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ORIGINAL ARTICLE

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Altered Brain Functional Connectivity in Female Athletes Over the Course of a Season of Collision or Contact Sports

Alyssia Wilson,¹ W. Dale Stevens,¹ Lauren Sergio,² and Magdalena Wojtowicz^{1,*}

Abstract

University athletes are exposed to numerous impacts to the body and head, though the potential cumulative effects of such hits remain elusive. This study examined resting-state functional connectivity (rsFC) of brain networks in female varsity athletes over the course of a season. Nineteen female university athletes involved in collision ($N=12$) and contact ($N=7$) sports underwent functional magnetic resonance imaging scans at both pre- and post-season. A group-level independent component analysis (ICA) was used to investigate differences in rsFC over the course of a season and differences between contact and collision sport athletes. Decreased rsFC was observed over the course of the season between the default mode network (DMN) and regions in the frontal, parietal, and occipital lobe (p false discovery rate, ≤ 0.05) driven by differences in the contact group. There was also a main effect of group in the dorsal attention network (DAN) driven by differences between contact and collision groups at pre-season. Differences identified over the course of a season of play indicate largely decreased rsFC within the DMN, and level of contact was associated with differences in rsFC of the DAN. The association between exposure to repetitive head impacts (RHIs) and observed changes in network rsFC supplements the growing literature suggesting that even non-concussed athletes may be at risk for changes in brain functioning. However, the complexity of examining the direct effects of RHIs highlights the need to consider multiple factors, including mental health and sport-specific training and expertise, that may potentially be associated with neural changes.

Keywords: contact sports; female athlete; functional connectivity; repetitive head impact

Introduction

Contact and collision sport athletes are exposed to repetitive head impacts (RHIs) attributable to rapid changes in head velocity as the result of a direct contact to the head or collision to the body.¹ These impacts

often lack visible signs of injury and/or may result in subthreshold clinical symptoms in comparison with hits resulting in concussion(s).² However, there is a growing literature examining potential cumulative effects of RHIs on athletes' physical, cognitive, and

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emotional health.^{3–6} To date, studies examining the possible cognitive effects of RHIs have revealed mixed findings. Several studies have identified decreases in neurocognitive performance over the course of an athletic season associated with sport exposure in the absence of reported concussions.^{4,5,7–12} However, collision, contact, and non-contact athletes are a heterogeneous group who have been shown to experience variable neurological outcomes based on their relative exposure to RHIs.¹³

The available research examining evidence of differences in structural brain metrics associated with RHIs has also reported mixed findings. Some studies have not observed white matter or cortical volume differences over the course of a season in collision athletes.^{14,15} However, others have reported changes in multiple structural and neurometabolic metrics across short-term^{16–18} and long-term findings,¹⁹ as well as differences between collision and non-contact athletes at baseline.^{17,18}

Using resting-state functional magnetic resonance imaging (rsfMRI), several studies have identified changes to resting-state functional connectivity (rsFC) after exposure to RHIs.^{4,8,15,20–25} Across brain regions, rsFC may detect subtle changes in the neural integrity of brain regions and networks that may be vulnerable to head impacts.^{26,27} Research on male football athletes has revealed differences in rsFC among asymptomatic football players over the course of a season.^{8,15,21,22} These studies have consistently observed changes associated with default mode network^{21,22} (DMN) connectivity.¹⁵ Collegiate rugby players showed connectivity differences after a single game between frontal, parietal, and subcortical regions.²⁴ In male soccer players, rsFC increases in the central autonomic network have been observed in association with the amount of head-to-ball impact exposure over a season.²⁵ Difference in global neural connectivity have been observed in varsity athletes at baseline, with the highest global connectivity observed in non-contact athletes and lowest global connectivity observed in collision athletes, suggesting potential better functional neural integrity in lower contact athletes.²³

The majority of the literature examining RHIs has focused on male football players. Of the total number of imaging studies examining RHIs ($N=12$), only three included both male and female athletes, whereas just one study included female athletes only. See the Supplementary Material for an in-depth literature review. Despite accounting for 43% of the collegiate athlete

population,²⁸ female athletes have been severely understudied in this literature. The type of impacts that female athletes sustain may be different than their male counterparts, attributable, in part, to smaller neck size and differences in type of play.^{29–33} In addition, some studies report that females experience more adverse symptoms,^{34,35} greater symptoms of depression,³⁶ and worse neurocognitive performance.^{16,34,37,38} This suggests potential sex-related differences in outcomes after RHIs. Few studies have examined neural differences in female athletes associated with RHI; however, two studies have shown structural brain changes in female hockey and rugby players that are not observed in male players.^{16,20}

This study examined cognitive and neural functioning of a cohort of female varsity athletes over the course of a season of play. Given the broad range of symptom presentations in female and male athletes after a head injury,^{34,37–40} and the previous focus in the literature on DMN findings, we decided to expand the scope of our study by taking a broader whole-brain network approach. Specifically, we examined changes in rsFC within the DMN, sensorimotor (SMN), frontoparietal (FPN), dorsal attention (DAN), and salience (SN) networks post-season compared to pre-season in female athletes involved in collision and contact sports. These networks have been implicated in head injury,^{24,41–43} motor function,^{44,45} executive functions,^{46–48} and attention processes,^{48–51} respectively. Potential rsFC differences in these networks associated with level of contact (i.e., collision vs. contact) were also explored.

This study hypothesized that: 1) there would be differences in rsFC between contact and collision athletes in the DMN and 2) a difference in rsFC would be observed over the course of a season. To further inform the literature, we also planned exploratory analyses in the following networks: SMN, FPN, DAN, and SN. A better understanding of rsFC differences in athletes over a season of play will improve our knowledge of the possible neurobiological changes associated with subclinical head impact that may compound over time and put exposed players at greater risk of clinical injury.

Methods

Participants

Nineteen female university athletes (ages 18–21) were recruited from York University. Participants were eligible if: 1) they were >18 years of age, 2) were rostered to play on a university team for the current season, and 3)



met the requirements for safe magnetic resonance imaging (MRI) scanning. Twelve were involved in collision sport (i.e., ice hockey), whereas the remainder ($n=7$) were involved in contact sports (i.e., basketball, soccer, or volleyball). Level of contact was determined in accordance with the classifications proposed by Rice,⁵² determined by estimating the level of relative risk for an acute injury. Collision sport athletes often come into rough contact with other players or objects usually at higher speeds, whereas contact sport athletes often come into contact with each other as a by-product of the sport and with relatively less force.

Procedure

This study was approved by the Human Participants Review Sub-Committee of York University's Ethics Review Board. Participants provided written informed consent and completed testing and MRI scanning before the start of their athletic season (before beginning contact practices) and immediately after their athletic season. Scans took place, on average, 166 days (standard deviation [SD] = 45) apart.

