

## RESEARCH PAPER

# Long-term health outcomes after exposure to repeated concussion in elite level: rugby union players

T M McMillan,<sup>1</sup> P McSkimming,<sup>2</sup> J Wainman-Lefley,<sup>1</sup> L M Maclean,<sup>1</sup> J Hay,<sup>3</sup>  
A McConnachie,<sup>2</sup> W Stewart<sup>3,4</sup>

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/jnnp-2016-314279>).

<sup>1</sup>Institute for Health & Wellbeing, University of Glasgow, Gartnavel Royal Hospital, Glasgow, UK  
<sup>2</sup>Robertson Centre for Biostatistics, University of Glasgow, Glasgow, UK  
<sup>3</sup>Department of Neuropathology, Laboratory Medicine Building, Queen Elizabeth University Hospital, Glasgow, UK  
<sup>4</sup>Institute of Neuroscience and Psychology, University of Glasgow, Glasgow, UK

## Correspondence to

Professor TM McMillan, Institute for Health & Wellbeing, University of Glasgow, Gartnavel Royal Hospital, Glasgow G120XH, UK; [thomas.mcmillan@glasgow.ac.uk](mailto:thomas.mcmillan@glasgow.ac.uk)

Received 24 June 2016  
Revised 12 September 2016  
Accepted 12 September 2016  
Published Online First  
5 October 2016



► <http://dx.doi.org/10.1136/jnnp-2016-315260>

► <http://dx.doi.org/10.1136/jnnp-2016-315510>



**To cite:** McMillan TM, McSkimming P, Wainman-Lefley J, et al. *J Neurol Neurosurg Psychiatry* 2017;**88**:505–511.

## ABSTRACT

**Background** There is continuing concern about effects of concussion in athletes, including risk of the neurodegenerative disease chronic traumatic encephalopathy. However, information on long-term health and wellbeing in former athletes is limited.

**Method** Outcome after exposure to repeated brain injury was investigated in 52 retired male Scottish international rugby players (RIRP) and 29 male controls who were similar in age and social deprivation. Assessment included history of playing rugby and traumatic brain injury, general and mental health, life stress, concussion symptoms, cognitive function, disability and markers of chronic stress (allostatic load).

**Results** The estimated number of concussions in RIRP averaged 14 (median=7; IQR 5–40). Performance was poorer in RIRP than controls on a test of verbal learning ( $p=0.022$ ) and of fine co-ordination of the dominant hand ( $p=0.038$ ) and not significantly different on other cognitive tests ( $p>0.05$ ). There were no significant associations between number of concussions and performance on cognitive tests. Other than a higher incidence of cardiovascular disease in controls, no group differences were detected in general or mental health or estimates of allostatic load. In RIRP, persisting symptoms attributed to concussion were more common if reporting more than nine concussions ( $p=0.028$ ), although these symptoms were not perceived to affect social or work functioning.

**Conclusions** Despite a high number of concussions in RIRP, differences in mental health, social or work functioning were not found late after injury. Subtle group differences were detected on two cognitive tests, the cause of which is uncertain. Prospective group comparison studies on representative cohorts are required.

## INTRODUCTION

There is growing concern about persisting consequences of concussion or mild traumatic brain injury (mTBI) in sports<sup>1</sup> including the potential for repeated mTBI to lead to long-term neurodegenerative changes, specifically chronic traumatic encephalopathy (CTE).<sup>2,3</sup> The late consequences of mTBI are reported as a cluster of non-specific symptoms that include depression, irritability, poorer concentration and memory, and in some, personality change and more widespread cognitive symptoms that can be consistent with mild cognitive impairment or dementia.<sup>2,4</sup> One study

reported an association between greater concussion exposure and more frequent self-report of memory and postconcussional symptoms in older and retired American football players, with no effect found on cognitive tests.<sup>5</sup> Again, in retired US National Football League (NFL) players, Guskiewicz *et al*<sup>6</sup> reported an association between lifetime depression and repeated concussion after controlling for age, years since retirement, years of play and physical comorbidities. Furthermore, a ‘dose–response’ effect is reported, where depression was more common in retired players with more than nine concussions.<sup>7</sup> Finally, death rates from neurodegenerative disease in ex-NFL players have been reported to be three times higher than in the general population<sup>8</sup> and greater risk of death late after mTBI has in part been found to be associated with repeated brain injury.<sup>9</sup> Autopsy studies in former athletes have fuelled anxieties over CTE as a late outcome of exposure to repeated concussion.<sup>10,11</sup> However, few studies have addressed long-term health in living, retired athletes and evidence to support a causative link between TBI and CTE is awaited.<sup>12</sup>

Rugby union is acknowledged as having a concussion incidence that is among the highest for contact sports, with estimates of between 4 and 13.4 concussions per 1000 player hours.<sup>13–15</sup> Despite this and the high levels of participation in rugby internationally, there are few formal studies that objectively investigate long-term outcomes in rugby players. The design of the present study takes into account a meta-analysis of studies on cognition after self-reports of repeated concussion<sup>16</sup> and investigates symptom and a range of cognitive and health outcomes including allostatic load (AL), a measure of accumulated physiological damage resulting from natural stress responses across the lifespan which can be associated with lifestyle, disease and mortality.<sup>17</sup>

## METHODS

### Approvals

Ethical approval for this study was obtained from the University of Glasgow College of Medical Veterinary and Life Sciences Research Ethics Committee.

