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Original research

Repetitive soccer heading adversely impacts short-term learning among adult women

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ABSTRACT

Objectives: To determine the impact of 12-month heading exposure on short-term learning.
Design: A total of 105 active amateur soccer players, 45 women and 60 men, were administered an EMA-based test of working memory, a version of the two-back, once daily for 14 days.
Methods: Heading exposure of the participants was assessed using "HeadCount", a validated structured questionnaire at the baseline visits. The short-term rate of learning of each individual is quantified by first fitting a quadratic model to the daily performance on the two-back test over a two-week period, then taking the instantaneous rate of the quadratic function at the 7th test. A linear regression model was used to test the association of heading exposure with rates of learning, including age, sex, years of education and history of concussion as covariates, as well as variables describing soccer play and heading within the two-week period. Sensitivity analyses were performed using different methods for quantifying the learning effects and different transformations on 12-month heading exposure.
Results: Greater 12-month heading was associated with lower rates of learning among women ($p = 0.008$) but not among men ($p = 0.74$).
Conclusions: We have identified evidence for an adverse, albeit subclinical, effect of soccer heading on brain function among young adult players, which selectively affects women in our sample.

Practical implications

- Prior soccer heading in adult amateur league players may be associated with diminished rate of learning across trials on a daily working memory task.
- Women exhibit disproportionate effects of heading on learning.
- Tests of day-to-day learning may be more sensitive to subclinical adverse effects of RSHI than point estimates of performance

1. Introduction

Repetitive head impacts (RHI) and concussion are common to soccer and other collision sports.[1] Soccer heading, in particular, has been independently associated with adverse profiles of brain microstructure and cognitive performance.[2–5] Studies have shown worse cognitive performance related to soccer heading among players at different ages and levels of play (e.g., [2,6–12]) and heading has been found to explain cognitive performance effects better than recognized concussion in amateur[13] and former professional players.[14] However, the severity of these effects is modest and clinical levels of impaired function have not been reported among the younger healthy players that have been studied to date. On the other hand, reports of late life neurodegeneration in long-time

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professional soccer players (e.g., [15,16]) have raised concern that accumulation of subclinical levels of injury may begin years before the onset of the neurodegenerative disease. Risk of long-term adverse effects from RHI remains an area of uncertainty. Early identification of cognitive dysfunction, even if subtle and subclinical, could be an indicator of future functional disturbances. Identifying subtle early signs could also be used to flag individuals at risk for irreversible changes or progression to overt disease, creating opportunities to mitigate adverse outcomes later in life for soccer players who head. Through daily monitoring of cognitive performance in this study, we sought to identify evidence of a real-time measurable effect on cognitive function that could be an important focus for future research and potentially serve as a foundation for safety management.

It is well-established that although women, depending upon age, are less likely to experience traumatic brain injury (TBI), including concussion, they sustain worse outcomes.[17] Similar findings have been reported in the case of sport related concussion.[18–20] Sex-divergence of adverse effects of sport related RHI, however, have received much less attention. Women have been found to experience greater head acceleration than men for similar intensity of heading[21] and similar heading exposure was found associated with more adverse effects on brain structure[22] in women compared to men. Sex-divergence of the association of heading with functional outcomes such as cognition has not been directly addressed.

Detection of change in cognitive function over time is limited by the frequency of measurement, by the reliability of the cognitive tests and by practice effects.[23,24] Moreover, episodic assessment relies upon comparison of individual performance to normative data, which limits the estimation of prior performance and is susceptible to confounding from individual characteristics (e.g., age, sex).[25,26] For example, an individual with very high baseline performance may fall well within a normal range, despite a large decline from their baseline level of functioning.[26] Thus, a significant degree of functional decline may be missed if the only criterion for functional decline is comparison of a single point performance measure to that of a normative sample. "Ecological Momentary Assessment" (EMA) involves repeated sampling of participants' performance in their natural environment,[27] by administering multiple assessments over brief periods, spaced closely together. EMA leverages the individual as their own control, yields better measurement reliability and permits assessment of features such as short-term learning.[28,29] The repeated measurement approach also reduces the effects of "good" or "bad" days on estimated performance.[26]

In this study, we tested the hypothesis that heading over 12-months would be adversely associated with short-term learning on an EMA test of working memory, to a greater degree among women compared to men.

