Horizontal and vertical saccades as a diagnostic marker of traumatic brain injury

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Abstract

Background: Eye tracking tests to measure horizontal and vertical saccades as a marker of damage to neural circuits associated with TBI was evaluated in the present study.

Methodology: 287 participants reporting either no TBI, mild, moderate or severe TBI participated in a suite of eye tracking tests to measure horizontal and vertical saccadic performance.

Results: The horizontal saccades test offered a sensitivity of 0.77 and a specificity of 0.78, similarly the vertical saccades tests offered a sensitivity of 0.64 and a specificity of 0.65.

Conclusions: The results indicated that using eye-tracking technology to measure these metric offers a as an objective, reliable and quantifiable way of differentiating between individuals with different severities of TBI, and those without a TBI.

Key words: *eye tracking, horizontal saccades, vertical saccades, VOMS, TBI*, *concussion*

Introduction

The rising incidence of traumatic brain injury (TBI) is an international public health concern and a significant cause of morbidity and mortality. In the United States alone, about 1.7 million people suffer from a TBI every year, and 52,000 of these cases result in death.[1] Oculomotor research contributes to the growing understanding of TBI by providing insight into neural functioning for clinicians and neuroscientists.[2] Oculomotor behavior is a promising neuropsychological endophenotype, as it reflects abnormalities of complex neurocircuitry.[2] Specifically, oculomotor impairments can be mapped to the location of neural dysfunction and offer objective examination of neurological health.[3]

Oculomotor behavior is commonly broken down into the following eye movement categories: fixations, smooth pursuits, and saccades.[4] Fixations keep the eye position in a relatively still state to hold the image of a stationary target on the fovea, a site of high visual acuity.[5] Smooth pursuits occur when the eyes track a moving stimulus to stabilize the image on the fovea.[6,7,8] Finally, saccades are rapid movements of the fovea between fixation points.[9] Depending on the type of eye movement, different brain regions become activated.[10] For example, several structures in the cerebral cortex control when and where saccades occur, including the Frontal Eye Field (FEF), the Supplementary Eye Field (SEF), the Dorsolateral Prefrontal Cortex (DLPFC), and the Parietal Eye Field (PEF).[10] Cerebellar structures also regulate saccade size and accuracy.[10]

Visual stimuli presented in different directions recruit specific brain regions to generate saccades. For horizontal saccades, the Paramedian Pontine Reticular Formation (PPRF) in the pons receives saccade initiation signals from the FEF and the Superior Colliculus (SC).[10] Excitatory burst neurons (EBNs) in the PPRF create a velocity command and project to the neural integrator (medial vestibular nucleus and adjacent nucleus prepositus hypoglossi), which yields an eye position command.[10] On the other hand, the rostral interstitial nucleus of the medial longitudinal fasciculus in the midbrain receives signals from the FEF and contains EBNs that produce upward and downward saccades.[10] These vertical saccades occur through different projections to the vertical neural integrator (the interstitial nucleus of Cajal).[10]

Saccades encompass a hierarchy of eye movements that includes visually guided (reflexive) saccades in response to visual stimuli and voluntary saccades.[10] Voluntary saccades are further divided into four types: saccades to command; predictive saccades produced in anticipation of a target; memory-guided saccades generated to the position of a previous target; and antisaccades made in the opposite direction of a target.[10] Specific oculomotor tests are able to examine self-paced saccades—voluntary saccades made between two stationary targets in a fixed period of time.[11] Execution of self-paced saccades involves a pathway from the FEF and DLPFC to the SC.[12] The anterior cingulate cortex also plays a role in sustaining motivation to perform self-paced saccade tasks.[11] Examining the neurocircuitry regulating oculomotor behavior is valuable to understanding both normal functioning and pathophysiology.

Several injuries and disorders can affect saccadic performance in humans, including TBI.[13] Individuals diagnosed with TBI have displayed abnormal antisaccades, memory-guided saccades, and self-paced saccades, and these impairments reflect the degree of head trauma.[1,13] The severity of a TBI is categorized as mild, moderate, or severe, depending on a patient's Glasgow Coma Score (GCS).[1] The GCS evaluates a patient's level of consciousness using a 3-15 point scale that rates a patient's best motor response (6 points), best verbal response (5 points), and eye opening ability (4 points), with higher scores indicating a higher state of consciousness.[14] Mild TBI (mTBI) is defined by a GCS between 13 and 15, moderate between 9 and 12, and severe between 3 and 8.[1] mTBI is the most common form of TBI and includes concussions, or brain injuries from blows to the head or body that induce neurological symptoms.[1,15]

