

Glymphatic system dysfunction associated with player position in collegiate American football players: A DTI-ALPS study

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A B S T R A C T

Purpose: The glymphatic system plays a crucial role in both short-term and long-term brain health through the clearance of neural waste and is vulnerable to disruption following head trauma. This study aimed to determine whether exposure to a season of sub-clinical head acceleration events (HAEs) in collegiate American football affects glymphatic function, and whether this effect varies by player position or concussion history.

Methods: Sixty-six male NCAA Division I football athletes underwent diffusion tensor imaging (DTI) before and after a competitive football season. Glymphatic function was quantified using the Diffusion Tensor Imaging Along the Perivascular Space (DTI-ALPS) index. Participants were categorized by player position (Speed vs. Non-Speed) and concussion history (Yes vs. No). Linear mixed-effects models were used to evaluate changes in DTI-ALPS index by time point, hemisphere, position, and concussion history.

Results: There were no significant changes in DTI-ALPS values from pre-to post-season in either hemisphere across the full cohort. However, a significant main effect of player position was observed in the right hemisphere ($p = 0.025$), with Speed position players demonstrating lower DTI-ALPS indices compared to Non-Speed players, suggesting reduced glymphatic function. No significant effects of concussion history or interaction terms were found.

Conclusions: These findings indicate that positional differences in HAEs experienced by Speed players, even absent clinical concussion, may contribute to impaired glymphatic function. Speed position players may be at increased risk due to the nature and magnitude of head impacts. The DTI-ALPS index may serve as a sensitive biomarker for early, sub-clinical brain dysfunction in athletes participating in contact sports.

1. Introduction

Participation in contact sports has many personal benefits to the athlete, from enhanced physical fitness and cardiovascular health (Torres, 2022) to improved mental wellbeing through stress relief and social connection (Eather, 2023). However, growing research over the past several decades has also highlighted the risk of short and long-term neurological consequences stemming from exposure to head acceleration events (HAE), with or without concussion, associated with participation in those contact sports (Daneshvar, 2021). Even in the absence of diagnosed concussions, these repeated blows to the head have been linked to a spectrum of cognitive, emotional, and behavioral impairments, and in some cases, progressive neurodegenerative conditions

such as amyotrophic lateral sclerosis (ALS), early onset dementia, Alzheimer's disease and chronic traumatic encephalopathy (CTE) (Daneshvar, 2021; van Amerongen, 2023; Baugh, 2012). The neural mechanisms underpinning these conditions continue to be explored by brain injury researchers using tools like neuropsychological testing, blood biomarkers, electroencephalography and neuroimaging or fMRI (Stamm, 2015; Joseph, 2018; Hirad, 2019; Mainwaring, 2018; Sattari, 2023; Johnson, 2014).

The glymphatic system is a brain wide network of perivascular structures primarily responsible for the movement and clearance of cerebrospinal (CSF) and interstitial (ISF) fluid in the brain (Ghanizada and Nedergaard, 2025). Normative functioning of the glymphatic system is crucial for maintaining neural health and preventing the accumulation

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of harmful metabolites that can eventually lead to neurodegenerative disease in the brain (Ghanizada and Nedergaard, 2025) and in the surrounding neuroanatomy of the eye (Cao, 2024). Research suggests that exposure to mild to moderate brain injuries can lead to a decrease in the functioning of this system (Dai et al., 2023; Li et al., 2024; Michalaki et al., 2025) having numerous downstream effects on neurological wellbeing with aging (Ghanizada and Nedergaard, 2025). Moreover, disruption of glymphatic system function compromises its ability to clear metabolic waste leading to the buildup of neurotoxic proteins (Peters, 2023). Compounding matters, these accumulated waste products then trigger inflammation and cellular stress throughout the brain's neural networks (Ferrara, 2022). Exposure to even mild traumatic brain injuries can trigger changes in glymphatic system activity, suggesting that HAE exposure, even those head impacts considered sub concussive, might have cumulative effects on this crucial waste-clearing mechanism, potentially contributing to long-term neurological consequences (Jung, 2024; Dai et al., 2023). Most concerning is that evidence suggests glymphatic failure may precede visible pathological changes, making it a critical early factor in the development of post-concussion neurodegeneration and subsequent cognitive, motor, and emotional disabilities (Huang, 2024).

Advances in brain imaging analysis have led to non-invasive methods for evaluating the overall health of this system, giving insight into the assessment of CSF clearance of metabolic waste in the brain. Assessment of glymphatic system function using a diffusion tensor imaging along the perivascular space (DTI-ALPS) index is an increasingly supported method in determining the relative health and function of the glymphatic system across a spectrum of brain injuries and pathologies (Dai et al., 2023; Taoka et al., 2022a). Moreover, this non-invasive measure of glymphatic system function has demonstrated the reliability and reproducibility of the DTI-ALPS index across different MRI platforms, establishing its potential as a standardized assessment tool (Liu et al., 2024). The utility of this method has been demonstrated in various clinical applications, with researchers demonstrating consistent correlations between DTI-ALPS index measurements and known glymphatic system impairments in various neurological conditions (Marecek, 2025). However, no research to date has measured the effect that repeated sub-clinical head acceleration events (HAE) may have on the function of this system.

It has been well documented that American football remains the sport with the highest rates of male adolescent participation in United States, and it yields the highest rates of reported concussive injuries among U.S. youth and adolescent sport participation (Hammer et al., 2020; Mueller & Colgate, n.d.). As such, football represents a unique observational research environment with respect to head trauma, as initially demonstrated by Barth et al. with the introduction of the "Sport as a Laboratory Model" (SLAM) (Barth et al., 1989). In this population of interest, sport-related head trauma, particularly concussion occurrence, has been empirically associated with short- and long-term functional deficits, including more severe symptom outcomes from subsequent sub-clinical HAE exposure (Alsalaheen et al., 2016; Chizuk et al., 2022; Howell et al., 2017).

Further, and critical to the evaluation of sub-clinical HAE outcomes, recent research has identified functional outcome differences between player position types in football. Generally, football athletes may be categorized as speed (quarterbacks, wide receivers, linebackers, defensive backs) and non-speed positions (defensive linemen, offensive linemen), based on the role of the player on the field (Baron et al., 2012; Lehman et al., 2012). In American football, research using xPatch accelerometers has shown that there are differing rates of HAEs based on player positions (Lee et al., 2021). Speed positions tend to expose athletes to higher velocity hits, and as such to a higher magnitude HAEs yielding greater rotational acceleration of the skull, which is more strongly associated with tissue deformation in the sulci, regions where chronic traumatic encephalopathy (CTE) pathology tends to accumulate (Broglia et al., 2011; Vike et al., 2022; Zimmerman et al., 2021).

Non-speed athletes, however, are more often exposed to lower velocity, head-to-head contact at the line of scrimmage, yielding lower magnitude HAE's albeit at a higher frequency (Broglia et al., 2011; Lee et al., 2021; Vike et al., 2022). Additionally, work from our group has shown that Speed players tend to demonstrate higher serum concentrations of blood biomarkers glial fibrillary acidic protein (GFAP) and neurofilament light chain (NFL) (Papa et al., 2022), as well as functional connectivity deficits in the Default Mode Network, compared to non-speed positions after a single season (Griffith et al., 2025).

This study aimed to utilize DTI images attained in a football cohort to assess changes in glymphatic system function over a single athletic season of HAE exposure. The researchers hypothesize that glymphatic system function will be compromised following exposure to HAE accumulated over the course of a football season. In addition, this compromise, as measured by DTI-ALPS index, will be greater in speed vs. non-speed positions.