### Participants

Retired international rugby players (RIRP) were identified as male former Scottish internationalists

on a database of former players held by the Scottish Rugby Union (SRU;  $n \sim 350$ ). Potential RIRP participants were contacted by the SRU by mass email, with information on the study and an invitation to participate. Those agreeing to take part were then contacted by the research team and written consent was obtained. Inclusion criteria were: age 18 or over, fluent in English, capable of giving consent and capable of assessment. Those continuing to play rugby were excluded.

Male controls were recruited from friends or relatives of the RIRP, from community groups or from school teachers. Inclusion criteria were: male, similar to RIRP in age and Scottish Index of Multiple Deprivation 2012 (SIMD)<sup>18</sup> quintile, fluent in English, capable of giving consent to take part and capable of assessment. SIMD ranks deprivation across Scotland and is derived from postcodes, each rank comprising a small section of the population. Exclusion criteria were: female, TBI (including concussion) on more than one occasion with loss of consciousness (LOC) and/or associated symptoms of confusion or disorientation, nausea, dizziness, poor balance, blurred vision or severe headache,<sup>19</sup> or any previous moderate or severe TBI (LOC > 30 min or more or post-traumatic amnesia (PTA) for > 1 day) or a diagnosis of chronic and debilitating neurological or psychiatric disorder.

### Assessments

All assessments were performed in face-to-face interviews between February 2014 and February 2015. The protocol for assessment comprised the following domains:

### Background information

This was a brief self-report inventory relating to demographic background, current diagnoses with disease, current medication and a brief history of rugby playing (years, position).

### History of TBI

A form to assess the history of concussion and of injury to the head that might be consistent with TBI. It estimated the number and approximate date of last concussion; details of any hospital admissions with TBI and assessment of PTA associated with any injuries without hospital admission that seem severe. Concussion was defined for participants during the interview as follows: 'a blow or injury to your head where you may or may not have lost consciousness and then had symptoms such as dizziness, blurred vision, nausea, vomiting, headache, poor concentration. It might be that symptoms were not noticeable straight away but you may have noticed them later or have had 'gaps' in your memory for the game that were unusual or you might have remembered little at all about the game' (see online supplementary file 1).

### Cognition

The Montreal Cognitive Assessment (MOCA; screening test of general cognitive function);<sup>20</sup> Symbol Digit Test (information processing speed);<sup>21</sup> Trail Making Test (executive function);<sup>22</sup> Rey Auditory Verbal Learning Test (RAVLT; memory and learning);<sup>23</sup> Sustained Attention to Response Task (SART; sustained attention);<sup>24</sup> Judgment of Line Orientation Test (visual perception)<sup>25</sup> and the Lafayette Grooved Pegboard (fine hand coordination).<sup>27</sup>

### Psychological assessment, disability outcome and alcohol use

The Hospital Anxiety and Depression Scale (HADS);<sup>28</sup> Rivermead Post Concussion Symptoms Questionnaire (RPQ);<sup>29</sup>

Short Form Health Survey (SF-36; questions 1 and 2);<sup>30</sup> Glasgow Outcome Scale-Extended (GOSE);<sup>31</sup> the Alcohol Use Disorders Identification Test (AUDIT).<sup>32</sup>

### Allostatic load

An AL score was created using biomarkers from its five components:<sup>33</sup> (1) neuroendocrine (aldosterone, dehydroepiandrosterone); (2) immune (C reactive protein, interleukin-6, tumour necrosis factor- $\alpha$ ); (3) metabolic (triglycerides, creatinine, high-density lipoprotein, albumin); (4) cardiovascular/respiratory (blood pressure, heart rate, forced expiratory volume); (5) anthropometric (waist hip ratio, body mass index). Markers for components (1)–(3) were measured from venous blood taken at the time of the assessment. Values for each biomarker were transformed, and z scores calculated and averaged for each component; the totals for each component were then summed to create the AL score.

### Statistical analyses

Data are summarised using the mean, SD and range for continuous variables and the number and percentage for categorical data. Continuous outcomes were investigated using linear regression models and non-parametric Kruskal-Wallis tests. Binary outcomes were compared using logistic regression models and Fisher's Exact tests. Comparisons of ordinal categorical outcomes were tested using the non-parametric Kruskal-Wallis test. Models to compare outcomes between the RIRP group and the control group were adjusted for the matching/design variables of age and SIMD quintile. Years of education was also adjusted for in models investigating cognitive outcomes.

