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Article *in* Journal of Science in Sport and Exercise · February 2021

DOI: 10.1007/s42978-020-00101-1

Kelsey Logan
Cincinnati Children's Hospital Medical Center

Weihong Yuan
Cincinnati Children's Hospital Medical Center

Kim Barber Foss
Cincinnati Children's Hospital Medical Center

Jed A. Diekfuss
Emory University

Journal of Science in Sport and Exercise
https://doi.org/10.1007/s42978-020-00101-1

ORIGINAL ARTICLE

Is it Possible to Protect the Adolescent Brain with Internal Mechanisms from Repetitive Head Impacts: Results from a Phase II Single Cohort, Longitudinal, Self-Control Study

Kelsey Logan[1,2] · Weihong Yuan[3,10] · Kim D. Barber Foss[1,4,11] · Jed A. Diekfuss[1,11,12] · Christopher A. DiCesare[1] · James Leach[5,10] · Mekibib Altaye[6] · Rhodri S. Lloyd[7] · Gregory D. Myer[1,8,9,11,12]

Received: 8 September 2020 / Accepted: 19 November 2020

Abstract

Purpose To quantify the effects of an externally worn collar device for mitigating the influence of repetitive head impacts on alterations to diffusion tensor imaging (DTI) metrics of white matter.

Methods Fifteen female high-school soccer athletes (age: 14.00–16.98 yrs) completed pre- and post-season DTI over two consecutive years, including measures of diffusivity, changes in which may be associated with brain dysfunction. The collar was worn during year 1 (Yr1) but not during year 2 (Yr2). Athlete exposures (AEs) and head impact exposure were recorded over the competitive seasons.

Results There were no significant differences in AEs or head impact exposures between Yr1 and Yr2 ($P > 0.05$). In Yr2, there was significant pre- to post-season mean diffusivity and/or axial diffusivity reduction in multiple WM regions (corrected $P < 0.05$). Pre- to post-season mean diffusivity, axial diffusivity, and radial diffusivity decreases were $3.04\% \pm 2.53\%$, $2.97\% \pm 2.19\%$, and $3.37\% \pm 3.34\%$, respectively, significantly greater than pre- to post-season changes in Yr1 (mean diffusivity: $-0.31\% \pm 1.78\%$, $P = 0.0014$; axial diffusivity: $-0.02\% \pm 2.25\%$, $P = 0.0014$; radial diffusivity: $-0.63\% \pm 2.10\%$, $P = 0.0030$).

Conclusions Mild bilateral compression to athletes' internal jugular vein through collar application may have increased intracranial blood volume and spatially redistributed head-impact-derived brain energy absorption. However, future research is needed to elucidate the potential clinical significance of WM changes of various degrees.

Clinical trails registration NCT03014492.

Keywords Soccer · Brain injury · DTI · Female athletes · White matter

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✉ Kim D. Barber Foss
Kim.Foss@cchmc.org

[1] The SPORT Center, Division of Sports Medicine, Cincinnati Children's Hospital Medical Center, Burnet Avenue, MLC 10001, Cincinnati, OH 45229, USA

[2] Departments of Pediatrics and Internal Medicine, University of Cincinnati, College of Medicine, Cincinnati, OH, USA

[3] Pediatric Neuroimaging Research Consortium, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

[4] Rocky Mountain University of Health Professions, Provo, UT, USA

[5] Division of Radiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

[6] Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

[7] Youth Physical Development Centre, Cardiff School of Sport and Health Sciences, Cardiff Metropolitan University, Cardiff, UK

[8] Departments of Pediatrics and Orthopedic Surgery, University of Cincinnati, College of Medicine, Cincinnati, OH, USA

[9] The Micheli Center for Sports Injury Prevention, Waltham, MA, USA

[10] Department of Radiology, University of Cincinnati, College of Medicine, Cincinnati, OH, USA

[11] Emory Sport Performance and Research Center, Flowery Branch, GA, USA

[12] Department of Orthopaedics, Emory University School of Medicine, Atlanta, GA, USA

Introduction

Girls' high school soccer has become increasingly popular over the past 20 years, with participation increasing from 226,636 athletes in the 1996–1997 school year to 388,339 athletes (a 58% increase) in the 2016–2017 school year [23, 24]. FIFA reports 30 million female players worldwide, with a goal to increase this to 60 million by 2026 [9]. This growth is reflected in the overall popularity of the sport, as it consistently remains the 4th most popular high school sport for girls, behind only track and field, volleyball, and basketball [24]. As the popularity of the sport has increased, so has the concussion injury rate [14]. It is difficult to determine whether this increase is due to more aggressive play, improved symptom recognition, or factors unique to female athletes (e.g. overall strength, neck strength, body size, etc.). A review of concussion etiology in girls' high school soccer showed that 51.3% of concussions occurred in athlete-athlete contact situations; contact with another player accounted for 61.9% of concussions sustained in heading situations [7]. In addition to increased concussion diagnoses, there is increased scrutiny on impacts to the head that do not result in a clinically diagnosable concussion. On their own, these hits, termed sub-concussive impacts (SCI), might not pose significant risk to an athlete after each individual event, but can be cumulatively detrimental [2, 6, 8]. The emergence of neuroimaging techniques has made examining the impacts of these potential injuries more viable to researchers. One such method, known as diffusion tensor imaging (DTI), has been used to evaluate the integrity of white matter (WM) tracts following repetitive SCI [3, 27, 33].