Measures

Sport Concussion Assessment Tool 5. The Sport Concussion Assessment Tool 5 (SCAT5)⁵³ was used to assess concussion symptoms by using scores from the Standardized Assessment of Concussion (SAC) and the total number of symptoms from the Symptom Evaluation.

Attention Network Test-Interaction. The Attention Network Test-Interaction (ANT-I) is a brief task of attention task and executive control that uses 2 (alerting) \times 3 (orienting) \times 2 (executive) design. It is described in detail elsewhere⁴¹ and has been previously used in concussion research.^{55–58} Briefly, efficiency of the alerting network is examined by the difference in reaction time on trials presented with a tone versus no tone. Efficiency of orienting is examined by differences in reaction time on trials with an invalid spatial cue (i.e., asterisk that appears in the opposite location of the target stimuli) versus a valid spatial cue. Finally, the efficiency of the executive network is examined by the difference in reaction time on incongruent flanker trials (i.e., the target arrow is surrounded by arrows pointing in the opposite direction) versus congruent trials (i.e., all arrows pointing in the same direction).

Magnetic resonance imaging acquisition. MRI data were acquired using a 3 Tesla Siemens TRIO MRI scanner (Siemens, Erlangen, Germany). Images were acquired for each subject before the beginning of the season and after the season. Whole-brain, high-resolution, T1-weighted anatomical scans were collected using an ascending multi-slice three-dimensional magnetization-prepared rapid acquisition gradient echo sequence (field of view [FOV] = 256 mm, $1.0 \times 1.0 \times 1.0$ mm voxels, repetition time [TR] = 2300, echo time [TE] = 2.62 ms). A whole-brain multi-echo planar imaging sequence (T2*-weighted) was used to acquire functional data in 240 volumes (43 slices, FOV = 216 mm, 64×64 matrix, $3.4 \times 3.4 \times 3.0$ mm³ voxels, TR = 3000 ms, TE_s = 14 ms, 30 ms, 46 ms, flip angle = 83 degrees). During rsfMRI scanning, patients were instructed to lay still with their eyes closed, but not to fall asleep.

Functional imaging pre-processing

rsfMRI data were pre-processed using the CONN toolbox Version 18.b(59) on the Matlab Version R2019a platform (The MathWorks, Inc., Natick, MA). The default pre-processing pipeline was used, and functional data were functionally realigned and unwarped, translated by centering to (0,0,0) coordinates, slice-time corrected, scrubbed with Artifact Detection Tools-based identification for outlier scans, segmented into gray matter, white matter, and cerebrospinal fluid, normalized to the Montreal Neurological Institute (MNI) template MNI152, and smoothed using an 8-mm Gaussian kernel, full width at half maximum. Denoising was performed using the toolbox's aCompCor protocol that involved linear regression of nuisance parameters to reduce physiological and movement effects. Finally, data were linearly detrended and band-pass filtered (0.008–0.090 Hz).

Independent component analysis

Using a whole-brain, multi-variate approach, rsFC data were analyzed with the independent component analysis (ICA) pipeline in CONN toolbox.⁵⁹ FastICA was used to estimate 20 independent spatial components. Group independent analysis setting was used to back-project individual subject-level spatial map estimation, and the dimensionality reduction value was 64. Spatial match-to-template correlations between each group-level spatial map and the CONN toolbox pre-defined Anatomical Labeling atlases, based on Harvard-Oxford and Automated Anatomical Labeling atlases, were used to identify resting-state networks. Specific networks were chosen



based on involvement in clinical symptoms associated with RHIs, including the DMN, SMN, FPN, DAN, and SN (see Fig. 1).

Statistical analysis

Behavioral variables. Because normality was found to be violated on some measures, non-parametric tests were used where relevant. Mann-Whitney U tests were used to compare mean rank of age, age at first sport, concussion history (number of previous concussions) between groups at pre-season and SCAT total number of symptoms, and SAC subtotal between groups at pre- and post-season. Wilcoxon's signed-rank tests were run between pre- and post-season scores to compare mean rank for all athletes assessed at both time points.

For the ANT-I, mean reaction times and intraindividual variability using the individual standard deviations⁵⁴ (ISDs) were calculated for each participant across trials and were both compared in separate repeated-measures analysis of variance (ANOVA). Twelve condition scores were calculated, one for every combination of alerting (tone vs. no tone), orienting (valid, invalid, or no cue), and executive control (congruent vs. incongruent flankers) factors, which were compared across group (level of contact) and time (pre- vs post-season) in a $2 \times 3 \times 2 \times 2 \times 2$ repeated-measures ANOVA. Repeated-measure ANOVAs for group and time were performed for ISDs. All analyses were adjusted for multiple comparisons.

Resting-state functional magnetic resonance imaging analysis

A 2×2 ANOVA was used to assess the main effects of group (contact and collision) and time (pre- and post-season), as well as any group \times time interaction. We performed follow-up analyses for the main effect of time on the rsFC of significant ICA components in each group independently. We also performed a follow-up analysis for the main effect of group at each time point independently, using between-subject *t*-tests. Non-parametric tests were used with an uncorrected voxel threshold of $p \leq 0.001$ and a cluster-mass correction of $p \leq 0.05$ false discovery rate (FDR) to control for multiple comparisons.

Results

Participant characteristics

At pre-season, there were no significant differences in age, age at first sport, concussion history, or SAC scores