2. Methods

2.1. Study population and procedures

This prospective cohort study recruited College age Division I NCAA American football athletes over 4 years (2015, 2019, 2021, 2022). Athletes were excluded if they met any criteria that were contraindicated for MRI scans. All participants completed a pre-season interview which included demographic information, relevant medical and concussion history. Self-report concussion considered a reliable method of recording lifetime concussion exposure (Wojtowicz et al., 2017), but to further improve reliability and reduce reporting bias a definition-based descriptor of concussion was utilized to capture self-report concussion history. Prior to the start of each pre-season of football, each participant underwent an MRI scan of the brain. During the fall football seasons, all participants included in the study participated in standard team activities, including football practices and games. Participants then completed a post-season MRI scan within 7–14 days immediately following the conclusion of the fall NCAA regular football season. See Fig. 1 for schematic overview of study design and data pipeline.

2.2. MRI acquisition

All imaging data were acquired on a the same 3 T S MAGNETOM Prisma scanner (Siemens Healthineers, Erlangen, Germany) equipped with the same 64-channel head coil and a locked protocol—identical gradient table, b-values, TR/TE, voxel size, FOV, slice prescription, and phase-encoding—across all four years (pre- and post-season). The software version and acquisition parameters remained constant throughout data collection. Routine QA (phantom SNR/ghosting) showed stable performance within site tolerances. High-resolution T1-weighted structural images were collected using a three-dimensional magnetization-prepared rapid acquisition gradient echo (MPRAGE) sequence with the following parameters: repetition time (TR) = 1700 ms, echo time (TE) = 1.77 ms, inversion time (TI) = 850 ms, flip angle = 9°, field of view (FOV) = 320 × 260 mm², voxel size = 1.0 × 1.0 × 1.0 mm³, 176 sagittal slices, and GRAPPA acceleration factor = 2. T1 images were reviewed by a neuroradiology specialist for gross white matter defects. Diffusion-weighted images were acquired using a single-shot spin-echo echo planar imaging (EPI) sequence with the following parameters: TR = 9800 ms, TE = 94 ms, FOV = 220 × 220 mm², matrix size = 110 × 110, voxel size = 2.0 × 2.0 × 2.0 mm³, and 72 contiguous axial slices acquired in interleaved order. Diffusion weighting was applied using 30 directions following the Siemens standard monopolar diffusion-weighted (MDDW) scheme, acquired at b = 1000 s/mm² and b = 2000 s/mm², with the same set of gradient directions applied at both b-values. In addition, seven b = 0 reference images were acquired with 7 averages. A GRAPPA acceleration factor of 2 was used to reduce echo

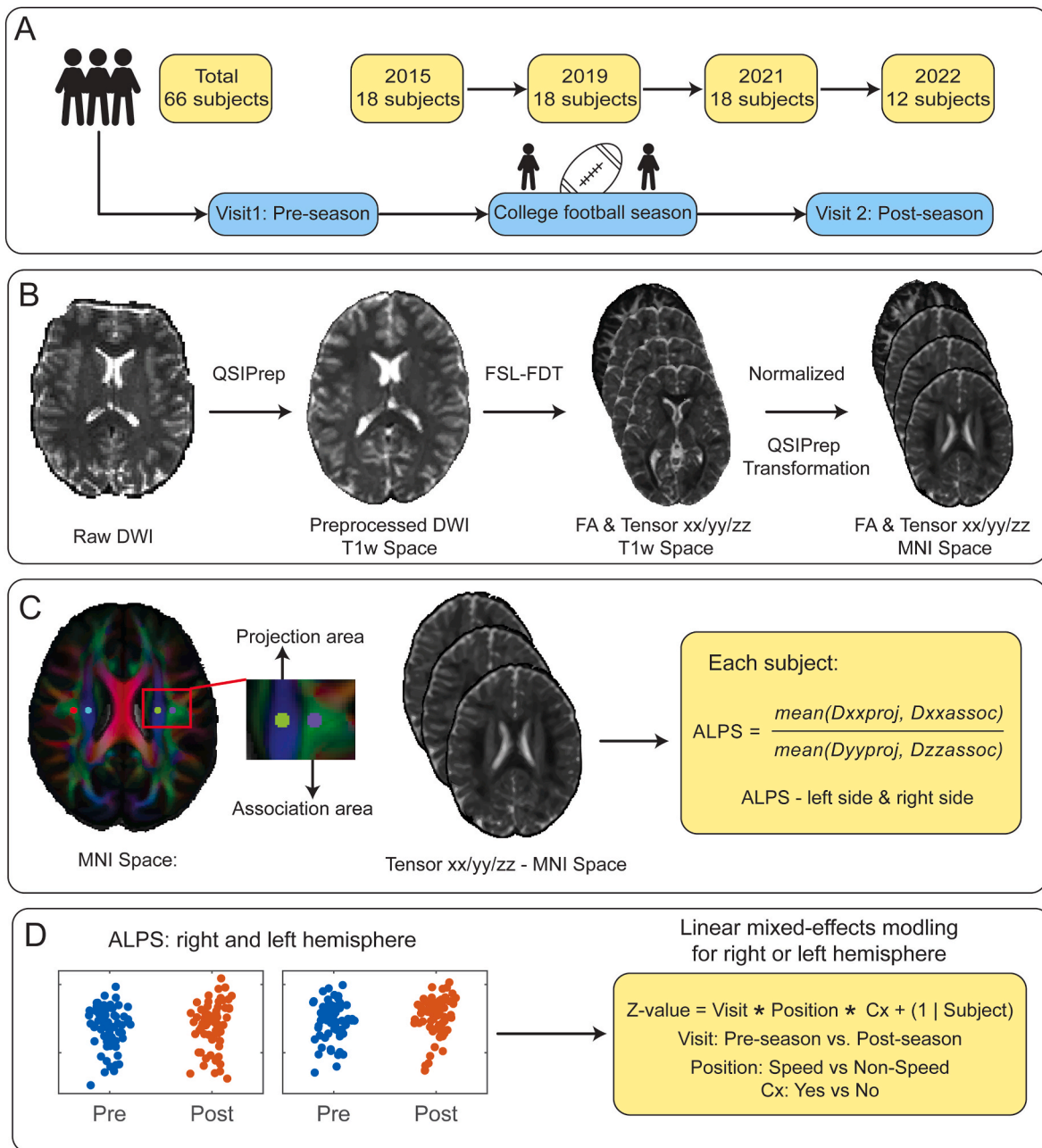


Fig. 1. Schematic overview of study design and analysis pipeline. (A) Timeline of data collection across four seasons (2015–2022) with pre- and post-season visits. (B) DWI preprocessing using QSIPrep and tensor estimation using FSL-FDT. (C) ROI definition and DTI-ALPS index calculation in MNI space. (D) Linear mixed-effects modeling of DTI-ALPS indices in the left and right hemispheres, examining effects of Visit, Position, and Concussion history.

train length and susceptibility distortions.

2.3. Diffusion tensor imaging processing

Diffusion-weighted imaging (DWI) data were preprocessed using QSIPrep (version 0.19.0), a containerized, standardized pipeline for diffusion MRI analysis (Cieslak et al., 2021). QSIPrep performed denoising, correction for eddy currents and susceptibility distortions, motion correction, and registration to each subject's T1w image. In addition to DWI preprocessing, QSIPrep also generated the spatial normalization transform from each subject's T1w image to the MNI152Nlin2009cAsym standard space using nonlinear registration.

