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Neurophysiological and cognitive impairment following repeated sports concussion injuries in retired professional rugby league players

Alan J. Pearce [a], Billymo Rist[a,b], Clare L. Fraser[c], Adrian Cohen[d], and Jerome J. Maller[e,f]

[a]Department of Rehabilitation, Nutrition and Sport, La Trobe University, Melbourne, Australia; [b]Mental Edge Consulting, Melbourne, Australia; [c]Save Sight Institute, Department of Ophthalmology, The University of Sydney, Sydney, Australia; [d]Central Clinical School, Discipline of Clinical Ophthalmology and Eye Health, University of Sydney, Sydney, Australia; [e]Monash Alfred Psychiatric Research Centre, The Alfred and Central Clinical School, Monash University, Melbourne, Australia; [f]General Electric Healthcare, Melbourne, Australia

ABSTRACT

Background: Concussion is regarded as a common injury in rugby league, however no studies have explored the long-term neurophysiological and cognitive effects of repeated concussion injuries in this sport.

Methods: Former professional rugby athletes (n = 25) were compared to 25 age-matched participants with no history of a concussion. All participants completed standardised motor dexterity, reaction time, and cognitive tasks for working memory, associative learning and rule acquisition and reversal. Single-pulse transcranial magnetic stimulation (TMS) acquired motor evoked potentials and cortical silent period (cSP), as well as paired-pulse TMS for short latency intracortical inhibition and long intracortical inhibition (LICI).

Results: Compared to controls, dexterity and visuomotor reaction time was slower in the rugby group compared to controls (p = 0.02, p < 0.01, respectively). The rugby group also demonstrated poorer cognitive performance than controls (p range 0.02 to < 0.01). TMS revealed significantly reduced cSP at suprathreshold stimulation intensities (p range 0.02 to <0.01), and increased LICI (p = 0.03) in the rugby group.

Discussion: These findings of motor and cognitive changes, along with neurophysiological alterations, particularly with intracortical inhibition, nearly two decades post-concussion provides evidence for long-term sequelae for athletes with a history of repeated head trauma in contact sports.

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Introduction

There is growing international attention towards understanding the relationship between repetitive concussions experienced in sport and the development of chronic neurological impairment later in life. To date, the majority of data has stemmed from North America in sports such as football, soccer and ice hockey. In retired athletes with a history of concussions, studies have reported ongoing neurological symptoms, neurophysiological abnormalities, and/or cognitive impairments (1–4). Recent neuroimaging studies have reported in retired US football players who played contact football from an early age, corpus callosum microstructural changes relating to chronic neurological impairments (5,6). Further, imaging of former professional soccer players, with and without a history of concussion, has revealed cortical thinning along with reduced memory performance compared to age-matched controls (7).

Despite concussion being regarded as a common injury in rugby codes (8–13), little research currently exists into the chronic effects of repeated head injuries. To date studies in retired elite rugby union players with a history of concussion have explored cognitive outcomes (14,15). Conversely, no studies have explored the long-term cognitive or neurophysiological effects of repeated concussion injuries in rugby league.

Similar to union, league is a full contact sport played internationally under the auspices of the Rugby League International Federation (16). Rugby league is comparable to rugby union in terms of the physicality of tackling and running. Differences between the codes include the number of players on the field (15 and 13 for union and league respectively), and league does not have 'rucks', 'mauls', 'lineouts', or have players pushing in the scrum (13). Players involved in league will have played union at some time, or vice versa (13).

To understand the chronic neurophysiological consequences of repeated concussions in contact sports, previous studies have employed electrophysiological techniques, such as electroencephalography (EEG) and transcranial magnetic stimulation (TMS) (2,17). De Beaumont et al. (2009) utilized EEG to demonstrate delayed and attenuated P3 event-related potentials; observing changes during episodic memory (P3a component), and the ability to shift attentional resources to novel stimuli presented (P3b component) in a mixed cohort of retired athletes who sustained their last concussion ~34 years prior. More recently, the utilisation