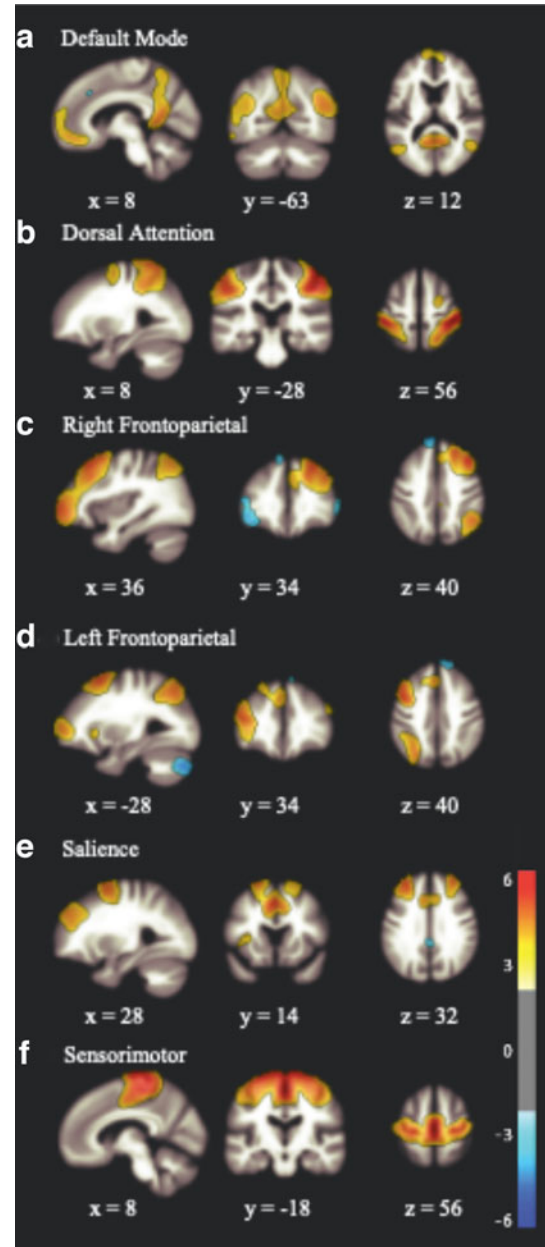


FIG. 1. Results of ICA showing components with high match to template for the (A) DMN, (B) DAN, (C) left FPN, (D) right FPN, (E) SN, and (F) SMN. DAN, dorsal attention network; DMN, default mode network; FPN, frontoparietal network; ICA, independent component analysis; SMN, sensorimotor network; SN, salience network.

Table 1. Demographic and Clinical Results for Contact and Collision Athletes

	Pre-season		p(g)	Post-season		p(g)
	Contact (n=7)	Collision (n=12)		Contact (n=7)	Collision (n=12)	
Age, years, M (SD)	19.71 (1.38)	19.50 (1.09)	0.65 (0.17)	—	—	—
Age at first sport, M (SD)	7.28 (3.68)	4.58 (0.90)	0.08 (1.12)	—	—	—
Concussion history, M (SD)	1.57 (1.51)	0.58 (0.90)	0.14 (0.82)	—	—	—
SCAT5 total symptoms, M (SD)	4.71 (3.40)	1.33 (3.11)	0.02 (1.00)	4.14 (4.60)	2.00 (3.22)	0.34 (0.54)
SAC subtotal, M (SD)	27.43 (1.81)	26.83 (1.19)	0.43 (0.39)	26.86 (0.90)	27.92 (1.56)	0.17 (0.74)

g = Hedge's *g*.

M, mean; SD, standard deviation; SCAT5, Sport Concussion Assessment Tool 5; SAC, Standardized Assessment of Concussion.

between contact and collision athletes ($ps > 0.05$; see Table 1). Contact athletes, however, did have significantly higher total SCAT5 symptom scores at preseason (see Table 1). There were no significant differences in scores between pre- and post-season scores ($ps > 0.05$; see Table 1). No athletes sustained a concussion over the course of the season.

Attention Network Test-Interaction results

ANT-I results are presented in Table 2. Overall scores showed within-subject effects of the alerting, orienting, and executive function networks (Alerting: $F_{(1,17)} = 5.66$, $p = 0.029$; Orienting: $F_{(2,34)} = 86.03$, $p < 0.001$; Executive: $F_{(1,17)} = 527.96$, $p < 0.001$). *Post hoc* analyses revealed that participants responded more quickly when there was a tone, valid cue, or congruent flanker in the alert, orient, and executive conditions, respectively ($ps \leq 0.05$).

There was also a significant main effect of time ($F_{(1,17)} = 6.91$, $p = 0.018$; partial eta squared = 0.29), with faster performance observed at post-season compared to pre-season ($M_{pre} = 599.15$ vs. $M_{post} = 574.25$). ANT-I performance did not differ by group ($F_{(1,17)} = 2.66$, $p = 0.121$, partial eta squared = 0.14), and there was no group by time interaction ($F_{(1,17)} = 0.917$, $p = 0.352$, partial eta squared = 0.05), indicating no group differences

in pre- and post-season testing (see Table 2 for mean (M) and SDs of ANT-I results by group at the two time points).

A repeated-measures ANOVA of ISDs did not show significant effects of time ($F_{(1,17)} = 2.47$, $p = 0.625$, partial eta squared = 0.014) or group ($F_{(1,17)} = 1.297$, $p = 0.270$, partial eta squared = 0.071).

Resting-state functional connectivity results

There was a main effect of time, such that the DMN (see Fig. 2) had decreased rsFC at post-season with a relatively large cluster primarily in the superior parietal lobule, with some voxels in the superior division of the lateral occipital cortex and spreading into the precuneus and post-central gyrus in the right hemisphere ($T = -6.85$, $pFDR = 0.001$) and a cluster across the supramarginal gyri and post-central gyrus bilaterally (left, $T = -6.13$, $pFDR = 0.004$; right, $T = -6.41$, $pFDR = 0.043$). Another cluster primarily in the left superior frontal gyrus with spread into the pre-central gyrus ($T = -7.61$, $pFDR = 0.006$) and one primarily in the superior parietal gyrus and lateral occipital cortex ($T = -5.82$, $pFDR = 0.043$) also showed decreased rsFC at post-season. Increased rsFC with the DMN was observed with a cluster in the right frontal pole ($T = 6.27$, $pFDR = 0.043$) at post-season.

Table 2. Attention Network Test-Interaction Results

	Pre-season		Post-season	
	Contact (n=7)	Collision (n=12)	Contact (n=7)	Collision (n=12)
Alerting				
Tone, M (SD)	617.11 (79.29)	580.21 (56.29)	596.92 (60.67)	543.35 (40.10)
No tone, M (SD)	618.44 (128.88)	580.83 (116.93)	606.97 (59.36)	549.76 (42.03)
Orienting				
Valid cue, M (SD)	573.47 (81.32)	539.84 (49.88)	559.18 (53.23)	508.12 (29.60)
Invalid cue, M (SD)	635.39 (80.11)	597.07 (63.64)	613.70 (64.91)	559.09 (51.00)
No cue, M (SD)	644.46 (77.57)	604.66 (60.75)	632.96 (64.85)	572.46 (50.03)
Executive Control				
Congruent, M (SD)	575.34 (75.83)	540.10 (52.00)	561.36 (57.98)	512.25 (37.20)
Incongruent, M (SD)	660.21 (81.10)	620.95 (61.41)	642.53 (62.35)	580.86 (44.76)

M, mean; SD, standard deviation.



