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Reliable sideline ocular-motor assessment following exercise in healthy student athletes

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ABSTRACT

Objectives: To assess the reliability and effect of exercise on sideline dynamic visual performance measures of ocular-motor function using a portable visual assessment system (*EYE-SYNC*®).
Design: Prospective cohort study.
Methods: Healthy student athletes, ages 18–25 years, performed eye-tracking six times—three times consecutively prior to and after practice—using EYE-SYNC® goggles. Ocular-motor performance was assessed by calculating five gaze error outcomes between target position and actual gaze position to inform dynamic visual synchronization. We assessed reliability by calculating the intraclass correlation coefficient (ICC) for each outcome (we defined the standard deviation of tangential error (SDTE) as our primary outcome) and calculated differences in mean pre- and post-practice scores.
Results: ICCs for the SDTE score were 0.86 (95% confidence interval, CI: 0.82–0.9) and 0.88 (0.84–0.91) at pre- and post-practice, respectively. 133 (89%) and 135 (90%) of 150 athletes had at least one measurement at pre- and post-practice, respectively. 117 (78%) and 122 (81%) athletes had more than one SDTE score at pre- and post-practice, respectively. The absolute mean (SD) differences between pre- and post-practice mean scores ranged from 0.02 (0.05) for horizontal gain to 0.1 (0.5) for SDTE.
Conclusions: We observed high ICC scores indicating excellent reliability of visual synchronization measurements, suggesting that one measurement would be sufficient. Most athletes had similar scores before and after practice, indicating little change in visual performance following exercise. *EYE-SYNC*® goggles have the potential for use in obtaining objective visual performance measures of ocular-motor function for sideline assessment of concussion and return to play decisions.

Practical implications

The portable EYE-SYNC® system can be used reliably in healthy student-athletes to obtain consistent visual performance scores.

Visual performance scores from the EYE-SYNC® goggles were similar before and after exercise.

EYE-SYNC® goggles have the potential to be used as a tool for obtaining objective measures for sideline assessment of concussion and return to play.

1. Introduction

Based on data from the Centers for Disease Control and Prevention, it is estimated that 1.6–3.8 million sports-related concussions occur annually in the United States.[1] In the past decade, sports-related concussions, a type of mild traumatic brain injury, have been recognized as a growing public health concern,[2,3] with an increasing incidence of sports-related concussions in student athletes. From 2009 to 2014, approximately 10,500 sports-related concussions were reported annually in collegiate athletes, with concussion rates increasing by almost 60%, from estimates in 2004.[4,5] Pediatric emergency department visits for sports-related concussions have doubled in the last decade, with an estimated 300,000 children being treated in U.S. emergency departments for sports-related concussions in 2012.[6] However, these estimates likely underestimate the true incidence of sports-related concussions given that athletes may not always seek medical attention following injury, may not be aware that they have a concussion, or may not report their injury in hopes of uninterrupted sports participation.[7–9]

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Despite it's extent, there is no medical consensus for concussion diagnosis.[10] Currently, diagnosis relies heavily on subjective questionnaires and cognitive screening supporting physical examination and clinical judgement.[11] Recovery tracking generally monitors the severity of post-concussive symptoms over time.[10] The impact of exercise on such subjective assessments is unknown, making it difficult to interpret test results. These factors are critical to understanding when an athlete should be removed from play following head injury or when an athlete should return-to-play.

In the United States, initial sideline assessment for suspected concussion after an athlete has sustained an injury is often performed by an athletic trainer and decisions regarding return-to-play can be extremely challenging.[12–14] Interpretation of post-injury performance measures may be challenging if baseline testing comparators were insincere or if repeated assessments resulted in a learning effect. To avoid variability in performance measures that may complicate trainers' decision-making, there is a critical need for objective sideline measures to assess concussion and guide decisions regarding return-to-play.

Ocular-motor impairments have been reported extensively following concussion[15,16] and prior research suggests that dynamic visual synchronization (DVS) assessments could objectively quantify impairment following head injury and track its resolution during concussion recovery.[17,18] Dynamic vision synchronization (DVS) is a term used to describe smooth pursuit predictive eye movements; smooth pursuit refers to the ability of the eyes to move smoothly in order to closely follow a moving object.[19] While desktop-based (non-portable) systems for visual tracking are available,[18,20] sideline assessment requires the use of portable devices, such as the *EYE-SYNC®* visual assessment system. *EYE-SYNC®* includes goggles with embedded eye tracking sensors and a high performance tablet, both enclosed in a portable aluminum case.[21] However, the reliability of the system to measure dynamic visual synchronization is unknown. The objectives of our study were to evaluate the reliability of the *EYE-SYNC®* portable system and explore the effect of exercise on visual measurement scores in a cohort of healthy student athletes. To address our objectives, we had the following specific aims: (1) evaluate reliability of pre-practice EYE-SYNC® goggles scores; (2) evaluate reliability of post-practice EYE-SYNC® goggles scores; (3) assess the effect of exercise on change in mean pre and post-practice scores; and (4) compare pre-practice EYE-SYNC® goggles scores to the non-portable desktop-based scores; the existing system available for assessing DVS.