CONTACT Alan J. Pearce alan.pearce@latrobe.edu.au Department of Rehabilitation, Exercise and Sport, La Trobe University, Australia.
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of TMS has quantified electrophysiological changes in retired players with a history of repeated concussions (2,17). While measures of corticomotor conduction time, motor-evoked potential (MEP) amplitude and intracortical inhibition changes have all been quantified following a concussion (18), intracortical inhibition, reflecting γ-aminobutyric acid (GABA) receptor activity has been cited as the most consistent TMS marker illustrating neurophysiological changes following concussion (18–20). Interestingly, research in chronic manifestations of repeated concussions has shown disparate results. For example, De Beaumont et al. (2) observed increased intracortical inhibition in retired North American athletes, whilst Pearce et al. (17) found reduced intracortical inhibition in former Australian rules football players. Whilst differences in these findings may reflect the characteristics of the cohorts studied (type of sport played and differences in time following last concussion when tested), as well as the TMS protocols employed (see methods section for description of TMS dependent variables), abnormalities in intracortical inhibition suggest further exploration is required. Further studies, across a range of contact sports, are required in exploring the long-term manifestations of multiple concussions on brain neurophysiology assessed by TMS (18).

This is the first study to present data on the long-term neurophysiological, motor and cognitive changes in retired professional rugby league players with a history of concussion injuries during their career. We hypothesized that compared to age-matched controls, retired rugby league players with a history of concussions would demonstrate reduced TMS intracortical inhibition; and associated decreased performance in cognitive tests for working memory, short-term learning and attention, fine dexterity and slowed visuomotor reaction time, compared to age-matched controls without history of head injury.

Methods

Approval and recruitment

Fifty male participants were recruited for the study. All participants were recruited through approved advertisement flyers and also via word of mouth. Twenty-five participants had played professionally at the elite level (National Rugby League, Australia), and were compared to 25 participants who had never received a concussion injury (Table 1). Control participants recruited, were age and educated matched, and had never played contact sport and had never sustained a concussion injury. Inclusion criteria for recruitment required all participants to be between 40 and 65 years of age, and not have been diagnosed with a neurological condition, or if they had sustained a brain injury outside of sport (e.g., motor vehicle accident). Recruited players were to have played in a formal competitive league with their last reported concussion a minimum of 10 years prior. With participant's self-reporting head injury from at least one decade previously, we used a definition of concussion as a head injury that results in the player missing the following game (17,22).

All participants were pre-screened for suitability to TMS, and all testing procedures were completed in one laboratory visit taking approximately 60 min. The University human research ethics committee, conforming to the Declaration of Helsinki, approved the study.

Motor control and cognitive assessments

Motor control and cognitive assessments were employed from previous sports concussion studies (17,23). Fine movement control was assessed via the established O'Connor Finger Dexterity test (Lafayette Instruments, USA) (24–26). Demonstrating good-to-excellent predictive ability (27), the O'Connor test requires individuals to pick up, manipulate and place three small pins into each hole. Similar to previous concussion studies (17,23), a modified form of the O'Connor test was utilised by measuring the time across three rows of the board (30 holes in total) (27). To account for learning effects (26,27) participants fully familiarised themselves prior to assessment.

Using the standardized tasks from the Cambridge Neuropsychological Test Automated Battery (Cambridge Cognition, UK), participants' cognitive performance was assessed using visuomotor reaction time, spatial working memory, associated learning, and intra-extra dimensional shift (17,23,28).

Visuomotor reaction time assessed both the participant's reaction time (difference in time of stimulation presentation and initiation of movement by releasing the button on the press pad) and movement time (time from release of press pad to touch the target displayed on the tablet screen) (28). Spatial working memory required participants to find tokens revealed behind boxes, whilst remembering boxes previously containing found tokens, with scores calculated for total errors (28), as well as utilisation of a strategy for improving working memory performance (29). Paired associative learning measured the participant's ability to learn new information via the locations of discrete patterns concealed behind

Table 1. Participant characteristics (mean and 95% CI).

	Elite	Control	*t* statistic	*p* value
Age (years)	48.4 [45.8, 51.0]	48.8 [45.9, 51.7]	0.69	0.49
Height (cm)	185.0 [182.0, 187.9]	178.1 [176.2, 180.1]	3.9	>0.01
Weight (kg)	100.7 [95.7, 105.7]	84.5 [80.8, 88.3]	5.2	>0.01
Handedness (Index) (21)	77.9 [57.6, 98.3]	68.2 [34.65, 91.7]	.75	0.46
Education (Years)	13.9 [10.5, 16.2]	14.8 [11.6, 17.5]	1.17	0.25
Number of concussions	8.5 [4.7,11.3]	n/a	n/a	n/a
Time since last concussion (years)	18.8 [15.9, 21.6]	n/a	n/a	n/a

n/a: not applicable.

boxes on the screen. Scores were calculated for errors detected at the 6-shape and 8-shape stages (28). Intra-extra dimensional shift assessed the participant's visual discrimination with shifting and flexibility of attention by displaying two random figures. Participants learn which is the correct figure and maintains the correct response until the computer changes the figures (without notice). Scores were calculated for errors detected and the stages successfully completed (28).