After preprocessing, FSL's FDT toolbox (version 6.0.7.4) was used to compute fractional anisotropy (FA) maps and diffusion tensor components (Dxx, Dyy, Dzz) in each subject's T1w space (Jenkinson et al.,

2012). The resulting maps were then transformed to MNI152Nlin2009cAsym space using the transformation outputs provided by QSIPrep, enabling standardized group-level analysis and consistent ROI placement across subjects (Hsu et al., 2023; Liu et al., 2024).

2.4. DTI-ALPS index calculation

The Diffusion Tensor Imaging analysis Along the Perivascular Space (DTI-ALPS) index method was used to assess diffusivity along perivascular pathways (Taoka et al., 2022a). In the normalized tensor maps, two spherical regions of interest (ROIs) with a diameter of 5 mm were placed in each hemisphere at the level of the body of lateral ventricles to capture projection and association fiber areas. The projection ROIs were centered at MNI coordinates (37, −12, 24) in the right hemisphere and (−26, −12, 24) in the left hemisphere. The association ROIs were

centered at (-26, -12, 24) in the left hemisphere and (-37, -12, 24) in the right hemisphere (Li et al., 2024). These ROIs were defined based on prior DTI-ALPS studies and positioned to capture white matter tracts perpendicular to the perivascular spaces (Li et al., 2024; Ueda et al., 2024).

Tensor components were extracted from each ROI, and the DTI-ALPS index was calculated separately for the left and right hemispheres using the following equation:

$$DTI - ALPS = \frac{\text{mean}(D_{xx}^{Proj}, D_{xx}^{Assoc})}{\text{mean}(D_{yy}^{Proj}, D_{zz}^{Assoc})}$$

Where D_{xx}^{Proj} and D_{xx}^{Assoc} represent diffusion along the x-axis in projection and association ROIs, respectively, and represent diffusion along the y- and z-axes in the corresponding projection and association ROIs.

2.5. Statistical analysis

Group-level differences in DTI-ALPS indices were analyzed using linear mixed-effects models implemented in MATLAB R2022b. Separate models were constructed for the left and right hemispheres. A random intercept was included for each subject, and the model was specified as:

$$ALPS = \text{Visit} * \text{Position} * Cx + (1 | \text{Subject})$$

where the fixed effects included Visit (Pre-season vs. Post-season), Position (Speed vs. Non-speed), and Concussion history (Cx: Yes vs. No), along with all interaction terms.

3. Results

3.1. Participant demographics

117 total athletes initially consented to participate in this study over the four seasons. After removal of participants' scans with missing data (n = 28) or individuals with non-useable DTI-ALPS images (n = 23), 66 participants were included in final analyses. These individuals had a mean age of 20.55 ± 1.52 years, were 100 % male, and had played football for 10.84 ± 4.85 years (Table 1). 33 % of participants reported

Table 1
Participant demographics.

Descriptive Variable	All Years	2015	2019	2021	2022
Sample Size, N	66	18	18	18	12
Age (yrs), mean sd	20.55 ± 1.52	20.94 ± 1.66	20.94 ± 1.55	20.28 ± 1.27	19.75 ± 1.36
Duration Played Sport (yrs), mean sd	10.84 ± 4.85	11.06 ± 3.68	11.22 ± 3.92	10.56 ± 3.65	10.42 ± 4.62
Body Type, mean sd					
Height (in)	74.35 ± 2.36	75.06 ± 2.10	74.28 ± 2.67	73.94 ± 2.24	74.34 ± 2.45
Weight (lbs)	252.18 ± 47.56	271.83 ± 40.33	247.72 ± 45.55	247.44 ± 55.36	236.50 ± 44.04
Sex, n (%)					
Male	66 (100 %)	18 (100 %)	18 (100 %)	18 (100 %)	12 (100 %)
Concussion History, n (%)					
Previous Concussion(s)	22 (33 %)	8 (44 %)	7 (39 %)	4 (22 %)	3 (25 %)
No Previous Concussion(s)	44 (67 %)	10 (56 %)	11 (61 %)	14 (78 %)	9 (75 %)
Position, n(%)					
Speed	32 (48 %)	7 (39 %)	9 (50 %)	7 (39 %)	9 (75 %)
Non-Speed	34 (52 %)	11 (61 %)	9 (50 %)	11 (61 %)	3 (25 %)

having had at least one previously diagnosed concussion and 48 % were speed position players. Participants did not differ significantly by season in any demographic factor.

3.2. DTI-ALPS findings

A linear mixed-effects model was used to assess the effects of Timepoint (Pre-season vs. Post-season), Position (Speed vs. Non-speed), and Concussion history (Cx: Yes vs. No) on the DTI-ALPS index in the left and right hemispheres. Results are summarized in Table 2.

In the left hemisphere, no significant main effects or interaction terms were observed (all p > 0.05). In contrast, the right hemisphere showed a significant main effect of Position (F(1,124) = 5.115, p = 0.025), indicating higher DTI-ALPS index values in Non-Speed players compared to Speed players across both timepoints. Neither Timepoint nor Concussion history showed significant effects in the right hemisphere, and no interaction terms reached statistical significance. These effects are visualized in Fig. 2, which shows group means and individual DTI-ALPS values stratified by position and concussion history in the right hemisphere.

As shown in Fig. 3, there were no significant pre-to-post season changes in DTI-ALPS index in either hemisphere when stratified by player position or concussion history. Patterns of individual variability were similar across all groups, with no consistent directional change from pre-to post-season.

Comprehensive descriptive summaries (mean ± SD) for Dxx-projection, Dxx-association, Dyy-projection, and Dzz-association at each timepoint, stratified by relevant covariates are represented in the Supplementary Table 1, Supplementary Table 2, and Supplementary Figs. 1–4.

4. Discussion

Proper glymphatic system function has a direct impact on several key functions in the brain including the elimination of neurometabolic waste, reabsorption of dissolved substances, interstitial movement of lipid signaling molecules, immune system neuroregulatory mechanisms among other supportive functions of the healthy brain (Ghanizada, 2025; Nycz, 2021; Benveniste, 2015). Recent literature has proposed brain trauma related glymphatic disruption as a crucial mechanism of short-term symptom presentation (Doustar, 2022) as well as long-term downstream neurodegeneration and cognitive decline (Peters, 2023). Therefore, early detection of glymphatic system dysfunction following trauma or HAE may prove to be of critical clinical importance for athletes following exposure. Further, while the glymphatic clearance system has been examined with respect to mild and severe traumatic brain injury, no studies to date have examined glymphatic alterations after sub-clinical HAE exposure. In this study, we evaluated glymphatic

Table 2
DTI ALPS linear mixed effect model findings.

Term	Left Hemisphere		Right Hemisphere	
	F-stat	p-value	F-stat	p-value
Intercept	662.26	< 0.0001	541.89	< 0.0001
Timepoint	0.785	0.377	1.376	0.243
Position	0.087	0.768	5.115	0.025
Concussion	0.092	0.762	1.065	0.304
Timepoint × Position	0.29	0.591	0.073	0.788
Timepoint × Concussion	0.009	0.926	1.295	0.257
Position × Concussion	1.995	0.16	0.542	0.463
Timepoint × Position × Concussion	0.173	0.678	0.295	0.588

Table 2 DTI-ALPS Findings ANOVA results from linear regression examining effects of Timepoint, Position, and Concussion history on DTI-ALPS index in left and right brain regions (N = 66 subjects × 2 timepoints). DFMethod = Residual; DF1 = 1, DF2 = 124 for all terms. Significant results are designated by bold font.