To investigate effects of repeated concussion within the RIRP group, the number of concussions sustained was included in models of cognitive and psychological outcomes as well as AL outcomes as the only covariate and grouped into three levels: no repeat concussions (0–1), moderate repeat concussion (2–9) and high repeat concussion (10 or more). Associations between cognitive and psychological outcomes and number of repeat concussions were also assessed using Spearman's rank correlation.

Similar analyses were carried out in relation to the number of international matches in the RIRP group; the only covariate in these models was defined by splitting the RIRP group at the median number of matches played.

All analyses were carried out using SAS for Windows V9.2, and a p value < 0.05 was considered to indicate statistical significance.

## RESULTS

### Recruitment

Enquiries were received from 76 RIRP, of whom 71 were eligible to take part. Of these, 52 (73%) were recruited and assessed; the remainder did not respond to repeated invitations or were not available over a period of several months. Forty-six controls enquired about the study; data were obtained on 29 (63%); 8 were excluded and 9 did not respond.

### Demographic characteristics and rugby history

Demographic differences between groups were non-significant with the exception of a higher number of years of education in controls than RIRP ( $p = 0.025$ ; table 1). In both groups, the mean years of education was high. As anticipated, RIRP had played rugby for longer, were older when they stopped playing and had played more recently than those controls that had ever

**Table 1** Demographic and rugby history

	RIRP	Controls	p Value*
Age			
Mean (SD) [minimum, maximum]	53.5 (13.0) [26, 79]	55.1 (9.0) [36, 72]	0.542
Social deprivation (SIMD) quintile			
1 (high)	0 (0%)	0 (0%)	0.320
2	2 (4%)	1 (3%)	
3	7 (16%)	6 (21%)	
4	8 (18%)	8 (28%)	
5 (low)	28 (62%)	14 (48%)	
Not resident in Scotland	7	0	
Years of education			
Mean (SD) [minimum, maximum]	16 (2.6) [10, 21]	17.3 (2.9) [12, 24]	0.025
Rugby history			
Ever played rugby (n %)	52 (100%)	19 (63%)	NA†
Number years rugby playing			
Mean (SD) [minimum, maximum]	22.4 (5.0) [8, 33]	8.4 (8.2) [1, 27*]	NA†
Age when stopped playing			
Mean (SD) [minimum, maximum]	33.2 (4.1) [24, 44]	19.9 (6.7) [9, 34*]	NA†
Years since stopped playing			
Mean (SD) [minimum, maximum]	20.3 (12.8) [1, 48]	34.3 (10.53) [0, 16*]	NA†
Position played <sup>‡</sup>			
Forward	21 (40%)	12 (63%)	NA†
Back	31 (60%)	4 (21%)	
Not specified	0	3 (16%)	

\*All regression models were adjusted for age and SIMD except age which was adjusted for SIMD only.

†Statistical comparisons between groups are not appropriate as RIRP are expected to have more rugby playing experience than controls.

NA, not available; RIRP, retired international rugby players; SIMD, Scottish Index of Multiple Deprivation 2012.

played rugby. The average number of international matches played within the RIRP group was 24 (SD 24) with an IQR from 5 to 40; 95% of RIRP played 77 matches or less.

### History of TBI

No participant reported a TBI with LOC for more than 30 min suggesting that all concussion events could have been 'mild' (table 2).<sup>34</sup> Almost all RIRP (92%) reported experiencing at least one concussion while playing rugby. The RIRP group experienced symptoms for more than an hour following a concussion on 2.7 occasions on average. In the RIRP the longest LOC reported for a single event ranged between 3 s and 17.5 min (median 1 min; upper and lower quartiles 19 s and 4.7 min). The history of TBI for controls is given in table 2. Statistical comparisons between RIRP and controls on variables

associated with frequency of concussion are not meaningful because of exclusion criteria for potential controls which included having more than one concussion.

### Health characteristics

Current and chronic health diagnoses were categorised as cardiovascular, respiratory, neoplastic, rheumatoid, orthopaedic, neurological, gastric, mental health, sensory, pain, alcohol use, allergic or dermatological. The frequencies in each category did not differ significantly between groups except for a higher frequency of chronic cardiovascular disorder in controls (21%) than in RIRP (2%;  $p=0.027$ ) and a non-significant trend towards a higher frequency of chronic orthopaedic problems in RIRP (14%) than in controls (3%;  $p=0.095$ ). History of smoking did not differ significantly between groups (table 3).

RIRP self-reported a less positive rating of health over the past year than controls on question 2 of the SF-36; note that the average health ratings over the past year for both groups translate to health as 'somewhat better' or 'about the same'. One RIRP had a current diagnosis of a deteriorating neurological condition (Parkinson's disease). Current diagnoses of mental health problems were reported in four RIRP (depression ( $n=2$ ); post traumatic stress disorder; sleep problems) and one control (depression). Current medication reflected this picture with psychotropic medication confined to antidepressants prescribed to two RIRP and one control. An opioid analgesic was prescribed to one RIRP.

### Mental health assessment and cognitive function

In terms of clinical 'caseness' on the HADS, the average scores were in the 'normal' range and no individual in either group scored in the 'severe' range for depression or anxiety (table 4).<sup>28</sup> Note that comparison between groups on the RPQ is not valid.