Transcranial magnetic stimulation, m-wave and electromyography (EMG) recordings

TMS allows for the examination of cortical excitability, via quantification of the MEP, that is useful for interpretation of changes in brain physiology for motor cortex plasticity or, conversely, with brain disorders (30). Using previously described methods (31–33), TMS was applied over the contralateral motor cortex with surface electromyography (sEMG; PowerLab 4/35, ADInstruments, Australia) recording 500 ms sweeps. sEMG activity was recorded using bipolar Ag/AgCl electrodes, with an intra-electrode distance of 2 cm positioned over the first dorsal interosseous (FDI) muscle of the participant's dominant hand adhering to the Non-Invasive Assessment of Muscles (SENIAM) guidelines for sEMG (34).

Active and resting MEPs were obtained using a MagPro R30 stimulator (MagVenture, Farum, Denmark) with a MC-B65 Butterfly Coil (MagVenture, Farum, Denmark). For reliability of coil placement participants wore a snugly fitted cap (EasyCap, Germany), positioned with reference to the nasion-inion and interaural lines. The cap was marked with sites at 1 cm spacing in a latitude–longitude matrix to ensure reliable coil position throughout the testing protocol (35).

Following identification of the 'optimal site', where the largest MEP could be observed, motor threshold determination was undertaken. Motor threshold provides a measure of the lowest stimulation intensity to generate a MEP waveform (36). Active motor threshold (aMT), where the participant holds a low-level tonic contraction, provides a measure of corticospinal excitability with dependence on the spinal segmental level excitability (30,37). In contrast, resting motor threshold (rMT) quantifies the corticomotor excitability of a central core of neurons reflecting both neuronal membrane excitability, and non-*N*-methyl-D-asparte (NMDA) receptors glutamatergic neurotransmission (36). aMT was identified by delivering TMS stimuli, during a controlled, low-level voluntary contraction of the FDI muscle at 10% of Maximal Voluntary Contraction (MVC), from a level below the participant's threshold, in 5% of stimulator output steps, and in 1% steps closer to threshold, until an observable MEP of at least 200 μV and associated cSP could be measured in at least five of 10 stimuli (35,38). rMT determination was completed using the same protocol as aMT, but with the muscle in a relaxed state. rMT was defined as an observable MEP being at least 50 μV in five of the 10 stimuli (39).

Stimulus-response curves for MEP excitability and cSP inhibition were completed using single pulse TMS of increasing intensities (17). Ten stimuli at random intervals between 8 and 10 s, were delivered at intensities of 110%, 130%, 150% and 170% of aMT (39). A break of 30 s was provided after each intensity level to avoid potential muscular fatigue. The MEP waveform, quantified as the peak-to-trough amplitude, represents the segment of corticomotor neurons activated by TMS (40) (see supplementary file A for examples of MEPs). As the MEP amplitude increases with stimulus intensity in a sigmoid manner, stimulus-response curves provide data on the physiological processes reflecting excitatory behaviour of corticomotor neurons. For example, at low intensities the MEP consists of a single wave (I1), whereas at higher stimulus intensities, the MEP is more complex, representing additional waves (I2-I4) contributed by trans-synaptic activation of excitatory interneurons mediated by a number of neurotransmitters including glutamate and neuromodulators, such as acetylcholine, dopamine, and norepinephrine (41). Pragmatically, the stimulus-response curve allows for comparison of corticomotor behaviour at low and higher stimulus intensities in a range of research designs, such as before and after an intervention (42), or between groups for brain disorders or injury (17,23).

Following the MEP, the cSP can be observed as interruption of EMG activity of the target muscle. Similar to the MEP, the duration of the cSP increases with stimulus intensity (38) with spinal mechanisms contributing to the first 50 ms (43) and corticomotor mechanisms contributing to the later part of the cSP (>50 ms) that are suggested to be mediated by $GABA_B$ receptor activity (38,44). For further in-depth discussion regarding the physiological mechanism of the MEP and cSP, the reader is directed to Ziemann (41).

