Analysis of head impact exposure and brain microstructure response in a season-long application of a jugular vein compression collar: a prospective, neuroimaging investigation in American football

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ABSTRACT
Background  Historical approaches to protect the brain from outside the skull (eg, helmets and mouthpieces) have been ineffective in reducing internal injury to the brain that arises from energy absorption during sports-related collisions. We aimed to evaluate the effects of a neck collar, which applies gentle bilateral jugular vein compression, resulting in cerebral venous engorgement to reduce head impact energy absorption during collision. Specifically, we investigated the effect of collar wearing during head impact exposure on brain microstructure integrity following a competitive high school American football season.

Methods  A prospective longitudinal controlled trial was employed to evaluate the effects of collar wearing (n=32) relative to controls (CTRL; n=30) during one competitive football season (age: 17.04±0.67 years). Impact exposure was collected using helmet sensors and white matter (WM) integrity was quantified based on diffusion tensor imaging (DTI) serving as the primary outcome.

Results  With similar overall g-forces and total head acceleration between the skull and its contents,10–12 we investigated mechanical-based slosh mitigation, in the form of a jugular vein compression collar fashioned off of the diagnostic Queckenstedt manoeuvre.13 This approach demonstrated an 83% reduction in amyloid precursor protein-positive axons—a widely accepted biomarker of TBI—during a 900 g impact protocol studied in animals.14 Further, an associated preclinical TBI model, which also used the same impact protocol, demonstrated a >45% reduction in degenerative neurons, reactive astrocytes and microglial activation with the application of jugular vein impedance.15 The proposed mechanism of protection was achieved via the mechanical impedance of the internal jugular vein (IJV) which is proposed to result in increased cerebral venous sinus engorgement to promote a ‘tightly’ fit of the brain inside the cranium.14 15

INTRODUCTION
Sports-related traumatic brain injury (TBI) is common in competitive sports and recreational activities, with 1.6–3.8 million cases reported annually in the USA.1 Children, adolescents and young adults are at the highest risk for sustaining mild TBI (mTBI).2 A recent review of personal protective equipment concluded that, while some items might confer a preventative effect from superficial head injury, they all failed to significantly prevent sports-related TBI in athletes.3 In American football specifically, prospective studies of mouthguards (both specialised and custom-fitted models) indicate that they may have minimal, if any, effect on sports-related TBI incidence.5–8 There is also limited high-level prospective, objective evidence indicating that any recent helmet design can prevent sports-related TBI. Helmets were developed for, and are effective in, preventing skull fractures and intracranial hematomas—they do not however protect the brain inside the cranium. This lack of measurable protection may be due to the limited ability of helmets to minimise the collision of the brain against the inside of the skull (ie, slosh) and from differential acceleration between the skull and its contents.10–12

We evaluated physiological-based slosh mitigation (ie, reduced movement of fluids within moving containers) with increased elevation found to be associated with reduced sports-related TBI rates at higher altitudes.11 12 We postulated that acclimatisation to altitude may have influenced an increased intracranial blood volume, resulting in a tighter fit of the brain within the cranium. The proposed physiological response to decreased ambient oxygen (ie, reduced movement of fluids within moving containers) was speculated to have protected the athletes at higher elevations against sports-related TBI.11 12

We also investigated mechanical-based slosh mitigation, in the form of a jugular vein compression collar, fashioned off of the diagnostic Queckenstedt manoeuvre.13 This approach demonstrated an 83% reduction in amyloid precursor protein-positive axons—a widely accepted biomarker of TBI—during a 900 g impact protocol studied in animals.14 Further, an associated preclinical TBI model, which also used the same impact protocol, demonstrated a >45% reduction in degenerative neurons, reactive astrocytes and microglial activation with the application of jugular vein impedance.15