2. Methods

The Einstein Soccer Study is an ongoing longitudinal study examining the impact of heading on brain structure and function in adult amateur soccer players. The study complied with the Health Insurance Portability and Accountability Act, was approved by the institutional review board, and all participants provided written informed consent. Amateur soccer players, ages 18–55, were recruited from the greater New York City area via local advertisement and social media. Inclusion criteria included soccer play for at least 5 years, current soccer play, active soccer play for at least 6 months per year, and English language fluency. Exclusion criteria included history of bipolar disorder, schizophrenia, neurological disorder, safety contraindication to MRI or claustrophobia (related to another arm of the study), recreational drug use within previous thirty days or a positive urine drug screen. We oversampled women soccer players relatively to their representation (10 %) in the regional population of active adult amateur soccer players. A subset of participants in the overall study were enrolled in this substudy, which employed daily measurement of cognitive performance. Participants in the substudy completed a period of daily at-home assessments, described below. We include, in this report, data from the in-laboratory enrollment visit and from the subsequent daily measurement period.

At enrollment, participants visited the laboratory, completed informed consent and a computer-administered questionnaire to obtain data on demographics and on soccer play, including heading, collisions and concussion history.

Heading was assessed during the laboratory visit using "HeadCount", a validated structured, web-based questionnaire[30–32] that has been used to estimate soccer head impact exposure in multiple studies of independent cohorts (e.g., [2,12,33,34]). HeadCount-12 m assesses heading over the prior 12 months, including frequency of heading during practice and play in both indoor and outdoor settings. The estimate of heading over the prior twelve months serves as the exposure measure of interest in the present study. Heading estimates were log-transformed for use as the explanatory variable in our models (below). In addition, we performed sensitivity analyses where heading was treated as a rank variable. HeadCount-12 m also captures years of soccer play and lifetime concussion history.

During the baseline laboratory visit (above), participants were issued a custom-programmed tablet PC (Android Table 2-Version 4.1.2; Hardware version i705.03 or Table 4-Version 4.4.4; Hardware Version T337V.03) to perform assessments at home. Research staff conducted face-to-face training to ensure that participants understood the operation of the device and its software. Participants were then trained on the actual tablet-based assessments and practiced the operation of the tablet and the entire assessment procedure under the research assistant's supervision.

During the designated 14-day measurement period, the tablet PC alarmed each evening at 7 PM to prompt completion of the assessment battery. Completion of the entire daily assessment battery requires 8–9 min. The software first asks whether the participant played soccer that day, followed by a hierarchical series of questions about soccer play that day, including number of headers, number of unintended impacts, concussion-related symptoms associated with either heading or unintended impacts and recognized concussion. A parallel set of distractor questions are incorporated, such that all participants must answer the same number of questions regarding soccer play. Participants then complete a version of the two-back task, optimized for administration on mobile devices, as part of an ecological momentary assessment (EMA). High between-person reliability, within-person variability, and construct validity are described in more detail in Sliwinski et al., 2018.[26] This task is designed to measure working memory, or the ability to hold information temporarily while completing a complex task demand. There is a 10-trial practice phase each day of testing, to ensure task comprehension, followed by the test phase. Participants are shown a series of playing card images and must maintain the identity of a playing card as it shifts spatial locations across the display. Participants are asked if a target card matches a card that they saw two trials earlier while simultaneously updating the identity of a new target card. After each response, there is a 500 msec. Delay. Participants were presented with 16 trials in each session, from which throughput per second (# of correct responses/response time) was derived as the performance measure for the session.[26]

Data were automatically uploaded to remote servers to facilitate test completion adherence monitoring. Participants were compensated on a sliding scale based on adherence. To receive the base compensation, participants were required to demonstrate >50 % compliance. Escalating bonuses were earned for 80 % and 90 % compliance. Compensation was loaded to an electronic debit card only after the conclusion of the entire daily measurement period.