Common tests for TBI include symptom evaluations and neuropsychological testing used for injury management.[16] While quick and convenient, symptom reports are subjective, vulnerable to underreporting, and may have limited long-term value, since cognitive and visual deficits can endure after symptoms diminish.[16] The standard test for concussion in sport, for example, is the third version of the Sport Concussion Assessment Tool (SCAT-3), which involves a physical exam, a GCS score, and cognitive and sensorimotor evaluations.[17] This testing battery includes other tests, such as the Standardized Assessment of Concussion (SAC) and the Balance Error Scoring System (BESS); however, none of these specifically test vision.[18] The Defense Automated Neurobehavioral Assessment (DANA) is a new mobile phone application that consists of cognitive and psychological tests to rapidly and reliably identify cases of TBI.[19] Yet, neuropsychological tests, such as DANA, have the potential for patient motivation to affect results.[20,21] Finally, the King-Devick Test (KDT) includes an evaluation of saccades but does not examine other eye movements often impaired after TBI.[17,18] Vestibular/Ocular Motor Screening (VOMS) provides a more complete assessment of eye movements to help clinicians evaluate vestibular and ocular abnormalities after concussion.[22] The VOMS tests saccades, smooth pursuits, fixations, convergence, and the vestibular-ocular reflex.[16] Although it can distinguish concussed athletes from healthy controls, the VOMS relies on subjective reports of symptoms that may introduce error from recall bias and underreporting.[18] Also, VOMS cannot detect specificity beyond gross eye movement observation by the clinican.[18]

Given the limitations of the common screening tools outlined above it is important to develop and implement more objective and specific methods to assist in concussion and TBI diagnostic decision-making. To this end, eye-tracking technology quickly delivers precise, objective eye movement recordings by surveying the eye several times per second.[6] Examining damaged circuits caused by TBI with oculomotor assessments produces quantifiable data to complement existing TBI screening methods.[23,24] Because both planning and rapidly producing saccades to targets in the visual field recruit frontoparietal areas vulnerable to damage from TBI, saccadic deficits are important to examine with eye-tracking metrics.[15,25] Common metrics for horizontal saccades include the number of fixations made during a saccade task, the ratio of saccadic velocity to accuracy (S/A ratio), and targeting metrics that measure accuracy. Accuracy metrics, such as saccade gain, measure how close eye gazes are to target stimuli by calculating the ratio of saccade amplitude to target amplitude. Position and direction errors are further indicated by the amount that saccades over or undershoot a target.[20] Vertical saccade metrics also include efficiency, which evaluates how well subjects follow the vertical path between target stimuli.

Several studies have revealed deficits on saccade tasks in patients with TBI or Post-Concussion Syndrome (PCS), with the majority focusing on measurements of horizontal saccades. These deficiencies, moreover, may reveal lingering consequences of even mTBI that traditional neuropsychological evaluations fail to identify.[26] Observed abnormalities include prolonged latencies and directional errors on memory-guided and antisaccade tasks in mTBI patients[3,12,27,28,29,30] and impaired antisaccades, memory-guided saccades, and self-paced saccades in PCS patients,[31] to name a few. In particular, several studies have revealed that TBI patients display impaired self-paced saccades compared to healthy controls.[3,12,32] Williams et al. (1997) and Mulhall et al. (1999) recorded the number of re-fixations within 30 seconds to examine the rate of self-paced saccades and found that TBI patients performed fewer saccades.[12,32] Heitger and colleagues, moreover, conducted two studies of saccadic behavior following head injury and found that mTBI and PCS patients performed fewer self-paced saccades with longer inter-saccadic intervals, suggesting impaired prefrontal function.[28,31] In the latter study, PCS patients also exhibited saccades with a lower peak velocity.[31] Also, Taghdiri and colleagues observed a lower number of self-paced saccades in PCS patients, especially in patients with more recent concussions.[11] The number of saccades negatively correlated with the number of self-reported concussion symptoms and positively correlated with the fractional anisotropy value of two white matter tracts often damaged after concussion.[11] In contrast, Phillipou et al. (2014) found no decrease in the rates of self-paced saccades in children with mTBI, possibly because of the small sample size used and the mild nature of patient injuries.[33]