Asymptomatic athletes may experience objective neurological deficits following repetitive sports-related head impacts [18]. Any disturbance of the brain's white matter may result in cognitive dysfunction; this disturbance can be seen on DTI as changes in diffusion, either increased or decreased, both of which may indicate abnormality in brain function. DTI has demonstrated efficacy in evaluating asymptomatic athletes for microstructural alterations of WM following repetitive SCI [2, 21, 22, 38] and allows for an objective evaluation of microscale WM alterations from these impacts. For instance, soccer headers was associated with altered microstructural integrity of temporo-occipital WM tracts that correlated with inferior memory scores in asymptomatic adults playing soccer [17, 26]. A previous study of asymptomatic high school girl soccer athletes, using both DTI and fMRI, also demonstrated microstructural WM changes following a single season of competitive play, with partial recovery seen 3 months post-season [39]. A relatively small but growing body of literature has documented that maturational WM DTI changes are seen throughout childhood development and continue more slowly through adolescence, with some stability occurring in young adulthood [34]. In general, normal maturation related increases in fractional anisotropy and decreases in radial diffusivity and mean diffusivity, are noted in most WM regions, with variable and more minimal changes in axial diffusivity. This may represent increased myelination, axonal density, and fiber compactness occurring with brain maturation [5]. How regular competitive sport play or concussive and SCI alter this normal maturation process is unknown. Diffusivity metrics (radial diffusivity, mean diffusivity, axial diffusivity) have been found to be more sensitive than FA values in detecting sports related head impact changes, with most (but not all) studies demonstrating diffusivity decreases [19, 21, 22, 38].

DTI uses four metrics to evaluate WM alterations: fractional anisotropy, mean diffusivity, radial diffusivity and axial diffusivity. Fractional anisotropy represents the normalized variance of three eigenvalues, which is an index for the degree of diffusion directionality. Mean diffusivity is the average of the three eigenvalues. The axial diffusivity is the eigenvalue along the principle eigenvector; radial diffusivity is the average of the eigenvalues along the two other eigenvectors. Alterations in diffusivity metrics have been associated with a range of neurologic sequala, including multiple sclerosis, Alzheimer's disease, and chronic traumatic brain injury [13, 16]. Research indicates that fractional anisotropy, more generally, reflects axonal integrity and the degree of myelination; whereas axial diffusivity, more specifically, provides a measure of axonal injury and radial diffusivity characterizes myelin abnormalities [1, 10, 25, 32]. Of these measures, mean diffusivity, axial diffusivity, and radial diffusivity generate consistent findings in detecting WM alterations in contact sport athletes [11].

To mitigate these effects, a novel internal jugular vein compression collar was designed to increase intracranial blood volume and reduce differential brain motion from head impacts [28]. *Internally* minimizing the movement of the brain fluids can limit the intracranial absorption of collision energy via elastic energy transfer. A type of internal brain cushioning appears to occur in g-force tolerant organisms via modulated intracranial volume and pressure [20, 28, 29, 35]. We reasoned that inducing mild dilation of cerebral veins (like that brought on by a yawn) may induce similar internal cushioning, using the brain's vascular system to reduce inelastic energy absorption upon head impact. The internal jugular vein compression collar (worn on the neck) was designed to promote cerebral vein filling by gently compressing the jugular veins, "taking up" the compensatory reserve volume of the cranial space. Previous studies have shown significant pre- to post-season alterations in DTI measures for those who did not wear the collar, but not in those who wore the collar during their athletic seasons [21, 22, 38]. However, none of these studies has investigated the collar effect within the same cohort of athletes based on longitudinal data from different seasons [19].

In the present study, we employed a two phase study design to capitalize on the unique opportunity to follow a cohort of athletes longitudinally, in which the collar was worn in year 1 (Yr1) and not worn in year 2 (Yr2). The purpose of the study was to quantify the effects of the collar device for mitigating the influence of repetitive head impacts on alterations to DTI metrics. This was accomplished by deconstructing inter-subject differences using a prospective, single cohort, longitudinal, self-control study design. We hypothesized greater pre- to post-season alterations in DTI-derived metrics of white matter during Yr2 (no intervention; collar not worn) compared to Yr1 (intervention; collar worn).

