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Heading and Unintentional Head Impacts Have Opposing Associations with Patient Reported Outcomes in Amateur Soccer Players

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Abstract

The effects of soccer-related head impacts, beyond overt concussions, on Patient Reported Outcomes (PROs) have not been explored to date. Generalized estimating equations were employed to determine the association between soccer-related head impacts (headers in the prior 2 weeks, unintentional head impacts in the prior 2 weeks, headers in the prior 12 months and lifetime concussions) on PROs including depression, anxiety, sleep disturbance and sleep impairment. Compared to players with no unintentional head impacts in the prior 2 weeks, players with one unintentional exposure reported more symptoms of anxiety ($p=0.002$) and players with 2+ exposures reported more symptoms of depression ($p=0.006$) and anxiety ($p<0.001$). In contrast, players in the 3rd Quartile of 12 mo. headers reported less anxiety ($p=0.001$), sleep disturbance ($p=0.002$) and sleep impairment ($p<0.001$) compared to those in the 1st quartile. Unintentional head impacts are associated with worse PROs while more headers are paradoxically associated with better PROs.

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Introduction

Soccer is the most popular sport in the world with over 265 million players globally (Kunz, 2007). In addition to concussions, which account for nearly 22% of all soccer related injuries (Covassin, Swanik, & Sachs, 2003), soccer players frequently head the ball and are therefore exposed to repetitive “subconcussive” head impacts, which are defined as impacts that do not lead to clinical diagnosis of concussion (Bailes, Petraglia, Omalu, Nauman, & Talavage, 2013). We have recently shown that repetitive sub-concussive impacts due to heading are associated with worse cognition (Levitch et al., 2017; Lipton et al., 2013; Stewart et al., in press) and that both heading and unintentional head impacts (e.g. head to head or head to goalpost) can produce CNS symptoms (Stewart et al., 2017). However, to date, the association between heading and unintentional head impacts and Patient Reported Outcomes (PROs) has not been explored.

PROs are emerging as an important tool to measure quality of life, mood, sleep hygiene and other factors based on self -report (Snyder, Jensen, Segal, & Wu, 2013). There is growing recognition that traditional neuropsychological batteries may not fully capture the scope of impairment in mild head traumas (Resch et al., 2016; Robert J. Sbordone, 2010; R. J. Sbordone, 2014). Instead, PROs provide a person-centered approach to accessing day-to day functioning in the general population as well as those with chronic disorders including Traumatic Brain Injuries (TBIs) (Polinder, Haagsma, van Klaveren, Steyerberg, & van Beeck, 2015). Moreover, PROs can identify individuals at risk for hospital readmission (Hinami, Smith, Deamant, DuBeshter, & Trick, 2015) and later mortality (DeSalvo, Bloser, Reynolds Kristi, He, & Muntner, 2006).

The National Institute of Health (NIH) Patient Reported Outcome Measurement Information System (PROMIS) is one of the most well regarded PROs. PROMIS utilizes advanced psychometric modeling as well as computerized adaptive testing to probe a range of physical, emotional and social health outcomes applicable to the general population (Cella et al., 2007).

The goal of the present study was to explore the association of soccer-related head impacts with selected PROs using PROMIS. We examined the association of PROs, including depression, anxiety and sleep hygiene, with heading in the prior 2 weeks, unintentional head impacts in the prior 2 weeks, heading in prior 12 months, and lifetime concussion history on PROs relevant to TBIs including depression and anxiety (Bryant et al., 2010) as well as poor sleep hygiene (Mollayeva, Mollayeva, & Colantonio, 2016; Sullivan, Edmed, Allan, Karlsson, & Smith, 2015). Guided by our previous findings (Levitch, et al., 2017; Stewart, et al., 2017), we hypothesized that soccer related head impacts would be associated with adverse effects on PROs and that the severity of impairment would differ based on the recall period (2 weeks vs. 12 months) and the type of head impact (headers vs. unintentional head impacts).

METHODS

Study Population

Players aged 18–55 were eligible if they played soccer for more than 5 years, currently play soccer more than 6 months per year, and are fluent in English. Exclusion criteria included schizophrenia, bipolar disorder, a known neurologic disorder, illicit drug use within 30 days. All study procedures were approved by the Institutional Review Board at the Albert Einstein College of Medicine. Adult amateur soccer players were recruited by print and Internet advertisement through soccer leagues, clubs and colleges in the New York City and surrounding areas from November 2013 to December 2016. Interested individuals were referred to the study website to collect screening information and were subsequently contacted by a research team member to confirm eligibility and willingness to participate.