Although few studies have specifically tested vertical saccadic performance following head trauma (and none have examined vertical self-paced saccades), there is some evidence of unusual vertical saccades in TBI patients. For example, significant differences were found between a group of mTBI patients and controls on a number of vertical saccadic parameters, including greater position errors, smaller amplitudes, and smaller peak velocities and accelerations detected in the mTBI subjects.[20] Also, results from VOMS assessments of patients with sports-related concussion indicated that vertical saccade tests positively correlated with the total symptom score on the Post-Concussion Symptom Scale.[18] Another study using VOMS found an association between prolonged recovery time from sports-related concussion and impaired vertical saccades.[34]

Additional studies with larger sample sizes are necessary to increase the reliability and precision of results.[11,26,35] Few studies of oculomotor impairments following TBI have concentrated on self-paced saccades, and even fewer have related specific deficits in self-paced saccades to TBI symptoms. The existing literature on TBI especially lacks studies investigating vertical self-paced saccades. Due to the limited research assessing self-paced saccade performance after TBI, additional research is needed. The purpose of this study, therefore, is to explore differences in horizontal and vertical saccades—measured by fixation number, S/A ratio, targeting, and efficiency—between people without a history of TBI and patients clinically identified as having TBI (either mild, moderate, or severe).

Method

Participants

195 participants were recruited to take part in the horizontal saccade test, and 92 for the vertical saccade test. The participants that took part in the horizontal saccade test were between the ages of 10-79 years (*M* = 37.75, *SD* = 16.49); 100 were males (51%), 95 were females (48.91%). Of the 195 participants, 70.65% were White, 5.43% were Hispanic, 5.43% were Asians, 4.35% were Black, and 14.14% opted not to report ethnicity. Among these participants there were 64 mild TBI, 57 moderate TBI, and 23 severe TBI cases that were clinically verified along with 51 participants reporting no history of TBI. The participants with TBI had sustained their head injuries within the last 30 days prior to testing.

The participants that took part in the vertical saccades test were between the ages of 10-79 years (*M* = 37.75, *SD* = 16.49); 47 were males (51.09%), 45 were females (48.91%). There were 23 (25%) clinically verified participants in each of the following TBI severity levels: No-TBI, mild TBI, moderate TBI, and severe TBI. Of the 92 participants, 70.65% were white, 5.43% were Hispanic, 5.43% were Asian, 4.35% were black, and 14.14% opted not to report ethnicity.

Apparatus

Stimuli were presented using the RightEye tests on NVIDIA 24-inch 3D vision monitor fitted with an SMI 12” 120 Hz remote eye tracker connected to an Alienware gaming system, and a Logitech (model Y-R0017) wireless keyboard and mouse. The participants were seated in a stationary (non-wheeled) chair that could not be adjusted in height. They sat in from of a desk in a quiet, private testing room. Participants’ heads were unconstrained. The accuracy of the SMI eye tracker was 0.4 degrees within the desired headbox of 32cm x 21cm at 60cm from the screen. For standardization of testing, participants were asked to sit in front of the eye tracking system at an exact measured distance of 60cm (ideal positioning within the headbox range of the eye tracker). A nine-point calibration was conducted with points spanning the computer screen.

Oculomotor Tasks

Two RightEye oculomotor tests are described below.

Horizontal Saccade Test (HS): In the HS test, participants were asked to look at a countdown of 3, 2, 1 in the center of the screen before moving their eyes back and forth between 2 dots. Their goal was to "target each dot" on the left and right of the screen as quickly and accurately as possible. The dots on the screen turned green when the participants' eyes hit the targets. The test lasted 10 seconds. The HS test provides measures of fixation percentages, saccade percentages, and target accuracy

Vertical saccades test (VS). The protocol for the VS test was the same as that for the HS test. However, the VS test was in a vertical plane.

Procedure

Participants were recruited through advertisements placed on the internet, social media, bulletin boards, and word of mouth. The study was conducted in accordance with the tenets of the declaration of Helsinki. The study protocols were approved by the Institutional Review Board of East Carolina University. The nature of the study was explained to the participants, and all participants were provided a written consent to participate. Following informed consent, participants were asked to complete a pre-screening questionnaire and an acuity vision screening where they were required to identify four shapes at 4mm in diameter. If any of the pre-screening questions were answered positively and any of the vision screening shapes were not correctly identified, then the participant was excluded from the study. Participants were excluded from the study if they reported any of the following conditions which may have prevented successful test calibration during the pre-screening process: vision-related issues such as extreme tropias [35, 36], phorias [37, 36], static visual acuity of greater than 20/400[38] nystagmus[38, 39] cataracts, eyelash impediments[39]; consumption of drugs or alcohol within 24 hours of testing. Participants were also excluded if they were unable to pass a 9-point calibration sequence.