2. Methods

In this prospective cohort study, from September 2016 to March 2017, we recruited male and female student athletes, ages 18–25 years, from the athletics department at a single university for enrollment in this study. Inclusion criteria included fluency in English and self-reported 20/30 or better eyesight (corrected vision allowed). Prior to a practice/game, athletes performed all three consecutive eye-tracking assessments using the *EYE-SYNC®* goggles over approximately 5 min in total. They repeated the three consecutive assessments within one hour of the said practice/game. Post-practice assessments were done to assess if exercise had any effect on the outcome measures. We used a total of 11 *EYE-SYNC®* goggles with identical software.

In addition, 20 athletes underwent eye-tracking assessment using a desktop system. The desktop system assessment was performed once prior to practice/game. This system performs the same assessment as the goggles using the same software, but with a different hardware system in which the athlete's head is stabilized using a chin- and head-rest and eye cameras track visual movement as the athlete looks at a target on a computer screen using a desktop computer.[19]

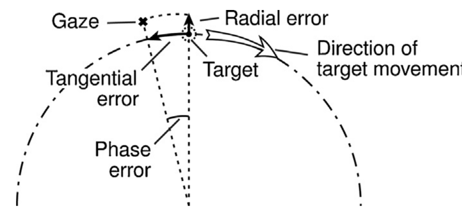

Fig. 1. Schematic definition of parameters. The target, moving clockwise along a circular trajectory (dot-dashed curve), is at the 12 o'clock position. The difference between the gaze and the target positions (gaze error) are indicated by the phase difference and the vectoral components in the radial and tangential directions.[18] Reprinted with permission.

Data were collected and managed by research coordinators. Athlete-specific information was collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools. REDCap is a secure, web-based application designed to support data capture for research studies.[22] Goggle assessments were collected directly by the software and goggle data were obtained from the SyncThink Inc. company.[21] Desktop data were obtained from the PDF report provided through the system and entered by research coordinators into Excel.

This study was approved by the University Institutional Review Board.

To assess dynamic visual synchronization as a measure of ocular-motor function, athletes were asked to follow a target moving in a clockwise circular trajectory at a constant speed (Fig. 1).[18] The automated software algorithm analyzes the eye position versus the target over the assessment time and produces the visual synchronization measures listed below. These measures provide information regarding the smooth pursuit of eye tracking and are the calculated errors between the target position and the athlete's gaze position.[18–20] These measures were obtained for the *EYE-SYNC®* goggles and desktop systems.

(a) Standard deviation of tangential error (SDTE): measures the standard deviation (SD) of the error between the target position and the gaze along the direction parallel to the target trajectory and is expressed as the degrees of visual angle. The values of this measure are non-negative with smaller values indicating better visual tracking; prior research indicates that in healthy young adults, mean SDTE scores range from 0.89 to 1.1 using the desktop system.[18,19]
(b) Standard deviation of radial error (SDRE): measures the SD of the error between the target position and the gaze along the direction perpendicular to the target trajectory and is expressed as the degrees of visual angle. The values of this measure are non-negative with smaller values indicating better visual tracking; prior research indicates that in healthy young adults, mean SDRE scores range from 0.62 to 8.9 using the desktop system.[18,19]
(c) Phase error: measures the angle formed by the gaze and a fixed target position at the 12 o'clock direction to assess the central tendency of the target position and gaze position and is expressed as the "degrees of phase angle".[20] The values of this measure can be negative or positive; positive values are typically considered to represent poor performance and indicate a situation where the gaze is ahead of the target along the circular path.
(d) Horizontal gain (HGain) and vertical gain (VGain): measure how well the gaze is tracking the target with respect to velocity by calculating the ratio of the average eye velocity to the average target speed in the horizontal and vertical dimensions,

Table 1
Intraclass correlation coefficients (ICCs) for EYE-SYNC® visual measures pre- and post-practice.