Methods

A cohort of 15 female high school soccer athletes were recruited from a local high school team, as part of a prospective longitudinal imaging study (age 16.7 ± 0.9 years; height 163.2 ± 5.4 cm; weight 59.8 ± 8.1 kg). All athletes in this study participated in a two-year two-stage study design, in which they wore the collar device, during all practices and games in Yr1 [19] but not in Yr2. Phase II, reported here, is a single cohort, longitudinal, self-control study. All participants underwent MRI at pre- and post-season in both Yr1 and Yr2.

The study was approved by the local Institutional Review Board. Parents/guardians and athletes provided written informed consent and assent prior to participation. Exclusion criteria for study participation included: inability to provide written consent, history of neurological deficits, previous cerebral infarction, severe head trauma, known increased intracranial pressure, metabolic acidosis or alkalosis, glaucoma (narrow angle or normal tension), hydrocephalus, recent (< 6 months) penetrating brain trauma, known carotid hypersensitivity, central vein thrombosis, known airway obstruction, or seizure disorder. Of the 15 participants, two were excluded from pre- to post-season comparison of DTI indices in Yr1 due to excessive head motion in the scan; final imaging analysis for Yr1 was based on imaging data from 13 participants. All 15 participants had valid scans at both pre- and post-season in Yr2 and were included in analysis of within-group pre- to post-season DTI change in Yr2. One participant experienced a diagnosed concussion during the study period, occurring in Yr1. Comparison of pre- to post-season DTI changes between the two years was based on data from 13 participants who completed MRI at all four time points.

At the first fitting of the collar in Yr1, a vascular technologist used ultrasound to ensure correct collar fitting and that jugular distension was achieved [22]. Following initial fitting, each athlete received instruction on proper device use for games and practices; in addition, follow up education and adjustment was made upon athlete request. Compliance of athlete attendance for the session (exposure), as well as collar wear compliance, was tracked through a custom designed app. There was 100% collar-wear compliance for games and practices throughout Yr1.

Each participant wore an X Patch accelerometer (X2 Biosystems; Seattle, Washington), during practices and competition. X2 is a small and durable device that is attached to the back of the neck behind the ear to track impacts, and it stores data for uploading to a PC. This X2 accelerometer accurately measures the severity of impacts by converting data such as high impact collision into usable data outputs. X2 data will be used in final analysis to normalize the exposures to potential concussive events. All impacts of greater than 10 g-force will be recorded and utilized in the post-season analyses. Total g-force is the cumulative g-forces over the course of the season. Average g-force is the average force per impact (i.e., total g-force / the # of impacts over the course of the season).

All MRI data were acquired on a 3 T Phillips Ingenia MRI scanner (Philips Medical Systems, Best, Netherlands), using a 32-channel head coil across all four time points. In both seasons, a similar single-shot EPI sequence was used in acquiring DTI data. In Yr1, the DTI sequence specifications were as follows: TR/TE = 8788/97 ms; field of view = 256 mm × 256 mm; acquisition matrix: 128 × 128; slice thickness = 2 mm; voxel size = 2 mm × 2 mm × 2 mm; number of slices = 68; SENSE factor = 3; number of noncolinear number of diffusion weighting directions = 61; diffusion weighting factor *b*-value = 1000 s/mm^2; number of non-diffusion weighted images (b0) = 7. In Yr2, the DTI sequence adopted a 64-direction gradient table, with the other parameters (TR, TE, FOV, matrix, b-value) remaining the same as those used in Yr1. To assess the potential effect of sequence difference, we also acquired DTI data at post-season in Yr2, using the same DTI sequence as that in Yr1. Using the same approach as later applied in the data analysis, no significant differences were found between the data acquired with the two slightly different DTI sequences based on the two datasets acquired from the 15 participants at the post-season time point of Yr2. At all four time points, a high-resolution 3D T1-weighted anatomical data set (voxel size = 1 mm × 1 mm × 1 mm) was acquired in the sagittal direction for image registration and review.

The Functional MRI of the Brain (FMRIB) Software Library (FSL) software package (www.fmrib.ox.ac.uk/fsl) was used in imaging data processing and analysis. Processed DTI parameters included fractional anisotropy, mean diffusivity, axial diffusivity, and radial diffusivity. The Tract-Based Spatial Statistics [30] approach was used in assessment of within group pre- to post-season DTI alterations in both Yr1, when all participants wore the collar device during practices and games, and in Yr2, when all participants practiced and played without the collar device. TBSS analysis was also used in assessment of pre- to post-season group difference, between Yr1 and Yr2. The "randomise" function, a FSL procedure for nonparametric permutation inference on statistical maps of imaging data that has unknown null-distribution, was used to generate null distribution to allow for modelling and inference using GLM design [37]. The 5000 permutations were used in all statistical analyses. Multiple-comparison correction was achieved through the threshold-free cluster enhancement (TFCE [31]) method incorporated into the "randomize" procedure in FSL.