Qualified participants who successfully passed the 9-point calibration sequence completed the eye tracking tests. The calibration sequence required participants to fixate one at a time on 9 points displayed on the screen. The participants had to successfully fixate on at least 8 out 9 points on the screen to pass the calibration sequence. Written instructions on screen and animations were provided before each test to demonstrate appropriate behavior required in each of the tests.

Data Analysis

The differences in the groups (No-TBI, Mild, Moderate, and Severe TBI) were analyzed on clinically verified data. The comparison was evaluated using one-way univariate ANOVA on the fixation (#), S/A ratio and targeting metrics. Fixation (#) is defined as the number of gaze fixations that occurred during the total duration of saccade task. S/A ratio is defined as the ratio of speed (saccadic velocity) over accuracy, where accuracy is the measurement of how close eye gaze to the target stimuli are, while performing a horizontal saccade. Targeting is a measurement of accuracy as explained in the previous sentence. A post-hoc analysis was conducted using Tukey's HSD (honest significant difference) test, to determine the mean differences and statistical significance, between each group. The alpha level was set at $p < 0.05$ for all statistical tests. In addition, Receiving Operating Characteristic (ROC), Area Under the Curve, Sensitivity and Specificity were calculated for a logistic regression to predict "No-TBI" versus "All categories of TBI" (Mild, Moderate and Severe).

Results

Horizontal Saccades

The ANOVA for fixation (#) metrics revealed significant differences between the groups. Fixation (#) metrics resulted in a significant main effect, F (3, 191) = 5.44; $p < 0.01$. In addition, Tukey's HSD test demonstrated significant differences between the moderate and severe group and the no-TBI group; however, there was no significant difference between the mild and TBI groups (see Figure 1).