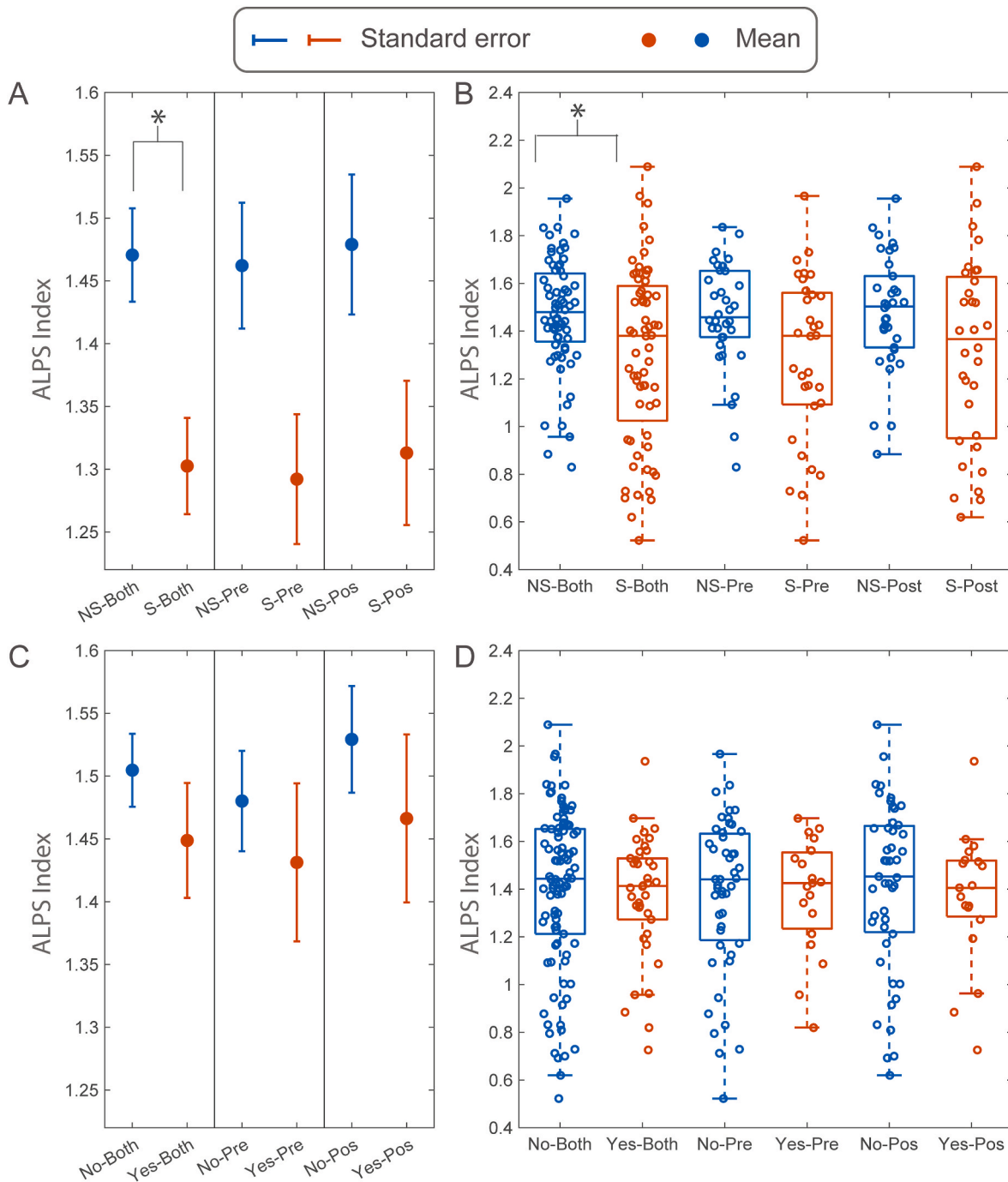


Fig. 2. DTI-ALPS index values in the right hemisphere grouped by player position (NS = Non-Speed, S = Speed; A-B) and concussion history (No vs. Yes; C-D) across pre-season, post-season, and their average (Both). (A) and (C) show group means with standard error; (B) and (D) display individual subject data with boxplots. A significant main effect of position was found ($p = 0.025$), with Non-Speed players showing higher DTI-ALPS values than Speed players. Error bars represent ± 1 standard error of the mean; * indicates statistical significance.

system function using the DTI-ALPS index. ALPS is an indirect diffusion metric localized to periventricular perivascular spaces, not a direct measure of glymphatic flow (Haller et al., 2024). Interpretations focus on perivascular-aligned interstitial diffusivity. Methodological factors—ROI placement, imaging plane alignment, gradient scheme, and TE—are clarified to align with current recommendations (Taoka et al., 2024a). Observed ALPS differences are considered alongside complementary structural and physiological markers. This method was utilized to determine if exposure to a season of HAE in American football had a negative impact on this system. Our study demonstrated that glymphatic system function may be impaired when evaluating the DTI-ALPS index

based on player position. However, we found that a player’s history of previous concussion had no effect on DTI-ALPS index measures.

4.1. No alteration of DTI-ALPS index values related to history of concussion

There were no significant changes in DTI-ALPS index from Pre-to Post-Season for either right or left hemisphere in all players (speed and non-speed) with a history of concussion vs. all players with no history of concussion. This is consistent with findings from our other investigations of this cohort demonstrating no change functional