	Pre-practice scores				Post-practice scores			
Visual measure	1 n = 114	2 n=116	3 n = 110	ICC (95% CI)[a]	1 n = 121	2 n = 135	3 n = 118	ICC (95% CI)[a]
SD tangential error	1.04 (0.7)	1.16 (0.8)	1.17 (0.8)	0.86 (0.82, 0.90)	1.0 (0.7)	1.0 (0.6)	1.0 (0.6)	0.88 (0.84, 0.91)
SD radial error	0.78 (0.4)	0.84 (0.4)	0.85 (0.4)	0.78 (0.71, 0.84)	0.8 (0.4)	0.8 (0.3)	0.8 (0.4)	0.91 (0.87, 0.93)
Phase error	−0.85 (3.4)	−0.73 (4.5)	−0.73 (3.8)	0.83 (0.77, 0.87)	−0.8 (4.0)	−1.4 (2.5)	−1.4 (2.5)	0.88 (0.84, 0.91)
Horizontal gain	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)	0.79 (0.72, 0.84)	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)	0.80 (0.74, 0.85)
Vertical gain	0.8 (0.1)	0.8 (0.1)	0.8 (0.1)	0.84 (0.79, 0.88)	0.9 (0.1)	0.8 (0.1)	0.8 (0.1)	0.87 (0.82, 0.90)

[a] Models were adjusted for goggle since 11 different goggles were used during the study.

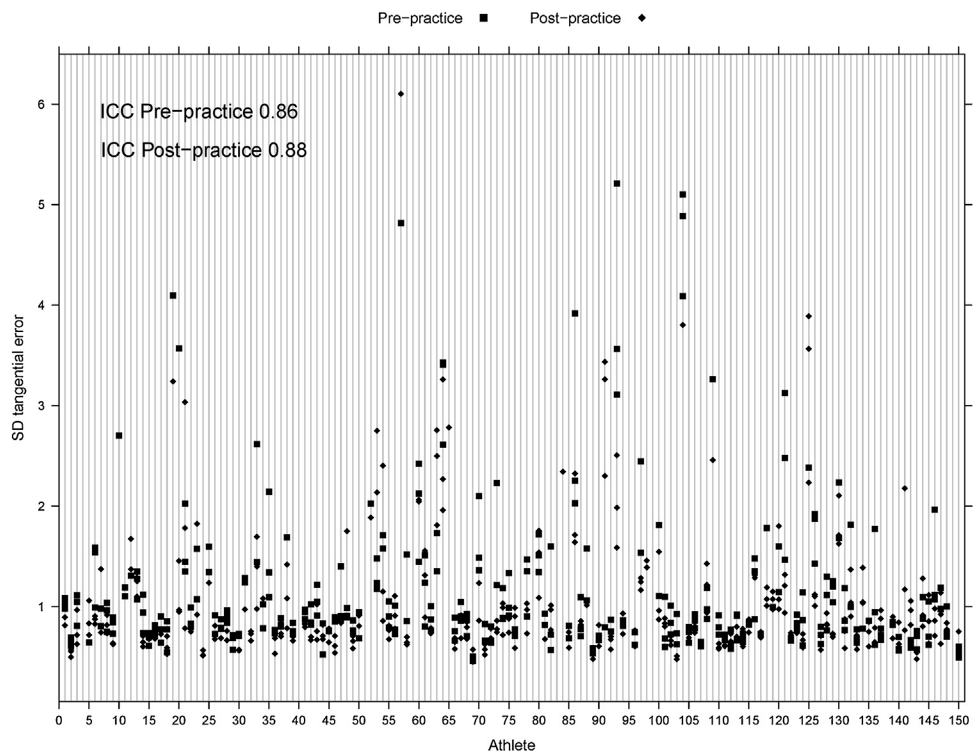

Fig. 2. Pre-practice and post-practice EYE-SYNC® goggles standard deviation of tangential error scores. This figure shows the pre- and post-practice SDTE scores for each athlete. Each line on the x-axis represents an athlete and the values on the y-axis show the SDTE score. Each square represents a specific value at pre-practice for an athlete and each diamond represents a specific value at post practice.

respectively. Values closer to 1 represent favorable performance and indicate a good velocity match between the gaze and the target with values closer to 0 indicating poor tracking. Values substantially higher than 1 also indicate poor tracking.

We defined our primary outcome as the SDTE score measured at the sideline prior to and after a practice/game. Our secondary outcomes were SDRE, phase error, HGain and VGain.