Study Procedures

At the baseline visit, players complete; 1) Informed consent; 2) A web-based questionnaire to obtain demographic information including age, gender, race, smoking history, and the average number of alcoholic beverages consumed in one week; 3) A web-based questionnaire to obtain medical history including a diagnosis of depression or anxiety 4) the Wide Range Achievement Test 4 reading subtest as an estimate of intelligence (Wilkinson and Robertson, 2006); 4) HeadCount-12m (described below) and; 5) PROMIS, which was installed on the computer in the study testing room. Immediately following this baseline visit, players were sent a link to the web-based HeadCount-2w (described below), which they were instructed to complete within 7 days.

At follow-up visits, which occurred at 3 or 6 month intervals over the course of 2 years players completed; 1) HeadCount-12m; and 2) PROMIS. Three weeks prior to each follow-up visit, players were then sent a link to the web-based HeadCount-2w, which they were instructed to complete prior to the visit.

Exposure Assessments

HeadCount-2w—HeadCount-2w estimates headers and unintentional head impacts in the prior 2 weeks. Details of HeadCount-2w have been reported previously (Catenaccio et al., 2016; Levitch, et al., 2017; Stewart, et al., 2017). In brief, players are asked a series questions about practice and competition in outdoor and indoor settings including: 1) The number competitive soccer games and practice sessions in prior 2 weeks; 2) The average number of headers during a typical game and; 3) The average number of headers during a typical practice. Total number of headers during the 2-week recall period was estimated as (headers per outdoor game × number of outdoor games) + (headers per outdoor practice × number of outdoor practices) + (headers per indoor game × number of indoor games) + (headers per indoor practice × number of indoor practices). Additionally, the questionnaire inquiries about the number of unintentional head impacts experienced in prior 2 weeks. Unintentional head impacts are defined as impacts to the head from causes such as the ball hitting the back of the head, head to goalpost, head to ground or head to head (or other body part) impact during player-to-player collisions.

HeadCount-12m—HeadCount-12m, described in detail previously (Levitch, et al., 2017; Lipton, et al., 2013), was administered to ascertain total number of headers during the prior 12 months and lifetime concussion history. Similar to HeadCount-2w (above), HeadCount-12m asks a series of questions about practice and competition in outdoor and indoor settings including: 1) The number of months per year active in each setting; 2) The average number of competitive soccer games per week; 3) The average number of headers per game; 4) The average number of practices per week; 5) The average number of headers per practice. HeadCount-12m also asks participants to report their main field position, the number of years they have been playing soccer at a similar frequency and their lifetime concussion history. To determine lifetime concussion history, players were instructed to report any head injury for which they sought or were advised to seek medical attention, related to soccer or for another reason (e.g. a fall or motor vehicle collision).

Patient Reported Outcomes (PROs)

We utilized the PROMIS short forms for depression, anxiety, sleep disturbance (i.e. poor sleep quality) and sleep impairment (i.e. daytime sleepiness) in the past 7 days. PROMIS short forms consist of 8–12 questions selected from the full PROMIS item bank that captures the spectrum of the construct being measured without sacrificing precision. PROMIS test scores are generated as T-scores based on an average US population mean of 50 and a standard deviation of 10. A higher T score corresponds to more of the concept being measured (Cella et al., 2010; Cella, et al., 2007).