As the first step in the analysis, for both Yr1 ($n=13$) and Yr2 ($n=15$), we performed voxel-wise analysis using the TBSS approach to calculate the pre- to post-season difference in DTI and tested the statistical significance of within-year pre- to post-season change based on one-sample t-test (which is equivalent to running a paired t-test in FSL) using the pre- to post-season difference DTI maps. This analysis was also repeated on the 13 athletes in Yr2. Since the findings were similar, only the results based on data from all 15 participants are included in the final reports for Yr2. Group difference of pre- to post-season change between Yr1 and Yr2 was calculated based on DTI data from the 13 participants who completed MRI scans at all four time points. In the second step in the analysis, DTI values were extracted from the WM area with significant pre- to post-season difference in Yr2 (the non-collar season) from the 13 subjects who had imaging data at all four time points. The pre- to post-season percentage changes were calculated for both Yr1 and Yr2 with the statistical significance of the year to year difference examined with paired t-test. Third, in addition to comparing the pre- to post-season percentage DTI change between the two years using data extracted from the significant regions as determined by the findings from the Yr2 (non-collar year), we also ran the voxel-wise analysis using the TBSS approach (still within the significant regions from Yr2) to compare the Yr1 with Yr2. In this analysis, a difference map was calculated between the DTI changes in Yr1 and DTI changes in Yr2 and a one-sample t-test was used to test whether the longitudinal changes in Yr1 was significantly different from Yr2.

In voxel-based TBSS analysis of group difference of pre- to post-season DTI change, in order to reduce multiple comparison penalty, area for comparison was limited to WM regions that presented pre- to post-season DTI change (mean diffusivity, axial diffusivity, radial diffusivity, or fractional anisotropy at corrected $P<0.1$) in Yr2. The threshold of P-level of 0.1 (corrected) was set subjectively and was selected to be more inclusive, while limiting the comparison to areas with at least trend level changes. The localization of the WM regions that presented either within-group, significant pre- to post-season DTI alteration in Yr2 or significant between-group difference of pre- to post-season alteration between Yr1 and Yr2 was determined based on the John Hopkins University WM tractography atlas [12].

To further explore and localize WM regions that were affected but could be protected by the collar device after a full season of exposure to repetitive head impact, a voxel-wise group comparison was made between pre- to post-season DTI change between Yr1, when participants wore the collar, and Yr2, when the cohort did not wear the collar. Comparison was made along the WM skeleton in the WM regions that presented pre- to post-season DTI change (fractional anisotropy, mean diffusivity, axial diffusivity, or radial diffusivity change at corrected P level of 0.1) in Yr 2.

Wilcoxon signed-rank test was used to test the difference of head impact exposure, in number of head impacts, average g-force, and cumulative g-force, at different g-force thresholds between Yr1 and Yr2 among the 13 participants who completed MRI at all four time points. Pearson correlation was used to test whether the significant DTI changes observed between the pre- and post-season time points in Yr2 was associated with exposure to repetitive head impacts experienced in Yr2. DTI median values (fractional anisotropy, mean diffusivity, axial diffusivity, and radial diffusivity) were extracted from brain regions that presented significant pre- to post-season alteration in Yr2 and were used in the correlation analysis.

Results

No significant differences were found in head impact exposure parameters (including number of head impacts, cumulative g-forces, and average g-force/impact) between Yr1 and Yr2 (Wilcoxon signed-rank test, all $P>0.05$). Detailed descriptive statistics at different g-force thresholds can be found in Table 1. AE exposures in year 1 (mean ± SD) 48.38 ± 5.87 were also not different from the AEs measured in follow-up year (47.92 ± 7.16; $P=0.857$).

No significant pre- to post-season DTI changes were found in any WM region during Yr1. In Yr2, significant pre- to post-season reduction was found in mean diffusivity, axial diffusivity, and/or radial diffusivity in a series of WM regions, including the anterior thalamic radiation, cortical spinal tract, forceps major, inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, and superior longitudinal fasciculus (Fig. 1, $P<0.05$, TFCE corrected; Table 2). There was a trend of fractional anisotropy increase that involved similar WM regions (only significant at $P=0.1$, corrected).