To assess the reliability of EYE-SYNC® goggles visual synchronization measures, we calculated the intraclass correlation coefficient (ICC) and its 95% confidence interval for each outcome measure.[23] The ICC – which in this case can be defined as proportion of total variation that is explained by the subject-to-subject heterogeneity in SDTE – describes the level of correlation between two or more observations made on the same student athlete; a higher ICC (closer to 1) indicates greater reliability of the measure. We used generalized linear mixed effects models, with a fixed effects to adjust for the 11 goggles and a random effects term for athlete, to estimate the ICC. We also calculated the total number of assessments done by each athlete at each time point to understand how many athletes had more than one assessment available.

To assess the effect of exercise on goggle visual synchronization measures, we calculated the difference between the mean scores pre- and post-practice and calculated an effect size; to test for statistical differences, we used the Wilcoxon signed-rank statistic. To evaluate the performance of the goggles' DVS measures compared to the desktop eye-tracking system, we used the mean values of the goggles' measures for each athlete at pre-practice and created a Bland–Altman plot to describe the agreement between measurements made by the different systems – EYE-SYNC® goggles and the desktop. If the observations are uniformly clustered around the horizontal reference line at 0, it suggests that there is no systematic bias in the measurements. To formally test agreement, we used the Wilcoxon signed-rank statistic to assess whether differences by system were significant at a two-sided alpha level of 0.05.

Analyses were conducted using Statistical Analysis Software version 9.4 (SAS Institute, Cary, NC) and R software.[24]

3. Results

We enrolled 150 athletes from 11 sports who met inclusion and exclusion criteria. Their mean (SD) age was 20 (1.3) years and 55% were female. Most were white/caucasian (57%) and born in the United States (97%) (Supplementary Table 1).

The means and standard deviations (SD) for all DVS measures were similar for the three assessments at pre-practice and post-practice times (Table 1). The mean values for the SDTE and SDRE scores as well as for HGain and VGain were all close to 1. Intraclass correlation coefficients (ICCs) for all visual score measures ranged from 0.78 to 0.86 at the pre-practice time and from 0.80 to 0.91 at post-practice (Table 1). For the SDTE score, the ICC (95% confidence interval) was 0.86 (0.82, 0.90) at pre-practice and 0.88 (0.84, 0.91) at post-practice (Fig. 2).

We obtained at least one pre-practice assessment from 133 (89%) athletes and at least one post-practice assessment from 135 (90%) athletes. We obtained all three pre-practice measurements from 60% of athletes and all 3 post-practice measurements from 71% of athletes (Supplementary Table 2).

We did not obtain any measurements from 11% and 10% of athletes pre- and post-practice, respectively. Reasons for inability to obtain measurements were overheating of the goggles, the program quitting unexpectedly, or athlete inability to complete the assessment due to sleepiness or inability to focus on the target. We were able to conduct assessments on average, for 10 (SD 6.3) athletes per hour, with a maximum of 25 athletes being assessed on a given day.

The mean (SD) SDTE score at pre-practice was 1.2 (0.79) and at post-practice was 1.09 (0.75) (Supplementary Table 3). The absolute mean (SD) differences between the pre- and post-practice mean scores ranged from 0.02 (0.05) for horizontal gain ($p < 0.01$) to 0.1 (0.5) for SD tangential error with statistically significant differences between pre- and post-measures ($p < 0.01$) but small effect sizes for most of the measures (Supplementary Table 3).

Twenty athletes underwent DVS assessment using the desktop eye-tracking system; of these, goggle measurements were not available for three athletes due to technical issues. SDTE ($p < 0.0001$), SDRE ($p < 0.0001$) and horizontal gain ($p = 0.0002$) measures were significantly higher for the goggles compared to the desktop; the mean (SD) difference in the SDTE scores was 0.58 (0.66). There was no significant difference in phase error and vertical gain by system (Supplementary Table 4). The difference in scores did not appear to be related to magnitude of the score (Supplementary Fig. 1).

4. Discussion

Our study included a large cohort of male and female student athletes of diverse ethnicities and playing a variety of sports. While we did not include traditionally high-impact sports such as football, other sports with high rates of concussion such as wrestling and soccer were included. We found high ICC scores for all gaze error outcomes indicating the reliability of the EYE-SYNC® goggle measurements for dynamic visual synchronization (DVS) in healthy student athletes. Additionally, the consistency of the measures suggests that a single assessment by the goggles is adequate for DVS assessment. We were able to collect data for one set of measurements from most athletes at pre- and post-practice times. Multiple assessments from EYE-SYNC® goggles at sidelines was limited; however, a majority of athletes had at least two pre or post-practice measurements to contribute toward the reliability assessment. In practice, visual testing would likely only be performed one time at the sideline and our findings indicate that the EYE-SYNC® goggles system can be used reliably for assessing DVS at the sideline.