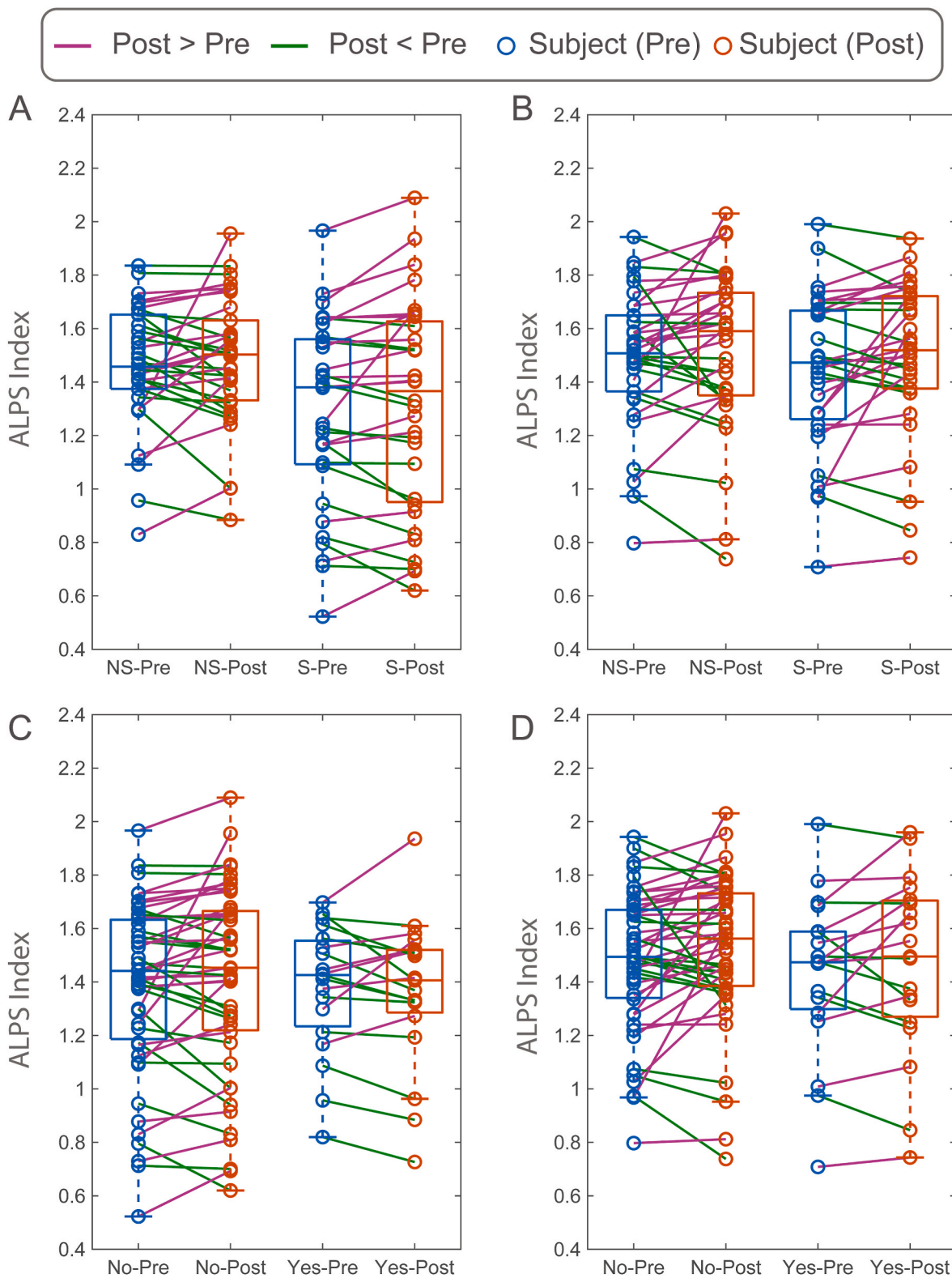


Fig. 3. Within-subject changes in DTI-ALPS index from pre-season to post-season by player position and concussion history. A and B show position-related changes for the right and left hemispheres, respectively (34 Non-Speed, 32 Speed). C and D show concussion history-related changes for the right and left hemispheres, respectively (47 No, 19 Yes). Lines connect individual subjects from pre to post. In the right hemisphere, DTI-ALPS increased in 17 Non-Speed and 19 Speed players; in the left hemisphere, DTI-ALPS increased in 21 Non-Speed and 20 Speed players. For concussion history, right hemisphere DTI-ALPS increased in 28 No-history and 8 Yes-history subjects; left hemisphere increases were observed in 29 No-history and 12 Yes-history subjects. Purple lines indicate post > pre; green lines indicate post < pre.

connectivity or clinical cognitive testing in players with a history of concussion (Griffith et al., 2025). The lack of statistical significance within this cohort may come from several factors associated with the “history of concussion” classification. The number of previous concussions (3 or more), increased symptom severity following concussion, and various mental health challenges can all influence the time course of functional and structural recovery following concussion (Broglio, 2022; Iverson, 2017), and thus may influence DTI-ALPS index measurements within the ‘history of concussion’ cohort analyzed in this investigation. Moreover, some investigations have found the DTI-ALPS index increases or improves following concussion in the chronic (6–12 month) phase of recovery (Zou, 2024), which would support why DTI-ALPS index values in this study may have recovered to normative values measured at our timepoints.

4.2. Alterations in DTI-ALPS index values related to position

When averaging DTI-ALPS index by player position across all timepoints, Football Speed players demonstrated a significantly lower DTI-ALPS index in the right hemisphere in comparison to Football Non-Speed players. This finding indicates that Football Speed players at large may be at risk for deficits in glymphatic waste clearance in this region. The positional differences found in this study are consistent with previous literature that has demonstrated structural and functional deficits in Football Speed players compared to their Non-Speed counterparts, as a result of heterogeneity in the magnitude, rate, and cranial location of the head acceleration events experienced by these two populations (Griffith et al., 2025). It has been well documented that Speed players (quarterbacks, running backs, wide receivers, tight ends, linebackers, and defensive backs) compared to Non-Speed positions (defensive and offensive linemen) (Baron et al., 2012; Lehman et al., 2012), are subject to lower rates, but higher magnitude head acceleration events, even in the absence of concussion (Lee et al., 2021; Vike et al., 2022). Additionally, Speed players experience more head acceleration events to lateral areas of the cranium which is understood to expose the brain to greater neural tissue strain in comparison to impacts to the frontal region which are generally experienced by Non-Speed players (Elkin et al., 2019; Lehman et al., 2012; Papa et al., 2022). As such, it’s theorized that despite a lower frequency of head acceleration events in Speed players, the elevated magnitude coupled with location elicits structural damage to the brain that, identifiable along the perivascular space.

4.3. Hemispheric asymmetry of ALPS index values

The primary finding related to positional differences in ALPS index values was specific to the right hemisphere of the brain. While glymphatic changes have been noted in brain injury literature (Dai et al., 2023; Park et al., 2023; X. Wang et al., 2024; Zhuo et al., 2024), indication of hemispheric asymmetry in ALPS index after brain injury has yet to be found. However, hemispheric asymmetry in perivascular space trauma is common in DTI literature across multiple other neurological morbidities. Still, there is a notable lack of clarity as to the mechanistic source of the asymmetries. As seen in Parkinson’s disease, decreased ALPS index findings are found in the left hemisphere early on in the pathology, but with a tendency to shift to the right hemisphere in more progressed cases (Shen et al., 2022; Si et al., 2022). In Alzheimer’s, decreased glymphatic function, as measured by ALPS index, was also found in the left hemisphere (Zhang et al., 2024). However, in patients diagnosed with major depressive disorder, lower ALPS index was identified in the right hemisphere, compared to the left (Bao et al., 2025). Perhaps the most important line of research for identifying mechanisms of hemispheric differences in ALPS index is in glioma imaging. Across several major studies, ALPS index was lower on the hemisphere of the glial brain tumor, rather than the contralateral side (Villacis et al., 2024; Zeng et al., 2025; Zhu et al., 2023), confirming that the decreased ALPS

index was observed around the focal point of tissue damage.

As such, it is theorized that the decreased ALPS index identified in Football Speed players, compared to Non-Speed players, may be a function of greater right sided brain trauma. Longitudinal studies of concussion using a football cohort demonstrate that the spatial distribution of head impacts is predictive of consequential localized fMRI activation changes. In two separate investigations researchers reported that impact location was associated with region-specific alterations in activation, and that these changes frequently involved right frontal and parietal regions (Robinson et al., 2015; Talavage et al., 2014). Their findings suggest that mechanical forces absorbed by the brain during play can preferentially affect one hemisphere over the other depending on play style and position.

In addition, serial task-based fMRI studies show that athletes with concussion often display increased activation of the right dorsolateral prefrontal cortex (DLPFC) during working memory and executive function tasks, even after clinical symptom resolution (Dettwiler et al., 2014; Pardini et al., 2010). This pattern has been interpreted as compensatory recruitment of right prefrontal resources to maintain cognitive performance under conditions of neural dysfunction following injury.

Lastly, there are cognitive networks with intrinsic right-hemisphere weighting that may amplify these patterns. The ventral attention network (VAN), essential for detecting unexpected stimuli, is right-lateralized (Corbetta and Shulman, 2011). Similarly, some networks show preferential hemispheric localization due to factors like left or right handedness which may affect localization of findings. For example, the vestibular cortical system shows right-hemisphere dominance in right-handed individuals (Dietrick et al., 2020), making it especially susceptible to disruption following concussion. Because vestibular and attentional symptoms are common after head trauma, its possible that subconcussive fMRI changes in these networks may manifest more strongly on the right side.

