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## Article:

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#### 2 **Objectives**

Current off-field concussion screening instruments have sub-optimal accuracy and additional testing
domains may be necessary to detect the full spectrum of concussion presentations. This study aimed to
determine if additional cognitive tests add utility to off-field screening for sport-related concussion.
Design
Reproducibility and diagnostic accuracy cohort studies were performed in the 2017 and 2018 seasons of
the Super Rugby competition, conducted in Argentina, Australia, Japan, New Zealand, and South Africa.
Methods

Abridged versions of Stroop (score, time), Spatial Memory (score, failed trials), and Trail Making Trial-B (time, errors) cognitive tests, modified for off-field use, were examined. Players performed baseline testing prior to each season. Cases undergoing off-field screening as part of the World Rugby Head lnjury Assessment Process underwent evaluation with the same cognitive tests during competition matches. Agreement between repeated pre-season baseline measurements, and the diagnostic accuracy of off-field testing against a clinical reference standard of concussion, were evaluated.

### 16 Results

Data were available for repeated preseason baseline testing in 644 players, and 100 cases undergoing
off-field concussion screening. There was little individual agreement across pre-season baseline
assessments for all tests (Lin's correlation and Gwets AC1 coefficients ranging between 0.2 and 0.3).
There was significantly worse performance for the time taken to complete the modified Stroop Test in
concussed players undergoing off-field screening, compared to non-concussed players (median time
21.1 v 18.4 seconds, p<0.01; area under the receiver operating characteristic curve 0.7 (AUROC, 95%CI</li>

1	0.5-0.8). Other cognitive measures did not discriminate between injured and un-injured players, with
2	no-statistically significant differences in distribution medians (p=0.6-0.9) and AUROC values close to 0.5.
3	Conclusions
4	The time taken to perform a modified Stroop Test may provide additional diagnostic accuracy if added
5	to current off-field concussion screening tools. Abridged Spatial Memory and Trail Making Trial-B tests
6	did not discriminate between concussed and non-concussed players.
7	Key words
8	Concussion, screening, sensitivity, specificity, agreement, Rugby
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1	Pra	actical implications:
2	1.	Current off-field concussion screening tools have sub-optimal accuracy. Stroop, Spatial memory, and
3		Trail Making Trial-B tests are commonly used cognitive tests. Abridged versions, suitable for side-line
4		use, could improve off-field detection of concussion if added to existing screening tools.
5		
6	2.	The time taken to perform a modified Stroop Test may provide additional diagnostic accuracy if
7		added to current off-field concussion screening tools.
8 9	2	Modified Spatial Memory and Trail Making Trial-B tests did not discriminate between injured and
10	5.	un-injured players
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12	4.	Reproducibility of repeated testing was low for all studied cognitive tests, suggesting limited benefit
13		from baseline testing.
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#### 1 Introduction

Concussion is a common and high profile injury in contact and collision sports.<sup>1</sup> Continuing to play when 2 3 concussed could worsen symptoms, delay recovery, and increase the risk of further injuries.<sup>2</sup> Elite 4 sports, following recommendations from the Berlin Concussion Consensus Statement, have therefore 5 introduced systems to identify and manage head impact events with the potential for concussion during 6 matches.<sup>3</sup> These typically involve off-field (often termed side-line) testing to detect suspected concussion following suspect head impact events.<sup>3</sup> 7 8 In elite Rugby, the World Rugby Head Injury Assessment off-field screening tool (HIA-1) is used to assess 9 players following identification of a meaningful impact event, without overt signs of concussion.<sup>4, 5</sup> This 10 instrument includes sub-tests assessing cognition (orientation, memory, and concentration), balance, 11 and symptomatology. It takes 10 minutes to administer and has demonstrated a sensitivity of 77% and 12 specificity of 87% for the diagnosis of concussion. The relatively low reported sensitivity of the HIA-1 off-

field tool may offer the opportunity to reduce the number of false negative cases through more detailedtesting.