We found that mean visual performance scores ranged from 0.8 (0.1) for gain scores to 1.2 (0.8) for the SD tangential error score. These results are similar to prior studies using desktop assessment of visual performance in normal adult subjects.[18] A few (8%) of our athletes had high SDTE scores (for example, SD tangential error score greater than 2.5) indicating poor tracking which is consistent with previously reported measures in normal adults.[19]

An important consideration for any concussion assessment tool is the ability to differentiate between the effect of exercise and concussion in athletes who sustain an impact. If measurements are affected after exercise, determining if the observed measurement after an impact indicates concussion or exercise effect can be challenging. Prior studies assessing cognitive functioning before and after exercise have found mixed results regarding the effect of exercise.[25–27] We found that exercise did not have a clinically meaningful effect on EYE-SYNC® goggles mean dynamic visual performance scores, as indicated by the small effect sizes observed in most of the pre-post practices measures. Despite a statistically significant difference in pre/post exercise scores, we found minimal changes in DVS measures pre-to-post practice, with absolute mean changes ranging from 0.02 (0.05) for horizontal gain to 0.1 (0.5) for SD tangential error.

We also found that most visual outcome scores from the *EYE-SYNC®* goggles were significantly higher than those observed from the desktop system, irrespective of magnitude of scores. This difference in scores is most likely a function of the differences in hardware between the two devices such that lower values in eye-target variance would typically be observed from the desktop system. As such, our findings indicate that the same system should be used in athletes to compare visual scores after sustaining an impact as the one used to obtain the baseline visual scores.

A limitation of this study is that it did not include athletes from traditionally high concussion sports such as football. While we did include other high contact sports, it would be important to investigate the impact of these measures at different training intensities. Future research will assess if dynamic visual synchronization measures change after concussion and if and how DVS can be used to support a diagnosis of concussion and to track recovery.

5. Conclusion

In conclusion, we found that the portable *EYE-SYNC®* goggles system can be used reliably in healthy student athletes to obtain consistent DVS assessments. Our findings suggest that *EYE-SYNC®* goggles can provide objective sideline assessment of DVS and have the potential to be used as an adjunct tool for concussion diagnosis and recovery tracking; clinically significant differences in DVS assessment post-injury as compared to baseline may support a concussion diagnosis. Additional research is required for a better understanding of the feasibility and reliability of the *EYE-SYNC®* portable system in athletes sustaining an impact.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jsams.2019.07.015.