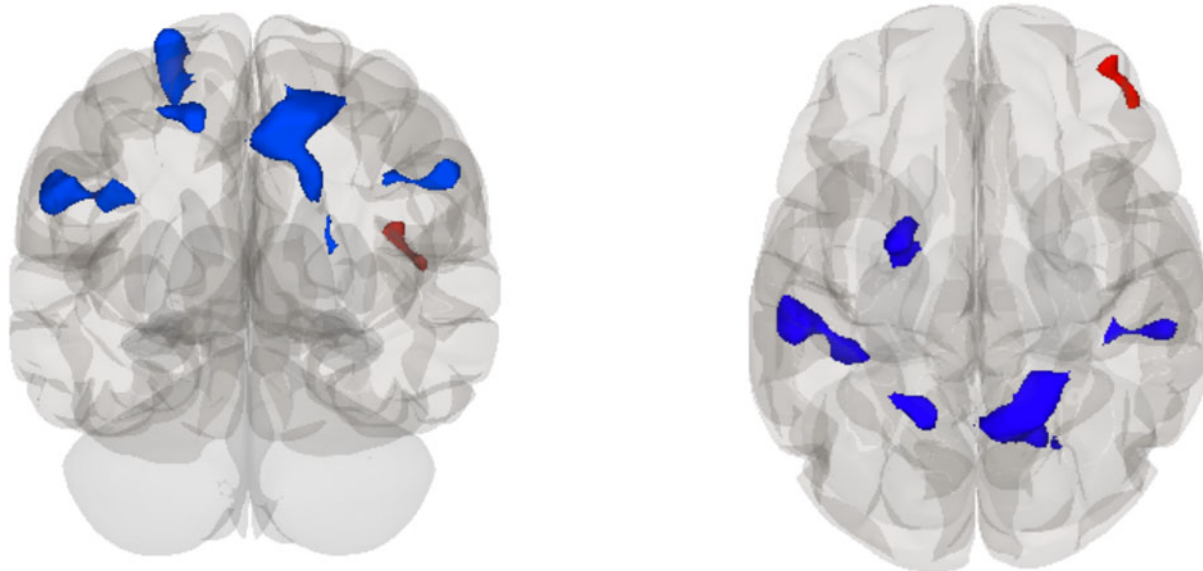


FIG. 2. Glass brain rendering showing the independent component analysis (ICA) main effect of time on rsFC of the default mode network (DMN): decreased connectivity with the right superior parietal lobule, left superior frontal gyrus, bilateral supramarginal gyrus, left superior parietal lobule, and increased connectivity with the right frontal pole at post-season compared to pre-season. rsFC, resting-state functional connectivity.

A follow-up within-subjects *t*-test analysis of the contact group only showed significantly decreased rsFC between the DMN and three clusters bilaterally in the lateral occipital cortex (right, $T = -19.32$, $pFDR = 0.001$; right, $T = -10.18$, $pFDR = 0.003$; left, $T = -16.42$, $pFDR = 0.003$), left supramarginal gyrus ($T = -27.85$, $pFDR = 0.001$), left superior frontal gyrus ($T = -13.75$, $pFDR = 0.003$), bilateral superior parietal lobules (left, $T = -12.81$, $pFDR = 0.010$; right, $T = -11.03$, $pFDR = 0.045$), and right pre-central gyrus ($T = -10.08$, $pFDR = 0.045$) at post- versus pre-season. No significant rsFC differences were observed between the DMN and other brain regions in a within-subjects *t*-test of the collision group at pre- versus post-season (see Table 3).

We observed a main effect of group in the DAN (see Fig. 3), such that collision sport athletes showed increased rsFC of this network with a cluster primarily in the right superior frontal gyrus and spread into the left superior frontal gyrus and paracingulate gyrus ($T = 7.33$, $pFDR = 0.035$) and decreased rsFC with the right supramarginal gyrus ($T = -6.09$, $pFDR = 0.037$). To examine this in more detail, we ran follow-up analyses. A follow-up between-subjects *t*-test contrasting the collision versus contact groups at pre-season showed increased rsFC between the DAN and a cluster primarily in the right superior frontal gyrus ($T = 6.43$, $pFDR = 0.021$) and decreased rsFC with a cluster in the right supramarginal gyrus ($T = -5.15$, $pFDR = 0.044$).

Table 3. ICA Results

Network	Primary regions	Cluster size	MNI coordinates			T value	Mass pFDR
			x	y	z		
Main effect of time ($n = 19$)							
DMN	Superior parietal lobule right	645	18	-46	70	-6.85	0.001
	Supramarginal gyrus, anterior division left	357	-50	-26	32	-6.13	0.004
	Superior frontal gyrus left	268	-22	-4	70	-7.61	0.006
	Supramarginal gyrus, anterior division right	145	56	-32	40	-6.41	0.043
	Superior parietal lobule left	133	-16	-58	68	-5.82	0.043
	Frontal pole right	115	42	48	-16	6.27	0.043
Follow-up: contact ($n = 7$) Pre(-1) Post(1)							



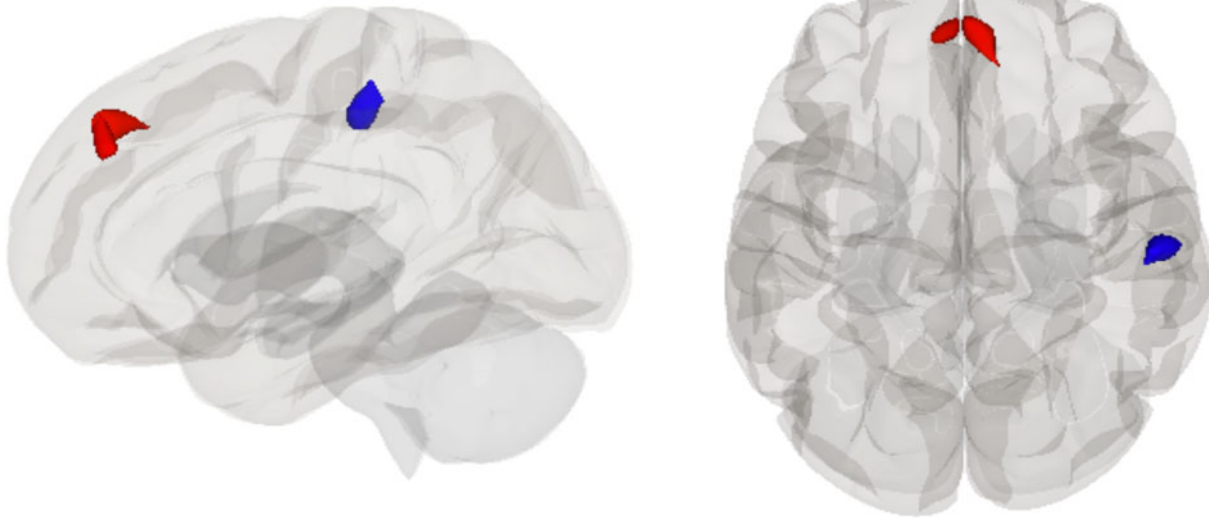


FIG. 3. Glass brain rendering showing the independent component analysis (ICA) main effect of group on rsFC of the dorsal attention network (DAN): increased connectivity with the right superior frontal gyrus and decreased connectivity with the right supramarginal gyrus in collision players compared to contact players. rsFC, resting-state functional connectivity.