15 Neuropsychological tests, including computerized neurocognitive tests, are used for diagnosis,

assessment of severity, and monitoring of recovery in neurological diseases e.g. traumatic brain injury,

- 17 hepatic encephalopathy.<sup>6, 7</sup> The Trail Making, Stroop, and Corsi block tapping tests are established
- 18 neuropsychological tests that have been studied in moderate and severe traumatic brain injury,<sup>8-10</sup>
- 19 Although not well studied in acute mild head injury, they evaluate a range of cognitive functions, and
- 20 involve different brain pathways that could conceivably be affected by concussion.<sup>6, 7</sup>

21 These detailed tests are not suitable for off-field application during sporting competitions due to time

22 constraints. However, it might be hypothesised that shortened versions, retaining the underlying

1	construct, could be effective as additional novel screening tests for concussion; although there is
2	currently an absence of evidence for their diagnostic accuracy following head impact events in sports. <sup>11</sup>
3	This study therefore aimed to determine if abridged versions of Trail Making, Stroop and Corsi block
4	tapping tests, modified for off-field use, could be useful additions to screening tools for sport-related
5	concussion. Specific objectives were to: describe the distribution, reproducibility and normative values
6	of baseline cognitive test values; describe the distributions of cognitive test scores in concussed and
7	non-concussed players; and evaluate diagnostic accuracy in Rugby Union players undergoing off-field
8	concussion screening.
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#### 1 Methods

2 Prospective reproducibility and diagnostic cohort studies were conducted in the male, adult, elite-level 3 Rugby Union 'Super Rugby' competition players over 2 seasons between 2017 and 2019. The source 4 population consisted of players rostered on Australian (5 teams), New Zealand (5), South African (6), 5 Argentinian (1) and Japanese (1) elite level rugby union teams (n=644). The study populations comprised 6 rostered players undergoing pre-season baseline testing; and those undergoing an off-field HIA-1 7 concussion screening tool assessment after identification of a meaningful head impact event during 8 competitive matches with the potential to cause concussion, but where the consequences were unclear 9 i.e. the possibility of concussion in the absence of overt manifestations, e.g. dangerous mechanism. The 10 indications for off-field screening assessments (termed 'criteria 2'), and details of the HIA-1 screening 11 tool, are provided in the web appendix (Table A1 and A2).<sup>4</sup> 12 According to the World Rugby HIA process, players demonstrating clear signs of concussion (e.g. loss of 13 consciousness, tonic posturing, ataxia, seizures) during matches are immediately and permanently 14 removed from the remainder of the match, without undergoing further off-field concussion screening. 15 These players were therefore outside of the scope of current study. The indications for immediate and 16 permanent removal (termed 'criteria 1'), and further details of the HIA process, are provided in the web appendix.<sup>4</sup> 17

The Trail Making, Stroop, and Corsi block tapping cognitive tests were chosen for evaluation based on the following factors: recognition as established and validated neurocognitive tests;<sup>6, 7</sup> previous use in traumatic brain injury;<sup>8-10</sup> availability, feasibility and practicality of application as a brief screening test; and complementation of cognitive domains assessed within the current HIA-1 off-field screening tool. In elite Rugby, the HIA-1 concussion screening tool is administered during a 10-15 minute off-field assessment period. As each of the chosen cognitive tests take approximately 5 minutes each to

complete, it was not possible to study the traditional versions alongside the existing HIA-1 screening tool
in the time available. Previously unvalidated, abridged (taking approximately 1-2 minutes each to
administer) versions of the Trail Making, Stroop, and Corsi block tapping tests were therefore developed
by CSx Systems (CSx Systems, Auckland, New Zealand) to allow off-field screening evaluation as
described below:

6 Trail Making Test: The Trail Making Test (TMT) provides information on visual search, scanning, speed of processing, mental flexibility, and executive functions.<sup>12, 13</sup> The TMT consists of two 7 parts. TMT-A requires an individual to draw lines sequentially connecting 25 encircled numbers 8 9 distributed on a sheet of paper. Task requirements are similar for TMT-B except the person must alternate between numbers and letters (e.g., 1, A, 2, B, 3, C, etc.).<sup>13</sup> This study only used the 10 11 TMT-B test, which was presented on a tablet and required the participant to complete the test 12 by tapping on the target stimulus in the order outlined above. Total time to completion and errors were recorded. 13

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15 Stroop test: The Stroop colour-word interference task measures selective attention, mental flexibility, and inhibitory control.<sup>14, 15</sup> Conventionally subjects are required to read three 16 17 different tables as fast as possible. Two of them represent the 'congruous condition' in which participants are required to read names of colours and name different colour patches. In the 18 19 third 'incongruent' table, colour-words are printed in an inconsistent colour (e.g. the word "red" 20 is printed in the colour green), and participants are required to name the colour instead of 21 reading the word. Unlike the traditional version of the Stroop, in this study the test taker was 22 not required to perform the priming subtests (word reading or colour naming) prior to completing the interference subtest (inconsistent colour-words). Study subjects were presented 23 24 with 10 colour-words of varying colour congruency on a tablet and required to respond by

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identifying the correct colour displayed. The time taken to perform the task and score were recorded.

