

Oculomotor Response to Cumulative Subconcussive Head Impacts in US High School Football Players

A Pilot Longitudinal Study

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IMPORTANCE Repetitive subconcussive head impacts in sports have emerged as a complex public health issue. Most of these head impacts remain asymptomatic yet have the potential to cause insidious neurological deficit if sustained repetitively. Near point of convergence (NPC) values have shown to reflect subclinical neuronal damage; however, the longitudinal pattern of NPC changes in association with subconcussive head impacts remains unclear.

OBJECTIVES To examine the NPC response to recurring subconcussive head impacts in a single high school football season through a series of repeated measurements.

DESIGN, SETTING, AND PARTICIPANTS This prospective case-series study of US varsity high school football players included baseline measurements of NPC, measurements at pregame and postgame points from 6 in-season games, and postseason follow-up measurements (a total of 14 points). An accelerometer-embedded mouthguard measured head impact frequency and magnitude from all practices and games. During the 6 games, players wore chest-strap heart rate monitors to record heart rate and estimate their excess postexercise oxygen consumption, accounting for possible physical exertion effects on NPC values.

EXPOSURES Players participated in practices and games with no restriction.

MAIN OUTCOMES AND MEASURES Near point of convergence.

RESULTS The 12 included players were all boys, with a mean (SD) age of 16.4 (0.5) years. A total of 8009 head impacts, 177 907 g of peak linear acceleration, and 16 123 371 rad/s² of peak rotational acceleration were recorded from the players in a single football season. There was a significant increase in NPC over time until the middle of the season (mean [SD] NPC: baseline, 5.25 [1.49] cm; pregame 3, 6.42 [1.93] cm; $P = .01$), which was significantly associated with subconcussive head impact frequency and magnitude (0.02 cm per 100 g of peak linear acceleration [SE, 0.0108; 95% CI, 0.0436-0.004]; $P = .01$; 0.023 cm per 10 000 rad/s² of peak rotational acceleration [SE, 0.009; 95% CI, 0.041-0.0105]; $P = .02$). However, NPC values began to normalize toward baseline level from midseason (mean [SD] NPC: baseline, 5.25 [1.49] cm; pregame 6, 5.75 [2.23] cm; $P = .32$), as supported by a significant quadratic trend (β [SE], -0.002 [0.001] cm/d; $P = .003$), while participants continued to incur subconcussive head impacts.

CONCLUSIONS AND RELEVANCE This longitudinal case series study suggests that NPC can be perturbed over the long term by subconcussive head impacts but may normalize over time. The oculomotor system may have an adaptational capacity to subclinical head impacts, yet the mechanism for such remains an open question and warrants further investigation.

JAMA Ophthalmol. 2019;137(3):265-270. doi:10.1001/jamaophthalmol.2018.6193
Published online December 20, 2018. Corrected on July 18, 2019.

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Repetitive head impacts observed in youth sports are becoming a major public health concern.¹ These subconcussive head impacts, which rarely elicit clinical symptoms of concussion,² may result in long-term neurological deficits if sustained repetitively.³ The near point of convergence (NPC), which measures the closest point of focus before diplopia occurs,⁴ has shown to detect subclinical neuronal damage.

Previously, we have demonstrated that 10 acute soccer headings immediately worsen NPC values by 40% compared with baseline measurements.⁵ A follow-up study in college football players revealed that the NPC values, assessed at 11 points during a summer camp (21 days), were chronically impaired among those who frequently sustained subconcussive head impacts.⁶ These sequential investigations yielded 2 questions: (1) How do adolescent NPC values respond to a seasonlong exposure to subconcussive head impacts? (2) Would NPC continue to worsen over time, or is there a limit of impairment?

To address these questions, we conducted a prospective observational study in high school football players and tested our hypotheses that NPC would be significantly worsened as a function of subconcussive head impacts but will reach its peak in the midseason and plateau thereafter. We further hypothesized that, after a 3-week resting period, postseason NPC values would normalize to baseline levels.