No significant group differences in rsFC were observed between the DAN and other brain regions at post-season (see Table 3).

There was no significant group \times time interaction.

Discussion

Because of growing concern about the effects of exposure to RHI, this study investigated pre- versus post-season differences in cognition and brain functional integrity in contact and collision female varsity athletes. By taking a network approach, we were able to more broadly investigate rsFC changes associated with a season of play. We identified changes in DMN rsFC that showed decreased connectivity bilaterally in the superior parietal lobule and supramarginal gyrus, as well as the left superior frontal gyrus, and increased connectivity with the right frontal pole across the season, which appeared to be driven by the contact athletes. Differences in rsFC were also identified within the DAN showing increased connectivity with the right superior frontal gyrus and decreased connectivity in the right supramarginal gyrus. In contrast, we did not observe differences in attentional and executive control performance (using the ANT-I) between groups; however, there was a reduction in overall mean reaction

time at post-season. This reduction may reflect a number of factors, including a test practice effect related to the ANT-I, specific training exposure associated with sport participation over the course of a season, or improvements in cognitive functioning related with cardiorespiratory fitness.⁶⁰

Several studies have highlighted changes in the DMN after a season of play related to level of contact exposure in athletes.^{15,20–22,24} Studies have shown that non-collision sport athletes displayed a consistent DMN connectivity between pre- and post-season scans, whereas collision sport athletes have shown variability in the rsFC of the DMN throughout the season.^{21,22} Other studies have reported greater DMN connectivity in higher-contact-level athletes compared to non-contact athletes throughout the season,²⁰ and in a study of football players, those who experienced a larger number of high-impact hits showed greater increases in DMN rsFC.¹⁵ It is striking that out of all the networks we investigated, our primary rsFC findings are consistent with the current literature, showing changes between DMN rsFC and other brain regions after a season of play, suggesting that this finding is relevant and is likely not attributable to noise.



In a comparison of pre- and post-season rsfMRI data, we observed decreased connectivity between the DMN and occipital, supramarginal, superior frontal, and superior parietal brain regions, and an increase in connectivity with the frontal pole in post-season scans. Follow-up *t*-test analyses revealed decreases in rsFC between the DMN and other brain regions after a season of play in contact sport athletes, but did not show any changes between pre- and post-season in collision sport athletes. Regions within the DMN have been associated with stability of performance.^{61–63} Specifically, decreased activity within nodes of the DMN have been associated with motor learning and improved performance.^{62,64,65} Thus, it is possible that within contact athletes, decreased rsFC between the DMN and other brain regions represents improvements in network functioning associated with visuo-motor training across the season.^{63,66} A similar pattern would be anticipated in collision athletes as well, but was not observed. Thus, the absence of rsFC changes in collision athletes observed in our study may reflect the effect of greater exposure to RHIs. However, observed changes may also be attributable to additional factors, such as differences in sport-related training, the number of practices and games, as well as differences in baseline symptoms.

To further explore potential baseline differences between groups, we examined rsFC between contact and collision athletes at pre-season. We observed rsFC differences between the DAN and other brain regions that included increased rsFC with the superior frontal gyrus and decreased rsFC with the supramarginal gyrus in collision sport athletes compared to contact sport athletes. This difference may represent distinctions in specialized sport-specific attentional requirements; however, there were no group differences in altering, orienting, or executive control components of the ANT-I. There were also no significant differences in mean concussion history between contact and collision groups in our sample, and the ranges of lifetime concussions in both groups were similar (i.e., between 0 and 4 in contact players and 0 and 3 in collision players).

Other literature has shown that differences in rsFC may reflect neuroplasticity required for expertise development associated with different sport requirements⁶⁷ and for specific relevant abilities such as motor skill learning.⁶⁸ The demands of different sports require specialized skills of the athletes playing them, such as various adaptations to different sport surfaces and techniques. Another consideration is that our contact

group was composed of athletes that played a larger variety of sports compared to the collision group, which may complicate the interpretation of the pre-season differences observed in the DAN. Additionally, no group by time interaction was observed; however, this could be attributable to small and/or unequal group sizes included in this study.

This study has several limitations, including a small sample size. However, it is notable that our sample is comparable to other neuroimaging studies examining changes in athlete functions associated with exposure to RHIs.^{4,8,13,14,16,20,22,23,61} Another limitation is the lack of accelerometry data; however, some studies have noted discrepancies between RHIs identified by accelerometry and video review,⁷⁰ and data collected by telemetry systems have been known to overestimate linear and rotational acceleration.^{71–74} This highlights the need for the development of more accurate measurements of head impacts. Our sample also investigated differences in attention measure scores to provide an objective cognitive measure; however, we were unable to compare these scores to healthy controls, which limits our ability to interpret these scores in relation to non-athletes.

A significant variable of interest in female athletes not controlled for in this study is hormonal fluctuations caused by the natural menstrual cycle or hormonal contraceptives. Hormonal fluctuations have been shown to affect symptom endorsement after brain injuries as well as neurological findings.^{17,75} Female sex hormones, such as estrogen and progesterone, have been suggested to potentially have a neuroprotective effect in brain injuries,^{76,77} and the effect of these biological factors on RHIs should be considered in future literature.

Conclusion

In conclusion, this study addresses important gaps in the literature and represents one of the few to examine rsFC associated with contact exposure in exclusively female athletes.²⁰ We identified differences primarily in the DMN after a season of play, emphasizing the robust nature of associations between contact exposure and DMN connectivity. Specifically, our findings suggested network differences between collision and contact athletes that may be driven by pre-season differences, potentially associated with inherent differences in sport requirements. These findings highlight the complexity of examining changes directly associated with RHIs and emphasize the need for considering multiple factors



(e.g., pre-season and sport differences) that might be associated with cognitive and neural changes observed over the course of a season, beyond just the suspected effects of RHIs.

Acknowledgments

The authors acknowledge Alanna Pierias, Diana Gorbet, and Melissa Miljanovski for their significant support and contribution to data collection, as well as the York University Sports Injury Clinic for their assistance with recruitment.

Author Contributions

A.W.: Conceptualization (equal); writing – original draft (lead); formal analysis (lead); writing – review and editing (equal). D.S.: Methodology (equal); writing – review and editing (supporting). L.S.: Review and editing (equal). M.W.: Conceptualization (equal); writing – original draft (supporting); formal analysis (supporting); writing – review and editing (equal).