Table 1 Head impact statistics in the 13 participants who wore the collar in Yr1 and did not wear the collar in Yr2

	Yr1 (collar)				Yr2 (non-collar)			
	Range	Median	Mean	SD	Range	Median	Mean	SD
Total hits								
> 10 g	279–856	512	523	158	267–674	450	449	103
> 20 g	78–327	131	155	66.7	63–204	126	130	39.7
> 50 g	13–53	25	26.5	11.6	11–45	25	26.4	10.6
> 100 g	0–6	3	3.23	1.69	1–8	3	3.69	2.02
Total g-force								
> 10 g	5839–19,124	10,712	10,566	3470	5550–12,706	9343	9349	1957
> 20 g	2942–11,901	5238	5710	2393	3007–8194	5245	5134	1519
> 50 g	957–3780	1675	1962	831	706–3429	2013	2057	787
> 100 g	0–776	403	394.9	215.8	117.1–991.9	397.1	479.8	273.3
Average g-force								
> 10 g	17.11–22.41	20.32	20.22	1.85	15.72–24.17	20.79	21.01	2.18
> 20 g	32.57–40.24	36.98	37.14	2.10	33.15–47.72	39.63	39.90	3.93
> 50 g	67.01–87.04	74.29	74.49	4.91	64.22–97.45	76.19	78.21	8.24
> 100 g	108.99–134.34	119.72	121.42	8.39	113.18–176.82	124.14	128.46	16.51

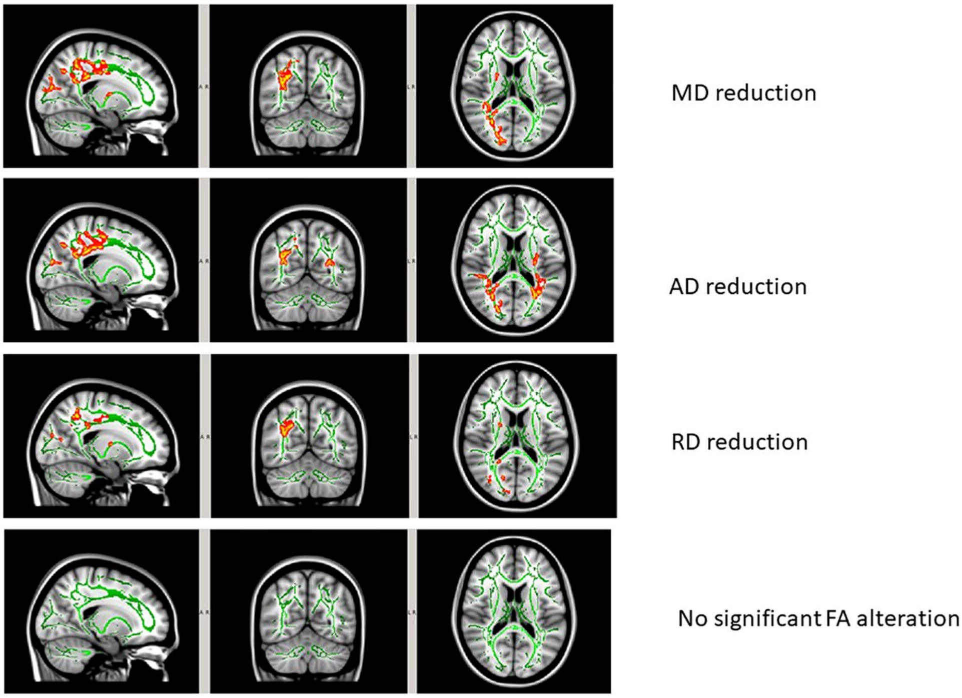

Fig. 1 Yr2, Pre to Post-Season DTI Alteration ($P<0.05$, corrected). *AD* axial diffusivity, *FA* Fractional anisotropy, *MD* mean diffusivity, *RD* radial diffusivity

Within significant regions, pre- to post-season percentage decreases in mean diffusivity, axial diffusivity, and radial diffusivity were 3.04% ± 2.53%, 2.97% ± 2.19%, and 3.37% ± 3.34%, respectively. Changes during Yr2 were significantly greater than pre- to post-season changes within the same areas during Yr1 (mean diffusivity: − 0.31% ± 1.78%, $P=0.001$, Cohen's $d=1.15$; axial diffusivity: − 0.02% ± 2.25%, $P=0.005$, Cohen's $d=0.96$; radial diffusivity: − 0.63% ± 2.10%, $P=0.003$, Cohen's $d=1.03$; paired t-tests). There was no significant group difference in the percentage change in fractional anisotropy ($P=0.13$).

As shown in Fig. 2, significantly greater mean diffusivity, axial diffusivity, and radial diffusivity reduction and/or fractional anisotropy increase ($P<0.05$, corrected) were found in WM regions in Yr2 when compared to Yr1. These WM regions include right anterior thalamic radiation, right cortical spinal tract, cingulum, forceps major, right inferior fronto-occipital fasciculus, right inferior longitudinal fasciculus, and right superior longitudinal fasciculus (Table 3).

