Recurrent Concussion Linked to Reduced CBF in Female Athletes

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> The long-term neurological sequelae of recurrent concussion, particularly in athletic populations, remain an area of ongoing investigation. While acute concussion typically results in transient cerebral blood flow (CBF) reductions that resolve, evidence suggests chronic alterations may occur. A recent study indicates that female collegiate-aged athletes with a history of recurrent concussion exhibit persistent reductions in global and regional gray-matter CBF, a finding not observed in male athletes.1

KEY TAKEAWAYS

- The Pivot: Recurrent concussion is associated with chronic cerebral hypoperfusion in female, but not male, collegiate athletes.
- The Data: The number of prior concussions was negatively associated with global and regional gray-matter CBF in female athletes.1
- The Action: Clinicians should consider sex-specific vulnerabilities when assessing long-term outcomes following recurrent concussion in athletic populations.

The susceptibility of athletes to long-term adverse outcomes following recurrent concussion is a subject of ongoing debate. Acute concussion is known to precipitate a transient reduction in cerebral blood flow (CBF), which typically returns to pre-injury levels. However, recent research suggests that long-term CBF alterations may exhibit sex-specific patterns. A study assessed whether a history of concussion was associated with chronic CBF alterations and whether sex moderated this relationship in otherwise healthy, active collegiate-aged athletes.1

Study Design and Findings

The study enrolled 204 collegiate-aged athletes from the community (37.8% female, mean age 21.0 ± 1.7 years). Participants underwent magnetic resonance imaging with pseudo-continuous arterial spin labeling to quantify global and regional CBF and spatial coefficient of variation. Additionally, participants completed measures of depression, anxiety, and cognition. Multiple linear regressions, incorporating prior concussion-by-sex interaction terms and adjusted for relevant covariates, were used to estimate the extent to which sex moderated the concussion history-CBF relationship. Exploratory analyses also assessed whether oral contraceptive use or pill formulation moderated this association in females.1

The number of prior concussions was negatively associated with global and regional gray-matter CBF in female athletes, but not in male athletes. The strongest associations were localized to frontotemporal regions. Notably, CBF metrics were

not related to cognitive performance or affective symptom burden in this cohort. Oral contraceptive use did not appear to substantially moderate the concussion history-CBF association in female athletes.1

Limitations and Next Steps

The study's findings indicate female-specific associations between concussion history and cerebral hypoperfusion in early adulthood, suggesting potential sex differences in the pathways and trajectories of adverse long-term outcomes. These early chronic CBF alterations may represent a vulnerability to future risk in a sex-specific manner. The study did not establish a direct link between these CBF changes and current cognitive performance or affective symptoms, which warrants further investigation into the clinical significance of these observed physiological changes. Future research should aim to elucidate the mechanisms underlying these sex-specific differences and their long-term clinical implications.1

Clinical Implications and Future Research Directions

The observed sex-specific reduction in CBF in female athletes with a history of concussion, particularly in frontotemporal regions, raises important questions regarding the long-term neurological health of this population. While the study did not find a direct correlation between these CBF changes and current cognitive or affective symptoms, it is crucial to consider that these physiological alterations may precede overt clinical manifestations. Early detection of such changes could potentially serve as a biomarker for identifying athletes at higher risk for developing neurodegenerative conditions later in life, or for experiencing more severe symptoms following subsequent head injuries.

The absence of a significant moderating effect of oral contraceptive use on the concussion history-CBF association in females is an interesting finding. This suggests that the observed sex differences may not be primarily driven by exogenous hormonal influences, but rather by intrinsic biological factors such as differences in brain structure, neuroinflammatory responses, or cerebrovascular reactivity between sexes. Future research should delve deeper into these potential underlying mechanisms, perhaps utilizing advanced neuroimaging techniques to assess microstructural integrity, white matter connectivity, and neurochemical changes.

Further longitudinal studies are essential to track the progression of these CBF alterations over time and to determine their ultimate clinical significance. It would be valuable to investigate whether these early chronic CBF reductions are predictive of future cognitive decline, increased susceptibility to mood disorders, or the development of chronic traumatic encephalopathy (CTE)-like pathologies. Incorporating a wider range of neurocognitive assessments, including more sensitive measures of executive function, processing speed, and memory, might reveal subtle cognitive deficits that were not captured by the current study's measures.

Another critical area for future investigation involves exploring the impact of concussion severity, number, and proximity of injuries on CBF changes in female athletes. Understanding the dose-response relationship between concussion history

and CBF alterations could inform more personalized return-to-play guidelines and prevention strategies. Additionally, research should explore potential interventions, such as targeted rehabilitation or pharmacological approaches, that could mitigate these CBF reductions and improve long-term outcomes in vulnerable female athletes.

In conclusion, this study provides compelling evidence for sex-specific vulnerabilities in the aftermath of recurrent concussion, highlighting the need for a more nuanced understanding of concussion pathophysiology. The identification of chronic cerebral hypoperfusion in female athletes, even in the absence of current symptomatic burden, underscores the importance of ongoing monitoring and further research to safeguard the neurological health of this athletic population.

CLINICAL IMPLICATIONS

The observation that recurrent concussion is associated with reduced cerebral blood flow in female collegiate athletes, but not their male counterparts, introduces a critical consideration for primary care and sports medicine clinicians. This sex-specific vulnerability, particularly in frontotemporal regions, suggests that current concussion management protocols may need to evolve to account for physiological differences. Relying on a one-size-fits-all approach could overlook a significant risk factor for long-term neurological sequelae in female athletes.

While the study did not correlate these CBF changes with current cognitive or affective symptoms, the presence of chronic hypoperfusion itself is a concerning biomarker. It implies a potential for future neurological compromise that may not be immediately apparent. Clinicians should consider this evidence when counseling female athletes with a history of recurrent concussions, emphasizing the importance of careful monitoring and potentially more conservative return-to-play guidelines. The lack of moderation by oral contraceptive use also simplifies the clinical picture, removing a potential confounding factor that might have complicated management strategies.

This research underscores the need for further investigation into the long-term clinical significance of these CBF alterations. For the industry, this could spur the development of sex-specific diagnostic tools or therapeutic interventions aimed at mitigating these chronic physiological changes. It also highlights a gap in our understanding of concussion pathophysiology that requires dedicated funding and research to ensure equitable and effective care for all athletes.

REFERENCES

1. 1. Andersson MJ, Goeckner BD, España LY. Reduced Cerebral Blood Flow in the Early Chronic Phase of Recurrent Concussion Among Female Collegiate-Aged Athletes. Hum Brain Mapp 2026. doi:10.1002/hbm.70584

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