Funding Information

This work is funded by a grant from the Natural Sciences and Engineering Research Council of Canada.

Author Disclosure Statement

This work is based on research done as part of Ms. Wilson's Master's thesis (<https://yorkspace.library.yorku.ca/xmlui/handle/10315/38727>).

Supplementary Material

Literature Table

Expanded rs-fMRI Methods

References

1. Dashnaw ML, Petraglia AL, Bailes JE. An overview of the basic science of concussion and subconcussion: where we are and where we are going. *Neurosurg Focus* 2012;33(6):E5: 1–9; doi: 10.3171/2012.10.FOCUS12284
2. Shaw NA. The neurophysiology of concussion. *Prog Neurobiol* 2002;67(4): 281–344; doi: 10.1016/S0301-0082(02)00018-7
3. Hwang S, Ma L, Kawata K, et al. Vestibular dysfunction after subconcussive head impact. *J Neurotrauma* 2017;34(1):8–15; doi: 10.1089/neu.2015.4238
4. Talavage TM, Nauman EA, Breedlove EL, et al. Functionally-detected cognitive impairment in high school football players without clinically-diagnosed concussion. *J Neurotrauma* 2014;31(4):327–338; doi: 10.1089/neu.2010.1512
5. McAllister TW, Flashman LA, Maerlender A, et al. Cognitive effects of one season of head impacts in a cohort of collegiate contact sport athletes. *Neurology* 2012;78(22):1777–1784; doi: 10.1212/WNL.0b013e3182582fe7
6. Bailes JE, Petraglia A I, Omalu BI, et al. Role of subconcussion in repetitive mild traumatic brain injury. 2013;119(November):1235–1245; doi: 10.3171/2013.7.JNS121822.
7. Davenport EM, Whitlow CT, Urban JE, et al. Abnormal white matter integrity related to head impact exposure in a season of high school varsity football. *J Neurotrauma* 2014;31(19):1617–1624; doi: 10.1089/neu.2013.3233
8. Breedlove EL, Robinson M, Talavage TM, et al. Biomechanical correlates of symptomatic and asymptomatic neurophysiological impairment in high school football. *J Biomech* 2012;45(7):1265–1272; doi: 10.1016/j.jbiomech.2012.01.034
9. McDonald BC, Saykin AJ, McAllister TW. Functional MRI of mild traumatic brain injury (mTBI): progress and perspectives from the first decade of studies. *Brain Imaging Behav* 2012;6(2):193–207; doi: 10.1007/s11682-012-9173-4
10. Zhang MR, Red SD, Lin AH, et al. Evidence of cognitive dysfunction after soccer playing with ball heading using a novel tablet-based approach. *PLoS One* 2013;8(2):e57364; doi: 10.1371/journal.pone.0057364
11. Gysland SM, Mihalik JP, Register-Mihalik JK, et al. The relationship between subconcussive impacts and concussion history on clinical measures of neurologic function in collegiate football players. *Ann Biomed Eng* 2012;40(1):14–22; doi: 10.1007/s10439-011-0421-3
12. Miller JR, Adamson GJ, Pink MM, et al. Comparison of preseason, mid-season, and postseason neurocognitive scores in uninjured collegiate football players. *Am J Sports Med* 2007;35(8):1284–1288; doi: 10.1177/0363546507300261
13. Churchill N, Hutchison MG, Leung G, et al. Changes in functional connectivity of the brain associated with a history of sport concussion: a preliminary investigation. *Brain Inj* 2017;31(1):39–48; doi: 10.1080/02699052.2016.1221135
14. Mayinger MC, Merchant-Borna K, Hufschmidt J, et al. White matter alterations in college football players: a longitudinal diffusion tensor imaging study. *Brain Imaging Behav* 2018;12(1):44–53; doi: 10.1007/s11682-017-9672-4
15. Slobounov SM, Walter A, Breiter HC, et al. The effect of repetitive subconcussive collisions on brain integrity in collegiate football players over a single football season: a multi-modal neuroimaging study. *NeuroImage Clin* 2017;14:708–718; doi: 10.1016/j.nicl.2017.03.006
16. Sollmann N, Echlin PS, Schultz V, et al. Sex differences in white matter alterations following repetitive subconcussive head impacts in collegiate ice hockey players. *NeuroImage Clin* 2018;17:642–649; doi: 10.1016/j.nicl.2017.11.020
17. Bari S, Svaldi DO, Jang I, et al. Dependence on subconcussive impacts of brain metabolism in collision sport athletes: an MR spectroscopic study. *Brain Imaging Behav* 2019;13(3):735–49; doi: 10.1007/s11682-018-9861-9
18. Svaldi DO, Joshi C, McCuen EC, et al. Accumulation of high magnitude acceleration events predicts cerebrovascular reactivity changes in female high school soccer athletes. *Brain Imaging Behav* 2020;14(1):164–174; doi: 10.1007/s11682-018-9983-0
19. Koerte IK, Mayinger M, Muehlmann M, et al. Cortical thinning in former professional soccer players. *Brain Imaging Behav* 2016;10(3):792–798; doi: 10.1007/s11682-015-9442-0
20. Manning KY, Brooks JS, Dickey JP, et al. Longitudinal changes of brain microstructure and function in nonconcussed female rugby players. *Neurology* 2020;95(4):E402–E412; doi: 10.1212/WNL.0000000000009821
21. Abbas K, Shenk TE, Poole VN, et al. Alteration of default mode network in high school football athletes due to repetitive subconcussive mild traumatic brain injury: a resting-state functional magnetic resonance imaging study. *Brain Connect* 2014;5(2):91–101; doi: 10.1089/brain.2014.0279
22. Abbas K, Shenk TE, Poole VN, et al. Effects of repetitive sub-concussive brain injury on the functional connectivity of default mode network in high school football athletes. *Dev Neuropsychol* 2015;40(1):51–56; doi: 10.1080/87565641.2014.990455
23. Churchill NW, Hutchison MG, Di Battista AP, et al. Structural, functional, and metabolic brain markers differentiate collision versus contact and non-contact athletes. *Front Neurol* 2017;8:390; doi: 10.3389/fneur.2017.00390
24. Johnson B, Neuberger T, Gay M, et al. Effects of subconcussive head trauma on the default mode network of the brain. *J Neurotrauma* 2014; 31(23):1907–1913; doi: 10.1089/neu.2014.3415
25. Monroe DC, Blumenfeld RS, Keator DB, et al. One season of head-to-ball impact exposure alters functional connectivity in a central autonomic network. *NeuroImage* 2020;223:117306; doi: 10.1016/j.neuroimage.2020.117306
26. Raichle ME. Behind the scenes of functional brain imaging: a historical and physiological perspective. *Proc Natl Acad Sci U S A* 1998;95(3): 765–772; doi: 10.1073/pnas.95.3.765