Drawing from these studies, a lightweight neck collaring compressive device was developed for humans (figure 1). Much like the effect of collar in
animal experiment, jugular vein compression in humans results in increased volume of the venous capacitance vessels of the cranium.\textsuperscript{16} Filling the compensatory reserve volume\textsuperscript{17} of the brain and spinal column appears to increase brain stiffness during jugular compression, as assessed by magnetic resonance elastography.\textsuperscript{18} Based on prior physiological models, we hypothesised that this would create a cradling effect to increase the brain’s resistance to movement or inertia, (ie, slosh mitigation of the brain inside the skull), potentially protecting the brain from external head impacts.\textsuperscript{11} A preliminary prospective longitudinal investigation showed that alterations in white matter (WM) microstructure and electrophysiological measures were ameliorated by application of jugular compression during head impact exposure in hockey.\textsuperscript{19} Therefore, the purpose of the current investigation was to examine the effects of a jugular vein compression collar worn during a competitive American football season to determine the potential effect on neuroimaging biomarkers associated with brain injury. Changes in brain diffusivity (a measure of WM brain injury\textsuperscript{20} that has been reported in neuroimaging studies of sports-related TBI\textsuperscript{21}) were evaluated in relation to the cumulative effects of repetitive head impacts accrued throughout the season.\textsuperscript{22}

**METHOD**

**Study participants**

The Cincinnati Children’s Hospital Medical Center Institutional Review Board (IRB) approved the data collection procedures and consent forms. The IRB approval number is IRB # 2015-2205 (ClinicalTrials.gov #: NCT02696200). Sixty-two healthy male varsity high school football players were enrolled from Southwest Ohio, USA. Parents, guardians and athletes provided informed consent prior to participation in the study. Primary exclusion criteria included history of neurological deficits, previous cerebral infarction, previous severe head trauma, known increased intracranial pressure, metabolic acidosis or alkalosis, glaucoma (narrow angle or normal tension), hydrocephalus, penetrating brain trauma (within 6 months), known carotid hypersensitivity, central vein thrombosis, known airway obstruction or seizure disorder. Teams were assigned to either the collar group or the control (CTRL) group prior to the start of the season. Of the 62 participants enrolled, 1 participant had contraindications for MRI (dental braces); 1 athlete had test anxiety with MR testing; 2 participants did not complete all testing due to medical issues that arose during the season unrelated to football participation; and 2 participants suffered a season-ending injury. Twelve participants had unusable MRI data on either preseason or postseason testing due to motion artefact during the scan and were excluded from all imaging analysis leaving 42 (21 collar and 21 CTRL) study participants (age 17.13±0.66 years; figure 2). In addition, one athlete in the collar group did not have accelerometer covariate information and, therefore, was not included in the correlation analysis. No significant difference was found between the athletes excluded for imaging reason and those who remained for analysis in age and all the impact-related variables (number of hits, cumulative

**Figure 1** (A) Visual representation of the jugular vein and intracranial venous system. (B) Visual representation of the collar application located near the omohyoid process. The increased jugular vein dilation superior to the collar application and resultant backfilling of the intracranial venous system are represented to provide the hypothesised tighter fit of the brain inside the cranium. (C) Neck collar device employed in current investigation.

**Figure 2** Study participant flow chart. (A) 11 excluded: no post-test (3), movement on MRI (7), season-ending injury (1); 2 reassigned from collar group due to non-compliance of collar wearing. (B) 7 excluded: movement on MRI (5), contraindication to MRI (1), season-ending injury (1). (C) 11 excluded: no post-test (3), movement on MRI (7), season-ending injury (1). (D) 7 excluded: movement on MRI (5), contraindication to MRI (1), season-ending injury (1). ITT, intention to treat.
g-force, average g-force per hit) at all the g-force thresholds (all hits, and g-force >20, 50, 100 or 150 g).

