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Oculomotor cognitive control abnormalities in Australian rules football players with a history of concussion

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Abstract

This study used oculomotor, cognitive, and multimodal magnetic resonance imaging (MRI) measures to assess for neurological abnormalities in current asymptomatic amateur Australian rules footballers (i.e., Australia's most participated collision sport) with a history of sports-related concussion (SRC). Participants were 15 male amateur Australian rules football players with a history of SRC greater than 6 months previously, and 15 sex-, age- and education-matched athlete control subjects that had no history of neurotrauma or participation in collision sports. Participants completed a clinical interview, neuropsychological measures and oculomotor measures of cognitive control. MRI investigation involved structural imaging, as well as diffusion tensor imaging and resting state functional MRI sequences. Despite no group differences on conventional neuropsychological tests and multimodal MRI measures, Australian rules football players with a history of SRC performed significantly worse on an oculomotor switch task: a measure of cognitive control that interleaves the response of looking towards a target (i.e., a prosaccade) with the response of looking away from a target (i.e., an antisaccade). Specifically, Australian footballers performed significantly *shorter* latency prosaccades and found changing from an antisaccade trial to a prosaccade trial (switch cost) significantly more difficult than control subjects. Poorer switch cost was related to poorer performance on a number of neuropsychological measures of inhibitory control. Further, when comparing performance on the cognitively more demanding switch task with performance on simpler, antisaccade/prosaccades tasks which require a single response, Australian footballers demonstrated a susceptibility to increased cognitive load, compared to the control group who were unaffected. These initial results suggest that current asymptomatic amateur Australian rules football players with a history of SRC may have persisting, subtle, cognitive changes, which are demonstrable on oculomotor cognitive measures. Future studies are required in order to further elucidate the full nature and clinical relevance of these findings.

Key words: mild TBI, cognition, functional MRI, DTI, cavum septum pellucidum, ocular motor

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Introduction

There is some evidence associating a history of sport-related concussion (SRC) with long-term neurological abnormalities.[1-9] For example, studies in retired American football players who sustained repetitive brain injuries earlier in life have reported evidence for structural brain changes such as cavum septum pellucidum (CSP),[5,6] as well as abnormalities in brain white matter detected by diffusion MRI.[7] However, most of these studies have been conducted in retired professional collision sport athletes, and the few studies that have investigated the potential long-term effects of SRC in current amateur athletes have reported mixed results. For example, asymptomatic amateur hockey players with a history of SRC had abnormalities detected by diffusion MRI and resting-state functional MRI (rs-fMRI) measures,[9] while other diffusion and rs-MRI studies found no significant differences between young athletes with or without a history of SRC.[10-12] Further, little is known about whether changes in cognitive function also occur in these players.

The oculomotor system is a widely distributed neural network that is susceptible to diffuse pathology, with damage manifesting as a measureable change in eye movement (i.e., saccades) metrics.[13-17] Even the simplest task of generating a saccade to a visual target (i.e., a prosaccade), requires the integration of sensory information with cognitive processes, in particular executive function, working memory, attention, and inhibitory control.[17] The antisaccade task is a classic oculomotor measure, that requires the inhibition of a prepotent response formed **in response to the** onset **of a** peripheral target in favour of generating a saccade in the opposite direction to the target.[17] A highly sensitive measure of cognitive control, the antisaccade task has been shown to be a useful measure in the acute stage of SRC, with deficits (increased saccade latency and erroneous responding) present up to six months post injury.[14,18] This suggests that concussion may affect the cognitive control of behaviour longer term.

Cognitive control may also be assessed using a task switching paradigm,[19] which ascertains the ability to flexibly shift between behavioural responses according to changes in environmental or internal demands. A common oculomotor version of this paradigm interleaves the dominant response of looking at a suddenly appearing peripheral stimulus

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(prosaccade) with the non-dominant response of looking away from a peripheral stimulus (antisaccade), increasing the difficulty of performing either task (higher cognitive load). An extreme dominance asymmetry between trial types is typical for the **prosaccade** response, due to the relative automaticity of its occurrence, resulting in a unidirectional switch cost; a switch cost is *only* evident when switching from an antisaccade to a prosaccade.[20-22] Generally, performance is poorer (prolonged latencies, increased errors) for switch trials compared to repeat trials, with the magnitude of the switch cost (switch – repeat) considered a measure of cognitive control; larger differences represent poorer cognitive control.[23] This measure has not been used previously in the context of SRC.