Table 2 Volume of white matter regions with significant pre- to post-season change in Yr2, without the collar device, based on number of voxels with statistically significant change

	WM tracts	WM volumes with Pre- to Post-season DTI change				
		MD↓	AD↓	RD↓	FA↑	All
Region 01	ATR, Left	14	80	1	0	82
Region 02	ATR, Right	297	159	152	0	364
Region 03	CST, Left	12	361	8	0	373
Region 04	CST, Right	713	817	236	0	1022
Region 05	Cingulum (CG part), Left	0	118	0	0	118
Region 06	Cingulum (CG part), Right	206	232	59	0	284
Region 07	Cingulum (HC part), Left	5	10	2	0	13
Region 08	Cingulum (HC part), Right	98	100	36	0	122
Region 09	Forcep major	885	687	340	0	1198
Region 10	Forcep minor	0	0	0	0	0
Region 11	IFOF, Left	0	325	0	0	325
Region 12	IFOF, Right	821	674	363	0	959
Region 13	ILF, Left	0	518	0	0	518
Region 14	ILF, Right	229	300	164	0	406
Region 15	SLF, Left	0	583	0	0	583
Region 16	SLF, Right	1516	1365	514	0	1964
Region 17	UF, Left	0	1	0	0	1
Region 18	UF, Right	0	0	0	0	0
Region 19	SLF (temporal), Left	0	35	0	0	35
Region 20	SLF (temporal), Right	20	15	1	0	24

ATR anterior thalamic radiation, *CST* cortico-spinal tract, *CG* Cingulate Gyrus, *HC* Hippocampal, *IFOF* Inferior fronto-occipital fasciculus, *ILF* Inferior longitudinal fasciculus, *SLF* Superior Longitudinal fasciculus, *UF* Unciate fasciculus, *ns* not significant

The values in these tables are the number of voxels with statistical significance based on within-group pre- to post-season comparison. Change in the 15 participants in Yr2 when they did not wear the collar device. The WM tracts were determined using WM atlas based on John Hopkins University's ICBM WM tract probability map

Across different g-force thresholds (g-force > 10 g, 20 g, 50 g, or 100 g), no significant correlation was found between head impact exposure and the significant DTI changes found in pre- to post-season comparisons reported in yr 2.

Discussion

This study demonstrates that microstructural changes were present in multiple WM tracts following a normal season of high school girls' soccer, without clinical evidence of brain trauma or concussion. The same cohort of participants did not present with any alterations in these WM regions in the prior season when a collar was worn.

Results of this study support prior findings of DTI WM alterations in soccer players without clinical symptoms of concussion. In a study comparing young adult male soccer players to similar age and handedness swimmers, increased radial diffusivity was found in multiple WM areas of soccer players, as was higher corpus callosum axial diffusivity; fractional anisotropy did not show significant differences between groups [15]. Research with non-concussed female soccer players has shown significant mean diffusivity, axial diffusivity, and radial diffusivity changes over one season [19]. These changes partially resolved 3 months after season's end, and while the length of time that changes are present is concerning, how this impacts cognitive function remains unknown.

There is growing evidence of WM changes in concussion that persist after concussion symptoms have resolved. A study of adolescent youth with sports-related concussion showed significant whole-brain fractional anisotropy increases and mean diffusivity decreases, two months after injury [36]. In that same cohort, fractional anisotropy and mean diffusivity changes were associated with lower Sports Concussion Assessment Tool 2 scores [36]. DTI changes have been documented in pediatric athletes with cognitive and behavioral symptoms, compared to asymptomatic athletes, 3–12 months after sport-related concussion [4].

The normal WM developmental changes can complicate DTI analysis of pathologic states in children and adolescents. This becomes particularly challenging in assessing sports related head impacts, with the changes seen likely reflecting impact related WM alterations acquired over the