Instrumentation and procedures

Testing was completed at preseason and postseason. Each testing session consisted of a preimaging screening questionnaire to assess for safety of brain MRI. Preseason (baseline) testing took place prior to the start of the first practice, while postseason testing took place after the completion of competitive play (including postseason play, when applicable). The average time between testing was 129.7±14.9 days (range 95–154 days). During the study period, 60 practices, 10 regular season games and 2 playoff games for the collar group and 50 practices, 10 regular season games and no playoff games for the CTRL group were completed. The postseason imaging data were acquired at 7.05±4.61 and 5.83±6.70 days (p=0.50) after the last competitive event in the CTRL group and the collar group, respectively (figure 2).

MRI data acquisition

All MRI data were acquired on the same 3 T Philips Achieva MRI scanner (Philips Medical Systems, Best, the Netherlands) using a 32-channel head coil. The diffusion tensor imaging (DTI) data were acquired with a spin echo-planar imaging sequence with the following specifications: repetition time/echo time (TR/TE)=9000/83 ms; field of view (FOV)=256×256 mm; matrix=128×128; in-plane resolution=2×2 mm; slice thickness=2 mm; 72 slices. Diffusion-weighted images were acquired along 61 non-collinear directions with 7 non-diffusion-weighted images (b0=1000 s/mm²). A high-resolution, three-dimensional (3D) T1-weighted anatomical dataset was acquired in the sagittal direction with the following specifications: TR/TE=8.1/3.7 ms; TI=1070 ms; FOV=256×256 mm; matrix=256×256; in-plane resolution=1×1 mm; slice thickness=1 mm; 180 slices. Susceptibility-weighted imaging (SWI) was also performed (venous blood-oxygen-level dependent (BOLD), TR/TE=14.7/20.7 ms; FOV=220×220 mm, flip angle=10°, matrix=220×221, slice thickness=2 mm). One board-certified neuroradiologist (JLL), blinded to treatment group assignment, evaluated all anatomical images (3D T1-weighted and SWI images). Clinically significant findings were reported to the study investigators, participants and parents as per study protocol. On subjective evaluation of any of the anatomical images (T1-weighted and SWI images), there were no traumatic abnormalities identified. There were no changes between the preseason and postseason anatomical images in any participant, and there was no evidence of any intracranial complication (eg, brain haemorrhage or lesion) from collar use.

DTI data were processed with the Functional MRI of the Brain (FMRIB) Software Library (FSL) software package (http://www.fmrib.ox.ac.uk/fsl). In FSL, skull stripping was performed using the brain extraction tool (BET) function. Eddy current and head motion artefact were corrected in FSL by aligning using the brain extraction tool (BET) function. Eddy current and head motion artefact were corrected in FSL by aligning

Neck ultrasound evaluation and collar fitting

The neck collar device was made up of the following: an outer collar that consists of a thermoplastic elastomer (durometer 80 Shore A), an inner collar that consists of a thermoplastic elastomer (durometer 50 Shore A) and a stainless steel mesh composite insert. Figure 1 shows the positioning of a collar compressing the jugular vein. The collar size for each individual was determined from the measured neck circumference, validated via spacing of the collar tips (1.25–2.5") and from visual evidence of ultrasound IJV dilation. At the initial fitting of the collar, a registered vascular technologist (JA) used ultrasound to ensure that the proper collar and IJV responses (eg, visual evidence of IJV dilation superior to collar) occurred as prescribed (figure 3).

A single sonographer performed all ultrasonography procedures and measurements, and the images and video clips were acquired using a LOGIQ e-unit (General Electric Inc, Fairfield, Connecticut, USA) with an ultrahigh frequency L8-18i-RS linear transducer. The study participants sat upright, facing forward during testing. IJV was identified in the transverse plane to verify normal anatomy. Each athlete was scanned for baseline, Valsalva (ie, bearing down against a closed glottis) and with the assigned collar on/off/on in sequence. A collar was then placed in proper position around the participant’s neck. A 15 s video clip of the collar in proper position, opening away from the neck, and returning to its proper position, was obtained. The IJV metrics were measured at their largest transverse dimensions upon initial placement of the collar, when the collar pressure was removed, and again after replacing the collar back on the neck.