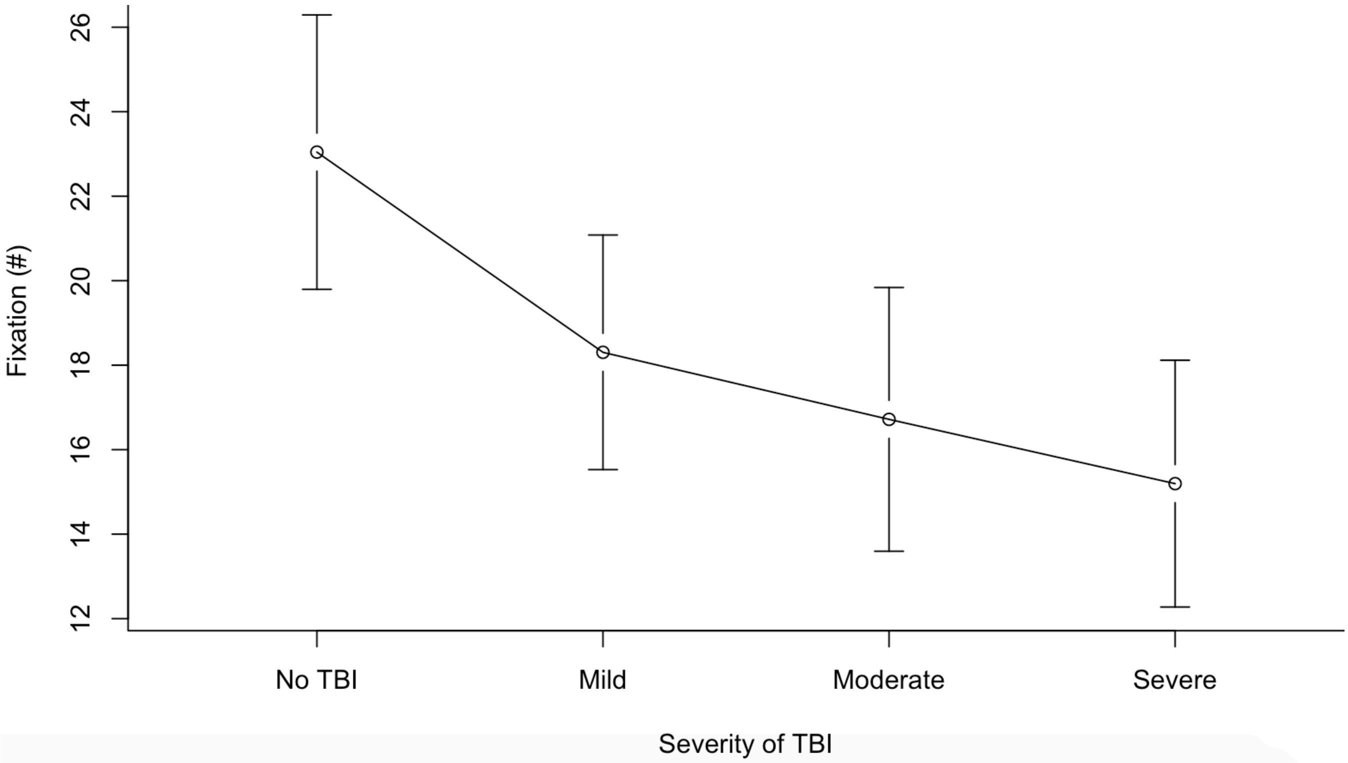

Figure 1: Mean Plot with 95% Confidence Interval

The ANOVA for S/A ratio metrics revealed significant differences between the groups. S/A ratio metrics resulted in a significant main effect, F (3, 191) = 12.38; p = < 0.001. In addition, Tukey's HSD test demonstrated significant difference between each TBI group and the no-TBI group (see Figure 2).