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4 Corsi block tapping test: The corsi block tapping test assesses visuo-spatial working memory and spatial attention.<sup>13</sup> The traditional forward version consists of nine cubical blocks irregularly 5 6 positioned on a board. An examiner taps the blocks starting with sequences of two cubes. The 7 subject has to reproduce a given sequence by tapping the blocks in the same sequence. If a 8 certain proportion of the sequences is reproduced correctly (usually 1/2, 2/3, or 3/5 of the trials 9 per sequence length), the sequence length increases by one item. The procedure ends when the number of wrong reproductions exceeds the proportion of admissible errors per length.<sup>16, 17</sup> In 10 11 this study a brief spatial memory test, modifying the forward Corsi block test, was investigated. 12 A symmetrical 3 x 3 grid of 9 objects (schematic flowers) was presented on a tablet. One item was randomly and sequentially highlighted at a time and respondents were asked to repeat the 13 order that these items appeared by tapping the corresponding objects on the grid. Five trials 14 15 were performed with the span (that is, the length of the pattern sequence) increasing after 16 successful completion of a sequence, and decreasing after failures, in the range from 3 17 (minimum span) to 7 (maximum span). The number of failed trials and score (calculated from 18 number of successful trials and spans, range 5 – 400) of the modified Corsi block test was 19 recorded.

Pictures of each cognitive test are shown in the web appendix (Figure A1). Players in participating Super
Rugby teams underwent baseline cognitive test evaluation after completion of a routine training
session. Post-exertional baseline testing was chosen to reflect the conditions present in off-field
concussion screening conducted during competitive matches. Testing was conducted in a standardised
format by the team doctor. This predominantly occurred prior to each season but was also repeated in

1 the event of transfer to another team. Thus, depending on team rosters, players could undergo baseline 2 testing: (i) once if participating in the first season of the study period only; (ii) twice if playing in the 3 Super Rugby competition during both study seasons; or (iii) more than twice if transferring to different 4 teams in the competition. 5 Participants requiring off-field HIA-1 concussion screening during competitive matches then underwent 6 assessment with the cognitive index tests during a 15 minute off-field medical room assessment 7 administered by the team doctor. Cognitive index test performance did not influence return to play 8 decisions, with tests implemented non-operationally after completion of the HIA-1 screening tool. Team 9 doctors could observe gross cognitive test performance, but were blinded to the final results (i.e. total 10 errors, score, time). 11 Following an off-field concussion screen, repeat clinical assessments were made by the team doctor

post-match (HIA-2 assessment) and after 48 hours rest (HIA-3 assessment), to determine a final clinical
 diagnosis of concussion.<sup>18</sup> The HIA-2 assessment consists of a clinical evaluation including the Sports
 Concussion Assessment Tool 5<sup>th</sup> Edition (SCAT-5 )instrument.<sup>19</sup> The HIA-3 assessment comprises a clinical
 evaluation, supported by an expanded SCAT-5 symptom checklist, a cognitive assessment (typically a
 computerised neuro-cognitive tool such as CogSport) and a balance assessment using the balance error
 scoring system and tandem gait balance tests.<sup>19, 20</sup>

HIA process data are routinely recorded at the point of assessment by doctors using a tablet based, webhosted platform, with standardised data collection forms (CSx Systems, Auckland, New Zealand). All
cognitive tests were administered using software applications embedded within the CSx data collection
system. Spanish and Japanese language-specific versions of the Stroop and TMT-B tests were available
for the Argentinean and Japanese teams.<sup>21-23</sup> Data was subsequently uploaded to the World Rugby HIA
database. HIA assessment forms, from each of the 3 HIA process stages, are linked deterministically
using unique player identifiers. Competition coordinators are responsible for data quality and collection

of outstanding information. Any missing CSx outcome data was collected by direct communication with
 team doctors.