27. Biswal BB, Yetkin FZ, Haughton V, et al. Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magn Reson Med* 1995;34(4):537–541; doi: 10.1002/mrm.1910340409
28. Lrick E. Student-athlete participation: 1981–82 – 2014–15; NCAA sports sponsorship and participation rates report. Natl Coll Athl Association: Indianapolis, IN; 2015.
29. Abrahams S, McFie S, Patricios J, et al. Risk factors for sports concussion: an evidence-based systematic review. *Br J Sports Med* 2014;48(2):91–97; doi: 10.1136/bjsports-2013-092734
30. Delaney JS, Lacroix VJ, Leclerc S, et al. Concussions among university football and soccer players. *Clin J Sport Med* 2002;12(6):331–338. doi: 10.1097/00042752-200211000-00003.
31. Gessel LM, Fields SK, Collins CL, et al. Concussions on U.S. high school and collegiate athletes. *J Athl Train* 2007;42(4):495–503; doi: 10.1016/S0162-0908(08)79294-8
32. Marar M, McIlvain NM, Fields SK, et al. Epidemiology of concussions among united states high school athletes in 20 sports. *Am J Sports Med* 2012;40(4):747–755; doi: 10.1177/0363546511435626
33. Covassin T, Swanick CB, Sachs ML. Sex differences and the incidence of concussions among collegiate athletes. *J Athl Train* 2003;38(3):238–244.
34. Broshek DK, Kaushik T, Freeman JR, et al. Sex differences in outcome following sports-related concussion. *J Neurosurg* 2005;102(5):856–863; doi: 10.3171/jns.2005.102.5.856
35. Zuckerman SL, Apple RP, Odom MJ, et al. Effect of sex on symptoms and return to baseline in sport-related concussion: clinical article. *J Neurosurg Pediatr* 2014;13(1):72–81; doi: 10.3171/2013.9.PEDS13257
36. Fenton G, McClelland R, Montgomery A, et al. The postconcussional syndrome: social antecedents and psychological sequelae. *Br J Psychiatry* 1993;162(APR):493–497; doi: 10.1192/bjp.162.4.493
37. Covassin T, Schatz P, Swanick CB. Sex differences in neuropsychological function and post-concussion symptoms of concussed collegiate athletes. *Neurosurgery* 2007;61(2):345–350; doi: 10.1227/01.NEU.0000279972.95060.CB
38. Majerske CW, Mihalik JP, Ren D, et al. Concussion in sports: postconcussive activity levels, symptoms, and neurocognitive performance. *J Athl Train* 2008;43(3):265–274; doi: 10.4085/1062-6050-43.3.265
39. Covassin T, Swanick CB, Sachs M, et al. Sex differences in outcome following sports-related concussion. *Neurosurgery* 2006;40:923–927; doi: 10.1136/bjmsm.2006.029496
40. Sollmann N, Echlin PS, Schultz V, et al. Sex differences in white matter alterations following repetitive subconcussive head impacts in collegiate ice hockey players. *NeuroImage Clin* 2018;17:642–649; doi: 10.1016/j.nicl.2017.11.020
41. Zhou Y, Milham MP, Lui YW, et al. Default-mode network disruption in mild traumatic brain injury. *Neuroradiology* 2012;265(3):882–892; doi: 10.1148/radiol.12120748
42. Abbas K, Shenk TE, Poole VN, et al. Alteration of default mode network in high school football athletes due to repetitive subconcussive mild traumatic brain injury: a resting-state functional magnetic resonance imaging study. *Brain Connect* 2015;5(2):91–101; doi: 10.1089/brain.2014.0279
43. Sharp DJ, Beckmann CF, Greenwood R, et al. Default mode network functional and structural connectivity after traumatic brain injury. *Brain* 2011;134(8):2233–2247; doi: 10.1093/brain/awr175
44. Vahdat S, Darainy M, Milner TE, et al. Functionally specific changes in resting-state sensorimotor networks after motor learning. *J Neurosci* 2011;31(47):16907–16915; doi: 10.1523/JNEUROSCI.2737-11.2011
45. Seidler R, Erdeniz B, Koppelmans V, et al. Associations between age, motor function, and resting state sensorimotor network connectivity in healthy older adults. *Neuroimage* 2015;108:47–59; doi: 10.1016/j.neuroimage.2014.12.023
46. Sauseng P, Klimesch W, Schabus M, et al. Fronto-parietal EEG coherence in theta and upper alpha reflect central executive functions of working memory. *Int J Psychophysiol* 2005;57(2):97–103; doi: 10.1016/j.jpsycho.2005.03.018
47. Desco M, Navas-Sanchez FJ, Sanchez-González J, et al. Mathematically gifted adolescents use more extensive and more bilateral areas of the fronto-parietal network than controls during executive functioning and fluid reasoning tasks. *Neuroimage* 2011;57(1):281–292; doi: 10.1016/j.neuroimage.2011.03.063
48. Dixon ML, De La Vega A, Mills C, et al. Heterogeneity within the fronto-parietal control network and its relationship to the default and dorsal attention networks. *Proc Natl Acad Sci U S A* 2018;115(7):E1598–E1607; doi: 10.1073/pnas.1715766115
49. Szczepanski SM, Pinsk MA, Douglas MM, et al. Functional and structural architecture of the human dorsal frontoparietal attention network. *Proc Natl Acad Sci U S A* 2013;110(39):15806–15811; doi: 10.1073/pnas.1313903110
50. Menon V, Uddin LQ. Saliency, switching, attention and control: a network model of insula function. *Brain Struct Funct* 2010;214(5–6):655–667; doi: 10.1007/s00429-010-0262-0
51. Uddin LQ. Saliency processing and insular cortical function and dysfunction. *Nat Rev Neurosci* 2015;16(1):55–61; doi: 10.1038/nrn3857
52. Rice SG. Medical conditions affecting sports participation. *Am Acad Pediatr* 2008;121(4):841–848; doi: 10.1542/peds.2008-0080
53. McCrory P, Johnston K, Meeuwisse W, et al. Summary and agreement statement of the 2nd International Conference on Concussion in Sport, Prague 2004. *Br J Sports Med* 2005;39(4):196–204; doi: 10.1136/bjmsm.2005.018614
54. Wojtowicz MA, Ishigami Y, Mazerolle EL, et al. Stability of intraindividual variability as a marker of neurologic dysfunction in relapsing remitting multiple sclerosis. *J Clin Exp Neuropsychol* 2014;36(5):455–463; doi: 10.1080/13803395.2014.903898.
55. Catena RD, Van Donkelaar P, Chou LS. Different gait tasks distinguish immediate vs. long-term effects of concussion on balance control. *J Neuroeng Rehabil* 2009;6(1):25; doi: 10.1186/1743-0003-6-25
56. Catena RD, Van Donkelaar P, Halterman CI, et al. Spatial orientation of attention and obstacle avoidance following concussion. *Exp Brain Res* 2009;194(1):67–77; doi: 10.1007/s00221-008-1669-1
57. Howell D, Osternig L, Van Donkelaar P, et al. Effects of concussion on attention and executive function in adolescents. *Med Sci Sports Exerc* 2013;45(6):1030–1037; doi: 10.1249/MSS.0b013e3182814595
58. Van Donkelaar P, Langan J, Rodriguez E, et al. Attentional deficits in concussion. *Brain Inj* 2005;19(12):1031–1039; doi: 10.1080/02699050500110363
59. Whitfield-Gabrieli S, Nieto-castanon A. Conn: a functional connectivity toolbox for correlated and anticorrelated brain networks. *Brain Connect* 2012;2(3):125–141; doi: 10.1089/brain.2012.0073
60. Voss MW, Weng TB, Narayana-Kumanan K, et al. Acute exercise effects predict training change in cognition and connectivity. *Med Sci Sports Exerc* 2020;52(1):131–140; doi: 10.1249/MSS.0000000000002115
61. Esterman M, Noonan SK, Rosenberg M, et al. In the zone or zoning out? Tracking behavioral and neural fluctuations during sustained attention. *Cereb Cortex* 2013;23(11):2712–2723; doi: 10.1093/cercor/bhs261
62. Sali AW, Courtney SM, Yantis S. Spontaneous fluctuations in the flexible control of covert attention. *J Neurosci* 2016;36(2):445–454; doi: 10.1523/JNEUROSCI.2323-15.2016
63. Eryurek K, Ulasoglu-Yildiz C, Matur Z, et al. Default mode and dorsal attention network involvement in visually guided motor sequence learning. *Cortex* 2022;146:89–105; doi: 10.1016/j.cortex.2021.10.006
64. Zhang H, Long Z, Ge R, et al. Motor imagery learning modulates functional connectivity of multiple brain systems in resting state. *PLoS One* 2014;9(1):e85489; doi: 10.1371/journal.pone.0085489
65. Martin A, Barnes KA, Stevens WD. Spontaneous neural activity predicts individual differences in performance. *Proc Natl Acad Sci U S A* 2012; 109(9):3201–3202; doi: 10.1073/pnas.1200329109
66. Baldassarre A, Lewis CM, Committeri G, et al. Individual variability in functional connectivity predicts performance of a perceptual task. *Proc Natl Acad Sci U S A* 2012;109(9):3516–3521; doi: 10.1073/pnas.1113148109
67. Chang CY, Chen YH, Yen NS. Nonlinear neuroplasticity corresponding to sports experience: a voxel-based morphometry and resting-state functional connectivity study. *Hum Brain Mapp* 2018;39(11):4393–4403; doi: 10.1002/hbm.24280
68. Dayan E, Cohen LG. Neuroplasticity subserving motor skill learning. *Neuron* 2011;72(3):443–454; doi: 10.1016/j.neuron.2011.10.008