Statistical Analyses

All analyses were done using STATA v.13.1. Baseline differences in self-reported diagnosis of depression and anxiety by exposure group (2 wk. headers, 2 wk. unintentional head impacts, 12 mo. headers and lifetime concussions) were calculated using a Chi-squared or Fisher's exact test. Players returned for follow-up visits every 3 to 6 months where identical exposure and PROMIS data were collected. Separate Generalized Estimating Equations (GEE) with independent covariance structure were fit to the data to determine the associations of each PRO (depression, anxiety, sleep disturbance and sleep impairment) with 2 wk. headers, 2 wk. unintentional head impacts, 12 mo. headers and lifetime concussions. GEE models data from each visit as a separate measurement while accounting for the within-subject correlations among visits (Hardin, 2005). Due to extreme positive skew in headers reported in both HeadCount-2w and HeadCount-12m, each exposure variable was transformed into a categorical variable comprising approximately equal size quartiles. Unintentional head impacts and lifetime concussion history were each characterized as ordinal variables (0, 1, 2+). For all analyses, the lowest exposure group was used as the reference category. Bivariate analyses were conducted to examine the association between PROs and potential confounders including age, gender, race (white vs. non-white), IQ, past or present history of smoking, average number of alcoholic beverage consumed weekly, main field soccer position played, years playing soccer at a similar frequency and lifetime concussion count. A backward step-wise selection approach, with $p<0.05$ as the criterion for retention of a variable in the model, was used to determine the final models. To correct for multiple comparisons, we applied the False Discovery Rate (FDR) at $p=0.05$. Finally, given the potential correlation between headers in the prior 2 weeks and headers in the prior 12

months, we conducted additional analyses using the same procedures as above but incorporating both heading exposure variables in the models.

RESULTS

Participants

The present study included 719 HeadCount-2w questionnaires collected from 305 players. Analysis was restricted to the 272 players that endorsed playing soccer in the prior 2 weeks: 125 players completed one HeadCount-2w questionnaire, 74 completed two HeadCount-2w questionnaires and 106 players completed 3 or more HeadCount-2w questionnaires. Demographics reported at baseline are presented in Table 1.

Baseline history of depression and anxiety disorders

History of a depression diagnosis significantly differed by lifetime concussion count (0,1,2+). 3.4%, 7.0 %, and 13.5 % of players with 0, 1, and 2+ lifetime concussions, respectively, reported a history of depression. Likewise, history of an anxiety disorder significantly differed by 12 mo. headers. 6.1 %, 11.6 %, 0%, and 7.8% of players in quartiles 1, 2, 3 and 4 of 12 mo. headers, respectively, reported a history of an anxiety disorder (Table 2).

PROs and soccer related head impacts

Depression and Anxiety: GEE linear regression models, adjusted for covariates, revealed that unintentional head impacts in the prior 2 weeks were associated with greater depressive and anxiety symptoms. Specifically, compared to players with no unintentional impacts, those with one unintentional impacts reported more anxiety symptoms ($\hat{\beta}$ = 2.19, p = 0.002) and players with 2 + unintentional impacts reported more depressive symptoms ($\hat{\beta}$ = 2.57, p=0.006) and anxiety symptoms ($\hat{\beta}$ = 3.48, p = <0.001). In contrast, the third quartile for heading in the prior 12 months was associated with less anxiety ($\hat{\beta}$ = −3.70, p=0.001) compared to the first quartile (Table 3). The interpretation of our results did not change when headers in the prior 2 weeks and headers in the prior 12 months were both incorporated in the models (Supplementary Table 1).

Sleep Disturbance and Sleep Impairment: GEE linear regression models, adjusted for covariates, demonstrated that the third quartile for heading in the prior 12 months was associated with fewer symptoms of sleep disturbance ($\hat{\beta}$ = −4.33, p=0.002) and sleep impairment ($\hat{\beta}$ = −5.36, p<0.001) compared to the first quartile (Table 3). The findings did not change when we included headers in the prior 2 weeks and 12 months in the same model (Supplementary Table 1).

DISCUSSION

We report the first study to examine the effects of soccer-related head impacts on PROs. Our focus on PROs reflects growing recognition that standardized cognitive batteries may be insensitive to deficits of complex functioning that characterize mild TBIs (Robert J. Sbordone, 2010; R. J. Sbordone, 2014) as well as the emergent awareness of the importance

of real-world, patient centered assessments in TBIs (Tulsky et al., 2016) and in health care at large (Snyder, et al., 2013). We examined the independent contributions of both recent and long-term intentional and unintentional head impacts on self-reported depression, anxiety, sleep disturbance and sleep impairment symptoms using NIH's PROMIS.

Previous studies in former NFL football players have shown that long-term exposure to concussions and (Didehbani, Munro Cullum, Mansinghani, Conover, & Hart, 2013) and mild repetitive head impacts (RHIs) is associated with more depression (Montenigro et al., 2017). Similarly, we have found that a greater percentage of players with a history of two or more lifetime concussions (13%) reported a history of depression compared to those with zero (3.4 %) or one (7.0%) lifetime concussion(s).