3 Analyses proceeded in 3 stages. Firstly, player flow through the study was described. Secondly, pre-4 season baseline results were examined. The distributions of pre-season baseline cognitive test scores 5 were examined using descriptive statistics. Only one baseline value was included per player, with the 6 first result used if repeated results were available. Normative ranges were then determined for each 7 cognitive test. Cut-offs were selected based on distribution percentiles consistent with previous SCAT 8 normative value studies and followed conventions used in cognitive assessments (e.g. Wechsler 9 intelligence quotient classifications).<sup>24-26</sup> The below average cut-off was defined as close as possible to the 25<sup>th</sup>/75<sup>th</sup> percentile ranks. Unusually low scores corresponded to the 10<sup>th</sup>/90<sup>th</sup> percentile ranks, and 10 extremely low scores aimed for the 2<sup>nd</sup>/98<sup>th</sup> percentile ranks. The reproducibility of cognitive tests was 11 12 then evaluated in players with repeated pre-season baseline results. In the event of multiple baseline 13 evaluations, the first two repeated measurements were examined. Scatter plots and frequency 14 histograms were used to visually compare the relationship between repeated measurements. Bland-15 Altman Limits of Agreement and Lin's concordance coefficient (continuous time and score variables); 16 and two-way bar charts, Cohen kappa using linear weights, and Gwets AC1 statistic (discrete score, test 17 errors, and failed trials variables), were then used to quantify agreement.

Thirdly, cognitive test performance in players undergoing off-field concussion screening during games was investigated. The distribution of test results was compared between concussed and non-concussed players graphically and with Mann Whitney U tests. The sensitivity, specificity, and area under the receiving operating characteristic curve (AUROC) were calculated for the cognitive index tests and the HIA-1 screening tool against the reference standard of a final clinical diagnosis of concussion. The primary threshold for cognitive index test positivity was the empirically derived normative threshold for poor performance (10<sup>th/90<sup>th</sup></sup> percentile ranks of baseline test result distribution, described above).

Secondary exploratory cut-points were explored according to any deterioration from the most recent
 baseline value and empirical thresholds derived using Youden's J statistic.

Buderer's formula was used to estimate sample size with the following assumptions from previous HIA data: a prevalence of concussion of 40% in players with significant head impact events requiring HIA-1 concussion screening assessment; a target sensitivity of 90%; and a target specificity of 80% for cognitive index tests to identify concussion.<sup>4, 5, 27</sup> To achieve a desired precision of 10% for the sensitivity estimate would require a sample size of 88 players undergoing off-field concussion screening assessments. Available case analyses were performed with the sample size determined by the number of players with complete data for each analysis. Statistical analyses were carried out in Stata version 13.1 (StataCorp, College Station, USA) with a conventional significance level ( $\alpha$ ) of 0.05 used. Ethical approval was provided by the University of Sheffield (Reference Number 017814). All players provided informed consent for participation prior to the start of the season. CSx provided an anonymised data set for analysis with player identifiers removed. 

#### 1 Results

2 Of the 644 players rostered on Super Rugby teams during the study, all were male with a median age of 3 24 years (IQR 22-28, range 18-37) and a median professional Rugby experience of 4 years (IQR 3-7, range 4 1-19). The majority of participants (85%) spoke English as their first language. Most players had been 5 diagnosed with at least one previous concussion (64%, median 1, IQR 0-2, range 0 - 10). Players had 6 predominantly completed education to secondary school level (82%, with a median of 13 years 7 education (IQR 12-14, range 7-20). 8 Baseline testing was performed on 896 occasions in the 15 participating teams over the 2 seasons of the 9 study. This testing was performed in 643 of 644 rostered players (Figure 1, once in 409 players, repeated 10 twice in 215 players, repeated thrice in 19 players). Data were missing due to incorrect or absent 11 baseline testing in a small number of cases (1.6% of total number of possible baseline tests across all 12 index tests, testing occasions, and players, n=5,286/5,376). 13 The cognitive tests generally exhibited a unimodal, positively skewed distribution, with a long tail; 14 indicating the majority of players performing well with a minority demonstrating increasingly poor 15 performance (web appendix Table A3, web appendix Figure A2). The normative classification ranges for

16 each cognitive test are presented in in the web appendix (web appendix Table A4).