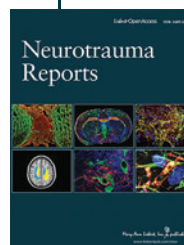
69. Sollmann N, Echlin PS, Schultz V, et al. Sex differences in white matter alterations following repetitive subconcussive head impacts in collegiate ice hockey players. *NeuroImage Clin* 2018;17:642–649; doi: 10.1016/j.nicl.2017.11.020
70. Press JN, Rowson S. Quantifying head impact exposure in collegiate women's soccer. *Clin J Sport Med* 2017;27(2):104–110; doi: 10.1097/JSM.0000000000000313
71. Beckwith JG, Greenwald RM, Chu JJ. Measuring head kinematics in football: correlation between the head impact telemetry system and hybrid III headform. *Ann Biomed Eng* 2012;40(1):237–248; doi: 10.1007/s10439-011-0422-2
72. Cobb BR, Urban JE, Davenport EM, et al. Head impact exposure in youth football: elementary school ages 9–12 years and the effect of practice structure. *Ann Biomed Eng* 2013;41(12):2463–2473; doi: 10.1007/s10439-013-0867-6
73. Young TJ, Daniel RW, Rowson S, et al. Head impact exposure in youth football: Elementary school ages 7–8 years and the effect of returning players. *Clin J Sport Med* 2014;24(5):416–421; doi: 10.1097/JSM.0000000000000055
74. Corbin-Berrigan LA, Wagnac É, Vinet SA, et al. Head impacts in Canadian varsity football: an exploratory study. *Concussion* 2021;6(3):CNC93; doi: 10.2217/cnc-2020-0024
75. Chen Y, Herrold AA, Gallagher V, et al. Preliminary report: localized cerebral blood flow mediates the relationship between progesterone and perceived stress symptoms among female collegiate club athletes after mild traumatic brain injury. *J Neurotrauma* 2021;38(13):1809–1820; doi: 10.1089/neu.2020.7217
76. Behl C. Oestrogen as a neuroprotective hormone. *Nat Rev Neurosci* 2002; 3(6):433–442; doi: 10.1038/nrn846
77. Djebaili M, Guo Q, Pettus EH, et al. The neurosteroids progesterone and allopregnanolone reduce cell death, gliosis, and functional deficits after traumatic brain injury in rats. *J Neurotrauma* 2005;22(1):106–118; doi: 10.1089/neu.2005.22.106

Cite this article as: Wilson A, Stevens WD, Sergio L, et al. Altered brain functional connectivity in female athletes over the course of a season of collision or contact sports. *Neurotrauma Reports* 2022;3(1):377–387. doi: 10.1089/neur.2022.0010.

Abbreviations Used

- ANOVA = analysis of variance
- ANT-I = Attention Network Test-Interaction
- DAN = dorsal attention network
- DMN = default mode network
- FDR = false discovery rate
- FOV = field of view
- FPN = frontoparietal network
- ICA = independent component analysis
- ISDs = individual standard deviations
- MNI = Montreal Neurological Institute
- MRI = magnetic resonance imaging
- RHIs = repetitive head impacts
- rsFC = resting-state functional connectivity
- rsfMRI = resting-state functional magnetic resonance imaging
- SAC = Standardized Assessment of Concussion
- SCAT5 = Sport Concussion Assessment Tool 5
- SD = standard deviation
- SMN = sensorimotor network
- SN = salience network
- TE = echo time
- TR = repetition time

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