2.1. Statistical methods

To quantify learning, we first fit a quadratic model for daily performance (throughput per second) over the entire assessment period

using the least square method, with the order of tests as the explanatory variable. We adopted the quadratic model based upon our observation that individual trajectories generally exhibited clear patterns of flattening after the first few assessments. The learning effect was then quantified as the derivative of the quadratic model at the 7th test, which is the slope of the tangent line of the quadratic curve at that point, also known as the instantaneous rate of change. The quantified rate of learning effect for each individual served as the outcome of interest in a multiple regression model where $\log_{10}$-transformed 12-month heading served as the primary explanatory variable and age, sex and years of education, as well as potential confounders or effect modifiers, were included. In the regression model, weighted least square was used, as each participant is weighted by the inverse of the standard error of the estimated learning effect. Other covariates were also investigated, including concussion history (Yes/No), proportion of heading days and proportion of soccer days within the two-week daily measurement period, as well as average number of headers per day during games or practices, alone and combined. In sensitivity analyses, other approaches to quantifying the learning effect and to representing the 12-month heading variable were explored. Variation in level of performance was measured as the mean squared residuals (MSE) of the quadratic model. We used a linear regression model to evaluate the association of MSE with heading exposure and the same covariates listed above, utilizing the log-transformation of MSE as the response. An additional linear regression model was also performed to assess LMN (mean of the $\log_{10}$ transformed reaction times for correct responses) as a measure of performance on the two-back test, which was administered within two weeks of the start of the daily assessment period.

3. Results

A total of 105 players enrolled were included, comprising 60 men and 45 women. Women, on average, were younger than men (mean 24.9 vs 26.7), and headed the ball less often than men (median 661 vs 1089), while years of education was similar for women and men (mean 15.8 vs 15.6). The distributions of these variables are shown in Fig. S1. Data from 86 participants who completed 10 or more daily tests, 47 men and 39 women, were included in our analyses. Although those excluded tended on average to be younger and men, we found no significant differences of age, sex or education for those included, compared to those excluded. Some participants missed days during the daily measurement period, completing daily measurements for fewer than 14 days and some completed >14 days of daily measurement. Fig. S2 shows the distribution of the number of daily two-back tests completed by each participant.

Fig. 1 shows the trajectory per player of two-back performance over the daily measurement period, stratified by sex. An overall upward trend is visible across the entire period, consistent with learning across repetitions of the test. Higher level of self-reported 12-month heading was associated with a smaller learning effect (p-value = 0.013). Separately, females demonstrated a stronger learning effect than males (p-value = 0.027) and older players exhibited a weaker learning effect than younger players (p-value = 0.00019). We found no association of two-back performance with education, history of concussion, proportion of days during the daily measurement period with soccer play or proportion of daily measurement period days with heading. Summary statistics of the linear regression model are shown in Table 1.