Head impact surveillance

Head impact was recorded using the GForce Tracker (GFT; GForce Tracker, Markham, Ontario, Canada) accelerometer device affixed to the inside of each football helmet. The accelerometers recorded linear acceleration and rotational velocity of the head (ie, 6 degrees of freedom) by directly measuring three axes of linear acceleration and three axes of angular acceleration. Prior to the initial exposure (ie, first practice), each accelerometer was calibrated according to device specifications and relative to the placement of the sensor in each helmet. Prior

Figure 3  Visual evidence of IJV dilation superior to omohyoid complex in response to Valsalva manoeuvre and with collar application. IJV, internal jugular vein.
evaluation of GForce Tracker accelerometers indicates that they provide a suitable impact-monitoring device across multiple helmet styles with coefficients of determination reported at \( r^2 = 0.82 \) for peak linear acceleration.\(^{20}\) The accelerometers were programmed to record data above 10 g, but only accelerations above 20 g threshold were used in the current investigation. Acceleration data were collected at 3000 Hz. A more detailed description of accelerometer methods can be found in the online supplementary appendix 1.

Compliance of collar use
Following the initial fitting, each athlete in the collar group received daily instruction on the proper usage of the collar. The collar usage was monitored by a study coordinator during routine visits, and recorded by the medical training staff in a daily log via custom software that tracked protocol compliance, attendance and any injury that occurred. These compliance logs were cross-referenced with accelerometer data daily to ensure data integrity for reported athlete exposures and collar compliance. Overall, the collar study participants (included in the reported per-protocol analysis) demonstrated 95.7% daily compliance (days of wear during impact practice or competition/ days possible) to collar usage as prescribed by the study protocol. It should be noted that the daily compliance collar usage was only 90.6% when evaluated by the intention-to-treat (ITT) methodology. A signiﬁcant effect of time was indicated, independent of group differences were determined by comparing with the John Hopkins University ICBM-DTI-81 WM labels atlas.\(^{31} \ 32\) For each of the areas, the longitudinal change of DTI values was extracted for each participant in the CTRL group. A Pearson correlation analysis was performed between the change in DTI and each of the three impact-related variables.

Initially, all participants were assigned to either the collar or CTRL group (with 19 athletes in the CTRL group and 25 athletes in the collar group). However, two of the participants assigned to the treatment (collar) group refused to comply from the outset, and two were partially compliant with collar use during the competitive season. Therefore, all the neuroimaging analyses reported in the present study were performed based on the per-protocol design. This involved 21 athletes from the CTRL group and 21 athletes from the collar group. We also conducted analyses based on the ITT principle using the original allocation regardless of compliance status. As expected, similar but reduced effects were observed when the ITT analyses were used. The ITT analyses and results are described more fully below with the details included in the online supplementary appendix 1 for comparison.

RESULTS
Responsiveness to collar
Ultrasound evaluation conﬁrmed that jugular vein size increased signiﬁcantly above the level of the collar following collar placement, implying a backﬁll into the venous capacitance vessels of the cranium. While signiﬁcant, the magnitude of change was less than that related to a quotidian physiologic sulcal manoeuvre. A signiﬁcant effect of time was indicated, independent of side, \( F(3,48) = 12.88 \), \( p = 0.002 \), \( \eta^2 = 0.45 \) (ﬁgure 4). Follow-up comparisons revealed that the per cent change for time point pair 1 (baseline to Valsa5) was signiﬁcantly greater than all other time points (\( p < 0.02 \)). Time points 2 (baseline to collar on, time 1) and 4 (baseline to collar on, time 2) did not differ from each other, but both were signiﬁcantly greater than time point 3 (baseline to collar off; \( p < 0.006 \)).