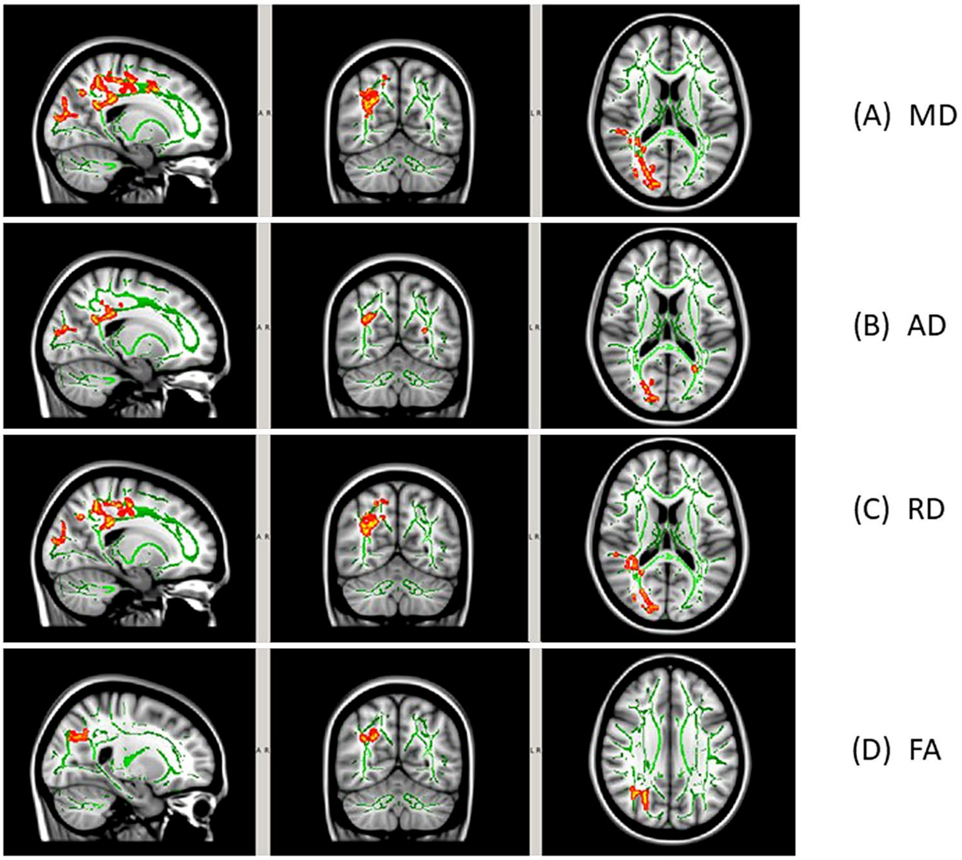

Fig. 2 WM areas with greater reduction in MD (**a**), AD (**b**), RD (**c**) or greater increase in FA (**d**) in Yr2 (when participants did not wear collar) than that in Yr1 (when participants wore collar)

entire season (accumulated acute, subacute and chronic injuries) as well as maturation related changes. In this study, we longitudinally evaluated the same subjects over two consecutive sports seasons. We expect that developmental changes in WM DTI metrics would be present over both seasons and be relatively minor (compared with earlier childhood development). Thus, the difference in the pre- to post-season changes in DTI metrics between the two seasons would likely represent the effects of the intervention (collar wearing).

Previous research has demonstrated that, despite similar quantities and magnitudes of head impacts, a non-collar wearing group showed significant WM changes pre- to post-season, whereas those wearing the collar did not show significant alterations [22]. Additionally, a significant relationship was found between head impact exposure experienced during the season and pre- to post-season DTI changes in the non-collar group. In this study, the absence of the collar in Yr2 was associated with DTI changes similar to the non-collar group in Yr1. This finding lends additional support to the concept that collar wearing limits head impact related DTI changes in female soccer players. It should be noted that the cross-over design in the present study was based on the assumption that collar wearing in Yr1 does not impact presence or absence of response in Yr2. Whether a season of wearing the collar device offered any potential persistent effect for WM protection in the next season, or whether the changes as found in Yr2 in the present study would have been greater without the device in Yr1, are questions that warrant further investigation.

Strengths of this study are the cohort and study design itself, with two years of high school soccer season data on head impacts, injury exposure, and repeat imaging on the same 13 subjects. A limitation of the study was the inability to monitor subjects year-round for head injury exposure. While the longitudinal study design from one season to the next allows for each subject to serve as their own control, there was potential for differences in skill and musculoskeletal development that might affect type and magnitude of head impact exposure. However, magnitude and quantity of head impact exposures were monitored closely for every game and practice and were similar for the current study participants. Optimally, a true control group would be beneficial in study design. A second limitation is the clinical relevance of these study findings, specifically the opportunity to link DTI derived metrics with clinical outcomes in future research. Additionally, the current report is not powered to do region of interest analysis by DTI; this is an area for future study and replication of the current results. Although we have previously described ultrasound procedure for

Table 3 Volume of white matter regions with significant changes seen in Yr2 (no collar device), compared to Yr1 (with collar device), based on number of voxels with statistically significant change