Distributions for repeated baseline measurements were similar for all cognitive tests, with inter-athlete baseline results before season 2 of the study mirroring the overall pattern of those from season 1 (web appendix Figures A3). In contrast, there was little intra-athlete agreement for each participant with scatter plots showing a lack of correlation between repeated measurements (web appendix Figure A4). Lin's correlation coefficient (pc) for TMT-B time, Stroop test time, and spatial memory test score ranged between 0.21 and 0.33 (Table 1), with Bland Altman plots showing large 95% limits of agreement exceeding plausible clinically acceptable interchangeability thresholds (Table 1, web appendix Figure A5). Agreement between repeated baseline results for TMT-B errors, Stroop test score, and spatial
memory test failed trials was low, with exact agreement evident in only 37.0%, 22.8% and 49.1% of
players (Table 1), respectively. The weighted kappa statistic also indicated poor agreement beyond that
expected for each cognitive test (Table 1): TMT-B errors 0.01 (95%CI 0.0-0.09); Stroop test score 0.20
(95%CI 0.12-0.28); Spatial memory test failed trials 0.11 (95%CI 0.01-0.21). Gwets AC1 coefficients
ranged between 0.2 and 0.3 (Table 1).

7 A total of 211 consecutive meaningful head impact events were detected in 165 individual players 8 (recurrent events occurring in 33 players, ranging from 24 players with 2, to 2 players with 5 incidents) 9 during competitive Rugby matches over the study period. Of these, 84 incidents (in 74 players) were 10 associated with overt signs or symptoms of concussion requiring immediate and permanent removal 11 from play. The remaining 127 incidents (in 106 players), where the consequences were unclear, 12 underwent off-field concussion screening comprising the study population. 100 players were assessed 13 with the cognitive index tests and were included in the final study sample (Figure 1). Of these cases, 33 14 players were diagnosed with concussion giving a prevalence of 33.0% (95% CI 24.4-42.9%). 15 There was significantly worse performance in the time taken to complete the Stroop Test in concussed, 16 compared to non-concussed players (median time 21.1 v 18.4 seconds, p<0.01, AUROC 0.66 (95% CI 17 0.54-0.76), n=100, Table 2, web appendix Figure A6). Using the normative threshold (web appendix 18 Table A4) as the cut-point for abnormal performance demonstrated low sensitivity, but high specificity, 19 of 15.2% (95%CI 5.1-31.9%) and 91.0% (95%CI 81.5-96.6%) respectively (Table 2). Using any worsening 20 from baseline as the threshold for test positivity offered the opposite pattern of higher sensitivity with 21 lower specificity with values of 75.0% (95%CI 53.4-90.2%) and 50.0% (95%CI 34.6-65.4%) respectively 22 (web appendix Table A5). An optimal cut-point of 19.8 seconds was indicated by the Youden method. 23 Sensitivity at this threshold was 66.7% (95%CI 48.2-82.0%) with a specificity of 68.7% (95%CI 56.2-24 79.4%).

The existing HIA01 screening tool in this cohort had a sensitivity of 78.8% (95%CI 61.1-91.0%) and
specificity of 64.2% (51.5-75.5%, n=100) for the detection of concussion in included players. Adding time
to complete the Stroop test to the HIA01 screening tool using its normative threshold resulted in the
detection of 2 additional concussion cases, at the cost of 4 false positives (combined sensitivity of 84.8%,
specificity 58.2%, AUROC 0.72). Using empirical Youden or baseline thresholds in a combined HIA01
screening tool detected additional concussion cases (3 and 3 respectively) but at the cost of a high
number of false positives (11 and 17 respectively).

8 Performance was similar regardless of injury status for all other cognitive index tests, with no-9 statistically significant differences in distributions (Mann-Whitney U tests, p=0.58-0.98, Table 2) or 10 frequency histograms (web appendix Figure A6). AUROC values were close to 0.5 indicating minimal 11 ability to differentiate between concussed and non-concussed players (web appendix Figure A7). 12 Diagnostic accuracy was poor for these other cognitive index tests regardless of whether normative 13 (sensitivity 12.1% - 24.2%; specificity 65.7% - 89.6%) or baseline (sensitivity 29.1% - 75.0%; specificity 14 50.0% - 73.8%) thresholds for positivity were used; with fewer additional concussions detected at the 15 cost of more false positive cases (Table 2 and web appendix Table A5).