Australian rules football is the most participated collision sport in Australia. Few studies have investigated the long-term effects of SRC in current/active Australian rules footballers and, to our knowledge, no study has used oculomotor measures to evaluate cognitive function or neuroimaging measures in this context. Therefore, the aim of this study was to use oculomotor assessments (prosaccade task, antisaccade task and task switching) and multimodal MRI methods, alongside conventional neuropsychological assessments, to investigate asymptomatic amateur Australian rules football players with a history of SRC. It was hypothesized that assessment of oculomotor tasks and advanced MRI methods would identify subtle abnormalities in Australian rules football players with a history of SRC relative to age-, education-, and sex-matched control athletes with no history of neurotrauma.

Materials and methods

Participants

Male Australian rules footballers with a history of SRC (n = 15) were recruited from a premier amateur division football club in the Victorian Amateur Football League. Age-, education-, and sex-matched athletes (n = 15) with no history of neurotrauma or participation in collision sports were recruited from local amateur sporting teams (i.e., basketball, tennis, cricket, swimming, and track and field) as controls. Any individuals with a medical history of neurosurgery, major psychiatric disturbance, or medical

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contraindications to MRI were also excluded. Australian football players who had been diagnosed with a neurotrauma in the past 6 months were excluded. Study procedures were approved by the Melbourne Health Human Ethics (#2015.012) committee and all participants provided written informed consent prior to the study.

Clinical Interview

A general medical history questionnaire was administered to each participant. This included information on demographics, concussion history (e.g., number, timing, persisting symptoms), sporting history, medical history, educational history, drug and alcohol use, as well as spelling, reading, speaking, math, and learning problems.[24] The Sports Concussion Assessment Tool 3 (SCAT3) was included as part of the medical history questionnaire.[25] The alcohol use disorders test (AUDIT) was used to detect any differences in risky or hazardous drinking.[24,26] The Beck Depression Inventory (BDI) was used to measure the severity of self-reported depression.[27]

Oculomotor Testing

Oculomotor assessment consisted of three discrete tasks: prosaccade block task (only prosacades performed), antisaccade block task (only antisaccades performed), and a switch task (interleaved prosaccades and antisaccades). Horizontal displacement of both eyes (i.e., saccades) was recorded using an Eyelink II dark pupil, video-oculography system (SR-Research Ltd., Mississauga, Canada). This is a high resolution (noise limited at < 0.01°) and high acquisition rate (500 Hz) system. Participants were seated in a darkened room, 840 mm in front of a **75hz** CRT monitor **(resolution: 1024 X 768)**. Task stimuli were presented on a black background and comprised crosses (**visual angle 1°**) all of equal luminance generated using Experiment Builder (version 1.6.121). A 5pt calibration sequence was performed prior to each task, with *in vivo* task calibrations performed to confirm accuracy of the initial calibration.

The prosaccade block task assesses ability to make visually guided saccades. Participants fixated on a central green cross for 1,250 – 1,750 ms, and performed saccades to a

suddenly appearing peripheral target (1,250 – 1,750 ms), as it stepped horizontally and pseudo-randomly (5° or 10° left or right of center).[15]

The antisaccade block task measures ability to inhibit a prepotent/reflexive response generated by a suddenly appearing target, and to generate a response in the equal and opposite direction. Participants fixated on a central green cross. Following 1,250-1,750 ms fixation, the central green cross disappeared concomitantly with the appearance of a green target cross at either 5° or 10° left or right of center (1,250-1,750 ms). Participants performed a saccade to the diametrically opposite position, without looking at the green target.[15]

The switch task requires a participant to switch between performing prosaccades and antisaccades.[28,29] Participants fixated a central cross that was either blue or purple. Following 1250, 1500, 1,750 ms, a green target cross appeared in one of four peripheral locations (5° left, 5° right, 10° left, 10° right). The color of the central cross indicated how a participant was to respond to the appearance of a peripheral green target cross (i.e., blue = prosaccade; purple = antisaccade). After 1500 ms a central fixation square appeared, reorienting the participants gaze centrally in preparation for the next trial. All participants were familiarized with the rules of the task by way of a guided example followed by a practice block of 12 trials (6 antisaccade trials, 6 prosaccade trials). Three test blocks were completed each consisting of 32 prosaccade trials and 32 antisaccade trials presented in a pseudo-random order. Trials were classified as a repeat trial where two consecutive trials required the same response, or a switch trial where a different response was required on two consecutive trials. Across the three test blocks 48 prosacade and 48 antisaccade trials were presented with even numbers of switch and repeat trials. The first trial of every block was excluded from switch/repeat trial analyses since they represented neither a switch nor repeat trial.