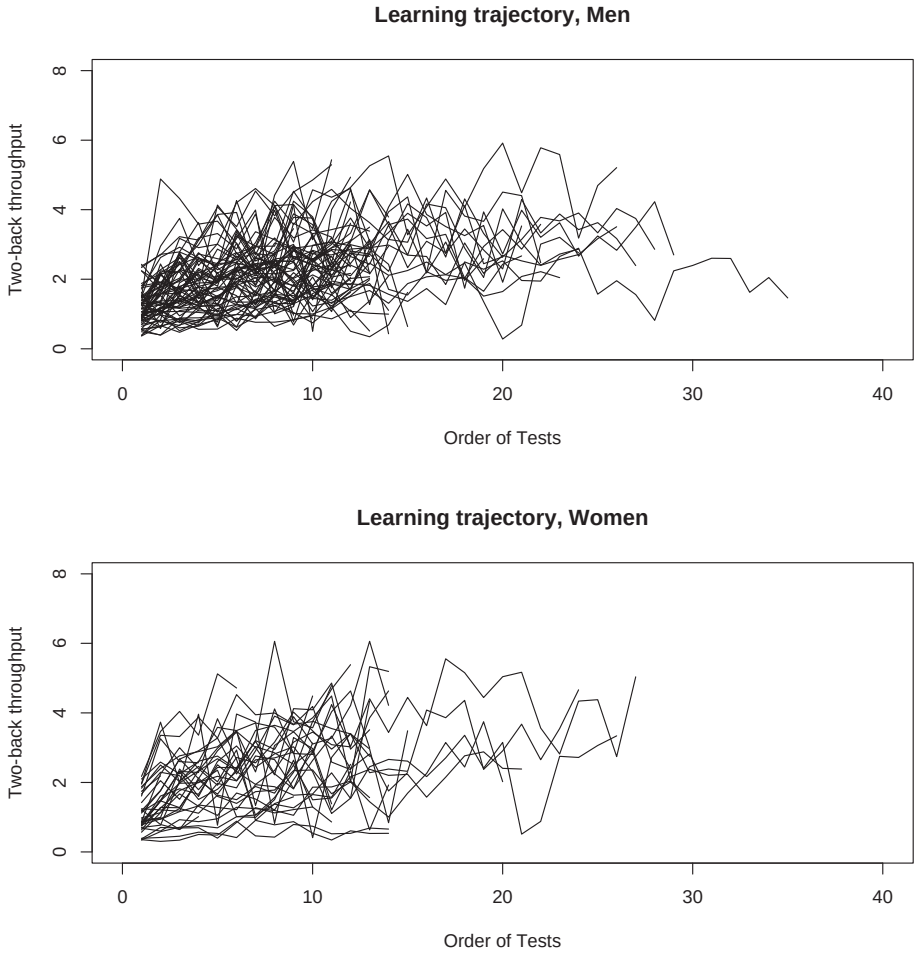

Fig. 1. Trajectories of daily performance. Trajectories of daily performance on the two-back test (throughput) over repeated daily administration, stratified by Sex. Each line represents one player.

Table 1
Results from the linear regression models of the association of **LOG** 12-month heading with early learning effects on the Two-Back memory test.

All participants				
Factors	Estimate	Std. error	t value	P-value (two-sided)
Sex	0.029705	0.01320	2.249	***0.0273***
Age	−0.002580	0.00066	−3.921	***0.000187***
log(12-month heading+10)	-0.012201	0.00480	−2.541	***0.0130***
Education (years)	0.002256	0.00312	0.723	0.4715
Soccer play (days)	0.073918	0.06257	1.181	0.2410
Daily heading	−0.016683	0.03653	−0.457	0.6492
Women only				
Age	−0.002382	0.00160	−1.485	0.1471
log(12-month heading +10)	−0.019075	0.00679	−2.807	***0.0083***
Education (years)	0.001716	0.00596	0.288	0.7754
Soccer play (days)	0.112993	0.06265	1.804	0.0804
Daily heading	0.063898	0.09852	0.649	0.5211
Men only				
Age	−0.002155	0.00069	−3.118	***0.0033***
log(12-month heading +10)	−0.002371	0.00728	−0.326	0.7463
Education (years)	0.001485	0.00374	0.397	0.6937
Soccer play (days)	−0.079153	0.04090	−1.935	0.0599
Daily heading	0.055706	0.07816	0.713	0.4801

P-values that are less than 0.05 are shown in bold and italics.

Given the sex differences in learning effects noted above, we completed separate linear regression analyses for men and women (Fig. 2). The negative association of 12-month heading with learning (Table 1) was stronger among women alone (p-value = 0.008) compared to the whole group, while the effect among men alone was not significant (p-value = 0.74). Age was significantly associated with learning among men (p-value = 0.003), but not among women (p-value = 0.147). For women, explained variance (R^2) in cognitive performance in the model without heading exposure was 0.269; R^2 increased by 15.4 % to 0.423 in the model with heading exposure. In comparison, for men, heading exposure only explains 0.16 % of the total variation of the response in our model.