Direct muscle responses (M-wave) were obtained from the FDI muscle by supramaximal electrical stimulation (pulse width 1 s) of the median nerve under resting conditions (DS7A, Digitimer, UK) (42). An increase in current strength was applied to the radial nerve until no further increase in amplitude was observed in the sEMG (M_{MAX}). To ensure maximal responses, the current was increased an additional 20% and the average M_{MAX} was obtained from five stimuli each separated by between 6 and 9 s (42).

Single pulse MEPs, from active conditions, were measured and normalized as a percentage of M_{MAX} (42). Corticomotor latency was calculated as the time between stimulation of the motor cortex to the onset of the MEP (18). cSP duration was taken from the onset of the MEP waveform (during active contraction of the FDI muscle) to the return of uninterrupted EMG (38).

Paired-pulse measures

Short latency intracortical inhibition (SICI) measured using paired-pulse TMS with an initial sub-threshold (conditioning) pulse followed by a suprathreshold (test) pulse between 1 and 5 ms through the same stimulating coil (41,45) producing a reduced, or inhibited, test MEP. It has been suggested that the conditioning pulse elicits short-lived inhibitory post-synaptic potentials which inhibits action potential generation mediated by $GABA_A$ receptor activity when the test stimulus is generated (45). SICI was measured with the FDI at rest using an interstimulus interval (ISI) of 2 ms, conditioning stimulus of 80% rMT and a test stimulus of 125% (17,23). Fifteen sweeps were delivered at random intervals between 8 and 10 s and

SICI was expressed as a ratio of the paired-pulse MEP to the single pulse resting MEP measured also at 125% (17,23,46).

Long intracortical inhibition (LICI), also tested by suprathreshold paired-pulse TMS at intervals between 50 and 200 ms, provides a complimentary measure of $GABA_B$ receptor activity to the cSP (41). This is because the physiological features can be disassociated through interventions such as different muscular contractions (47) or with fatiguing exercise (48). LICI was quantified in the resting FDI with 15 sweeps, delivered between 8 and 10, with an ISI of 100 ms, and suprathreshold conditioning and test stimuli at 125% of rMT (17).

Data analyses

All data were screened for normal distribution using Shapiro-Wilk tests, and were normally distributed. All data were compared between groups using independent samples *t*-test. Values are presented as mean and 95% confidence intervals (CI), and effect size (Cohen's *d*) was used to calculate effect differences between groups (≤0.5 = small; 0.51–0.8 = medium; ≥0.81 = large) (49). Correlations (Pearson's *r*) were performed between significant TMS variables and movement tests (O'Connor, reaction time, movement time). Alpha was set at $p \leq 0.05$.

Results

Participants recruited completed all tests with no adverse effects. Group comparisons (Table 1) showed no difference in age ($p = 0.49$; $d = 0.05$), or education, ($p = 0.25$; $d = 0.33$); but differed in height ($p > 0.01$; $d = 1.09$) and weight ($p > 0.01$; $d = 1.46$). Retired players self-reported an average of 8.5 concussions (where they missed competing the following week), with their last concussion occurring a mean 18.7 years previously.

Motor control and cognitive assessments

Cognitive and motor control assessments are presented in Table 2. Motor testing revealed that the retired rugby league group performed significantly poorer in the O'Connor fine motor task compared to controls ($p = 0.02$, $d = 0.8$).

Visuomotor reaction times showed that while movement time to the stimulus was not different between the groups ($p = 0.47$; $d = 0.24$), the rugby league group was significantly slower in reacting to the stimulus ($p < 0.01$; $d = 0.89$).

Cognitive testing generally showed that the rugby league participants were able to complete the final stage for paired associative learning ($p = 0.06$; $d = 0.63$), and intra-extra dimension shift ($p = 0.10$; $d = 0.47$). Similarly with the spatial working memory testing, rugby league participants utilized a strategy (29), similar to controls, to complete all stages of the working memory protocol ($p = 0.11$; $d = 0.52$). However, overall performance across all tests showed significantly difference between groups (paired associative learning: $p < 0.01$; $d = 1.06$; spatial working memory $p = 0.02$; $d = 0.77$; Intra-extra dimension shift: $p < 0.01$; $d = 1.04$).