Methods

Participants

High school football players at 1 high school volunteered for this study. The study was conducted during the 2017 football season, including a preseason baseline examination, 6 in-season games, and the postseason. The inclusion criterion was being an active football team member. Exclusion criteria included a history of head and neck injury in the previous year or neurological disorders. Since our aim was to study the NPC response to seasonlong subconcussive head impacts, the data from players who did not complete the season were excluded in the analyses.

All participants and legal guardians gave written informed consent. The Washington Hospital Healthcare System institutional review board approved the study.

Study Procedures

During the preseason physical examination, participants were custom-fitted with the Vector mouthguard (Athlete Intelligence) that measured the number of head hits and magnitude of head linear and rotational acceleration.^{6,7} Players wore the Vector mouthguard for all practices and games. Players were also fitted with a chest-strap heart rate monitor (Firstbeat Technologies) to record heart rate variability and estimate players' excess postexercise oxygen consumption during the 6 games, which was used to account for physical exertion effects on acute NPC changes between pregame and postgame measurements.⁸ The NPC values were assessed based on our established protocol^{5,6} at baseline, pregame and postgame for each of 6 games, and postseason (a total of 14 points). Briefly, participants were seated with their

Key Points

Question What is the association between near point of convergence (NPC) values and subconcussive head impacts in high school football players across repeated measurements in a single football season?

Findings This longitudinal case-series study assessed NPC measurements at 14 different points in a football season in 12 football players and found that NPC values were impaired beyond baseline. The impairment was associated with cumulative subconcussive head impacts, and NPC values began normalizing to baseline levels in midseason while players continued to incur head impacts.

Meaning These data suggest the NPC has the potential to reflect subclinical brain damage but may develop tolerance at a certain point to recurring subconcussive impacts.

head in the neutral anatomical position. No spectacles were permitted; participants wore contact lenses if needed at all points. Using the accommodative ruler (Gulden Ophthalmics), an accommodative target (14-point letter) was moved toward the eyes at a rate of approximately 1 to 2 cm per second. The NPC was recorded when the tester observed eye misalignment or when participants verbally signaled diplopia had occurred. On verbal signal, the tester stopped moving the target and recorded the distance between the participant and object. The assessment was repeated twice, and the mean NPC was used for analyses. One trained tester, whose intrarater reliability was excellent (intraclass correlation coefficient of 0.94 [95% CI, 0.92-0.95]; $P < .001$), was masked from the head impact data and assessed all players at all points.

Statistical Analysis

The primary aim was to examine the longitudinal pattern of NPC in association with subconcussive head impacts. We conducted a mixed-effects regression model (MRM) on the primary outcome (pregame NPC values), a similar approach to our previous study.⁶ The rationale of using the pregame NPC as the outcome measure is because postgame NPCs are likely influenced by subconcussive head impacts sustained during games. Conversely, 1 to 2 days prior to each game, the team underwent light-conditioning practices that did not involve tackling; therefore, pregame NPCs were considered free of acute subconcussive effects. The MRM was used to accommodate repeated measurements across 14 points to account for between-participant differences in unmeasured factors (ie, genetic variance, socioeconomic background). The MRM accounts for missing data (3 measurements from 2 participants who were absent during data collection), which increases statistical power and preserves the representation of the results to the larger population.⁹ Because we learned in the previous study that NPC normalizes to baseline levels after 2 weeks of a resting period,⁶ we conducted polynomial trend (quadratic) modeling using (pregame) NPC as an outcome, time as a fixed effect, and participants as a random effect to account for individual NPC differences at the baseline. Corrective lens status was treated as a covariate, given its

unknown effect on NPC measurements. Since the interest was to identify when NPC values are significantly elevated (worsened) compared with baseline measurements, we tested the difference between the pregame NPC values and baseline NPC values by 2-tailed paired *t* tests, with a concept similar to that of the Dunnett post hoc test, if a quadratic trend was present.¹⁰

The second MRM tested whether the chronic increases in NPC values were modulated by cumulative subconcussive head impacts. We conducted 3 individual sets of MRMs for impact frequency, and linear (*g*) and rotational (rad/s²) head accelerations. The models included pregame NPC values as an outcome measure, cumulative head impact kinematics (frequency, linear, or rotational) prior to each game as a fixed effect, and participants as a random effect to account for individual NPC differences at the baseline. For instance, 1 model tests the association between cumulative impact frequency and NPC up to pregame 3, followed by subsequent individual models testing such associations up to pregame 4, pregame 5, and pregame 6. (Only pregame data were used, to minimize acute subconcussive effects during games.)