Oculomotor Analyses

For all oculomotor tasks, saccadic latency (ms) was calculated from a monocular recording, as the temporal difference between peripheral target onset and saccade onset, with

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saccade onset calculated using a velocity criterion of 30° per second. Trials were removed from the analysis of latency where; (1) the task was not completed in accordance with task rules (error); (2) fixation was not maintained within 1.5° of the central target; (3) a blink occurred around trial onset that was thought to affect saccade onset; (4) no response was made within the trial period; (5) a saccade made within 100 ms of **target** onset. Independent of task errors, approximately 3.1% of total trials were removed across all tasks.

Proportion of errors were calculated for all oculomotor tasks as a proportion of total trials.

Prosaccade block task: saccades made in the opposite direction to the peripheral target.

Antisaccade block task: saccades made towards the peripheral green target cross.

Switch task: performance of an prosaccade during an antisaccade trial or vice versa.

In addition, for the switch task, switch cost was calculated for both latency and error and was defined as the relative difference between a switch trial and a repeat trial (i.e., switch trial performance – repeat trial performance). For this task design, previous studies have shown that only prosaccade trials elicit a switch cost (unidirectional switch cost: prosaccade switch – prosaccade repeat).[20-22] As such, switch cost was only investigated for prosaccade trials. A larger switch cost indicates increased difficulty with switching and poorer cognitive control. For the analysis of latency, only trials not preceded by an error were included since evidence suggests that switch costs are only evident when the previous trial is correct.[20]

To investigate the effect of cognitive load, performance on the prosaccade block task was compared with performance on the switch task prosaccade trials, and the antisaccade block task performance was compared with performance on the switch task antisaccade trials. Switch task trials were considered as having a higher cognitive load because they require additional cognitive processing due to the requirement to maintain both task sets simultaneously whilst inhibiting the unrequired task set.

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Neuropsychological Testing

Participants underwent a neuropsychological battery that included the Hayling's Sentence Completion Test (HSCT),[30] the Stroop Color Word Test (Golden version),[31] the Symbol Digit Modalities Test (SDMT),[32] the Digit Span subset from the Wechsler Adult Intelligence Scale,[33] and the Paced Auditory Serial Addition Test (PASAT).[34] These tests provide measures related to inhibitory control, mental flexibility, working memory, and attention, and were chosen because performance on these tasks has been associated with performance on the oculomotor tasks that were also tested.[30-34] The National Adult Reading Test (NART) was used to estimate premorbid intelligence.[35] All tests were administered in a quiet room by a trained researcher.

MRI Acquisition

MRI acquisition was performed on a 3 T scanner (Magnetom Prisma, Siemens, Erlangen, Germany). A three-dimensional magnetization prepared rapid gradient echo (MP-RAGE) sequence was used to obtain T1-weighted images for structural analyses with the following parameters: Repetition time (TR) = 2400 ms; echo time (TE) = 2.24 ms; inversion time (TI) = 1060 ms; flip angle = 8°; field of view (FOV) = 256 x 256 mm^2; 192 slices with thickness = 0.8 mm; resolution = 0.8 x 0.8 x 0.8 mm^3; and total acquisition time = 6 minutes 38 seconds.

Two-dimensional rs-fMRI blood oxygen level dependent (BOLD) images were acquired using a single-shot gradient-echo echo planar imaging (EPI) sequence (TR = 2500 ms; TE = 31.0 ms; 34 slices; resolution = 3.4 × 3.4 × 3.4 mm^3; acquisition time = 7 minutes 35 seconds) for functional connectivity analysis. During rs-fMRI acquisition, subjects were asked to lie motionless with their eyes closed and to think about nothing.

Two-dimensional diffusion tensor images were acquired with a spin-echo EPI sequence with diffusion weighting gradients applied in 64 directions with b-value = 3000 s/mm^2. Other imaging parameters included: TR = 10400 ms; TE =83 ms; FOV = 256 x 256 mm^2; matrix = 128 x 128; slice thickness = 2 mm; resolution = 2 x 2 x 2 mm^3; and total acquisition time = 11 minutes 59 seconds.

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MRI Analyses

The incidence and severity of CSP was assessed using MP-RAGE images. CSP was defined as cerebrospinal fluid (CSF) being visible between two leaflets of the septi pellucidi on the coronal slices.[6] An investigator, blinded to the study design, assessed for the presence of the CSP and characterized it according to previously described methods.[36] The CSP length was measured by counting the number of consecutive coronal slices resolving the CSP and multiplying by slice thickness. The CSP was graded using the coronal slice that showed the greatest cavity. Grades were defined as: 0 (absent), 1 (questionable), 2 (mild), 3 (moderate) and 4 (severe).