TMS motor threshold and corticomotor excitability

Table 3 presents TMS motor threshold (active and resting) and corticomotor excitability (latency and normalized MEP amplitude) measures. There were no significant differences observed between groups for aMT ($p = 0.29$ and $d = 0.31$) or rMT ($p = 0.54$ and $d = 0.16$), and corticomotor latency (active: $p = 0.06$; $d = 0.69$; resting: $p = 0.11$; $d = 0.49$). Normalized MEP ratio showed no differences between groups at all stimulus intensities (130%: $t = 0.36$, $p = 0.72$; 150%: $t = 0.33$, $p = 0.75$; 170%: $t = 0.41$, $p = 0.65$, Figure 1a).

TMS intracortical inhibition

Intracortical inhibition differences (Figure 1b) were observed between the two groups, with the rugby group showing a significant reduction in cSP duration at stimulation intensities at 130% ($t = -3.11$, $p < 0.01$ and $d = 0.92$), 150% ($t = -2.44$, $p = 0.02$ and $d = 0.78$) and 170% ($t = -3.06$, $p < 0.01$ and $d = 1.11$) above aMT. Supplementary file A illustrates overlaid EMG sweeps for all participants in the rugby group compared to typical examples in the control group at 130% aMT. No differences were observed between groups for SICI ($p = 0 \cdot 69$; $d = 0 \cdot 22$; Table 3), but significant differences were found in LICI between groups ($p = 0 \cdot 03$; $d = 0 \cdot 77$; Table 3). Significant correlations were found between cSP duration and O'Connor at 130% ($r = -0 \cdot 41$, $p < 0{\cdot}01$), 150% ($r = -0 \cdot 39$, $p = 0 \cdot 01$) and 170% ($r = -0 \cdot 45$, $p < 0 \cdot 01$) of aMT; and cSP duration and reaction time at 130% ($r = -0 \cdot 52$, $p < 0 \cdot 01$), 150% ($r = -0 \cdot 33$, $p = 0 \cdot 03$) and 170% ($r = -0 \cdot 30$, $p = 0 \cdot 05$) of aMT. No significant correlations were found between cSP duration and movement time. A significant correlation was observed between LICI and O'Connor ($r = -0 \cdot 53$, $p < 0 \cdot 01$). No significant correlations were found between LICI and reaction or movement time.

Table 2. Motor and cognitive assessment (mean, 95% CI).

	Elite	Control	*t* statistic	*p* value
O'Connor (s)	263.25 [239.1, 287.4]	225.4 [205.6, 245.1]	2.4	0.02
Visuomotor reaction time (ms)	324.0 [307.4, 340.6]	289.3 [271.1, 307.6]	2.74	>0.01
Visuomotor movement time (ms)	336.66 [306.2, 367.1]	321.2 [295.5, 346.9]	0.73	0.47
Paired associative learning (8-shape stage errors)	26.4 [18.0, 34.8]	10.5 [6.0, 15.0]	3.12	>0.01
Paired associative learning (6-shape stage errors)	4.3 [2.6, 6.0]	2.1 [0.9, 3.4]	1.95	0.06
Spatial working memory (errors)	28.3 [19.9, 36.7]	15.0 [8.4, 21.6]	2.35	0.02
Spatial working memory (strategy)	32.4 [29.8, 34.9]	29.33 [26.9, 31.8]	1.63	0.11
Intra-extra dimensional shift (stages)	8.7 [8.5,9.0]	9 [9.0, 9.0]	1.71	0.10
Intra-extra dimensional shift (errors)	23.3 [15.8, 30.7]	10.8 [7.3, 14.3]	2.85	>0.01

Table 3. Single and paired pulse TMS measures (mean, 95% CI).

	Elite	Control	*t* statistic	*p* value
Active motor threshold (%)	39.4 [36.5, 42.2]	36.9 [33.4, 40.5]	1.05	0.29
Resting motor threshold (%)	50.5 [45.5, 55.6]	49.3 [44.1, 54.5]	0.61	0.54
Active latency (ms)	24.3 [23.2, 25.3]	22.9 [22.4, 23.5]	1.95	0.06
Resting latency (ms)	25.9 [23.6, 28.3]	24.8 [23.9, 25.7]	1.63	0.11
Short latency intracortical inhibition (% rest MEP amplitude)	0.29 [0.23, 0.36]	0.27 [0.19, 0.34]	0.39	0.69
Long intracortical inhibition (% test MEP amplitude)	0.56 [0.46, 0.67]	0.39 [0.28, 0.50]	2.17	0.03