Lastly, we assessed the acute changes between pregame and postgame NPC values from 6 games using 2-tailed paired *t* tests. The third MRM examined whether the acute NPC changes between pregames and postgames were modified by subconcussive head impact during the games, with the pregame and postgame changes in NPC as outcome measures, head impact during games as fixed effect, and individual baseline difference in NPC as a random effect. Pregame NPC values and excess postexercise oxygen consumption data were included as covariates. All analyses were conducted using statistical software R version 3.4.1 (R Foundation for Statistical Computing) with the package nlme. Significance was set at *P* values less than .05.

Results

Of the 17 players initially enrolled, 2 actively withdrew in the first month, 2 sustained season-ending injuries in the midseason, and 1 did not wear the mouthguard and heart rate monitor after the second game. As a result, the data from 12 players were included in the study (eFigure 1 in the [Supplement](#)). Included participants had a mean (SD) age of 16.4 (0.5) years. All were boys.

A total of 8009 hits, 177 907 *g* of peak linear acceleration, and 16 123 371 rad/s² of peak rotational acceleration were recorded from the 12 players during the football season. Demographics and impact data are summarized in [Table 1](#). Briefly, the median (interquartile range [IQR]) impact count was 543 (331.5-1011.0) hits, median (IQR) peak linear acceleration was 10 826 (7172-24 618) *g*, and median (IQR) peak rotational acceleration was 1 126 008 (620 915-2 231 629) rad/s². Comprehensive impact data are detailed in [Table 2](#) and the eTable in the [Supplement](#).

There was a significant increase (worsening) in NPC values over time (mean [SD] NPC: baseline, 5.25 [1.49] cm; pregame 3, 6.42 [1.93] cm; *P* = .01), but NPC values began to normalize toward the preseason baseline level from the mid-

Table 1. Demographics and Head Impact Kinematics

Variable	Participants, No. (%) (N = 12)
Demographic, mean (SD)	
Age, y	16.4 (0.5)
BMI	28.1 (4.3)
Football experience, y	2.9 (1.5)
Previous concussion	0.5 (0.6)
Players with concussions	
0	8 (75)
1	3 (25)
2	1 (8)
Contact lens	
Yes	3 (25)
No	9 (75)
Race	
White	7 (58)
Black/African American	0 (0)
Asian	3 (25)
American Indian/Alaska	1 (8)
Multiracial	1 (8)
Ethnicity	
Not Latino/Hispanic	8 (67)
Latino/Hispanic	4 (33)
Football position	
Offensive and defensive linemen	5 (42)
Linebacker	1 (8)
Tight end	1 (8)
Skill players ^a	5 (42)
Impact kinematics for season, median (IQR)	
Impact count	543 (331.5-1011.0)
Peak linear acceleration, <i>g</i>	10 826 (7172-24 618)
Peak rotational acceleration, rad/s ²	1 126 008 (620 915-2 231 629)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); IQR, interquartile range.

^a Includes wide receiver, defensive back, and running back positions.

season (mean [SD] NPC: baseline, 5.25 [1.49] cm; pregame 6, 5.75 [2.23] cm; *P* = .32), as illustrated by a significant quadratic trend (β [SE], -0.002 [0.001] cm/d; *P* = .003; [Figure](#)), although participants continued to incur subconcussive head impacts. (The eTable in the [Supplement](#) shows exact NPC values at each point and pairwise comparisons.) The NPC value increase observed from baseline to game 3 was significantly and positively associated with cumulative subconcussive head impact frequencies and magnitudes. For example, NPC values are estimated to have increased 0.04 cm per 10 head impacts (SE, 0.02 [95% CI, 0.08-0.001] cm; *P* = .01), 0.02 cm per 100 *g* (SE, 0.01 [95% CI, 0.04-0.004] cm; *P* = .01), and 0.023 cm per 10 000 rad/s² (SE, 0.009 [95% CI, 0.04-0.01] cm; *P* = .02). However, the magnitudes of the association began to lessen when the model included game 4 (with *P* values > .08), game 5 (*P* values > .16), and game 6 (*P* values > .35). By the postseason point, NPC values were normalized to baseline levels (mean [SD] values: baseline, 5.25 [1.49] cm; postseason, 5.15 [2.46] cm; *P* = .87).