Head impact surveillance
There were no signiﬁcant differences between the collar group and the CTRL group for any head impact measures (all \( p > 0.05 \); table 1). As presented in ﬁgure 5, the distribution of number of impacts at different g-force indices was similar...
between the two study groups (figure 6A, B). Table 1 presents descriptive values relative to each impact variable.

Cross-sectional comparison of preseason DTI metrics between the CTRL group and the collar group
At preseason, no significant differences were found in any of the four DTI measures in any WM region between the two groups.

Longitudinal change and group difference in preseason to postseason DTI metrics
Significant preseason to postseason decreases in MD, AD and RD (corrected $p<0.05$) were found in extensive WM areas in the CTRL group (details below). No statistically significant preseason to postseason FA change was found in the CTRL group. No statistically significant longitudinal changes were found in any DTI measure in any WM region in the collar group ($p>0.05$).

Derived from the above within-group analyses, there is a consistent reduction of the diffusivity measures in the CTRL group, while the direction of change is more variable in the collar group (figure 7). For example, at an individual level, all 21 athletes in the CTRL group exhibited decreases in AD (per centage of reduction $=2.43\pm1.02\%$; figure 8A). Within the same areas, 11 out of the 21 athletes in the collar group exhibited decreases in AD ($0.95\pm0.77\%$), 8 out of the 21 athletes exhibited increases in AD ($1.22\pm0.68\%$) and 2 did not exhibit any change, with an overall average reduction of AD at the level of $0.03\pm1.27\%$ or absolute change of AD ($0.96\pm0.67\%$; figure 8B).

Between-group analysis showed significantly larger preseason to postseason DTI changes in the CTRL group within the corpus callosum, the internal and external capsule, and a series of other WM regions (figure 9; corrected $p<0.05$, see table 2 for location and volume of specific WM regions involved based on the AD measurement) when compared with the collar group (figure 10).

Correlation between preseason to postseason DTI change in the no-collar (CTRL) group and head impacts
Among the WM regions with significant group difference of AD, the superior longitudinal fasciculus in the CTRL group was found to present significant correlation between the preseason and postseason decreases in diffusivity and impact burden. As shown in table 3, the AD reduction in the superior longitudinal fasciculus in the CTRL group was significantly correlated with the number of hits and cumulative g-force (all hits or hits $\geq20\,g$) and marginally correlated with number of hits at the $\geq50\,g$ threshold. The MD reduction in superior longitudinal fasciculus in the CTRL group was mildly correlated with the number of hits and cumulative g-force (all hits or cut-off $>20\,g$). In addition, we also found that the change of FA in posterior thalamic radiation was significantly correlated with the number of hits and with cumulative g-force (all hits or cut-off $>20\,g$). No other WM region was found to have significant correlation between change in DTI measures and impact measures.

Neuroimaging findings based on ITT protocol
The results based on the ITT protocol are similar to the above-reported findings based on the per-protocol design. Briefly, based on the ITT design, we found significant preseason to postseason reduction in MD, AD and RD in the CTRL group but...
The group difference of preseason to postseason reduction in MD, AD and RD remained statistically significant after using the collar group as the CTRL (see online supplementary figure S4). The WM regions with significant group difference of longitudinal diffusivity change were similar to the findings based on the per-protocol design (see online supplementary table S1). In the correlation analysis, the superior longitudinal fasciculus was found to present significant correlation between the AD reduction and the total number of hits. It should be noted that the number of WM regions with significant group difference and the number of WM regions with significant correlations in the ITT analysis were both smaller than that in the per-protocol design. This difference may be attributed to the lower compliance in the ITT design (90.6% for ITT vs 95.7% for per-protocol as reported in Method-Compliance of collar use). The ITT analysis which included two non-compliant athletes and the two partially compliant in the collar group weakened the homogeneity of the group analysis and, as expected, led to less significant findings. When compared to the formally presented per-protocol design, these data provide further support that the effect of collar wear to reduce changes in DTI was a valid outcome.