No study to date has examined the association between short-term exposure to mild RHIs and mental health-related PROs. Herein, we are the first to report an association between short-term unintentional impacts in the prior 2 weeks and worse self-reported depression and anxiety symptoms not explained by a prior diagnosis of depression or anxiety. These findings dovetail on previous findings that unintentional impacts are associated with moderate to severe CNS symptoms (Stewart, et al., 2017) and provide additional evidence that repetitive head impacts in soccer, independent of recognized concussion, are associated with worse function.

An unexpected finding in our current study is the paradoxical association of 3rd quartile intentional heading with better PROs. Given presumed pathophysiological mechanisms (Lipton, et al., 2013), it is unlikely that repetitive headers lead to better PROs. Instead, for patient- reported symptoms of anxiety and depression these findings may be attributed to the fact that significantly fewer players in the 3rd quartile of 12 mo. headers had a psychiatric diagnosis of anxiety and a similar trend exists for a history of diagnosed depression.

Another plausible explanation for this unexpected result across all PROs we examined is that headers are a proxy for overall soccer activity. Physical activity confers clear physical and mental health benefits (Hiles, Lamers, Milaneschi, & Penninx, 2017). It is therefore plausible that 3rd quartile 12 mo. headers who are more active (more games and practice sessions) than both 1st and 2nd quartile headers would demonstrate better PROs due to the benefit of greater physical activity. In this context, the absence of a significant association between 4th quartile headers and improved PROs suggests the benefits of physical activity on mood and sleep hygiene may be contravened by excessive exposure to repetitive impacts. This notion is consistent with our finding microstructural tissue damage (Lipton, et al., 2013), worse cognitive performance (Levitch, et al., 2017), and more CNS symptoms (Stewart, et al., 2017), only in players reporting greatest exposure to headers (i.e., 4th quartile). Another possible explanation for the observed relationship between more headers and better PROs is selection bias; perhaps players vulnerable to the effects of heading chose to head less or players who experienced impaired functioning after heading dropped out of the study or selectively quit playing soccer, biasing recruitment for this study.

Prior research on sleep dysfunction and concussion (Gosselin et al., 2009; Mathias and Alvaro, 2012; Mollayeva, et al., 2016) have not distinguished the effect of single vs. multiple

concussions on sleep hygiene. We have found a trend towards multiple lifetime concussions associated with more sleep disturbance and sleep impairment that did not pass our strict threshold for multiple comparisons. Further research is warranted to explore this association; particularly in light of a recent study of combat veterans (Bryan, 2013), which reported multiple concussions are more detrimental to sleep than a single concussive event.

There are several limitations to our findings. We cannot make inferences regarding the lifetime cumulative effects of heading and unintentional impacts on PROs given that our exposure measurements, HeadCount-2w and HeadCount-12m, only quantify heading in the prior 2 weeks and 12 months, respectively. Moreover, this study did not include a non-collision sport control group, which would have permitted us to control for the normal variations in PRO amongst athletes. We employed a structured self-report instrument, HeadCount, for estimation of exposure, which is based on the demonstrated validity of HeadCount-2w (Catenaccio, et al., 2016). Nonetheless, Headcounts is a self-report measure and recall bias cannot be excluded (Harriss, Walton, & Dickey, 2018), including the possibility of recall bias whereby players with more anxiety and depressive symptoms over-reported two-week unintentional impacts. Likewise, HeadCount does not capture kinematic variations in intensity, linear and rotational forces associated with heading and unintentional impacts (Caccese et al., 2018; Caccese, Lamond, Buckley, & Kaminski, 2016). Moreover, HeadCount-12m, which has not been validated by direct observation for practical reasons. Nonetheless, associations between headers in the prior 12 months and PROs still emerged. Finally, we examined relatively young US amateur soccer players and cannot explicitly generalize these findings to other demographics. However, the demographic features of our sample have been noted to generally reflect the population of amateur players worldwide (Lingsma and Maas, 2017).