	WM tracts	WM volumes with significant group difference				
		MD↓	AD↓	RD↓	FA↑	All
Region 01	ATR, Left	12	8	6	0	14
Region 02	ATR, Right	166	65	138	6	203
Region 03	CST, Left	1	0	0	0	1
Region 04	CST, Right	574	101	397	0	597
Region 05	Cingulum (CG part), Left	0	0	0	0	0
Region 06	Cingulum (CG part), Right	166	79	133	0	191
Region 07	Cingulum (HC part), Left	3	0	1	0	3
Region 08	Cingulum (HC part), Right	83	53	43	18	93
Region 09	Forcep major	696	343	504	47	825
Region 10	Forcep minor	0	0	0	0	0
Region 11	IFOF, Left	0	0	0	0	0
Region 12	IFOF, Right	576	121	544	70	681
Region 13	ILF, Left	0	1	0	0	1
Region 14	ILF, Right	187	60	192	34	233
Region 15	SLF, Left	0	0	0	0	0
Region 16	SLF, Right	1482	115	1163	74	1646
Region 17	UF, Left	0	0	0	0	0
Region 18	UF, Right	0	0	0	0	0
Region 19	SLF (temporal), Left	0	0	0	0	0
Region 20	SLF (temporal), Right	20	2	27	0	31

ATR anterior thalamic radiation, *CST* cortico-spinal tract, *CG* Cingulate Gyrus, *HC* Hippocampal, *IFOF* Inferior fronto-occipital fasciculus, *ILF* Inferior longitudinal fasciculus, *SLF* Superior Longitudinal fasciculus, *UF* Unciate fasciculus

The values in these tables are the number of voxels with statistical significance based on between group comparison of pre- to post-season change (between Yr1 and Yr2. 13 participants successfully completed MRI at all four time points. The WM tracts were determined using WM atlas based on John Hopkins University's ICBM WM tract probability map

fitting the collar device (12), it is not practically possible at this time to measure jugular distention with the collar device during strenuous activity, and there is no evidence that the distention is maintained during these activities. This a goal of future research where we can do cerebrovascular flow during exercise with multi-vascular technologies, such as fNIRS. Finally, as reported in the manuscript, there was a significant pre- to post-season DTI alteration in Yr2 when the athletes did not wear the collar device. While the magnitude of change based on percentage difference is only at the level of ~ 3%, the effect size as reflected in the comparisons suggest that these changes are clinically important and warrant further investigation in a larger scale prospective study.

Implications for Clinical Practice

This study shows that despite comparable exposure to repetitive head impacts in two sports seasons, participants demonstrated significant WM diffusivity reductions when they did not wear the jugular vein compression collar. By contrast, no similar changes were evidenced when the same cohort wore the device during practices and games in their previous competitive season. This further documents that WM changes can occur in normal sport seasons without clinical symptoms of concussion. The difference in WM alterations observed between the two seasons suggests this may be related to a neuroprotective effect of increased blood volume, achieved via jugular vein compression, by reducing energy absorption in the brain from head impacts. Further investigation is needed to study whether WM changes seen in girls' high school soccer play is associated with long-term cognitive deficits and whether the study findings are generalizable in different age ranges or sports, where the profiles of head impact are different.

Acknowledgements The authors would like to thank from Seton High School: Ron Quinn, Lisa Larosa, Holly Laiveling, and the entire soccer coaching staff as well as the Seton administration and athletic director Wendy Smith; from Madeira High School soccer head coach Dan Brady, athletic director Joe Kimling, and principal David Kennedy for their support and assistance to conduct this study. Thank you to the soccer parents and players. We appreciate their patience with the testing scheduling, follow-ups, and equipment additions. Their enthusiastic support made this study possible. Special acknowledgement goes to the Athletic Trainers at Seton High School, Cindy Busse and Madeira High School, Glenna Knapp. Without their time, commitment, and passion for the health and well-being of their student athletes, this study would not have been possible. We would also like to thank University of Cincinnati interns Casey McCall, Danielle Reddington, Preston Heath and Jacob Snyder for their assistance with the daily accelerometer tracking. The authors would like to thank Lacey Haas, Brynne Williams, Kaley Bridgewater, and Matt Lanier in the Imaging Research Center, as their support made this study possible.

Funding The Heidt Family Foundation, Robert S. Heidt, Sr. —Wellington Foundation and Q30 Sports Innovations, LLC. Gregory D. Myer consults with Q30 Innovations to support application to the US Food and Drug Administration but has no financial interest in the commercialization of the Q-Collar. Dr. Myer also received current and ongoing funding support from National Institutes of Health/NIAMS Grants U01AR067997, R01 AR070474, R01 AR056259-01, and industry sponsored research funding related to brain injury prevention and assessment with Q30 Innovations, LLC and ElMinda, Ltd, and book royalties from Human Kinetics. The other authors have indicated they have no financial relationships relevant to this article to disclose.

Compliance with Ethical Standards

Conflict of interest The authors have no conflicts of interest relevant to this article to disclose.

Ethics Approval Study approved by the Cincinnati Children's Hospital Institutional Review Board.

Informed Consent All subjects and parent/legal guardians provided written informed assent/consent. All authors provide consent for publication.

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