**Table 2** Concussions from rugby or other causes\*

	RIRP	Controls
Ever had a concussion†	48 (92%)	10 (34%)
Rugby related	48 (92%)	3 (10%)
Non-rugby related	15 (27%)	7 (24%)
Estimated number of concussions‡	13.9 (18.9) [0, 100]	0.3 (0.5) [0, 1]
Estimated number of concussion symptoms lasting more than an hour‡	2.7 (5.3) [0, 25]	0.1 (0.3) [0, 0]
Estimated cumulative loss of consciousness (mins) ‡	4.7 (10.4) [0, 60]	0.6 (3.3) [0, 17.5]

\*Statistical comparisons between groups are not appropriate as controls were excluded if having more than one concussion.

†n (%).

‡Mean (SD) [minimum, maximum].

RIRP, retired international rugby players.

The RPQ specifically asks about symptoms in relation to concussion and would not describe a baseline prevalence of these non-specific symptoms in controls, most of whom had no history of concussion and automatically score zero.

Differences between groups on the HADS and on cognitive tests were non-significant, except for poorer performance in the RIRP group on a test of verbal learning (RAVLT-immediate recall) and on a test of fine motor coordination in the dominant hand (Grooved Pegboard Test). On the MOCA (a screening test for cognitive decline) there was no overall group difference.

**Table 3** Health characteristics

	RIRP	Controls	p Value*
Current diagnosis (any)†	26 (50%)	14 (48%)	0.728
Chronic diagnosis (any)†	26 (50%)	10 (35%)	0.116
General health now (SF-36 question 1)†			
Excellent	18 (34%)	10 (35%)	0.848
Very good	27 (52%)	16 (55%)	
Good	5 (10%)	3 (10%)	
Fair	2 (4%)	0 (0%)	
Poor	0 (0%)	0 (0%)	
General health compared with a year ago (SF-36 question 2)†			
Much better	4 (8%)	1 (3%)	0.024
Somewhat better	8 (15%)	12 (42%)	
About the same	33 (63%)	16 (55%)	
Somewhat worse	6 (12%)	0 (0%)	
Much worse	1 (2%)	0 (0%)	
Alcohol use ‡	7.0 (4.2) [0, 25]	6.0 (4.1) [0, 16]	0.235
Smoking†			
Current	2 (4%)	2 (7%)	0.488§
Past	7 (14%)	6 (21%)	
Never	43 (83%)	21 (72%)	

\*Regression models adjusted for age and SIMD.

†n (%).

‡Mean (SD) [minimum, maximum].

§Unadjusted Fisher's exact test p value; logistic regression model was not appropriate due to small numbers.

RIRP, retired international rugby players; SF-36, Short Form Health Survey; SIMD, Scottish Index of Multiple Deprivation 2012.

However, this test is often used clinically with a cut-off to indicate impairment. One RIRP scored below a conservative cut-off score of <22. If using the more commonly used cut-off of <26, which has a lower specificity<sup>35</sup> nine RIRP (17%) and one control (3%) fell below the cut-off ( $p=0.087$ ; unadjusted Fisher's Exact test).

### Number of concussions and outcomes in retired international players

RIRP subgroups were created on the basis of no repeat concussions (0–1), moderate (2–9) and high number of repeats (10 or more; table 5).<sup>7</sup> No RIRP subgroup differences were found for mental health (HADS) or general health (SF-36). Persisting concussion symptom scores (RPQ) differed between the three subgroups ( $p=0.028$ ; unadjusted Kruskal-Wallis test), with higher scores in 'high' repeat than in no repeat concussion subgroups. Overall, the average score on the RPQ was 4.6 (SD 8.4; range 0–28).

There were no significant differences between the three RIRP subgroups on cognitive tests and no significant correlations with overall frequency of concussion, including for RAVLT-immediate recall ( $r=0.16$ ;  $p=0.268$ ), Grooved Pegboard (dominant hand;  $r=-0.10$ ;  $p=0.482$ ) and the MOCA ( $r=-0.08$ ;  $p=0.554$ ).

There was no significant difference on the GOSE between the three concussion subgroups. There was a significant correlation between GOSE and concussion exposure overall ( $r=-0.32$ ,  $p=0.020$ ) with lower GOSE ratings (less perfect recovery) associated with higher repeat concussion. Specifically, 11/52 RIRP reported symptoms linked to concussion that had some impact on daily life but were not disabling (Lower Good Recovery GOSE=7) and 2 (1 moderate and 1 high frequency of concussion) reported Upper Moderate Disability (GOSE=6). The remaining 39 were in the Upper Good Recovery category (no persisting effect; GOSE=8).