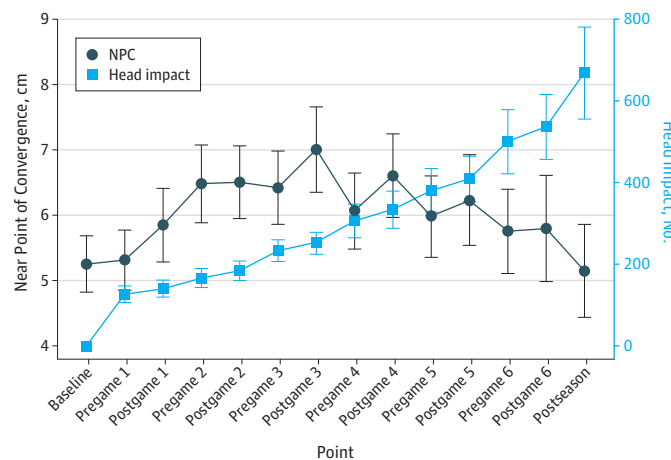
An acute increase in NPC values between pregame and postgame was found only in game 3 (mean [SD] NPC values, pregame, 6.42 [1.94] cm; postgame, 7.00 [2.27] cm; *P* = .03;

Table 2. Cumulative Head Impact Kinematics

Game ^a	Median (Interquartile Range) Value		
	Impact Count	Peak Linear Acceleration, g	Peak Rotational Acceleration, rad/s ²
1			
Up to game	106 (69-165)	2243 (1475-3331)	180 592 (34 367-286 978)
During game	14 (4-21)	258 (73-368)	15 847 (6995-29 485)
2			
Up to game	136 (99-223)	3006 (2040-4479)	235 606 (185 864-392 131)
During game	10 (9-25)	219 (149-535)	18 495 (10 634-48 421)
3			
Up to game	218 (158-314)	4241 (3346-6034)	385 582 (268 180-519 711)
During game	19 (9-25)	380 (178-600)	35 321 (19 008-45 300)
4			
Up to game	267.5 (205-363)	5585 (4294-7502)	512 445 (341 438-606 609)
During game	20 (17-61)	421 (293-1230)	39 711 (220 98-100 673)
5			
Up to game	347 (234-517)	6603 (4883-11 101)	657 433 (384 051-928 073)
During game	31 (10-39)	482 (188-830)	56 045 (16 682-82 711)
6			
Up to game	410 (305-734)	8178 (6302-16 464)	767 293 (517 359-1 502 156)
During game	36 (12-65)	859 (302-1299)	76 648 (24 774-127 067)

^a Preseason camp began on August 8, 2018; dates of games 1, 2, 3, 4, 5, and 6 were September 22, September 29, October 16, October 20, October 28, and November 4, 2018, respectively.

Figure. Trajectories of Near Point of Convergence Values and Head Impacts in a High School Football Season



Near point of convergence gradually increased in direct association with cumulative head impacts and peaked at game 3. The associations between increase in near point of convergence values and head impacts diminished after game 3 and began normalizing toward the baseline level, as illustrated by a significant quadratic trend. Values are expressed as mean (the standard error of

the mean); significant findings occurred at pregame 2 (6.48 [2.06] cm; $P = .02$), postgame 2 (6.50 [1.93] cm; $P = .006$), pregame 3 (6.43 [1.93] cm; $P = .01$), postgame 3 (7.00 [2.27] cm; $P = .003$), and postgame 4 (6.60 [2.22] cm; $P = .01$), and between pregame 3 and postgame 3 (6.43 [1.93] cm vs 7.00 [2.27] cm; $P = .02$).