For functional connectivity analysis, rs-fMRI images from each subject were processed using an in-house automated pipeline developed from freely available software packages.[37] A parcellation atlas was used to define cortical regions related to seven resting-state networks (RSNs): visual, somato-motor, dorsal attention, ventral attention, limbic, frontal-parietal, and default mode.[38] Regions within each RSN were extracted based on four pre-specified anatomical lobes (i.e., frontal, parietal, temporal, occipital) and resulted in the identification of forty distinct cortical regions across both hemispheres. Cortical surface labels, obtained using T1-weighted images, were obtained from each subject (FreeSurfer; http://surfer.nmr.mgh.harvard.edu) and were used to transform each region from the atlas space to the subject native space. Subsequently, the forty cortical regions were transformed to the subject rs-fMRI spaces for analysis.

The rs-fMRI data were first processed using the FSL package and included skull stripping (Brain Extraction Tool, BET),[39] interleaved slice timing correction and motion correction (MCFLIRT algorithm),[40] spatial smoothing (6mm full width at half maximum), and temporal high-pass filtering (>0.01 Hz) to eliminate low frequency artifacts. Noise components in the pre-processed data were removed using independent component analysis-based methods (FSL Xnoiseifier, FIX).[41] In addition, the time-points of large motion perturbations in the original four-dimensional resting-state time series dataset were identified (FSL Motion Outliers) using a threshold of 0.2 mm (a stringent threshold for scrubbing) applied for frame-wise displacement.[42] A confound matrix was created for the large motion time-points and was included as additional event variable in the analysis to remove nuisance

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variables from the resting-state dataset (fMRI Expert Analysis Tool, FEAT). CSF and WM masks were defined on the MNI152 template space and then transformed into the subject rs-fMRI image space. Six motion parameters and the average time series from CSF and WM masks were regressed out as nuisance variables (FEAT) from the pre-processed noise reduced (FIX) four-dimensional rs-fMRI dataset. The time-point volumes with motion greater than the threshold were removed from the "cleaned" rs-fMRI dataset. Average BOLD signal of all voxels within individual regions from this processed dataset was computed for all time points for subsequent analysis. The Pearson correlation coefficients (r) of averaged rs-fMRI-obtained BOLD signal time series between pairs of regions in each network were converted to z-scores using Fisher's r-to-z transformation ($z = 0.5 \times \ln [(1 + r)/(1 - r)]$).

Diffusion tensor imaging (DTI) was used to calculate fractional anisotropy (FA), apparent diffusion coefficient (ADC), axial diffusivity (AD), and radial diffusivity (RD), all of which are markers for white matter integrity.[8,9,43-45] A study template was generated using the MRtrix software package (www.mrtrix.org) from 10 control subjects selected at random. A reverse phase-encoded image was used with FSL's topup tool for distortion, and eddy current, correction.[46] Bias field correction was performed using N4 bias field correction and images were normalized using the b_0 white matter image intensity.[47] Images were upsampled by a factor of two, as this has been suggested to improve image registration and statistical analysis when subsequently using cluster-based statistical methods.[48] Fibre orientation distributions (FODs) were computed using constrained spherical deconvolution (CSD) with a group (n=10) average response function and the study template image was constructed using symmetric diffeomorphic FOD registration.[49,50] After template construction, FOD images for all participants were registered to the study template using symmetric diffeomorphic FOD registration (subject-to-template warp).[50]

Tract-based spatial statistics (TBSS) were used for all statistical analyses related to DTI.[51] FA, ADC, AD, and RD maps were calculated for each subject and warped into template space using the calculated subject-to-template diffeomorphisms. Group differences were assessed using non-parametric permutation testing and threshold-free cluster enhancement (TFCE). An FWE-corrected $p < 0.05$ was considered significant.

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Statistical Analyses

SPSS 22.0 (IBM Corp., Armonk, USA) was used for statistical analyses, with the exception of the TBSS analyses of diffusion MRI described above. Chi-squared tests were used to assess differences in the presence and grade of CSP. For oculomotor tasks and neuropsychological tests, comparisons between players and controls for each dependent variable were performed by way of a multivariate ANOVA. **T**o investigate**, the effect of cognitive load, that is** whether **antisaccade/prosaccade** performance was different between block and switch task design, a 2 (group: players, controls) by 2 (task design: block task, switch task) by 2 (trial type: antisaccade, prosaccade) repeated measures ANOVA was performed. Post hoc analyses were performed using paired samples t-test or Wilcoxon signed rank tests where violations to normality were found. Statistical significance was set at $p < 0.05$. Pearson's correlations were used to compare oculomotor performance with neuropsychological test performance. Where violations to normality occurred, Spearman's rho was used instead.