We have addressed the ever-growing need for broader outcome assessments in sports related head injury by examining the effect of soccer related head impacts on PROs. Unintentional head impacts are associated with adverse mental well- being. On the other hand, we observed a perplexing association of moderately, but not extremely high levels of heading with better PROs. Future research that utilizes non-collision sport athletes as a control group or explicitly characterizes aerobic activity, such as by actigraphy, is warranted to further understand the relationship of heading with PROs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1:

Summary of baseline characteristics in players who endorsed two- week soccer activity at baseline (N=272)

Variable (continuous)	Mean (sd)	Median (IQR)
Age	25.9 (7.8)	23 (20–29)
Concussion Count *	0.67 (1.1)	0 (0–1)
WRAT-4 Reading *	105.2 (14.3)	105 (97–115)
Years playing at similar frequency	12.3 (7.4)	11 (7–16)

Variable (categorical)		Frequency (%)
Gender	Male	207 (76)
	Female	65 (24)
Race	Non -white	106 (39)
	White	166 (61)
Smoker	No	191 (70)
	Yes	81 (30)
Alcoholic drinks/week	0	75 (28)
	1–2	109 (40)
	3–7	69 (25)
	8–14	17 (6)
	14+	2 (1)
Main Position **	Forward	53 (20)
	Midfield	102 (38)
	Defense	92 (34)
	Goaltender	22 (8)

* Data missing in 1 player

** Data missing in 3 players

Table 2:

Baseline history of depression and anxiety disorders by exposure group

	Group	No	Yes	p-value
Depression				
		Frequency (row%; column %)	**Frequency (row%; column %)**	
2 wk. Headers	1	53 (96.4; 20.7)	2 (3.6; 12.5)	0.28
	2	73 (91.2; 28.5)	7 (8.8; 43.7)	
	3	56 (91.8; 21.9)	5 (8.2; 31.3)	
	4	74 (97.4; 28.9)	2 (2.6; 12.5)	
2 wk. Unintentional Impacts	0	164 (95.3; 64.1)	8 (4.7; 50.0)	0.27
	1	49 (94.2; 19.1)	3 (5.8; 18.8)	
	2+	43 (89.6; 16.8)	5 (10.4; 31.2)	
12 mo. Headers	1	62 (93.9; 24.2)	4 (6.1; 25.0)	0.11
	2	61 (88.4; 23.8)	8 (11.6; 50.0)	
	3	59 (98.3; 23.1)	1 (1.7; 6.2)	
	4	74 (96.1; 28.9)	3 (3.9; 18.8)	
Lifetime Concussion	0	170 (96.6; 66.7)	6 (3.4; 37.5)	0.02 *
	1	40 (93.0; 15.7)	3 (7.0; 18.8)	
	2+	45 (86.5; 17.6)	7 (13.5; 43.7)	
Anxiety				
2 wk. Headers	1	52 (94.5; 20.5)	3 (5.5; 16.7)	0.46
	2	76 (95.0; 29.9)	4 (5.0; 22.2)	
	3	54 (88.5; 21.3)	7 (11.5; 38.9)	
	4	72 (94.7; 28.3)	4 (5.3; 22.2)	
2 wk. Unintentional Impacts	0	164 (93.3; 64.6)	8 (4.7; 44.4)	0.17
	1	47 (90.4; 18.5)	5 (9.6; 27.8)	
	2+	43 (89.6; 16.9)	5 (10.4; 27.8)	
12 mo. Headers	1	62 (93.9; 24.4)	4 (6.1; 22.2)	0.03 *
	2	61 (88.4; 24.0)	8 (11.6; 44.4)	
	3	60 (100.0; 23.6)	0 (0.0; 0)	
	4	71 (92.2; 28.0)	6 (7.8; 33.3)	
Lifetime Concussion	0	167 (94.9; 66.0)	9 (5.1; 50)	0.21
	1	40 (93.0; 15.8)	3 (7.0; 16.7)	
	2+	46 (88.5; 18.2)	6 (11.5; 33.3)	

* significant at $p < 0.05$ based on chi-squared or fisher's exact test

Table 3:

Generalized Estimating Equation models of mean difference in PROMIS T-score by exposure