We also examined the initial performance and the best performance of each individual during the daily assessments. Both are comparable between women and men, with P-values = 0.43 and 0.53 respectively (by two-sided Welch two-sample *t*-tests). This suggests that the lower learning effects among men and the lack of heading effect on them are unlikely the results of them having a higher floor and or a lower ceiling of the two-back test.

To address the possibility that the results could be a function of the way we treated the 12-month heading variable, we repeated the regression analyses, expressing the 12-month heading variable as the rank instead of its log-transform. Results of these analyses (Table S1) are equivalent to those described above, supporting the robustness of the associations. Our choice of the instantaneous rate of change at the 7th test was somewhat arbitrary. To ensure the results were robust to how the learning effect was quantified, we explored other ways to quantify the response. In addition to the instantaneous rate at the 7th test, we tested the slope of a linear model, and the instantaneous rates at the 4th, 5th, 6th and 8th tests using the quadratic model. Results obtained using each of these possible approaches to the characterization of learning similarly supported the association of 12-month heading with learning during the daily measurement period.

We found no association of 12-month heading exposure with variance of two-back performance, taken as the mean squared residuals of the least square quadratic curve. However, variance was negatively associated with age ($p = 1.03 \times 10^{-6}$). We found no association of the variance of two-back performance with other covariates such as sex, education, history of concussion, and days with heading or soccer play during the daily measurement period.

In addition to the learning effect (i.e., change in performance over time), we assessed level of performance on the two-back test given at the initial study visit prior to start of the daily assessments. Performance was measured as the mean of the $\log_{10}$ transformed reaction times for correct responses (see Methods) and lower score indicates better performance.

We found no significant association of the level of performance with sex. Performance was, however, negatively associated with age