#### 1 Discussion

2 There are several important findings from the present study. Firstly, abridged Stroop (score, time), 3 Spatial memory (score, failed trials), and TMT-B (time, errors) tests demonstrated poor intra-athlete 4 agreement, with players often having markedly different results across repeated pre-season baseline 5 assessments. Secondly, in players undergoing off-field screening assessments, there was significantly 6 worse performance for the time taken to complete the abridged Stroop test in concussed players 7 compared to non-concussed players (median time 21.1 v 18.4 seconds, p<0.01; AUROC 0.66 (95% CI 8 0.54-0.76; n=100). Adding this test to the HIA01 screening tool, using a normative cut-point, detected a 9 small number of additional concussion cases, at the cost of relatively few false positives. Finally, errors 10 in the abridged Stroop test, and abridged Spatial memory and TMT-B cognitive index tests, did not 11 appear to discriminate between injured and un-injured players, with no-statistically significant 12 differences in distribution medians (p=0.58-0.98) and AUROC values close to 0.5. 13 The time taken to complete a 10-word Stroop colour-word interference task was the only studied 14 cognitive measure that discriminated between concussed and non-concussed players undergoing off-15 field screening assessments. Processing of the Stroop task is performed by the anterior cingulate cortex and the dorsolateral prefrontal cortex.<sup>11,12</sup> Impairment in both of these cerebral regions has been 16 observed in human MRI imaging studies, and animal models, following mild traumatic brain injury.<sup>28</sup> 17 Although evidence is limited in concussion and mild head injury,<sup>29</sup> studies have shown worsened 18 19 performance in the traditional Stroop task in moderate and severe traumatic brain injury.<sup>8</sup> An increased 20 cognitive interference effect (delayed reaction time due to mismatch in stimuli) has also been found in 21 other neurological disorders including dementia, attention-deficit hyperactivity disorder, and 22 Parkinson's disease strengthening the biological plausibility of a detectable deficit in concussion.<sup>30-32</sup> 23 Further modification of the Stroop test to include other sensory modalities and variables, for example 24 testing the reverse Stroop effect (reading a colour-word printed in the congruent colour, an incongruent

colour, or a neutral colour), could conceivably magnify this effect. The observed lack of utility of the
 abridged Spatial Memory and TMT-B tests suggests that either the associated cognitive functions are
 not commonly impaired acutely post-concussion, or that the studied tasks were not sufficiently
 demanding.

5 Current concussion screening tools consist of multiple sub-tests conducted in parallel, in which all tests 6 need to be normal to give a negative result and any abnormal finding results in a positive test. In this 7 testing paradigm, as further sub-tests are added sensitivity will increase, and specificity fall, dependent 8 on the performance and overlap of individual sub-tests. The sensitivity and specificity of these 9 constituent sub-tests can also be varied in opposite directions as the cut-point for test positivity is 10 altered; with the optimal trade-off dependent on how false negative and false positive cases are valued. 11 The World Rugby HIA01 multi-modal concussion screening tool has previously shown moderate sensitivity and high specificity.<sup>4, 5</sup> The key aim when expanding off-field concussion screening is 12 13 therefore to select sub-tests and test thresholds that detect additional concussion cases, without an 14 unacceptable increase in false positives. The individual sub-tests currently included in the HIA01 15 screening tool have previously demonstrated AUROC values between 0.51 and 0.73.<sup>4</sup> The time to 16 complete the abridged Stroop test AUROC of 0.66 compares favourably to these. Using normative 17 thresholds for Stroop test time demonstrated high specificity, and therefore if sufficiently sensitive, 18 offers promise to detect extra concussion cases at the cost of very few extra false positives. Using 19 baseline thresholds, or the empirically derived cut-point using Youden's index, for the abridged Stroop 20 test would detect a small number of additional concussions but would likely result in an unacceptable 21 loss of specificity.