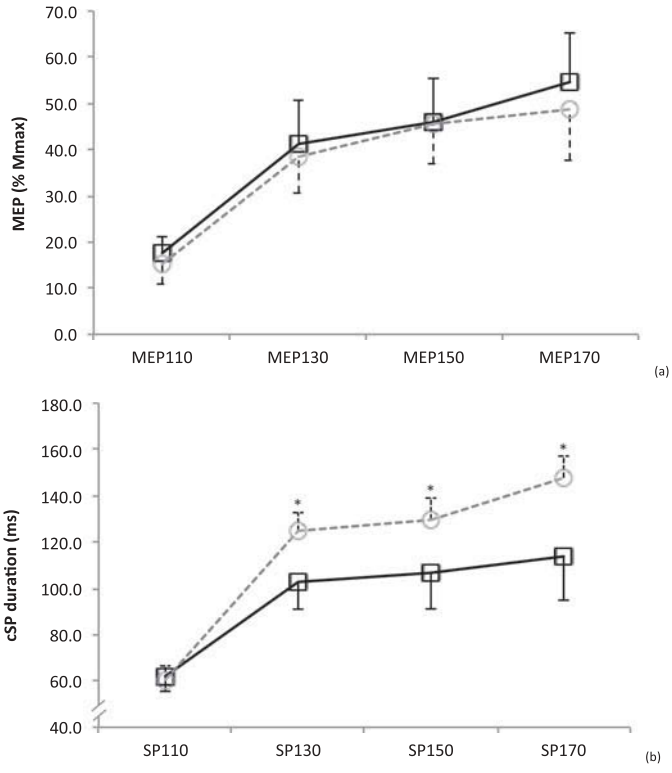

Figure 1. Stimulus response curves for normalised MEP amplitude (a) and CSP duration (b) between the rugby group (solid line) and the controls (dashed line). No differences were observed for normalised MEP amplitude between groups (a), however at suprathreshold stimulus intensities at 130%, 150%, and 170% there was a significant reduction in CSP duration seen in the rugby group (b). Asterisk indicates significance ($p < 0.05$), error bars indicate 95% confidence intervals.

Discussion

This study is the first to report alterations in neurophysiological measures and functional cognitive-motor outcomes in retired professional rugby league players with a history of concussions during their careers. To date, studies on concussion history in either rugby code have been limited to hospital admissions (50), or chronic cognitive changes in self-reported concussion (14,15). Whilst our cognitive-motor results supports previous data on retired professional athletes with a history of concussions (2,14,15,17,51,52), the novel finding of our study was the observation of significant neurophysiological changes in intracortical inhibition and the correlations between intracortical inhibition and cognitive-motor outcomes. The study also found increased corticomotor latency in the rugby players; however, this is likely to be due to the significant difference in height, and subsequent limb length (53–56).

It is important to note that the relative novelty of TMS for the assessment of long-term manifestations of repeated concussions makes clinical translation, at this point in time, difficult. However, emerging evidence suggests potential sequelae of repeated sports concussion on the motor system. Indeed, Rabadi and Jordan (57) assert that the motor system is typically the earliest clinical manifestation of chronic repeated head trauma, preceding cognitive decline (2,17). Therefore, with increasing utilisation of TMS in concussion research, the sensitivity of the technique is now being recognised as a confirmatory modality to detect chronic physiological changes in the cortico-motor system (58). In particular, TMS can highlight neurophysiological alterations that can be used to detect the cumulative effects of repeated concussions in sport (19).

Although the exact mechanisms for intracortical inhibition are not fully understood (59), the significant changes observed in intracortical inhibition (cSP and LICI) in the retired group suggest altered $GABA_B$ receptor activity which play an important inhibitory role in neural transmission (60,61). The robustness of TMS intracortical inhibition has been demonstrated across various populations. For example, differences in inhibition have been reported in cross-sectional studies in healthy older versus healthy younger adults (46,62,63), as well as investigations comparing brain injury, neurodegenerative conditions or psychiatric disorders to age-matched controls (64–68). It is worth noting, however, that the observed changes have not been uniform. Difference in data may be attributed to the dynamic process of chronic neurophysiological changes in the motor cortex at an individual level. For example in healthy older and younger adults Sale and Semmler (62) and Oliviero et al. (63) reported reductions in cSP in older adults whilst McGinley et al. (46) found lengthening in cSP in older adults, attributing the different findings to the muscle studied and TMS protocols employed. Similarly studies in brain injury, such as stroke, have also reported shortening or lengthening in the cSP as a result lesion location (64). Decreased cSP duration has been found in some, but not all, TMS studies of Alzheimers/dementia (69). Reviews by Magnus-Haraldsson et al. (66) and more recently by Bunse et al. (67) in psychiatric disorders have reported increased and decreased cSP that are likely to reflect medication (type and whether medicated at time of testing).