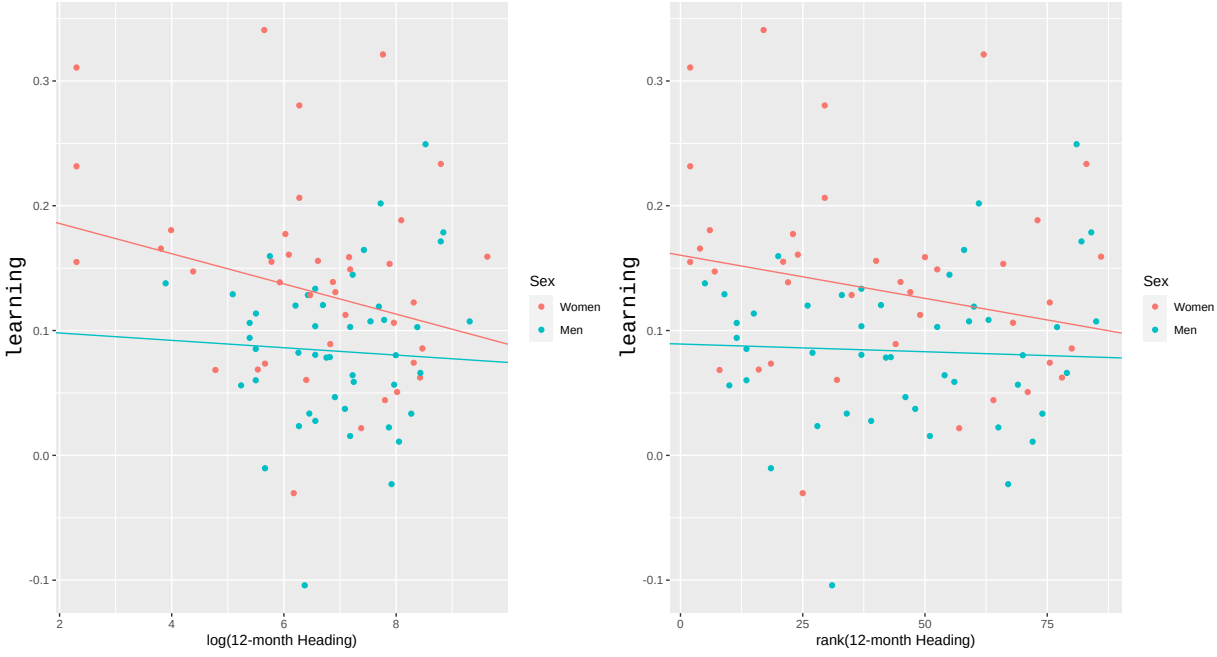

Fig. 2. Association with learning effects stratified by sex. Association of 12-month heading with learning on the two-back test, stratified by sex. The association is significant in women (pink), but not in men (blue). In the left panel, the log-transformed 12-month Heading estimate is used for the linear association. In the right panel, the ranking of 12-month Heading estimate is used.

(p-value = 0.024). In sex-stratified analyses designed to test the association of heading exposure with level of performance, we found a marginally significant negative association of 12-month heading exposure with performance level among women (p = 0.076 using the log-transform of total heading and p = 0.04 using the rank of total heading), but no association among men (p = 0.47 using the log-transform of total heading and p = 0.54 using the rank of total heading).

4. Discussion

Utilizing EMA to assess daily working memory performance among adult amateur soccer players, we demonstrate an adverse association of prior longer-term (12-month) exposure to heading with learning over a 2-week period. This finding is consistent with adverse brain effects engendered by cumulative exposure to heading, which impair short-term learning capacity on a new cognitive task. We detected this effect across a group comprising men and women soccer players and found a significant effect of sex in the overall exposure-response model. Stratified analyses revealed that, overall, women in our sample exhibit cognitive performance at a superior level compared to men. However, the adverse effect of RHI on learning was specific to women. We therefore suggest that greater susceptibility of women to adverse effects of RHI on brain structure and function may underly the adverse association of RHI with learning we found to be specific to women in our sample.

Cross-sectional comparison of cognitive performance common to many studies may be confounded by normal day-to-day variation in level of performance, capturing individuals on particularly "good" or "bad" days.[26] In our study, the repeated administration of a task spaced over a 14-day assessment period yields a more stable measure of performance and permits characterization of unique features such as learning across repeated daily administration of the same test.[26] In our sample, average level of performance was not associated with prior exposure; a separate single administration of the same task at the onset of the study yielded effects that were marginally significant. Leveraging the daily repeated measurements, we confirmed learning over the daily measurement period, an expected feature of normal functioning, as well as a positive effect of female sex, across the entire sample, on the rate of learning. At the same time, we found that prior 12-month RHI attenuated learning during the daily measurement period in women, but not in men. Given the generally better learning we identified among women in our sample, in whom the distribution of exposure to RHI is highly right skewed and the most common level of exposure is zero, the flat learning trajectory detected among women with high-level exposure to RHI implicates a disproportionate sensitivity to the adverse effects of RHI on brain function among women.

Daily EMA assessment could, in principle, be leveraged to characterize very short-term (day-to-day) effects of activity and RHI exposure on cognitive performance. However, due to the very strong learning effects we found in our young healthy cohort, day-to-day effects must be assessed either using detrended data or by sampling after learning has reached an asymptote. In this regard, we have limited pilot experience with repeated epochs of testing in a small subset of our sample. A subset (n = 23) of participants completed four daily measurement periods spaced at 3-month intervals. These limited data (not shown here) suggest that a strong learning effect persists during the second and third daily measurement periods. Learning effects are no longer evident during the 4th epoch. However, our sample for this epoch is too small to support the analyses we have reported for the whole group over a single two-week daily measurement period. Assessment of day-to-day effects might be feasible were a larger sample to complete multiple repeated daily measurement periods. This is an important area for future study.