### Influence of number of international matches played on outcomes in RIRP

Comparisons were made within the RIRP group using a median split (17 or more matches and <17 matches). General health compared with a year before was self-reported to be better in

**Table 4** Self-report of mental health and tests of cognition (total score unless otherwise indicated)

	RIRP mean (SD) [minimum, maximum]	Controls mean (SD) [minimum, maximum]	p Value *
Mental health			
HADS depression	2.8 (2.1) [0, 9]	2.6 (2.8) [0, 10]	0.941
HADS anxiety	4.8 (3.0) [0, 12]	5.2 (3.6) [0, 12]	0.157
Cognition			
MOCA	27.4 (2.3) [21, 30]	28.0 (1.5) [25, 30]	0.806
RAVLT immediate recall	50.2 (11.1) [26, 71]	56.1 (8.4) [42, 72]	0.022
RAVLT delayed recall	10.5 (3.6) [2, 15]	11.6 (2.3) [8, 15]	0.165
SART (commission errors)	10.3 (5.0) [8, 13]	10.0 (6.0) [6, 12]	0.860
SART (reaction time)	336 (68) [186, 563]	313 (65) [258, 570]	0.618
Symbol Digit Test	50.9 (11.2) [25, 76]	53.0 (7.5) [31, 70]	0.490
Trail Making Test B (s)	56.1 (18.5) [4, 23]	51.9 (17.6) [26, 91]	0.434
Judgement of Line Orientation	28.2 (1.9) [23, 30]	28.1 (2.3) [21, 30]	0.442
Grooved Pegboard Test (s)			
Dominant hand	74.9 (12.3) [54.7, 105.0]	68.7 (14.0) [49.4, 108.0]	0.038
Non-dominant hand	85.4 (15.3) [47.9, 118.0]	80.1 (20.0) [55.9, 149.1]	0.126

\*Linear regression model adjusted for age, SIMD and years of education.

HADS, Hospital Depression and Anxiety Scale; MOCA, Montreal Cognitive Assessment; RAVLT, Rey Auditory Verbal Learning Test; RIRP, retired international rugby players; SART, Sustained Attention to Response Task; SIMD, Scottish Index of Multiple Deprivation 2012.

**Table 5** Mental health, persisting concussion symptoms and disability outcomes in 'no', 'moderate' (2–9) and 'high' (>9) repeat concussion subgroups

	Repeat concussion			p Value*
	No (n=7)	Moderate (n=27)	High (n=18)	
HADS depression†	3.1 (3.3) [0, 9]	2.6 (1.9) [0, 7]	3.1 (1.7) [0, 6]	0.630
HADS anxiety†	3.7 (2.9) [1, 9]	4.7 (2.6) [0, 10]	5.4 (3.5) [1, 12]	0.389
RPQ†	0.3 (0.8) [0, 2]	2.3 (5.5) [0, 19]	9.6 (11.1) [0, 28]	0.028‡
GOSE§<8	0	6 (22%)	7 (39%)	0.142¶

\*Unadjusted linear regression model p value.

†Mean (SD) [range].

‡Unadjusted Kruskal-Wallis non-parametric test p value; linear model inappropriate due to non-normal distribution.

§n (%); note a score <8 indicates persisting effect of brain injury on daily life, but may not be disabling (see text).

¶Unadjusted Fisher's exact test p value; logistic regression model not appropriate due to small numbers.

GOSE, Glasgow Outcome Scale-Extended; HADS, Hospital Anxiety and Depression Scale; RPQ, Rivermead Post Concussion Symptoms Questionnaire.

those who had played more than 17 matches ( $p=0.008$ ; 95% CI 0.12 to 0.78). No significant differences in mental health or cognitive function were found.

### Allostatic load

There were no significant differences between RIRP and control groups for total AL ( $p=0.635$ ) or its components (cardiovascular/respiratory  $p=0.498$ ; neuroendocrine  $p=0.856$ ; metabolic  $p=0.624$ ; immune  $p=0.682$ ). An exception was the anthropometric component ( $p=0.043$ ; 95% CI  $-0.94$  to  $-0.02$ ); this reflects higher body mass index ( $p=0.006$ ) and hip circumference ( $p=0.004$ ) in the RIRP group. Within the RIRP group, no significant associations were found between no, moderate or high repeat concussions and total AL score ( $p=0.315$ ) or the components of AL (see online supplementary file 2 for further details).

### DISCUSSION

A high number of repeat concussions/mTBI was associated with participation in rugby union in this cohort of retired international players, given the overall median of 7 self-reported concussions and that 34% self-reported at least 10 concussions. On the basis of self-report of duration of LOC and of symptom persistence, all TBIs seem to have been mild,<sup>34</sup> and this context is important when considering the similarity between RIRP and controls in terms of mental health and cognitive outcome. The average scores in these domains for both groups were generally 'normal' and where differences between groups were found, poorer scores for cognition or concussion symptom reporting in the RIRP group were in the normal range for these tests;<sup>36</sup> furthermore, no significant relationship was found between the frequency of concussion, and mental health ratings (depression or anxiety) or cognitive function in the RIRP group. This suggests a detectable but 'non-clinical' effect of concussion in RIRP.