Results

Clinical History

The values presented in this section represent the mean ± standard error of mean. There were no significant differences between the Australian footballers and control subjects in terms of age and education ($p > 0.05$). For the Australian footballers, the average age was 24.3 ± 0.9 years and the average education was 15.1 ± 0.4 years. For the control group, the average age was 23.4 ± 0.4 years and the average education was 15.2 ± 0.3 years. There were no significant differences between the groups on the NART (Australian footballers = 117.2 ± 0.74; control subjects = 117.14 ± 0.71; $p > 0.05$) and BDI (Australian footballers = 3.4 ± 0.60; control subjects = 3.21 ± 1.05; $p > 0.05$). The AUDIT scores did not differ significantly between the two groups (Australian footballers = 10.6 ± 0.9; control subjects = 8.4 ± 1.5; $p > 0.05$). One control participant reported problems with spelling and learning. One of the Australian rules footballers reported problems with reading, spelling and learning. No participants reported any problems with mathematics or speech.

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The Australian footballers had played 14.33 ± 1.49 years of collision sport, and reported an average number of 2.2 ± 0.3 previous concussions. Five footballers reported a single previous concussion, three footballers reported two previous concussions, six footballers reported three previous concussions, and one reported four previous concussions. The average time since the last concussion was 60.8 ± 9.6 months. There were no significant differences between the groups identified by the SCAT3 (i.e., number of symptoms, symptom severity score, SAC total, BESS). None of the footballers reported any persisting symptoms as a result of their previous concussion(s).

Oculomotor Assessment

Oculomotor findings are presented in Table 1. For the switch task, a significant effect of group was found (p = 0.03) with **post hoc analyses indicating that** Australian footballers performed significantly *shorter* latency prosaccades than control subjects (prosaccade repeat trials: p = 0.010) and demonstrated a significantly larger switch cost (prosaccade errors) than control subjects (p = 0.021). **No significant effect of group was found for the prosaccade block task or the antisaccade block task (p > 0.05).**

A significant group by task design by trial interaction was found (**Error:** p = .002**; Latency:** p = .02). **Specifically,** Australian footballers demonstrat**ed** significantly more antisaccade errors on **the cognitively more difficult** switch task antisaccade trials compared with **the simpler** antisaccade **block** task (p < 0.001), and shorter latency prosaccade on **the cognitively more difficult** switch task trials compared with the **simpler** prosaccade **block task** (p = 0.010). In contrast, **the control group did not perform differently on each task**.

[Insert Table 1 here]

Neuropsychological Assessment

There were no significant differences between the groups on any of the neuropsychological measures (p > 0.05, Table 2). However, for Australian football players

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only, poorer switch cost (error), was significantly related to poorer performance on the Digit Span (forward: r = .67, p = 0.010, backwards: r = .61, p = 0.015), PASAT (r = .56, p = 0.029), and HSCT (r = .53, p = 0.040).

[Insert Table 2 here]

MRI

The groups did not significantly differ in the prevalence, length, and severity of CSP (p > 0.05, Figure 1).

[Insert Figure 1 here]

There were no significant group differences on functional connectivity, computed from rs-fMRI-derived BOLD signals, for all 7 networks (p > 0.05, Table 3).

[Insert Table 3 here]

TBSS analysis of DTI metrics found no significant differences between the groups on FA, ADC, AD, and RD (p > 0.05, Figure 2).

[Insert Figure 2 here]

Discussion

This study used oculomotor, neuropsychological, and multimodal MRI methods to compare active/current asymptomatic male amateur Australian rules footballers with a history of SRC to active/current athlete control subjects without a history of neurotrauma or participation in collision sport. Significant group differences were found on the oculomotor switch task, with Australian footballers performing significantly worse than the control group. There were no significant group differences in any of the neuropsychological or MRI measures.