**DISCUSSION**

We examined the effect of a bilateral jugular vein compression collar device on the mitigation of brain microstructure changes as assessed by WM integrity in response to a season-long head impact exposure. The collar is a novel approach for the potential internal protection of the brain against repetitive head impact. As hypothesised, the wearing of the device was effective to prevent diffusion changes after a full season of repetitive head impacts in high school football athletes. Specifically, the CTRL group showed consistent and statistically significant reduction in diffusion coefficients—a change that has been reported frequently in mTBI and sports-related TBI literature—contrasting with the absence of change in the football players who wore the collar. Combined with the association found between the decrease of diffusivity in the CTRL group and their impact burden, our study has generated initial evidence for a potential protective effect of the collar device. It supports the notion that the approach of protecting the brain internally via jugular vein compression may be a promising alternative, or at least a complementary tool, that helps to prevent and mitigate potential injury from repetitive head impact in competitive contact sports.

**Figure 6** (A) Graphical representation of average magnitude of head impacts (represented by height and colour) distributed about the sphere of the head for the CTRL (left, no-collar) and collar group (right). (B) Graphical representation of average frequency of head impacts (represented by height and colour) distributed about the sphere of the head for the CTRL (left, no-collar) and collar group (right). CTRL, control.
Brain slosh and increased intracranial blood volume

Slosh mechanisms have been primarily studied in their relation to fluid-filled containers.15 When an impact is sustained to a container filled with fluids (by extrapolation of the skull and brain), maximising volume within the container (ie, by reducing compliance of the venous sinuses and maximising intracranial blood and brain volume) reduces energy absorption.14 15 It is likely that only a very small amount of intracranial blood volume change is necessary for this effect to occur. Accordingly, previous work has demonstrated that cerebral volume needs to rise only by 3–4 mL before concomitant pressure increases occur.45 Since the cerebral blood space is ∼150 mL, we speculate that a 3% rise in intracranial volume will take up excess compliance and may provide protection from shear stress, cavitation and impact on the interior cranium.11 12 The degree of venous dilatation documented in this study with neck collar placement would not be expected to be dangerous and is likely less than the normal physiologic range noted with sneeze, cough and the Valsalva manoeuvre (ie, forced exhale against closed glottis; figures 3 and 4).

Objectifying brain injury biomarkers in response to head impacts

In contrast to the relatively subjective end point of concussion, DTI has been used as an objective imaging biomarker in quantifying WM structural changes in patients with mTBI and collision sport athletes during acute, semiacute and chronic stages after discrete head trauma or a season of repetitive head impacts.22 38–44 WM integrity changes based on DTI have been correlated with postconcussive symptoms and cumulative risk-weighted exposure.40 Prior analyses of DTI in mTBI and sports-related TBI have shown changes of varying severity and direction, including abnormally lower FA and/or higher diffusivity (MD, AD, RD) in patients, concussed athletes, athletes with a history of concussion,25 27 43 46 or decreased FA and/or increased diffusivity measures in athletes when tested for preseason to postseason changes.39 42 47 48 However, other studies have shown changes in the opposite direction (ie, higher FA and/or lower diffusivity for MD, AD and RD) in acute mTBI33–37 and in collision sport athletes with either concussive or subconcussive

Figure 7 White matter regions with significant within-group AD reduction at postseason compared with preseason baseline. The significant regions (red-yellow regions, p<0.05, FWE corrected for multiple comparisons) were overlaid on to the white matter skeleton (green) and standard T1-weighted image in MNI 152 space (grey scale). The significant regions were filled in using thsv_fill in FSL to improve visualisation. Image orientation is in radiological convention. AD, axial diffusivity; CTRL, control; FSL, FMRIB Software Library; FWE, family-wise error rate; MNI, Montreal Neurological Institute. Top row: no-collar (CTRL) group; bottom row: collar group.