Baseline test results are commonly used in off-field screening assessments to aid interpretation of post injury scores, although they are not considered mandatory in the Berlin Concussion Consensus
 Statement.<sup>3</sup> The studied cognitive tests were imprecise with significant natural variation apparent with

1 repeated testing. The relatively high intra-athlete variability noted for each cognitive test between each pre-season measurement, is similar to that reported previously for serial SCAT assessments,<sup>33</sup> and would 2 3 seem to limit the utility of baseline testing. Worse results than baseline would be frequently expected 4 secondary to random natural variation in test performance rather than underlying cognitive impairment. 5 More importantly, the lack of precision of the cognitive tests (closeness of the repeated measurements) 6 will undermine test performance, even if relatively accurate (closeness of the measurements to a 7 specific value). The lack of agreement observed with repeated Stroop test time measurements, implies 8 high measurement error for the task and an inability to attribute change to a concussion unless there 9 change of large magnitude. This could therefore support the use of normative, rather than baseline 10 thresholds. 11 The source population of professional Rugby players should ensure that these results are largely 12 generalisable throughout elite Rugby Union competitions. However, previous research has suggested 13 that team doctors often use clinical judgement to interpret off-field screening subtest results with 14 improved overall discrimination for concussion compared to strict application of baseline or normative 15 thresholds.<sup>4</sup> Cognitive tests were implemented non-operationally and it is therefore possible that 16 modified Stroop test performance could differ if applied in actual practice. External validity to the elite 17 level of other sports with different frameworks for evaluating head impact events is less certain,

although cognitive index test administration should largely be independent of context-specific factors
such as test setting (on field v pitch-side v medical room) or equipment (boots v skates). Results could
also differ if alternative formats of the abridged tests are administered, for example using paper-based
forms rather than a tablet application.

This study provides a pragmatic evaluation of novel cognitive tests for rapid sports related concussion screening on the off-field and has several strengths. The cognitive tests and reference standard were applied to all included participants with no potential for partial or differential verification biases. The

reference standard was determined after serial standardised examinations by experienced team doctors
 reducing the risk of differences in diagnostic thresholds and misclassification. Furthermore, blinding, and
 sequential outcome assessments prevented test and diagnostic review biases.

4 Conversely, there are a number of limitations which could challenge internal validity. Firstly, as a real-life 5 study using routinely collected clinical data there were inevitably missing data with the potential for 6 selection bias. However, this is likely of less magnitude than performing a two-gate 'case-control' study 7 design common in this research field. Secondly, there is the possibility of incorporation bias. During 8 normal sports medicine practice the team doctor predominantly conducts both off-field screens and 9 subsequent diagnostic assessments. Although blinded to the final cognitive index test results, it is 10 possible that team doctors incorporated a global impression of screening test performance into their 11 overall diagnostic assessment. Thirdly, the diagnosis of concussion is inherently subjective and ill-12 defined, as acknowledged in the Berlin concussion consensus document. Imperfect diagnosis of 13 concussion could therefore lead to misleading accuracy metrics. The extent of any systematic error 14 would be dependent upon the frequency of misclassifications and the degree of correlation between 15 cognitive test and reference standard errors. Fourthly, language-specific tests were not available for all 16 participants and some players may have completed the cognitive tests in a non-native language. In 17 mitigation, the vast majority of players were fluent in English and previous studies examining differences 18 in the Stroop effect in bilingual individuals are inconclusive. Moreover, language-specific versions were 19 available for use in Spanish and Japanese teams, with similar baseline results observed across different 20 languages (web appendix Figure A8). Fifthly, although the cognitive index tests were implemented in a 21 uniform fashion, we did not investigate inter-observer variability in performance between team doctors. 22 Finally, atypical testing paradigms were used for each investigated cognitive index test. The observed 23 lack of diagnostic utility could reflect the ineffectiveness of these non-validated testing approaches or 24 sub-optimal administration by non-experts. However, the construct for the abridged tests remains

consistent with the traditional versions. Furthermore, the formal versions of these tests are not practical
 for brief off-field concussion screening and testing by non-neuropsychologists reflects the reality of real world sports medicine. As stated in the Berlin concussion consensus statement 'abbreviated testing
 paradigms are designed for rapid sports related concussion screening on the sidelines and are not
 meant to replace a comprehensive neurological evaluation'.<sup>3</sup>