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The testing of the oculomotor network provides a sensitive tool to explore neuronal processes that may be adversely affected by SRC.[13,14,52] Although the majority of the previous literature implicates oculomotor impairments in the acute stages of SRC,[13,14,52] there is some initial research indicating that dysfunction on oculomotor tests also occurs in the chronic stages of mild TBI.[14,18] In particular, a previous study found that mild TBI patients had deficits on the antisaccade task that were present at least six months post-injury.[14] While our study did not find group differences in the antisaccade task, we did find an increased susceptibility of Australian footballers to cognitive load on antisaccade error performance. The performance of an antisaccade error represents the failure to inhibit a prepotent response elicited by the peripheral target.[53] For the Australian footballers with a history of SRC, increasing the cognitive load on the inhibitory system might have increased the likelihood of erroneous responding, which was not similarly evident in the control group. The Australian footballers also performed significantly shorter latency saccades both in comparison to control subjects and as a function of increasing cognitive load. Previous research in patients with clinically isolated syndrome, who have subtle disseminated pathology, have similarly showed shortened latency saccades relative to healthy controls.[15] This finding was considered a consequence of poorer inhibitory control altering the balance of excitation/inhibition at the superior colliculus, resulting in the expedited release of saccades and thus shortened latency saccades.

The oculomotor switch task also allows a measure of cognitive control. Generally, task switching requires the formation of accurate and persistent task-set representations for each of the required responses (i.e., prosaccade response, antisaccade response), as well as inhibitory control to prevent the execution of an erroneous task set. During a switch trial, the facilitation of the appropriate task set concomitant to the clearance of the previous task set generally incurs a behavioral cost (i.e., switch cost) relative to a task repeat trial, and provides a measure of cognitive control.[54] Australian footballers demonstrated a significantly larger switch cost (error) compared to control subjects, suggesting poorer cognitive control and susceptibility to switching. Interestingly, switch cost differences were only evident for error not latency, suggesting that Australian footballers had increased difficulty inhibiting the unwanted antisaccade task set when the following trial required a prosaccade response. However, when able to inhibit the

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unwanted antisaccade task set, Australian footballers were no slower than controls at performing subsequent prosaccade. In support of this, poorer performance on cognitive measures of inhibition (i.e., PASAT, Digit span, and HSCT) was related to poorer switch cost.

A multimodal MRI examination consisting of assessment for the presence of CSP, as well as DTI and rs-fMRI analyses did not identify any significant group differences. This is inconsistent with some previous studies reporting that a history of SRC is associated with increased incidence of CSP in retired professional American football players.[6,7] These discrepancies are likely due to the younger age of our cohort and their relatively low exposure to SRC. Findings have been mixed from diffusion MRI and rs-fMRI studies that involve participants with a similar age and SRC history to those in our study. Consistent with our findings, Churchill and colleagues found no significant differences on rs-fMRI between athletes with or without a history of concussion.[10] Furthermore, a study by Meirer *et al.* found no significant difference between American football players with or without a history of SRC on fractional anisotropy, a diffusion MRI measure.[11] On the other hand, Orr *et al.* found abnormalities in young adult ice hockey players on both diffusion MRI and rs-fMRI measures.[9] However, this study involved participants that had suffered a concussion as early as 3 months prior to testing, and may have been confounded by the sub-acute effects of the most recent SRC. Furthermore, they utilized additional diffusion MRI measures (e.g., diffusion kurtosis) that may be more sensitive than the traditional DTI measures that we employed in the present study. It should also be noted that each of these studies were similar to our study in that they were limited by low participant numbers.

In conclusion, this study found significant differences between Australian footballers with a history of SRC and control subjects on the oculomotor switch task. These occurred in the absence of any group differences on the MRI or neuropsychological outcomes that were examined. Potentially, these deficits may be related to poorer inhibition and cognitive control in the Australian footballers with a history of SRC, however future research is required to confirm these findings, identify the underlying causes, and further elucidate their clinical significance. There are some limitations with the study that should be noted.

For example, because all of the Australian rules footballers in this study had a history of concussion it is not possible to distinguish between the possible effects of concussion versus participation in collision sport (i.e., subconcussive impacts) on the measures that were examined. Future studies could include collision sport athletes with and without a history of concussion to provide insight into this question. This study was also limited to amateur athletes, and it would be of interest to expand this research into professional athletes who may have increased exposure to Australian rules football and associated mild brain injuries. It is also important to consider the small group sizes when interpreting the present findings, and future longitudinal studies with increased subject numbers should be conducted.

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Author Disclosure Statement

No competing financial interests exist.

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Tables

Table 1: Oculomotor measurements for controls and Australian footballers (Mean, Confidence intervals). * significantly lower than control; # significantly greater than Switch task – Antisaccade switch error (i.e., cognitive load); $p < .05$.