Several other findings are consistent with this interpretation. The average concussion symptom score on the RPQ in the RIRP group was low in relation to base rates for these symptoms; it was about half that found in healthy controls when not associated with concussion and considerably lower than the average in non-sportsmen reporting persisting postconcussion symptoms.<sup>37–38</sup> On the GOSE, an association was found between having more repeat concussions and reporting that persisting symptoms had some impact on daily life. The impact caused occasional strain, but did not restrict or limit social or employment functions, and as such was not disabling. Similarly there were no clear differences in general health between the groups, and in fact cardiovascular disease was more common in

controls. Nor was there evidence for an association between exposure to concussion and indicators of accumulated life stress (AL). Systematic studies on AL in people with TBI have not been published, although there is evidence to suggest that this model is associated with chronic health symptoms and disease trajectories in other groups.<sup>33</sup>

Although there was no statistically significant difference between RIRP and control groups on the MOCA, the difference in the number of participants falling below the cut-off in the RIRP (17%;  $n=9$ ) versus control (3%;  $n=1$ ) groups is worthy of comment, as scores below the cut-off indicate that clinical assessment can be warranted. It is of note that 7/9 RIRP with MOCA scores below the cut-off were at maximum on the GOSE (Upper Good Recovery) and the remaining two with Lower Good Recovery. Further, as there was no association between MOCA scores and the number of concussions reported in this RIRP subgroup, these findings also support a view of detectable differences that do not generalise to symptoms about disability in daily life.

In a meta-analysis of the neuropsychological effects of exposure to concussion/mTBI, poorer delayed memory recall and executive function was reported in those exposed to repetitive injury versus those reporting a single injury.<sup>16</sup> However, the effect size was small and the clinical significance unclear. The number of mTBI in the repeat group in these studies was also unclear, but where reported averaged three.<sup>16</sup> The present study is broadly in line with this, despite the median number of reported concussions being higher, and with detectable but non-clinical effects evident.

The picture for retired players is similar in recent studies and reviews where in general, it is thought that there is an insufficient number of longitudinal studies with a high-quality design.<sup>1–39–40</sup> A recently reported study on retired national/international rugby players in France found depression and mild cognitive impairment to be more common than in controls; with depression associated with a higher frequency of self-reported concussion.<sup>41</sup> Of interest the mean number of concussions (3) was considerably lower than in the present study (14). In a study on retired NFL players an association between risk of depression and number of concussions was also reported<sup>7</sup> although evidence for this was not found in the present study.

The current study benefits from inclusion of a control group that was similar in age and social deprivation to RIRP and also from a range of outcome data comprising cognitive, mental and general health, disability and assessment of cumulative life stress. Nevertheless, our study is limited by the modest response from the potential pool of ~350 retired players. No data are

available on the non-respondents and whether the sample presented here is representative of the population is not known. The higher frequency of self-reported cardiovascular disease in controls could raise a question over whether there was associated cognitive impairment which might reduce the likelihood of finding group differences on cognitive tests; however, the numbers here are small, and this finding should be seen in its context of the control group all reporting their general health to range between good and excellent (table 3), making such an effect unlikely. Future studies may however consider including a comparison group of athletes to control for health factors that may be associated with competitive team sport, such as high levels of physical fitness, late impact of orthopaedic injury or drug use (eg, opioid analgesics, anabolic steroids) during their playing careers. Undoubtedly large-scale prospective studies on representative cohorts of athletes with matching to appropriate control populations are required to further consider any association between exposure to repetitive concussion/mTBI and longer term outcomes.

In common with many such retrospective studies, there is an absence of objective information about TBI in terms of actual number and severity; recent evidence suggests that the concordance between recorded incidence of concussion in sports and self-report may be poor.<sup>42</sup> Also of note is that many in the present sample played rugby in the preprofessional era where the impact of 'hits' may have been less than in recent years, as also was the rigour with which concussion was identified and return to play managed. Hence, findings may not generalise to the modern professional era of rugby union. Other studies on repeat mTBI and their long-term effects vary in terms of their definition of concussion, reporting of the incidence of concussions, exposure period, time since stopped playing and characteristics of controls groups and have not demonstrated that samples are representative of their parent population. Future studies need to overcome these methodological difficulties. Finally, although detectable but 'non-clinical' differences were found on some cognitive measures between the groups, the reason for this is uncertain. Although brain pathology could be the cause, these differences could reflect psychological attributions about mTBI and the impact of retrospective recall bias on symptom reporting.<sup>12 43 44</sup> The latter interpretation may even seem more plausible given the absence of significant relationships between scores on cognitive or mental health measures and the high number of repeat mTBI in RIRP.

## CONCLUSIONS

The number of self-reported concussions in RIRP was high relative to many other studies, and although signs of long-term effects were detectable they were overall, mild. General health and mental health of the retired international players was not poorer than controls, and on cognitive tests, the retired international players performed in the 'normal range', and where differences were found, they were not associated with a higher number of repeat concussions. More repeat concussions were associated with self-report of persisting concussion symptoms, and a poorer outcome on the GOSE, and again although detectable, these effects were mild and did not reflect disability in terms of social or work function. However, given the limitations of a retrospective study with self-reported recall of concussion events and a modest sample size, further work is required using a number of the methodological features of this study, but in a larger cohort of retired athletes.