5. Limitations

This study was subject to several inherent limitations. First, the sample was comprised of contact-sport, male athletes only, as a function of funding availability and lack of female age-matched controls in Football. The lack of female participants inhibits the generalizability of findings because biological sex is not included as a covariate. The lack of non-contact sport controls was primary a funding-related limitation, as the research team chose to prioritize sample size in the population of interested using the current pretest-posttest within-subjects repeated measures study design. Additionally, while there are well recognized and consistent differences in the angle, rate, and magnitude of hits experienced by the current binomial classification of position, ‘speed’ or ‘non-speed’, this classification does not in itself offer an objective measure of HAE exposure rates without helmet accelerometer data. Moreover, several ‘non-speed’ athletes may also participate in special teams plays which have the potential for higher-speed collisions like ‘speed’ position athletes experience during their regular course of practice and games. This type of HAE may be similar to speed positions albeit at a much lower number and frequency than what a traditional speed player absorbs during their normal play. Further, concussion history was recorded using a self-report questionnaire, which while still a reliable measure of lifetime concussion exposure, remains subject to individual reporting bias compared to electronic medical records. Additionally, the DTI-ALPS index, is a non-invasive proxy for supposed glymphatic function in humans. However, this method is notably vulnerable to partial volume effects, particularly at the gray–white matter interface where voxel contamination can artificially influence anisotropy values and confound ALPS measurements (Taoka et al., 2024b). The ALPS index is also highly sensitive to region of interest (ROI) placement, and small differences in positioning may yield substantial variability, limiting its reproducibility (Taoka et al., 2022b; Y. Wang et al., 2025).

Independent, blinded ROI placements by multiple raters was not performed in current study. ROIs were finalized by two physicians using a consensus approach, and inter-rater reliability was not calculated. Future work could include blinded, duplicate ROI placement with agreement metrics to better quantify reproducibility of the ALPS index. Third, while the ALPS index correlates with neurological and vascular pathophysiology in other studies, DTI-ALPS index should be interpreted cautiously as a standalone marker, as it reflects only an indirect approximation of perivascular fluid dynamics rather than a direct quantification of glymphatic clearance and function (Ringstad, 2024). Nevertheless, when considered alongside other measures, the ALPS index may serve as a valuable proxy for glymphatic system function, providing non-invasive insights into fluid transport that remain otherwise challenging to capture in vivo (Taoka and Naganawa, 2020). White matter lesions may also affect DTI-ALPS measurements. White matter lesions are commonly observed as age-related small vessel ischemic changes that are highly uncommon in the young populations that represent this study sample, and review of 3D T1 images from this study were deemed negative for gross white matter changes. However, independent review of FLAIR or T2 MRI sequence in future studies may definitively rule out their presence.

6. Conclusions

Our study found that glymphatic system function as measured by DTI-ALPS was impaired based on player position and not history of concussion after exposure to a season of HAE. Assessment of glymphatic system dysfunction is an important clinical indicator correlating to several adjacent areas of cognitive impairment following impacts to the brain. This is a critical factor to consider when addressing the short- and long-term neurological health of athletes participating in contact sports, particularly given the accumulating findings of systemic alterations in functional systems following sub-clinical HAE exposure, including alterations in neurocognitive functions (Griffith et al., 2025), functional connectivity of the Default Mode Network (Griffith et al., 2025), levels of blood-serum protein including GFAP, Tau, and NF-L (Pappa, 2022), and additionally retinal nerve fiber thinning can occur and has been recently corroborated (Kelly J, Retinal Thinning is Experienced by Collegiate Rugby Players Following a Single Season, unpublished data, June 2025). Our study adds to the growing body of evidence that exposure to HAEs, even in the absence of clinical symptom reporting, may reveal compromised brain integrity and yield high risk for functional and structural neurophysiological deficits.

CRedit authorship contribution statement

Michael Gay: Writing – review & editing, Writing – original draft, Visualization, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Xiaoxiao Bai:** Writing – review & editing, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Owen Griffith:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Project administration, Investigation, Conceptualization. **Linda Papa:** Writing – review & editing, Validation, Supervision, Project administration, Conceptualization. **Wayne Sebastianelli:** Writing – review & editing, Visualization, Supervision, Project administration, Investigation, Funding acquisition, Conceptualization. **Kevin Cockroft:** Writing – review & editing, Validation, Project administration. **Krishnamoorthy Thamburaj:** Writing – review & editing, Validation, Supervision, Project administration. **Semyon Slobounov:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Investigation, Funding acquisition, Conceptualization.

Ethics statement

The studies involving humans were approved by Penn State University Central Applied Tracking System Institutional Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

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Declaration of Competing interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.yinrp.2025.100295>.

Data availability

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

References

- Alsalaheen, B., Stockdale, K., Pechumer, D., Broglio, S.P., 2016. Measurement error in the immediate postconcussion assessment and cognitive testing (ImPACT): systematic review. *J. Head Trauma Rehabil.* 31 (4), 242–251. <https://doi.org/10.1097/HTR.000000000000175>.
- Bao, W., Jiang, P., Xu, P., Lin, H., Xu, J., Lai, M., Yuan, J., Xu, J., 2025. Lower DTI-ALPS index in patients with major depressive disorder: correlation with fatigue. *Behav. Brain Res.* 478, 115323. <https://doi.org/10.1016/j.bbr.2024.115323>.
- Baron, S.L., Hein, M.J., Lehman, E., Geric, C.M., 2012. Body mass index, playing position, race, and the cardiovascular mortality of retired professional football players. *Am. J. Cardiol.* 109 (6), 889–896. <https://doi.org/10.1016/j.amjcard.2011.10.050>.
- Barth, J.T., Alves, W.M., Ryan, T.V., Macciocchi, S.N., Rimel, R.W., Jane, J.A., Nelson, W.E., 1989. Mild head injury in sports: neuropsychological sequelae and recovery of function. In: *Mild Head Injury*. Oxford University Press, pp. 257–275.
- Broglio, S.P., Eckner, J.T., Martini, D., Sosnoff, J.J., Kutcher, J.S., Randolph, C., 2011. Cumulative head impact burden in high school football. *J. Neurotrauma* 28 (10), 2069–2078. <https://doi.org/10.1089/neu.2011.1825>.
- Chizuk, H.M., Cunningham, A., Horn, E.C., Thapar, R.S., Willer, B.S., Leddy, J.J., Haider, M.N., 2022. Association of concussion history and prolonged recovery in youth. *Clin. J. Sport Med.: Offic. J. Canadian Academy of Sport Med.* 32 (6), e573–e579. <https://doi.org/10.1097/JSM.0000000000001044>.
- Cieslak, M., Cook, P.A., He, X., Yeh, F.-C., Dhollander, T., Adebimpe, A., Aguirre, G.K., Bassett, D.S., Betzel, R.F., Bourque, J., Cabral, L.M., Davatzikos, C., Detre, J.A., Earl, E., Elliott, M.A., Fadnavis, S., Fair, D.A., Foran, W., Fotiadis, P., et al., 2021. QSIprep: an integrative platform for preprocessing and reconstructing diffusion MRI data. *Nat. Methods* 18 (7), 775–778. <https://doi.org/10.1038/s41592-021-01185-5>.
- Corbetta, M., Shulman, G.L., 2011. Spatial neglect and attention networks. *Annu. Rev. Neurosci.* 34, 569–599. <https://doi.org/10.1146/annurev-neuro-061010-113731>, 34, 2011.
- Dai, Z., Yang, Z., Li, Z., Li, M., Sun, H., Zhuang, Z., Yang, W., Hu, Z., Chen, X., Lin, D., Wu, X., 2023. Increased glymphatic system activity in patients with mild traumatic