Task	Measure	Control	Australian Footballer
Prosaccade	Latency (ms)	176 (165, 191)	177 (163, 192)
	Error (%)	0.1 (-.07, .35)	.2 (-.11, .51)
Antisaccade	Latency (ms)	266 (241, 286)	274 (257, 300)
	Error (%)	10.0 (5.0, 16.1)	9.4 (4.0, 15.3)
Switch task	Prosaccade repeat latency	182 (168, 194)	163 (157, 172)*
	Prosaccade switch latency	194 (173, 207)	177 (167, 189)
	Prosaccade switch cost (latency)	12.2 (-1.6, 19.8)	13.5 (5.3, 21.6)
	Prosaccade repeat error (%)	1.4 (.1, 2.9)	0.0 (0, 0)
	Prosaccade switch error (%)	2.6 (.5, 5.1)	5.1 (2.5, 7.7)
	Prosaccade switch cost (error)	1.1 (-1.4, 3.9)	5.1 (2.5, 7.8)*
	Antisaccade repeat latency	273 (245, 297)	269 (256, 287)
	Antisaccade switch latency	260 (234, 284)	267 (256, 284)
	Antisaccade repeat error (%)	11.8 (5.6, 17.1)	17.1 (9.3, 26.7)#
	Antisaccade switch error (%)	10.6 (5.3, 16.2)	8.5 (2.8, 15.4)

Table 2. Neuropsychological data for controls and Australian footballers (Mean ± SE).

Neuropsychological Test	Controls	Australian Footballers
HSCT	6.07 ± .18	5.67 ± .23
Stroop	58.15 ± 1.72	54.87 ± 4.20
SDMT	62.54 ± 3.03	64.93 ± 1.54
PASAT	89.86 ± 2.48	90.44 ± 2.14
Digit Span		
Forward	12.29 ± 0.63	12.13 ± 0.70
Backward	7.86 ± 0.51	8.33 ± 0.72
Total	11.00 ± 0.94	12.20 ± 0.97

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Table 3. Averaged functional connectivity measure for the seven resting-state networks in controls and Australian footballers. The values shown are functional connectivity (Mean ± SE) in each group.

Network	Controls	Australian Footballers
Visual network	1.25 ± 0.05	1.28 ±0.04
Somato-motor network	1.30 ± 0.04	1.25 ± 0.05
Dorsal attention network	0.98 ± 0.04	0.92 ± 0.06
Ventral network	1.04 ± 0.03	1.04 ± 0.05
Limbic network	0.75 ± 0.05	0.80 ± 0.06
Frontal-parietal network	0.82 ±0.03	0.82 ±0.06
Default mode network	0.92 ± 0.03	0.95 ± 0.04

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Figure Legends

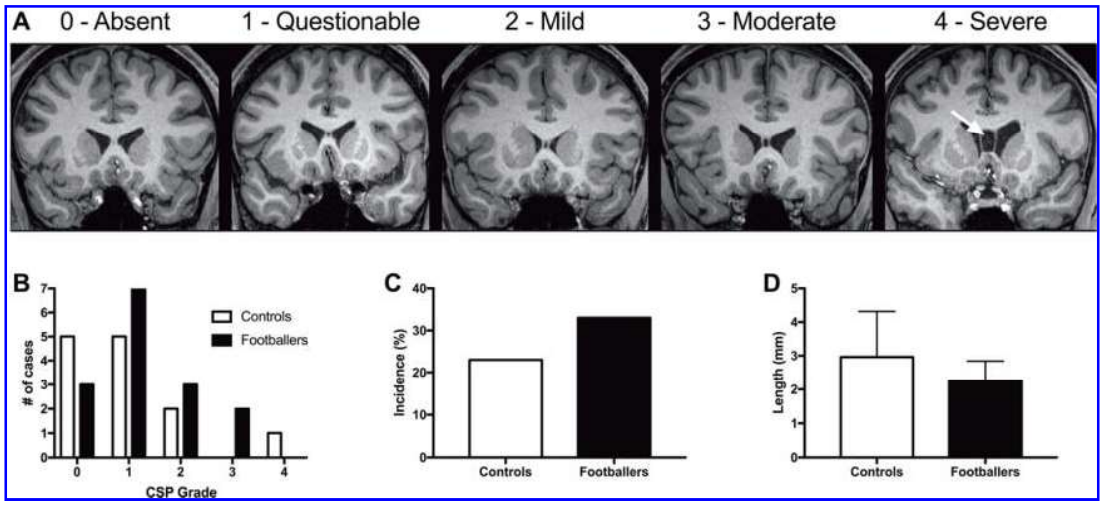

Figure 1. Cavum septum pellucidum (CSP) in controls and Australian footballers. **(A)** Representative images of each CSP grade. CSP was considered 'present' for grades 2 and above. White arrow indicates CSP. **(B)** Number of cases of each CSP grade in each group. **(C)** Incidence of CSP in each group. **(D)** Average length (mm) of CSP in each group. There were no significant differences found between the groups on any of the CSP measures.