The pathologic substrate of brain dysfunction due to mild trauma is generally understood to arise, via a range of molecular and cellular mechanisms, from microscopic traumatic axonal injury (TAI).[35] Neuroimaging has provided correlates of TAI related to neurocognitive effects[36,37] and specifically due to soccer heading.[2,38] We recently reported sex-divergence of microstructural features consistent with TAI among male and female soccer players matched for exposure to RHI, which were independent of concussion.[22] Microstructural pathology at very low levels will not, however, necessarily induce detectable functional effects; it must first accumulate to a level sufficient to impair function.

Our finding that women have, overall, superior working memory performance compared to men in our sample and exhibit a greater adverse effect of RHI on working memory learning, despite lesser overall exposure to RHI compared to men, suggests greater biological susceptibility to RHI among women. Prior studies of traumatic brain injury, including concussion, have shown that women are at greater risk than men for poor outcome.[39,40] Although men are more likely to sustain sport-related concussion, women are more likely to experience persistent adverse sequelae.[18–20] The mechanisms underlying this sex divergence is incompletely understood. Lesser strength of the head and neck segment among women has been demonstrated[41] and shown to contribute to head acceleration.[42] However, biomechanical differences have not been shown to account for excess risk among women compared to men. Sex hormones are central to many aspects of cerebral homeostasis. Changes related to development, the menstrual cycle and hormonal contraceptives, among others, may confer epochs of vulnerability, such as during decline of progesterone following ovulation (reviewed by Blaya, et al.[17]). Finer substructure of axons has also been reported among women and suggested as a source of inherent vulnerability to trauma.[43]

Our findings must be considered in light of several limitations. Our performance measure is based on the two-back test of working memory only and may not generalize to other functional domains. We included a flanker task and a test of spatial memory as part of the daily measurement period. However, the vast majority of participants reached a performance ceiling after only a few days of assessment. Therefore, these two tests, previously shown to be effective in older adults,[26] were not effective in differentiating cognitive function across our sample. An inherent feature of our "real world" EMA approach that it occurs in an uncontrolled environment. Participants are instructed on parameters for test completion, but confounding due to variability in the test environment, time of day, distractions and, potentially, completion of the task by someone other than the participant, cannot be entirely excluded. Balancing this limitation, environmental variability is a key component strength of EMA, which contributes to its ecological validity. We determine exposure (heading, etc.) based on self-report, which may be subject to recall bias. However, the instruments we employ have demonstrated reliability and validity across multiple settings and timeframes, with concurrent validity tested against sideline observation and video recording review.[2,34,44,45] While direct observation may be considered a gold standard for exposure assessment, it too is subject to observer bias. Additionally, while observation may be feasible for short exposure periods, it is not practical to employ over long periods of time in adult recreational settings, which account for the largest pool of soccer players. We estimated exposure over the prior 12 months and thus cannot inform with regard to individual impacts. Such biomechanical characterization was not a component of this study. We studied adult amateur soccer players from one region of the United States, with oversampling of women relative to their representation (10 %) in the regional soccer player population. As such, we cannot necessarily generalize our findings to soccer play among other geographic and age (e.g., children, adolescents) groups, who may experience different patterns of exposure, for example, professional players who generate higher ball velocities and therefore engage in higher intensity heading. However, the mean activity level of our study participants has been deemed comparable to that of amateur players worldwide.[46]

In conclusion, we have identified evidence for an adverse, albeit subclinical, effect of soccer heading on brain function among young adult players, which selectively affects women in our sample. Further study is warranted to understand the longer-term implications of this finding

as well as how it is related to overt clinical effects later in life. Understanding the role of individual characteristics, such as biological sex, on risk of RHI can ultimately be leveraged to provide personalized guidance to players that will maximize their benefit from sports relative to inherent risks.

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Declaration of Interest Statement

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Confirmation of Ethical Compliance

The study complied with the Health Insurance Portability and Accountability Act, was approved by the institutional review board at Albert Einstein College of Medicine, and all participants provided written, informed consent.

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Appendix A. Supplementary data

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