References

1. Langlois JA, Rutland-Brown W, Wald MM. The epidemiology and impact of traumatic brain injury: a brief overview. *J Head Trauma Rehabil* 2006; 21(5):375–378.
2. Patel DR, Fidrocki D, Parachuri V. Sport-related concussions in adolescent athletes: a critical public health problem for which prevention remains an elusive goal. *Transl Pediatr* 2017; 6(3):114–120. http://dx.doi.org/10.21037/tp.2017.03.08.
3. Lippman H. Concussion—A Public Health Crisis. Available at: https://www.mdedge.com/neurologyreviews/article/81884/alzheimers-cognition/concussion-public-health-crisis. Accessed 30 March 2018.
4. Hootman JM, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports: summary and recommendations for injury prevention initiatives. *J Athl Train* 2007; 42(2):311–319.
5. Zuckerman SL, Kerr ZY, Yengo-Kahn A et al. Epidemiology of sports-related concussion in NCAA athletes from 2009–2010 to 2013–2014: incidence, recurrence, and mechanisms. *Am J Sports Med* 2015; 43(11):2654–2662. http://dx.doi.org/10.1177/0363546515599634.
6. Coronado VG, Haileyesus T, Cheng TA et al. Trends in sports- and recreation-related traumatic brain injuries treated in US Emergency Departments: The National Electronic Injury Surveillance System-All Injury Program (NEISS-AIP) 2001–2012. *J Head Trauma Rehabil* 2015; 30(3):185–197. http://dx.doi.org/10.1097/HTR.0000000000000156.
7. Chrisman SP, Quitiquit C, Rivara FP. Qualitative study of barriers to concussive symptom reporting in high school athletics. *J Adolesc Health* 2013; 52(3):330–335. http://dx.doi.org/10.1016/j.jadohealth.2012.10.271, e3.
8. McCrea M, Hammeke T, Olsen G et al. Unreported concussion in high school football players: implications for prevention. *Clin J Sport Med* 2004; 14(1):13–17.
9. Torres DM, Galetta KM, Phillips HW et al. Sports-related concussion: anonymous survey of a collegiate cohort. *Neurol Clin Pract* 2013; 3(4):279–287. http://dx.doi.org/10.1212/CPJ.0b013e3182a1ba22.
10. Sharp DJ, Jenkins PO. Concussion is confusing us all. *Pract Neurol* 2015; 15(3):172–186. http://dx.doi.org/10.1136/practneurol-2015-001087.
11. Dessy AM, Yuk FJ, Maniya AY et al. Review of assessment scales for diagnosing and monitoring sports-related concussion. *Cureus* 2017; 9(12):e1922. http://dx.doi.org/10.7759/cureus.1922.
12. Dompier TP, Kerr ZY, Marshall SW et al. Incidence of concussion during practice and games in youth, high school, and collegiate American football players. *JAMA Pediatr* 2015; 169(7):659–665. http://dx.doi.org/10.1001/jamapediatrics.2015.0210.
13. Putukian M. Clinical evaluation of the concussed athlete: a view from the sideline. *J Athl Train* 2017; 52(3):236–244. http://dx.doi.org/10.4085/1062-6050-52.1.08.
14. Concussion Resources for Coaches and Athletic Trainers. Available at: http://www.concussiontreatment.com/forcoaches.html. Accessed 15 May 2019.
15. Ventura RE, Balcer LJ, Galetta SL et al. Ocular motor assessment in concussion: current status and future directions. *J Neurol Sci* 2016; 361:79–86. http://dx.doi.org/10.1016/j.jns.2015.12.010.
16. Ventura RE, Balcer LJ, Galetta SL. The concussion toolbox: the role of vision in the assessment of concussion. *Semin Neurol* 2015; 35(5):599–606. http://dx.doi.org/10.1055/s-0035-1563567.
17. Cifu DX, Wares JR, Hoke KW et al. Differential eye movements in mild traumatic brain injury versus normal controls. *J Head Trauma Rehabil* 2015; 30(1):21–28. http://dx.doi.org/10.1097/HTR.0000000000000036.
18. Maruta J, Suh M, Niogi SN et al. Visual tracking synchronization as a metric for concussion screening. *J Head Trauma Rehabil* 2010; 25(4):293–305. http://dx.doi.org/10.1097/HTR.0b013e3181e67936.
19. Maruta J, Heaton KJ, Kryskow EM et al. Dynamic visuomotor synchronization: quantification of predictive timing. *Behav Res Methods* 2013; 45(1):289–300. http://dx.doi.org/10.3758/s13428-012-0248-3.
20. Maruta J, Spielman LA, Rajashekar U et al. Visual tracking in development and aging. *Front Neurol* 2017; 8:640. http://dx.doi.org/10.3389/fneur.2017.00640.
21. No Title. Available at: https://syncthink.com/. Accessed 9 April 2018.
22. Harris PA, Taylor R, Thielke R et al. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009; 42(2):377–381. http://dx.doi.org/10.1016/j.jbi.2008.08.010.
23. Hankinson SE, Manson JE, Spiegelman D et al. Reproducibility of plasma hormone levels in postmenopausal women over a 2–3-year period. *Cancer Epidemiol Biomarkers Prev* 1995; 4(6):649–654.
24. R Core Team. *R: A language and environment for statistical computing*, Vienna, Austria, R Foundation for Statistical Computing, 2019. URL https://www.R-project.org/.
25. Chang YK, Labban JD, Gapin JI et al. The effects of acute exercise on cognitive performance: a meta-analysis. *Brain Res* 2012; 1453:87–101. http://dx.doi.org/10.1016/j.brainres.2012.02.068.
26. Cottle JE, Hall EE, Patel K et al. Concussion baseline testing: preexisting factors, symptoms, and neurocognitive performance. *J Athl Train* 2017; 52(2):77–81. http://dx.doi.org/10.4085/1062-6050-51.12.21.
27. Covassin T, Weiss L, Powell J et al. Effects of a maximal exercise test on neurocognitive function. *Br J Sports Med* 2007; 41(6):370–374. http://dx.doi.org/10.1136/bjsm.2006.032334, discussion 374.