- brain injury. *Front. Neurol.* 14, 1148878. <https://doi.org/10.3389/fneur.2023.1148878>.
- Dettwiler, A., Murugavel, M., Putukian, M., Cubon, V., Furtado, J., Osherson, D., 2014. Persistent differences in patterns of brain activation after sports-related concussion: a longitudinal functional magnetic resonance imaging study. *J. Neurotrauma* 31 (2), 180–188. <https://doi.org/10.1089/neu.2013.2983>.
- Dietrick, B., Molloy, E., Massaro, A.N., Strickland, T., Zhu, J., Slevin, M., Donoghue, V., Sweetman, D., Kelly, L., O'Dea, M., McGowan, M., Vezina, G., Glass, P., Vaidya, D., Brooks, S., Northington, F., Everett, A.D., 2020. Plasma and cerebrospinal fluid candidate biomarkers of neonatal encephalopathy severity and neurodevelopmental outcomes. *J. Pediatr.* 226, 71–79.e5. <https://doi.org/10.1016/j.jpeds.2020.06.078>.
- Elkin, B.S., Gabler, L.F., Panzer, M.B., Siegmund, G.P., 2019. Brain tissue strains vary with head impact location: a possible explanation for increased concussion risk in struck versus striking football players. *Clin. Biomech.* 64, 49–57. <https://doi.org/10.1016/j.clinbiomech.2018.03.021>.
- Ghanizadeh, H., Nedergaard, M., 2025. Chapter 10—The glymphatic system. In: Verkhratsky, A., de Witte, L.D., Aronica, E., Hol, E.M. (Eds.), *Handbook of Clinical Neurology*, vol. 209. Elsevier, pp. 161–170. <https://doi.org/10.1016/B978-0-443-19104-6.00006-1>.
- Griffith, O., Bai, X., Walter, A.E., Gay, M., Kelly, J., Sebastianelli, W., Papa, L., Slobounov, S., 2025. Association of player position and functional connectivity alterations in collegiate American football players: an fMRI study. *Front. Neurol.* 15. <https://doi.org/10.3389/fneur.2024.1511915>.
- Haller, S., Moy, L., Anzai, Y., 2024. Evaluation of diffusion tensor imaging analysis along the perivascular space as a marker of the glymphatic system. *Radiology* 310 (1), e232899. <https://doi.org/10.1148/radiol.232899>.
- Hammer, E., Brooks, M.A., Hetzel, S., Arakkal, A., Comstock, R.D., 2020. Epidemiology of injuries sustained in boys' high school contact and collision sports, 2008–2009 through 2012–2013. *Orthopaedic J. Sports Med.* 8 (2), 232596712090369. <https://doi.org/10.1177/2325967120903699>.
- Howell, D.R., Beasley, M., Vopat, L., Meehan, W.P., 2017. The effect of prior concussion history on dual-task gait following a concussion. *J. Neurotrauma* 34 (4), 838–844. <https://doi.org/10.1089/neu.2016.4609>.
- Hsu, J.-L., Wei, Y.-C., Toh, C.H., Hsiao, I.-T., Lin, K.-J., Yen, T.-C., Liao, M.-F., Ro, L.-S., 2023. Magnetic resonance images implicate that glymphatic alterations mediate cognitive dysfunction in Alzheimer disease. *Ann. Neurol.* 93 (1), 164–174. <https://doi.org/10.1002/ana.26516>.
- Jenkinson, M., Beckmann, C.F., Behrens, T.E.J., Woolrich, M.W., Smith, S.M., 2012. *Fsl Neuroimage* 62 (2), 782–790. <https://doi.org/10.1016/j.neuroimage.2011.09.015>.
- Lee, T.A., Lycke, R.J., Lee, P.J., Cudal, C.M., Toroliski, K.J., Bucherl, S.E., Leiva-Molano, N., Auerbach, P.S., Talavage, T.M., Nauman, E.A., 2021. Distribution of head acceleration events varies by position and play type in North American football. *Clin. J. Sport Med.* 31 (5), E245–E250. <https://doi.org/10.1097/JSM.0000000000000778>.
- Lehman, E.J., Hein, M.J., Baron, S.L., Gersic, C.M., 2012. Neurodegenerative causes of death among retired national football league players. *Neurology* 79 (19), 1970–1974. <https://doi.org/10.1212/WNL.0b013e31826daf50>.
- Li, W.-X., Liu, Z.-Y., Zhai, F.-F., Han, F., Li, M.-L., Zhou, L.-X., Ni, J., Yao, M., Zhang, S.-Y., Cui, L.-Y., Jin, Z.-Y., Zhu, Y.-C., 2024. Automated diffusion-weighted image analysis along the perivascular space index reveals glymphatic dysfunction in association with brain parenchymal lesions. *Hum. Brain Mapp.* 45 (11), e26790. <https://doi.org/10.1002/hbm.26790>.
- Liu, S., Sun, X., Ren, Q., Chen, Y., Dai, T., Yang, Y., Gong, G., Li, W., Zhao, Y., Meng, X., Lin, P., Yan, C., 2024. Glymphatic dysfunction in patients with early-stage amyotrophic lateral sclerosis. *Brain: J. Neurol.* 147 (1), 100–108. <https://doi.org/10.1093/brain/awad274>.
- Michalak, E., Pulliam, A.N., Datta Roy, P.M., Dixon, J.B., LaPlaca, M.C., 2025. Near-infrared imaging of glymphatic clearance in a pre-clinical model of repetitive closed head traumatic brain injury. *Neurotrauma Reports* 6 (1), 115–128. <https://doi.org/10.1089/neur.2024.0128>.
- Mueller, F. O., & Colgate, B. (n.d.). ANNUAL SURVEY OF FOOTBALL INJURY RESEARCH 1931–2010.
- Papa, L., Walter, A.E., Wilkes, J.R., Clonts, H.S., Johnson, B., Slobounov, S.M., 2022. Effect of player position on serum biomarkers during participation in a season of collegiate football. *J. Neurotrauma* 39 (19–20), 1339–1348. <https://doi.org/10.1089/neu.2022.0083>.
- Pardini, J.E., Pardini, D.A., Becker, J.T., Dunfee, K.L., Eddy, W.F., Lovell, M.R., Welling, J.S., 2010. Postconcussive symptoms are associated with compensatory cortical recruitment during a working memory task. *Neurosurgery* 67 (4), 1020. <https://doi.org/10.1227/NEU.0b013e3181ee33e2>.
- Park, J.H., Bae, Y.J., Kim, J.S., Jung, W.S., Choi, J.W., Roh, T.H., You, N., Kim, S.-H., Han, M., 2023. Glymphatic system evaluation using diffusion tensor imaging in patients with traumatic brain injury. *Neuroradiology* 65 (3), 551–557. <https://doi.org/10.1007/s00234-022-03073-x>.
- Ringstad, G., 2024. Glymphatic imaging: a critical look at the DTI-ALPS index. *Neuroradiology* 66 (2), 157–160. <https://doi.org/10.1007/s00234-023-03270-2>.
- Robinson, M.E., Shenk, T.E., Breedlove, E.L., Leverenz, L.J., Nauman, E.A., Talavage, T.M., 2015. The role of location of subconcussive head impacts in fMRI brain activation change. *Dev. Neuropsychol.* 40 (2), 74–79. <https://doi.org/10.1080/87565641.2015.1012204>.
- Shen, T., Yue, Y., Ba, F., He, T., Tang, X., Hu, X., Pu, J., Huang, C., Lv, W., Zhang, B., Lai, H.-Y., 2022. Diffusion along perivascular spaces as marker for impairment of glymphatic system in Parkinson's disease. *npj Parkinson's Dis.* 8 (1), 1–10. <https://doi.org/10.1038/s41531-022-00437-1>.