Figure 8 Bar plots of preseason and postseason AD values from individual athletes. (A) No-collar (CTRL) group; (B) collar group. AD, axial diffusivity; CTRL, control.
impacts. The inconsistency of these findings may be explained by the differences in timing of imaging, as well as differing severity and chronicity of brain injury.

In general, lower FA and higher MD, AD and/or RD are often interpreted as damage to the myelin sheath and axonal membrane. Conversely, higher FA and lower MD, AD and/or RD are often attributed to extracellular space compression, cytotoxic oedema (axonal swelling) or inflammation. In the present study, no significant change in FA was noted; the primary findings were significant decreases in WM diffusivity at postseason in the CTRL group. The areas affected included the corpus callosum, anterior and posterior internal capsule, corona radiata, posterior thalamic radiation, external capsule, cingulum and superior longitudinal fasciculus, which are consistent with previous studies of TBI and head impacts.

Previously, a prospective randomised controlled trial was performed in hockey players to evaluate the effects of external jugular compression applied during head impact exposure on longitudinal changes in brain neuroanatomical and neurophysiological biomarkers. A prospective randomised controlled trial was performed in hockey players to evaluate the effects of external jugular compression applied during head impact exposure on longitudinal changes in brain neuroanatomical and neurophysiological biomarkers. A similar to the current results, athletes not wearing the collar and exposed to head impacts showed a disruption of WM microstructure, including mean diffusivity and radial diffusivity. Hockey players who wore the compressive collar did not show a significant change in either MD or RD despite similar accumulated linear accelerations from head impacts. In addition to these anatomical findings, electrophysiological network analysis demonstrated concomitant changes in brain network dynamics in the no-collar group.

**Figure 9** WM areas with significant between-group differences (CTRL vs collar), preseason versus postseason. (A) MD; (B) AD; and (C) RD. The significant regions (red/yellow regions, p<0.05, FWE corrected for multiple comparisons) were overlaid on to the WM skeleton (green) and standard T1-weighted image in MNI 152 space (grey scale). The significant regions were filled in using tbss_fill in FSL to improve visualisation. Image orientation is in radiological convention. AD, axial diffusivity; FSL, FMRI Software Library; FWE, family-wise error rate; MNI, Montreal Neurological Institute; MD, mean diffusivity; RD, radial diffusivity; WM, white matter.

**Table 2** The WM regions corresponding to the brain regions with significant preseason versus postseason changes (figure 10) were determined using John Hopkins University’s WM atlas

<table>
<thead>
<tr>
<th>Volume (mm³)</th>
<th>WM region located</th>
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<tbody>
<tr>
<td>Region 01</td>
<td>173 Genu of corpus callosum</td>
</tr>
<tr>
<td>Region 02</td>
<td>960 Body of corpus callosum</td>
</tr>
<tr>
<td>Region 03</td>
<td>384 Splenium of corpus callosum</td>
</tr>
<tr>
<td>Region 04</td>
<td>3 Anterior limb of internal capsule R</td>
</tr>
<tr>
<td>Region 05</td>
<td>40 Posterior limb of internal capsule R</td>
</tr>
<tr>
<td>Region 06</td>
<td>84 Retrolenticular part of internal capsule R</td>
</tr>
<tr>
<td>Region 07</td>
<td>2 Retrolenticular part of internal capsule L</td>
</tr>
<tr>
<td>Region 08</td>
<td>216 Anterior corona radiata L</td>
</tr>
<tr>
<td>Region 09</td>
<td>490 Superior corona radiata R</td>
</tr>
<tr>
<td>Region 10</td>
<td>77 Superior corona radiata L</td>
</tr>
<tr>
<td>Region 11</td>
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<tr>
<td>Region 12</td>
<td>266 Posterior corona radiata L</td>
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<td>18 Posterior thalamic radiation (include optic radiation) L</td>
</tr>
<tr>
<td>Region 15</td>
<td>22 External capsule R</td>
</tr>
<tr>
<td>Region 16</td>
<td>42 Cingulum (cingulate gyrus) L</td>
</tr>
<tr>
<td>Region 17</td>
<td>365 Superior longitudinal fasciculus R</td>
</tr>
<tr>
<td>Region 18</td>
<td>197 Superior longitudinal fasciculus L</td>
</tr>
<tr>
<td>Region 19</td>
<td>2 Tapetum R</td>
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WM, white matter.
Division I Football Bowl Subdivision collegiate level, the average number of impacts per player over the course of a season has varied widely, ranging from 171 to 1354. Our results showed no significant effect of impact per player or any other impact-related variable in any of the covariate analyses on the potential collar effects on reduced change in DTI. The current data are generalisable in relative head impact exposure (magnitude and quantity) to high school and collegiate football players over a single season.