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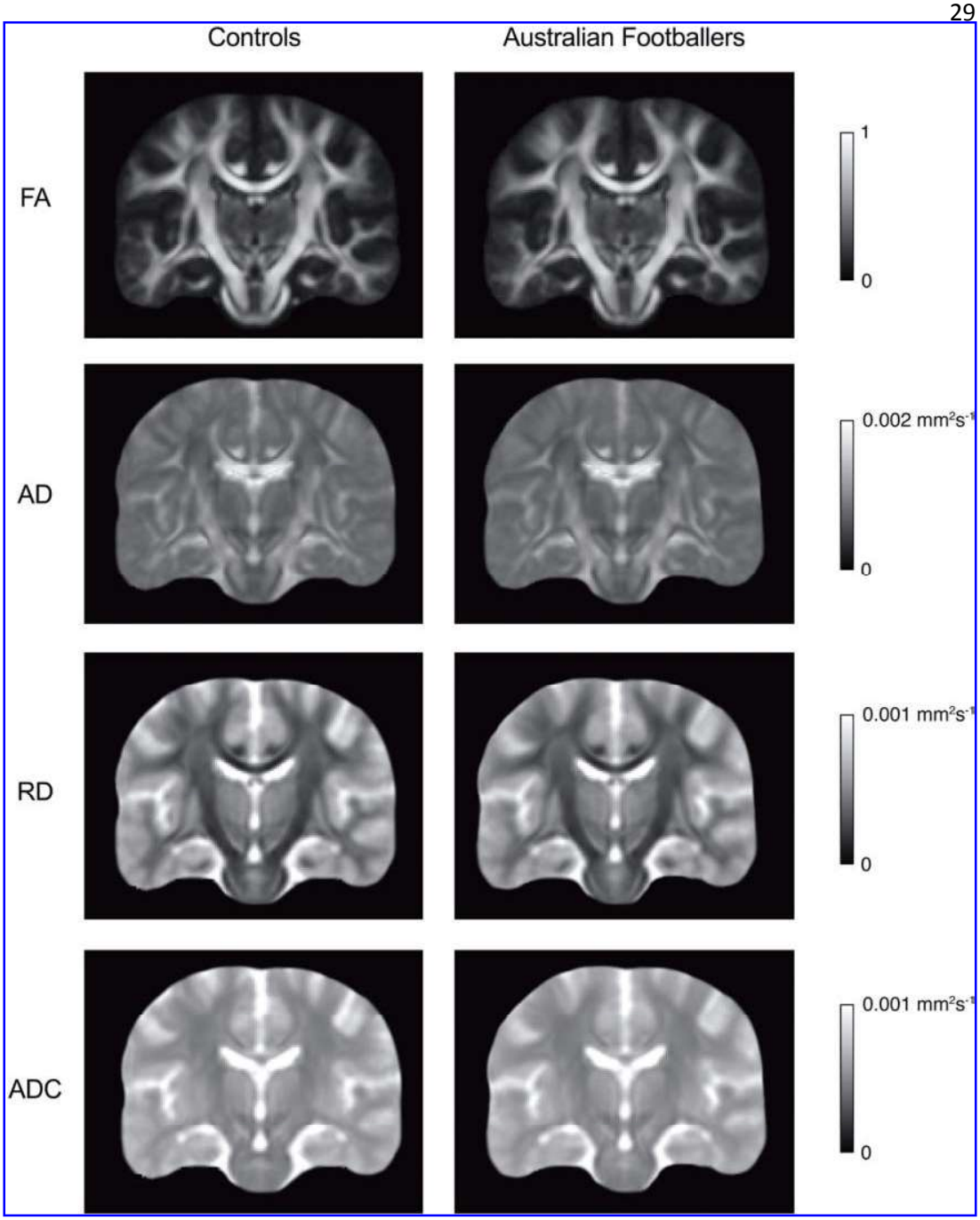

Figure 2. Diffusion tensor imaging (DTI) in controls and Australian footballers. **(A)** Fractional anisotropy (FA), **(B)** axial diffusivity (AD), **(C)** radial diffusivity (RD), and **(D)** apparent diffusion coefficient (ADC) template images for each group. Tract-based spatial statistics (TBSS) found no significant differences between the groups on any of the DTI measures.