6 This is the first study to evaluate the Stroop, Spatial memory and TMT-B tests for off-field sports-related 7 concussion screening. However, there is a larger literature examining normative values for the TMT-B 8 and evaluating the performance of the cognitive tests in patients with confirmed traumatic brain injury. 9 The distribution of TMT-B times observed in the current study are significantly quicker than previously 10 published normative values (median 17 v 47 seconds). This is likely to reflect different test taking 11 conditions using a tablet application compared to traditional administration with paper and pencil. In contrast to TMT-B time, a cut-point of 3 errors has been suggested in previous studies,<sup>34</sup> which appears 12 13 consistent with the normative range derived from the current investigation. A number of studies have 14 demonstrated impaired performance of the Stroop, Spatial memory, and TMT-B in traumatic brain injury patients, <sup>35,29,30</sup> however the relevance of these to the milder sub-set of concussed patients is 15 16 uncertain.

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#### 18 Conclusions

assessments.

The time to perform an abridged Stroop test, modified for off-field use, may provide additional diagnostic accuracy if added to current off-field concussion screening tools. Reproducibility of repeated testing was low, suggesting limited benefit from baseline testing, and supporting use of a normative threshold for test positivity. Modified Spatial memory and TMT-B tests did not discriminate between concussed and non-concussed players and do not appear to have utility in off-field screening

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Table 1. Agreement of repeated pre-season baseline cognitive tests evaluated using the Bland-Altman limits of agreement, concordance correlation, and weighted kappa approaches.

	Cognitive test					
	TMT-B time n=216	TMT-B errors n=216	Stroop test time n=219	Stroop test score n=219	Spatial memory test score n=226	Spatial memory test failed trials n=226
Mean of paired differences (95% CI)	1.2 (0.1-2.4)	-	1.8 (0.8-2.7)	-	12.6 (1.8-23.4)	-
Lower 95% limit of agreement	-15.1	-	-12.0	-	-149.2	-
Upper 95% limit of agreement	17.6	-	15.6	-	174.3	-
Concordance correlation coefficient (95% CI)	0.3 (0.2-0.4)	-	0.2 (0.1-0.3)	-	0.2 (0.1-0.3)	-
Bias correction factor	0.9	-	0.9	-	0.9	-
Pearson's correlation coefficient (95% Cl)	0.3 (0.2-0.5)	-	0.2 (0.1-0.4)	-	0.2 (0.1-0.3)	-
Absolute agreement (%, 95% CI)	-	37.0% (30.5-43.5)	-	22.8% (17.2-28.4)	-	49.1% (42.6-55.7)
Weighted kappa (95% CI)	-	0.01 (0.0- 0.1)	-	0.2 (0.1 - 0.3)	-	0.1 (0.0 - 0.2)
Gwets AC1	-	0.3 (0.3- 0.4)	-	0.1 (0.1-0.2)	-	0.3 (0.2-0.4)

N=100	Median value of distribution		AUROC	Normative test threshold	Diagnostic accuracy using Normative cut-point		Additive performance to HIA01 off-field screening tool		
Cognitive test	Concussed	Non- concussed	p-Value	AUROC (95% CI)		Sensitivity (%)	Specificity (%)	Additional concussions detected	Additional false positives
				(95% CI)					
Trail Making Test B - Time	17.2	17.8	0.8	0.5 (0.4-0.6)	≥27.7	12.1 (3.4-28.2)	86.6 (76.9-93.7)	0	4
Trail Making Test B – Errors	1	1	1.0	0.5 (0.4-0.6)	≥4	15.2 (5.1-31.9)	86.6 (76.0-93.7)	1	6
Stroop test – Time (secs)	21.1	18.4	0.01*	0.7 (0.5-0.8)	>25.5	15.2 (5.1-31.9)	91.0 (81.5-96.6)	2	4
Stroop test- Score	10	9	0.6	0.5 (0.4-0.6)	≤4	12.1 (3.4-28.2)	89.6 (79.7-95.7)	1	5
Spatial memory test – Score	280	270	1.0	0.5 (0.4-0.6)	≤205	24.2 (11.1-42.3)	79.1 (67.4-88.1)	1	8
Spatial memory test – Failed trials	1	1	0.6	0.5 (0.4-0.6)	≥2	33.3 (18.0-51.8)	65.7 (53.1-76.8)	2	13

## Table 2. Performance of cognitive tests for the detection of concussion

\*Significant at  $\alpha$ =0.05

# Figure legends

Figure 1. Flow diagram showing derivation of study sample.