

## **Elevated Systemic Oxidative-Nitrosative Stress and Cerebrovascular Function in Professional Rugby Union Players: The Link to Impaired Cognition**

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Sports-related concussion (SRC) represents a growing public health concern in rugby union, yet remains one of the least understood injuries facing the community today. There is concern that prior SRC may contribute to long-term neurologic sequelae in later-life(1). This may be due to an accelerated decline in cerebral perfusion, a major risk factor for neurocognitive decline and neurodegeneration(2), though the underlying mechanisms remain inconclusive. It was hypothesised that recurrent SRC in current professional rugby union players would result in elevated systemic oxidative-nitrosative stress(3), reflected by a free radical-mediated reduction in bioactive nitric oxide (NO) metabolite bioavailability and impaired cerebrovascular and cognitive function.

A longitudinal study design was adopted across the 2017-2018 rugby season. Ethical approval was obtained from the University of South Wales Ethics Committee. All experimental procedures were carried out in accordance with the Declaration of Helsinki of the World Medical Association. Data collection is ongoing and the current report documents result from the pre-season data collection. Participants were divided into two separate groups; 23 professional rugby union players (aged  $26 \pm 5$  years) and 22, age- and physical activity-matched non-concussed controls ( $27 \pm 8$  years). Pre-season measurements were performed for cerebrovascular function (Doppler ultrasound of middle cerebral artery velocity (MCAv) at rest and in response to hypocapnia/hypercapnia), venous concentrations of the ascorbate radical (A•-, electron paramagnetic resonance spectroscopy), and cumulative bioactive NO metabolites (nitrite and S-nitrosothiols, ozone-based chemiluminescence) including cognition (neuropsychometric tests).

The rugby players expressed greater oxidative-nitrosative stress confirmed by a systemic elevation in A•- ( $P < 0.05$  vs. control) and reduction in cumulative bioactive NO ( $P < 0.05$  vs. control). The players performed worse in the Rey Auditory Verbal Learning Test B (learning and memory) and the Grooved Pegboard test using both the dominant and non-dominant hands (visuomotor coordination,  $P < 0.05$  vs. control). No between-group differences in cerebral perfusion at rest (MCAv:  $54 \pm 13$  vs.  $59 \pm 12$ ,  $P > 0.05$ ) or in response to the CO<sub>2</sub> challenges were observed (CVR<sub>CO<sub>2</sub>Hypo</sub>:  $2.58 \pm 1.01$  vs.  $2.58 \pm 0.75$ ,  $P > 0.05$  and CVR<sub>CO<sub>2</sub>Hyper</sub>:  $2.69 \pm 1.07$  vs.  $3.35 \pm 1.28$ ,  $P > 0.05$ ).

The present study identified that the rugby players are characterised by impaired cognitive function subsequent to elevated systemic-oxidative-nitrosative stress. This appears to be independent of any functional impairment in cerebrovascular function. Given the potential long term trajectory towards accelerated cognitive decline following SRC, prophylaxis to increase NO bioavailability warrants consideration(4).

## References

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