	Group	N of HeadCount	Range of Headers	Mean Difference (95% CI)	p-value
Depression Symptoms[1]					
2 wk. Headers[a]	1	182	0–5	---	---
	2	188	6–15	−0.18 (−1.45, 1.10)	0.79
	3	167	16–49	−1.25 (−2.88, 0.39)	0.14
	4	178	50–680	−0.90 (−2.76, 0.96)	0.35
2 wk. Unintentional Impacts[a]	0	470	---	---	---
	1	134	---	1.04 (−0.24, 2.32)	0.11
	2+	111	---	2.57 (0.73, 4.40)	0.006*
12 mo. Headers[b]	1	186	0 −313	---	---
	2	174	314–717	−0.40 (−2.04, 1.25)	0.64
	3	178	718–1590	−2.26 (−4.31, −0.21)	0.03
	4	175	1591–22838	−1.25 (−3.07, 0.56)	0.18
Lifetime Concussion[b]	0	471	---	---	---
	1	116	---	−0.19 (−1.91, 1.67)	0.90
	2+	128	---	−0.85 (−2.59, 0.89)	0.34
Anxiety Symptoms[2]					
2 wk. Headers[a]	1	181	0–5	---	---
	2	188	6–15	−0.50 (−1.85, 0.86)	0.47
	3	167	16–49	−1.24 (−2.95, 0.47)	0.16
	4	178	50–680	−1.77 (−3.83, 0.30)	0.09
2 wk. Unintentional Impacts[a]	0	469	---	---	---
	1	134	---	2.19 (0.79, 3.60)	0.002*
	2+	111	---	3.48 (1.59, 5.36)	<0.001*
12 mo. Headers[b]	1	185	0–320	---	---
	2	174	321–719	−0.14 (−1.99, 1.70)	0.88
	3	178	720–1597	−3.70 (−5.95, −1.45)	0.001*
	4	175	1598–22838	−0.81 (−2.77, 1.14)	0.41
Lifetime Concussion[b]	0	470	---	---	---
	1	116	---	− 0.17 (−2.09, 1.74)	0.86
	2+	128	---	− 0.87 (−2.64, 0.89)	0.33
Sleep Disturbance Symptoms[3]					
2 wk. Headers[a]	1	176	0–5	---	---
	2	187	6–15	−0.97 (−2.61, 0.67)	0.25
	3	166	16–49	−1.22 (−3.20, 0.76)	0.23
	4	176	50–680	−2.45 (−4.97, 0.72)	0.06
2 wk. Unintentional Impacts[a]	0	461	---	---	---
	1	132	---	1.98 (0.25, 3.71)	0.02

	Group	N of HeadCount	Range of Headers	Mean Difference (95% CI)	p-value
12 mo. Headers[b]	2+	110	---	1.77 (−0.43, 3.97)	0.11
	1	181	0 −326	---	---
	2	174	327–717	−1.34 (−3.53, 0.83)	0.23
	3	174	718–1668	−4.33 (−7.06, −1.60)	0.002*
	4	174	1669–22838	−2.06 (−4.59, 0.47)	0.11
Lifetime Concussion[b]	0	463	---	---	---
	1	115	---	1.78 (−0.27, 3.83)	0.09
	2+	127	---	2.00 (0.03, 4.00)	0.05
Sleep Impairment Symptoms[4]					
2 wk. Headers[a]	1	181	0–5	---	---
	2	188	6–15	−0.94 (−2.63, 0.74)	0.27
	3	167	16–49	−2.68 (−4.78, −0.58)	0.01
	4	178	50–680	−2.59 (−5.45 0.27)	0.08
2 wk. Unintentional Impacts[a]	0	470	---	---	---
	1	133	---	2.21 (0.23, 4.19)	0.03
	2+	111	---	2.30 (0.06 4.53)	0.04
12 mo. Headers[b]	1	185	0–320	---	---
	2	174	321–719	−2.05 (−4.25, 0.15)	0.07
	3	178	720–1597	−5.36 (−8.38, −2.35)	<0.001*
	4	175	1598–22838	−2.73 (−5.19, −0.28)	0.03
Lifetime Concussion[b]	0	470	---	---	---
	1	116	---	1.31 (−0.59, 3.20)	0.18
	2+	128	---	2.12 (−0.008, 4.25)	0.05

[a]- Model included 2 wk. headers and 2wk. unintentional impacts

[b]- Model included 12 mo. headers and lifetime concussion.

[1]- Covariates: Alcohol us

[2]- Covariates: Alcohol use, years playing at a similar frequency (only (a) model), gender (only (b) model)

[3]- Covariates: Main field position.

[4]- Covariates: Alcohol use, age.

* Significant after FDR correction.