Figure), and none of the acute NPC increases were correlated with subconcussive head impacts sustained during games (eFigure 2 in the Supplement for individual NPC patterns).

Discussion

To our knowledge, this prospective, longitudinal study is the first clinical study to date to examine the seasonlong pattern of NPC response to repetitive subconcussive head impacts in

high school football players. The data confirmed some previous findings, generated critical knowledge about subconcussive effects on oculomotor function, and might introduce an entirely new concept to the neuroophthalmology and neurotrauma research communities. First, high school football players experienced a median frequency of 543 subconcussive head impacts in a single season, with some players exceeding 1000 impacts. These numbers are consistent to previous studies in high school and college football,¹¹ rugby,¹² and soccer.^{13,14} Second, NPC values worsened concurrently with

subconcussive impacts, and impaired NPC did not recover rapidly, illustrating the slow nature of oculomotor system recovery.^{15,16} Third, as with college football players (whose NPC worsened from 29% to 38% from baseline levels),⁶ the impairment in NPC values in the high school cohort peaked at 33% greater distance than the baseline value, suggesting that NPC responses between adolescents and young adults are similar. Fourth, acute NPC elevations between pregame and postgame measurements were blunted by chronic NPC elevation at the pregame points. Last, NPC values began recovering toward the baseline level in the midseason, despite players continually sustaining head impacts. Taken together, the data suggest that oculomotor function has the potential to reflect subclinical brain injury, but at a certain point, it may also adapt to recurring subconcussive head impacts.

Concussive and subconcussive effects on NPC performance have been studied in a sequential manner. Mucha et al¹⁷ first demonstrated that NPC values were able to distinguish concussed athletes from healthy controls with a 73% accuracy. The result was successfully corroborated in athletes and military personnel with an acute concussion¹⁸⁻²⁰ and prolonged concussion symptoms,²¹ of whom 54% showed exponential increases in NPC (range, 13 cm to 80 cm).²² Impairment in NPC is also notable when children and adolescents sustain a concussion,^{21,23} and a rehabilitative eye movement training does not aid in NPC recovery.²⁴ The data from our current and previous subconcussion studies demonstrated that NPC is sensitive enough to reflect subclinical neural damage in such a way that NPC gradually increases with subconcussive head impacts and plateaus at approximately 30% to 40% beyond baseline values.^{5,6}

The importance of the current study is that, in this cohort, the impaired NPC values began to normalize toward the baseline level in the middle of the season while the participants continued to sustain subconcussive head impacts. Neither our data nor available literature can address whether the oculomotor system develops a tolerance to head impacts or if this pattern is part of an oculomotor plasticity to injury. Thus, future in vitro experiments may apply repetitive minor shear and stretch forces to axons and examine longitudinal morphological response and axolemmal permeability. We simultaneously encourage clinical studies with a larger sample size and various oculomotor assessments to confirm whether the adaptation can be observable in saccades and smooth eye

pursuits. While the current study generated a new concept that warrants further study, there are also several clinical implications. During an early-to-middle phase of a football season, NPC values are likely to have carryover effects from cumulative subconcussive neural burden. Based on evidence from our sequential studies,^{5,6} when evaluating a suspected concussion case, we recommend clinicians to account for 30% to 40% of NPC increase from baseline owing to subconcussive head impacts if the patient has repeatedly incurred head impacts prior to a concussion. However, the changes in NPC caused by subconcussive head impacts are subclinical, with no proven effects on sports performance and activity of daily living. This may be owing to a lack of sensitive metric to translate clinical significance of subtle neural damage.

Limitations

Although the sample size was limited to 12 players, we confirmed that the NPC data for each point were normally distributed by Shapiro-Wilk tests (with nonsignificant *P* values), because the normality assumption is required to avoid type I and II errors. The primary analyses included NPC measurements at 7 different points (baseline and 6 pregames; 81 observations, with 3 missing data points), which yielded a large effect size estimated at the peak, pregame 3, compared with baseline (Cohen *d*, 0.854), as well as sufficient statistical power (2-tailed $t_{11} = 2.957$; power, 0.768; $P = .01$) to support our preliminary findings. However, the limited sample size coupled with a lack of control group composed of athletes playing noncontact sports precludes the generalizability of the findings. The pilot study nonetheless supports the feasibility of repeated data collection in adolescent athletes, encouraging a larger-scale longitudinal study in the near future.