**Acknowledgements** The authors thank the Scottish Rugby Union for facilitating this research. They also thank Ms K Chung for contributing to data checking.

**Contributors** TMM was involved in planning the project, the development of the protocol, obtained ethics approval, supervised the research workers, provided the funding, was involved in the analysis, wrote the initial draft manuscript and led the development of the manuscript to submission and acceptance. PM and AM carried out the statistical analysis, were involved in discussions of interpretation of data and commented on drafts of the manuscript. JW-L and LMM were involved in helping to set up the protocol, recruited and consented the participants, carried out all assessments, organised meetings and notes, scored all data and developed and inputted to the database. They commented on drafts of the manuscript and provided insights in relation to their experience in assessing all participants. The data on allostatic load in the paper were gathered as part of JW-L's PhD. JH was involved in helping set up the protocol, processing blood, recruiting participants and reviewing the manuscript and attending meetings. WS was involved in planning the project, the development of the protocol and commented on drafts of the manuscript.

**Funding** LMM and JH were partly funded by the Sackler Foundation. JW-L was funded by the Chief Scientist Office (DTF/12/13). WS was supported by an NHS Research Scotland Career Researcher Fellowship.

**Competing interests** None declared.

**Ethics approval** University of Glasgow.

**Provenance and peer review** Not commissioned; externally peer reviewed.

## REFERENCES

- 1 McCrory P, Meeuwisse WH, Kutcher JS, *et al*. What is the evidence for chronic concussion related changes in retired athletes: behavioural pathological and clinical outcomes? *Br J Sports Med* 2013;47:327–30.
- 2 Smith DH, Johnson VE, Stewart W. Chronic neuropathologies of single and repetitive TBI: substrates of dementia? *Nat Rev Neurol* 2013;9:211–21.
- 3 McKee A, Cairns NJ, Dickson DW, *et al*. The first NINDS/NIBIB consensus meeting to define neuropathological criteria for the diagnosis of chronic traumatic encephalopathy. *Acta Neuropathol* 2016;131:75–86.
- 4 Guskiewicz KM, Marshall SW, Bailes J, *et al*. Association between recurrent concussion and late-life cognitive impairment in retired professional football players. *Neurosurgery* 2005;57:719–26.
- 5 Thornton AE, Cox DN, Whitfield K, *et al*. Cumulative concussion exposure in rugby players: neurocognitive and symptomatic outcomes. *J Clin Exptl Neuropsychol* 2008;30:398–409.
- 6 Guskiewicz KM, Marshall SW, Bailes J, *et al*. Recurrent concussion and risk of depression in retired professional football players. *Med Sci Sports Med* 2007;39:903–9.
- 7 Kerr ZY, Marshall SW, Harding HP, *et al*. Nine-year risk of depression diagnosis increases with self-reported concussions in retired professional football players. *Am J Sports Med* 2012;40:2206–12.
- 8 Lehman EJ, Hein MJ, Baron SL, *et al*. Neurodegenerative causes of death among retired National Football League players. *Neurology* 2012;79:1970–4.
- 9 McMillan TM, Weir CJ, Wainman-Lefley J. Mortality 15 years after Hospital admission with mild head injury: a prospective case-controlled population study. *J Neurol Neurosurg Psychiatr* 2014;85:1214–20.
- 10 McKee AC, Cantu RC, Nowinski CJ, *et al*. Chronic traumatic encephalopathy in athletes: progressive tauopathy after repetitive head injury. *J Neuropathol Exp Neurol* 2009;68:709–35.
- 11 Hay J, Johnson VE, Smith DH, *et al*. Chronic traumatic encephalopathy: the neuropathological legacy of traumatic brain injury. *Annu Rev Pathol* 2016;11:21–45.
- 12 Meehan W, Mannix R, Zafonte R, *et al*. Chronic traumatic encephalopathy and athletes. *Neurology* 2015;85:1504–11.
- 13 Hollis SJ, Stevenson MR, McIntosh AS, *et al*. Incidence, risk, and protective factors of mild traumatic brain injury in a cohort of Australian nonprofessional Male rugby players. *Am J Sports Med* 2009;37:2328–33.
- 14 Kemp SP, Hudson Z, Brooks JH, *et al*. The epidemiology of head injuries in English professional rugby union. *Clin J Sport Med* 2008;18:227–34.
- 15 England Professional Rugby Injury Surveillance Project Steering Group. England Professional Rugby Injury Surveillance Project 2014–2015 Season Report. 2016.
- 16 Belanger HG, Spiegel E, Vanderploeg RD. Neuropsychological performance following a history of multiple self-reported concussions: a meta-analysis. *J Int Neuropsychol Soc* 2010;16:262–7.
- 17 McEwen BS. Protective and damaging effects of stress mediators. *N Engl J Med* 1998;338:171–9.
- 18 Scottish Executive (2012). The Scottish Index of Multiple Deprivation 2012. The Scottish Government, Edinburgh. ISBN 978-1-78256-258-0. 2012. <http://simd.scotland.gov.uk/publication-2012/> (accessed 19 Feb 2016).
- 19 Kerr ZY, Marshall SW, Guskiewicz KM. Reliability of concussion history in former professional football players. *Med Sci Sports Exerc* 2012;44:377–82.

