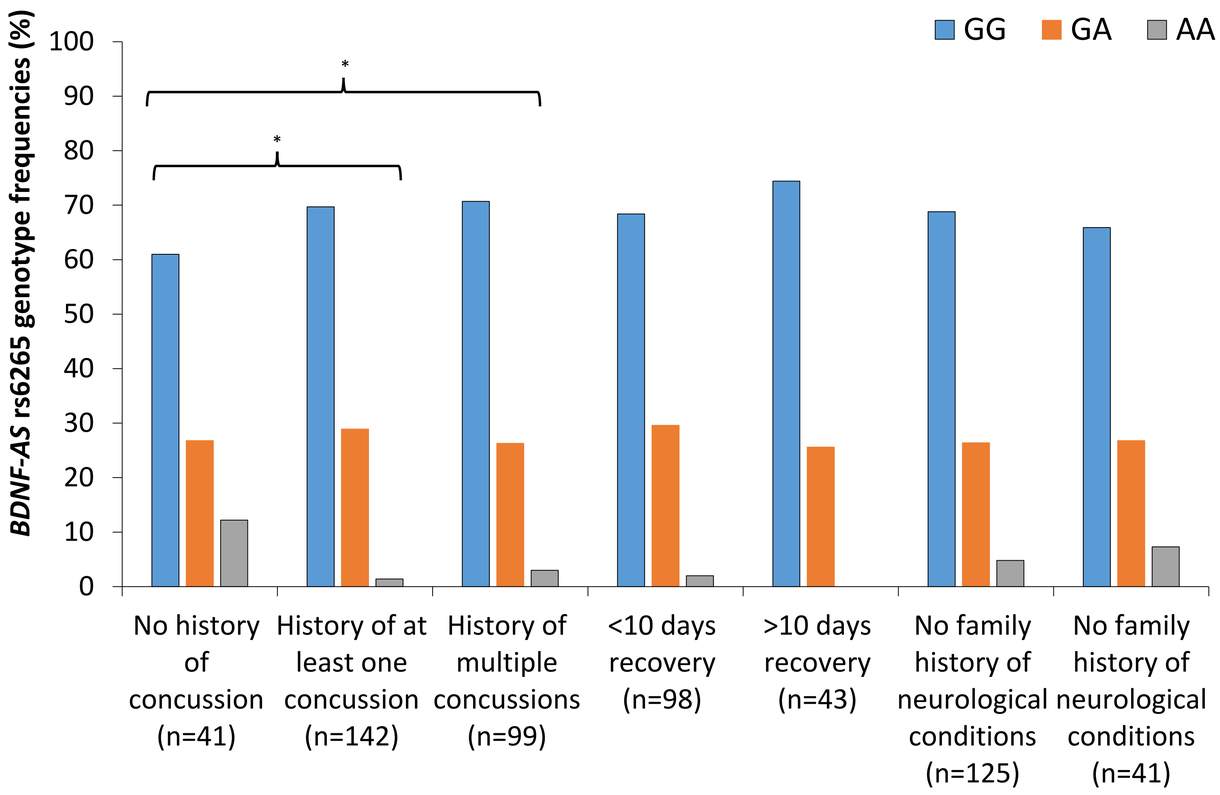


**Fig. 1** Genotype frequency of *BDNF-AS rs6265* for athletes. * GG less common in RANC ($P \leq 0.041$).

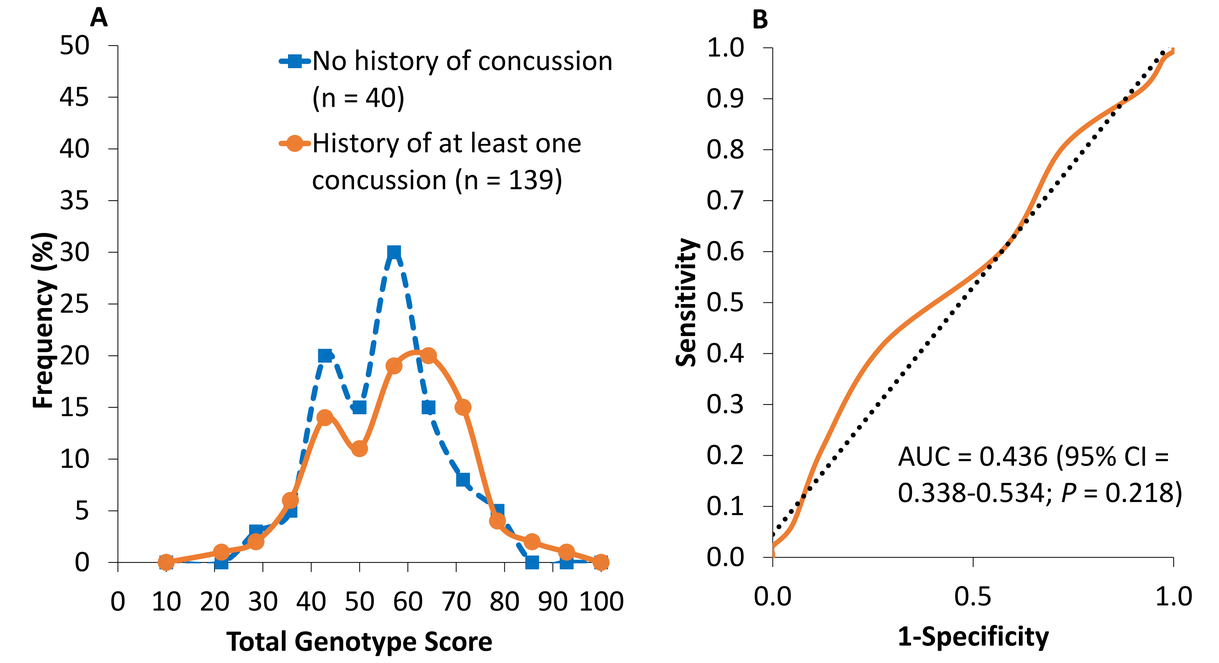


**Fig. 2 .** Similar frequency distribution of TGS for RANC (54.6 ± 11.6) and RAC (57.4 ± 12.8); $P$ = 0.212 (**2A**). Receiver operating characteristic curve displays the inability of the TGS to discriminate RANC from RAC. Dotted line = no discrimination. AUC; area under the curve (**2B**).

## Conclusion

These findings support the growing evidence that incidence and recovery from concussion could be influenced by an athlete's genetic predisposition. Such knowledge could be used in the future and when additional relevant variants have been identified, to inform individualised management strategies for athletes in possession of risk genotypes.

## References

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[2] W. J. Panenka *et al.*, "Systematic Review of Genetic Risk Factors for Sustaining a Mild Traumatic Brain Injury," *Journal of Neurotrauma*, vol. 34, no. 13. Mary Ann Liebert Inc., pp. 2093–2099, Jul. 01, 2017. doi: 10.1089/neu.2016.4833.

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