- Si, X., Guo, T., Wang, Z., Fang, Y., Gu, L., Cao, L., Yang, W., Gao, T., Song, Z., Tian, J., Yin, X., Guan, X., Zhou, C., Wu, J., Bai, X., Liu, X., Zhao, G., Zhang, M., Pu, J., Zhang, B., 2022. Neuroimaging evidence of glymphatic system dysfunction in possible REM sleep behavior disorder and Parkinson's disease. *npj Parkinson's Dis.* 8 (1), 1–9. <https://doi.org/10.1038/s41531-022-00316-9>.
- Talavage, T.M., Nauman, E.A., Breedlove, E.L., Yoruk, U., Dye, A.E., Morigaki, K.E., Feuer, H., Leverenz, L.J., 2014. Functionally-detected cognitive impairment in high school football players without clinically-diagnosed concussion. *J. Neurotrauma* 31 (4), 327–338. <https://doi.org/10.1089/neu.2010.1512>.
- Taoka, T., Ito, R., Nakamichi, R., Kamagata, K., Sakai, M., Kawai, H., Nakane, T., Abe, T., Ichikawa, K., Kikuta, J., Aoki, S., Naganawa, S., 2022a. Reproducibility of diffusion tensor image analysis along the perivascular space (DTI-ALPS) for evaluating interstitial fluid diffusivity and glymphatic function: changes in alps index on multiple condition acquisition experiment (CHAMONIX) study. *Jpn. J. Radiol.* 40 (2), 147–158. <https://doi.org/10.1007/s11604-021-01187-5>.
- Taoka, T., Ito, R., Nakamichi, R., Kamagata, K., Sakai, M., Kawai, H., Nakane, T., Abe, T., Ichikawa, K., Kikuta, J., Aoki, S., Naganawa, S., 2022b. Reproducibility of diffusion tensor image analysis along the perivascular space (DTI-ALPS) for evaluating interstitial fluid diffusivity and glymphatic function: changes in alps index on multiple condition acquisition experiment (CHAMONIX) study. *Jpn. J. Radiol.* 40 (2), 147–158. <https://doi.org/10.1007/s11604-021-01187-5>.
- Taoka, T., Ito, R., Nakamichi, R., Nakane, T., Kawai, H., Naganawa, S., 2024a. Diffusion tensor image analysis Along the perivascular space (DTI-ALPS): revisiting the meaning and significance of the method. *Magn. Reson. Med. Sci.: MRMS: An Offic. J. Japan Soc. Magnetic Resonance in Med.* 23 (3), 268–290. <https://doi.org/10.2463/mrms.rev.2023-0175>.
- Taoka, T., Ito, R., Nakamichi, R., Nakane, T., Kawai, H., Naganawa, S., 2024b. Diffusion tensor image analysis Along the perivascular space (DTI-ALPS): revisiting the meaning and significance of the method. *Magn. Reson. Med. Sci.: MRMS: An Offic. J. Japan Soc. Magnetic Resonance in Med.* 23 (3), 268–290. <https://doi.org/10.2463/mrms.rev.2023-0175>.
- Taoka, T., Naganawa, S., 2020. Glymphatic imaging using MRI. *J. Magn. Reson. Imag.: JMIR* 51 (1), 11–24. <https://doi.org/10.1002/jmri.26892>.
- Ueda, R., Yamagata, B., Niida, R., Hirano, J., Niida, A., Yamamoto, Y., Mimura, M., 2024. Glymphatic system dysfunction in mood disorders: evaluation by diffusion magnetic resonance imaging. *Neuroscience* 555, 69–75. <https://doi.org/10.1016/j.neuroscience.2024.07.026>.
- Vike, N., Bari, S., Susnjari, A., Lee, T., Lycke, R., Auger, J., Music, J., Nauman, E., Talavage, T., Rispoli, J., 2022. American football position-specific neurometabolic changes in high school athletes: a magnetic resonance spectroscopic study. *J. Neurotrauma* 39 (17–18), 1168–1182. <https://doi.org/10.1089/neu.2021.0186>.
- Villacis, G., Schmidt, A., Rudolf, J.C., Schwenke, H., Küchler, J., Schramm, P., Ulloa, P., 2024. Evaluating the glymphatic system via magnetic resonance diffusion tensor imaging along the perivascular spaces in brain tumor patients. *Jpn. J. Radiol.* 42 (10), 1146–1156. <https://doi.org/10.1007/s11604-024-01602-7>.
- Wang, X., Deng, L., Liu, X., Cheng, S., Zhan, Y., Chen, J., 2024. Relationship between glymphatic system dysfunction and cognitive impairment in patients with mild-to-moderate chronic traumatic brain injury: an analysis of the analysis along the perivascular space (ALPS) index. *Quant. Imag. Med. Surg.* 14 (12), 9246–9257. <https://doi.org/10.21037/qims-24-895>.
- Wang, Y., Yang, M., Zeng, X., Wang, S., Zhang, W., Wang, W., Du, Y., Ding, J., Ding, X., 2025. Glymphatic dysfunction assessed by DTI-ALPS index predicts early cognitive impairment in acute subcortical infarcts: a prospective clinical cohort study. *Front. Neuroim.* 16, 1605889. <https://doi.org/10.3389/fneur.2025.1605889>.
- Wojtowicz, M., Iverson, G.L., Silverberg, N.D., Mannix, R., Zafonte, R., Maxwell, B., Berkner, P.D., 2017. Consistency of self-reported concussion history in adolescent athletes. *J. Neurotrauma* 34 (2), 322–327. <https://doi.org/10.1089/neu.2016.4412>.
- Zeng, S., Huang, Z., Zhou, W., Ma, H., Wu, J., Zhao, C., Yang, Z., Qiu, H., Chu, J., 2025. Noninvasive evaluation of the glymphatic system in diffuse gliomas using diffusion tensor image analysis along the perivascular space. *J. Neurosurg.* 142 (1), 187–196. <https://doi.org/10.3171/2024.4.JNS232724>.
- Zhang, X., Wang, Y., Jiao, B., Wang, Z., Shi, J., Zhang, Y., Bai, X., Li, Z., Li, S., Bai, R., Sui, B., 2024. Glymphatic system impairment in Alzheimer's disease: associations with perivascular space volume and cognitive function. *Eur. Radiol.* 34 (2), 1314–1323. <https://doi.org/10.1007/s00330-023-10122-3>.
- Zhu, H., Xie, Y., Li, L., Liu, Y., Li, S., Shen, N., Zhang, J., Yan, S., Liu, D., Li, Y., Zhu, W., 2023. Diffusion along the perivascular space as a potential biomarker for glioma grading and isocitrate dehydrogenase 1 mutation status prediction. *Quant. Imag. Med. Surg.* 13 (12), 8259–8273. <https://doi.org/10.21037/qims-23-541>.
- Zhuo, J., Raghavan, P., Li, J., Roys, S., Njokou Tchoquessi, R.L., Chen, H., Wickwire, E. M., Parikh, G.Y., Schwartzbauer, G.T., Grattan, L.M., Wang, Z., Gullapalli, R.P., Badjatia, N., 2024. Longitudinal assessment of glymphatic changes following mild traumatic brain injury: insights from perivascular space burden and DTI-ALPS imaging. *Front. Neurol.* 15, 1443496. <https://doi.org/10.3389/fneur.2024.1443496>.
- Zimmerman, K.A., Kim, J., Kartou, C., Lochhead, L., Sharp, D.J., Hoshizaki, T., Ghajari, M., 2021. Player position in American football influences the magnitude of mechanical strains produced in the location of chronic traumatic encephalopathy pathology: a computational modelling study. *J. Biomech.* 118, 110256. <https://doi.org/10.1016/j.jbiomech.2021.110256>.