Conclusions

The present study suggests that NPC can be chronically perturbed by subconcussive head impacts, but NPC can begin recovering to baseline levels while individuals continue to sustain subconcussive impacts. Our data support the concept that the oculomotor system may adapt to what is considered subclinical brain injury, yet such mechanism remains an open question and warrants further investigation.

ARTICLE INFORMATION

Accepted for Publication: November 1, 2018.

Published Online: December 20, 2018.
doi:10.1001/jamaophthalmol.2018.6193

Correction: This article was corrected on July 18, 2019, to fix the units in the Figure caption from mm to cm for the values reported for pregame 2 (6.48 [2.06] cm), postgame 2 (6.50 [1.93] cm), pregame 3 (6.43 [1.93] cm), postgame 3 (7.00 [2.27] cm), and postgame 4 (6.60 [2.22] cm), and between pregame 3 and postgame 3 (6.43 [1.93] cm vs 7.00 [2.27] cm).

Author Contributions: Dr Kawata had full access to all of the data in the study and takes responsibility

for the integrity of the data and the accuracy of the data analysis.

Concept and design: Zonner, Kawata.

Acquisition, analysis, or interpretation of data:

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Drafting of the manuscript: Zonner, Ejima, Fulgar, Kawata.

Critical revision of the manuscript for important intellectual content: Ejima, Charleston, Huibregtse, Bevilacqua, Kawata.

Statistical analysis: Ejima, Kawata.

Obtained funding: Kawata.

Administrative, technical, or material support:

Zonner, Fulgar, Charleston, Bevilacqua, Kawata.

Study supervision: Kawata, Zonner, Charleston, Huibregtse.

Conflict of Interest Disclosures: Ms Charleston reports that she is now on an advisory board for Athlete Intelligence; however, she was independent during the study period. No other disclosures were reported.

Funding/Support: This work was supported from the Indiana Spinal Cord & Brain Injury Research Fund from the Indiana State Department of Health (grant 0019939; Dr Kawata) and Indiana University School of Public Health faculty research grant program (grant 2246237; Dr Kawata).

Role of the Funder/Sponsor: Sponsors had no role in the design or conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: We thank Ms Lamiya Sheikh, MS, for her statistical advice and administrative assistance. Ms Sheikh participated in initial analytical brainstorming but did not participate in data analysis; thus she is not listed as a co-author of this paper. Also, we thank Michelle Stone, BS, and Kimberly Hartz, MS, for their administrative assistance. These individuals were not compensated for their contributions.

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Invited Commentary

Assessing Subconcussive Head Impacts in Athletes Playing Contact Sports—The Eyes Have It

Ann C. McKee, MD; Michael L. Allosco, PhD

Converging research has shown that subconcussive head impacts are a substantial source of acute and chronic structural and functional changes in the brains of contact sport athletes. Subconcussive head impacts involve the transmission of mechanical energy

to the head from a force sufficient to cause neuronal injury or dysfunction, but they do not result in immediate overt clinical symptoms. From high school through professional play, athletes playing contact sports can experience hundreds of unrecognized subconcussive impacts in a single season, through which they continue to play, seemingly unharmed. Although large prospective studies are needed to understand this phenomenon, the

frequency of subconcussive head impacts has been correlated with acute microstructural changes in cortical and deep gray matter structures of the brain, as well as impairments on neuropsychological testing in various samples of athletes playing contact sports, including football, soccer, and ice hockey.¹ Growing evidence, primarily in former football players, further suggests that repetitive exposure to subconcussive impacts can lead to long-term neurobehavioral disturbances,² including those from the neurodegenerative disease chronic traumatic encephalopathy (CTE).^{3,4} Recent experimental models of unilateral impact injuries that replicate subconcussive hits, not concussions, are associated with neuropathological changes resembling CTE in the brains of wild-type mice, including a progressive spread of fo-



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