Limitations
In the present study, the similar impact exposure between the two study groups strengthens the conclusion that the significantly lower levels of DTI alterations in the collar group are attributed to the intervention. However, despite best efforts for control, the changes reported could be potentially explained by other factors such as physiologic responses to other stresses in addition to trauma, developmental changes of the immature brain, genetics and/or other susceptibilities. The utilisation of a controlled longitudinal study design can mitigate, but does not eliminate, the risk of these potential confounding variables. Regardless, the cumulative results of the current investigation represent a substantive and important finding in the field of sports injury prevention. The exact pathologic substrate and clinical significance of the diffusion changes identified in this study are unknown. The diffusion changes and locations identified in the CTRL group are consistent with those identified in prior studies of severe TBI (sTBI), lending support to the premise that they are traumatic in origin. In addition, the current investigation was focused on the assessment of objective biomarkers that are associated with brain injury, and the study design was not appropriate to evaluate the subjective and often nebulous outcome of clinically diagnosed concussion. The authors acknowledge future large-scale epidemiological clinical trials are needed to determine the potential of the investigated

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**Table 3**

<table>
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<tr>
<th></th>
<th>Hits</th>
<th>Hits (&gt;20 g)</th>
<th>Hits (&gt;50 g)</th>
<th>Cumug</th>
<th>Cumug (&gt;20 g)</th>
<th>Cumug (&gt;50 g)</th>
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<td>-0.21/NS</td>
</tr>
</tbody>
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Correlation coefficient p value. All statistics were tested using one-tailed Pearson correlation at p<0.05. AD, axial diffusivity; CTRL, control; DTI, diffusion tensor imaging; FA, fractional anisotropy; MD, mean diffusivity; NS, not significant; PTR, posterior thalamic radiation; SLF: superior longitudinal fasciculus.
collar device for mitigating concussion incidence. Finally, future research is warranted to understand and document the intracranial effects of jugular venous compression, to assess for any long-term effects of playing sport with jugular venous compression and presumably increased cerebral blood volume, as well as to validate its mitigating effects on brain injury from head impact exposure.

CONCLUSION
The current investigation tested a neck collar device that produces physiologic distension of the superior jugular veins to encourage cerebral venous engorgement to ameliorate the changes in brain microstructure associated with a season of contact sport. These prospective longitudinal data using an internal in vivo approach indicate that it may be possible to protect the brain from ‘inside the skull’ from sports-related head impacts.

What are the findings?
- Analyses of brain injury biomarkers and head impacts in response to the season-long application of a jugular compression collar indicate a consistent reduction in altered white matter diffusivity parameters.
- These results represent prospective, longitudinal and objective data demonstrating a potential approach to protect the brain from changes sustained within a competitive football season, as evidenced by brain microstructure integrity.

How might it impact on clinical practice in the future?
- These prospective longitudinal data using an internal in vivo approach indicate that it may be possible to protect the brain from ‘inside the skull’ from sports-related head impacts.
- The novelty of this device, as well as the tolerance and general compliance, may help drive future efforts to prevent sports-related brain injury.

REFERENCES