Despite disparities across studies, our data reporting a significant decrease in cSP duration and increased LICI

shows for the first time that intracortical inhibition is altered in retired rugby league players. It also supports previous studies that have also shown alterations in cSP in retired contact sport athletes with a history of concussions (2,17). The reduction in cSP and increased LICI in this study appear to support, in part, previous findings of reduced intracortical inhibition in retired Australian rules football players (17) but differ to the findings of increased cSP duration in retired North American athletes (2). The inconsistencies between studies may reflect the TMS protocols employed such as the stimulus intensities and ISIs. Our study used stimulus intensities from 110% to 170% aMT and ISIs of 2 ms and 100 ms, similar to studies in Australian football (17) but different to studies in North American football and hockey reporting MEP data recorded at 110–130% aMT and ISIs of 2, 3, 9 and 12 ms (2).

It may also be argued that the nature of concussions specific to these sports contributed to differences in findings. For example, concussion impact studies have shown that the majority of impacts resulting in concussion in rugby occurred in the temporal region (70) and Australian football occurred mainly in the temporal but also the occipital region (70) whereas biomechanical data in US football have reported forces directed mainly to the frontal area (71). However, given the limited availability of both head impact biomechanics and TMS data in these football codes, caution should be employed interpreting associations of cSP changes to characteristics of head impacts between these sports. Whilst the sport studied may be an influencing factor on neurophysiological outcomes, it would seem that the disparate measurement protocols employed by different studies have implications on the understanding of the long-term effects of repeated concussions on neurophysiological function at the group level. It is therefore important that gaining consensus for future protocols will allow for a more comprehensive understanding on the mechanisms of neurophysiological changes following head trauma while appreciating the characteristics of different sports which may contribute to different findings.

As with many retrospective studies, the main limitation of this study concerns the historical self-reporting of player concussions, as well as lack of diagnosis from medical staff at time of concussion. Our finding of 8.5 self-reported concussions is consistent with a number of prior studies that presented actual number of self-reported concussions (72–74). However, as suggested previously (75), reliance on self-reported concussion history needs to be viewed with caution as the under-reporting of concussion may be as high by a factor of 6–10. To assist with player recollections of their concussions, inclusion criteria for recruitment required a classification of concussion, which involved a player to miss the following game due to a head injury (22). However, players participating in the study anecdotally reported that they were not adequately assessed at the time of the concussion, and generally overlooked by the medical personnel unless they suffered loss of consciousness or experienced post-traumatic amnesia, similar to previous reports (2,76). Therefore, it was not possible for recruited players to provide full diagnostic reports of their concussions.

Future research should consider longitudinal designs, as opposed to the cross-sectional design currently employed. For example, differences in weight between groups may have contributed to observed differences in corticomotor outcomes (although this is unlikely as a number of experimental and clinical studies have demonstrated that weight does not influence the MEP (77–80)). By undertaking a repeated measures design, allowing for intra-subject comparison, rather than between-groups comparison will provide greater confidence in players' longer-term outcomes following multiple concussions sustained during their professional careers. Longitudinal studies, and incorporation of other measures, for example investigating functional or evoked effective connectivity using TMS-EEG (81), or neuroimaging techniques such as GABA magnetic resonance (MR) spectroscopy or MR diffusion tensor imaging, will be valuable to contextualise changes in TMS intracortical inhibition observed in this study.

In conclusion, this study is the first to show neurophysiological evidence of alterations in intracortical inhibition and changes in cognitive function in retired professional rugby league players with a history of concussions. Further studies in different contact sports are required to assess the chronic effects of repetitive sports concussions on long-term neurological outcomes.

Declaration of Interest

The authors report no conflicts of interest.

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ORCID

Alan J. Pearce http://orcid.org/0000-0002-9264-9880

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