- 20 Nasreddine ZS, Phillips NA, Bédirian V, *et al.* The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* 2005;53:695–9.
- 21 Smith A. *Symbol Digit Modalities Test. SDMT.* Manual (revised). Los Angeles: Western Psychological Services, 1982.
- 22 Tombaugh TN. Trail making test A and B: normative data stratified by age and education. *Arch Clin Neuropsychol* 2004;19:203–14.
- 23 Lezak MD. *Neuropsychological assessment.* 2nd edn. New York: Oxford Press, 1983.
- 24 Robertson IH, Manly T, Andrade J, *et al.* 'Oops!': performance correlates of everyday attentional failures in traumatic brain injured and normal subjects. *Neuropsychologia* 1997;35:747–58.
- 25 Smilek D, Carriere JSA, Cheyne JA. Failures of sustained attention in life, lab, and brain: ecological validity of the SART. *Neuropsychologia* 2010;48:2564–70.
- 26 Benton AL, Sivan AB, Hamsher K deS, *et al.* *Contributions to neuropsychological assessment.* Orlando, Florida: Psychological Assessment Resources, 1983.
- 27 Matthews CG, Klove K. *Instruction battery for the adult neuropsychology test battery.* Madison, Wisc: University of Wisconsin Medical School, 1964.
- 28 Snaith RP, Zigmond AS. *The hospital anxiety and depression scale.* Berkshire: NFER-NELSON, 1984.
- 29 King NS, Crawford S, Wenden FJ, *et al.* The Rivermead post concussion symptoms questionnaire: a measure of symptoms commonly experienced after head injury and its reliability. *J Neurol* 1995;242:587–92.
- 30 Ware JE Jr, Sherbourne CD. The MOS 36-item Short-Form Health Survey (SF-36): I. Conceptual framework and item selection. *Med Care* 1992;30:473–83.
- 31 Wilson JT, Pettigrew LE, Teasdale GM. Structured interviews for the Glasgow outcome scale and the extended Glasgow outcome scale: guidelines for their use. *J Neurotrauma* 1998;15:573–85.
- 32 Babor TF, Ramon de la Fuente J, Saunders J. *AUDIT: the alcohol use disorders test: guidelines for use in primary care.* Geneva: World Health Organisation (WHO), 1992.
- 33 Juster RP, McEwen BS, Lupien SJ. Allostatic load biomarkers of chronic stress and impact on health and cognition. *Neurosci Biobehav Rev* 2010;35:2–16.
- 34 Carroll JD, Cassidy LJ, Peloso PM, *et al.* Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO collaborating centre task force on mild traumatic brain injury. *J Rehabil Med* 2004;(Suppl 43):28–60.
- 35 Lees RA, Selvarajah J, Fenton C, *et al.* Test accuracy of cognitive screening tests for diagnosis of dementia and multidomain cognitive impairment in stroke. *Stroke* 2014;45:3008–18.
- 36 Strauss E, Sherman EMS, Spreen O. *A compendium of neuropsychological tests.* Oxford: Oxford University Press, 2006.
- 37 Chan RCK. Base rate of post-concussion symptoms among normal people and its neuropsychological correlates. *Clin Rehabil* 2001;15:266–73.
- 38 King NS, Kirwilliam S. Permanent post-concussion symptoms after mild head injury. *Brain Inj* 2011;25:462–70.
- 39 Randolph C, Karantzoulis S, Guskiewicz K. Prevalence and characterization of mild cognitive impairment in retired national football league players. *J Int Neuropsychol Soc* 2013;19:873–80.
- 40 Hart J, Kraut MA, Womack KB. Neuroimaging of cognitive dysfunction and depression in aging retired national football league players. *JAMA Neurol* 2013;70:323–44.
- 41 Decq P, Gault N, Blandeau M, *et al.* Long-term consequences of recurrent sports concussion. *Acta Neurochir (Wien)* 2016;158:289–300.
- 42 Kerr ZY, Mihalik JP, Guskiewicz KM *et al.* Agreement between athlete-recalled and clinically documented concussion histories in former collegiate athletes. *Am J Sports Med* 2015; 43:606–13.
- 43 Gunstad J, Suhr JA. Expectation as “etiology” versus “the good old days”: postconcussion syndrome symptom reporting in athletes, headache sufferers, and depressed individuals. *J Int Neuropsychol Soc* 2001;7(3):323–33.
- 44 Kristman VL, Borg J, Godbolt AK, *et al.* Methodological issues and research recommendations for prognosis after mild traumatic brain injury: results of the International Collaboration on Mild Traumatic Brain Injury Prognosis. *Arch Phys Med Rehabil* 2014;95(Suppl 3):S265–77.