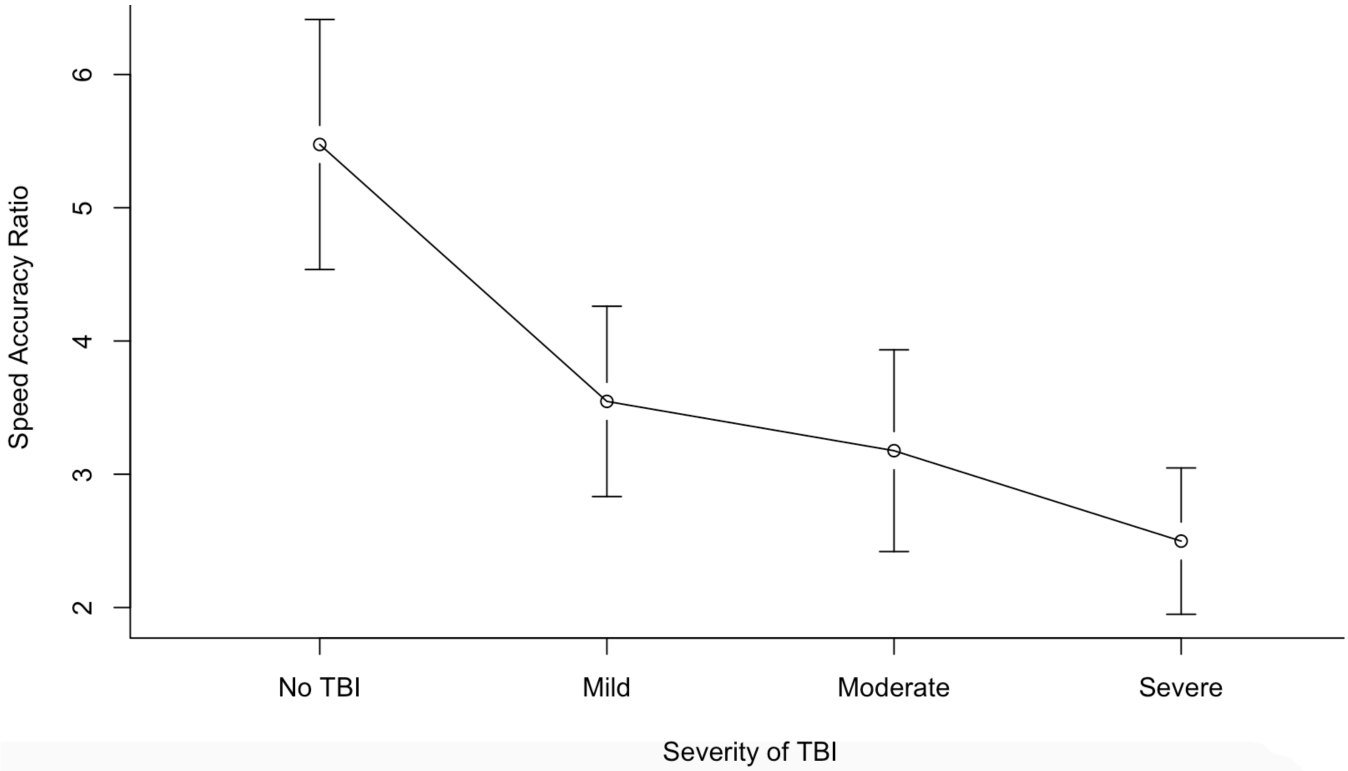

Figure 2: Mean Plot with 95% Confidence Interval

The ANOVA for targeting metrics revealed significant differences between the groups. Targeting metrics resulted in main effect, F (3, 191) = 6.31; $p < 0.05$. However, Tukey's HSD test demonstrated significant difference between TBI groups and the no-TBI group (see Figure 3).

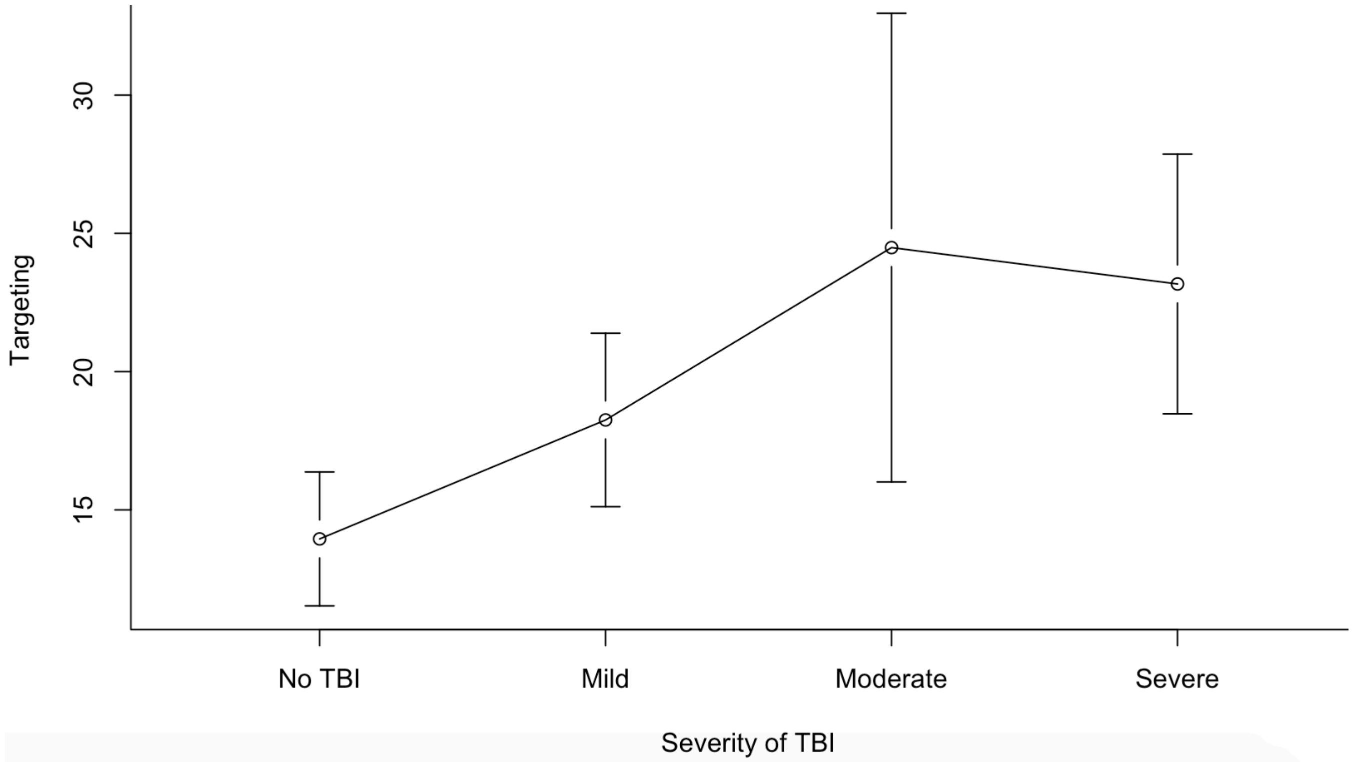

Figure 3: Mean Plot with 95% Confidence Interval

The logistic regression model for fixation # and S/A ratio revealed differentiated no-TBI and TBI groups. The resulting ROC curve produced an Area Under the Curve (AUC) value of 0.825 with sensitivity = 0.77 and specificity = 0.78 (see Figure 4).

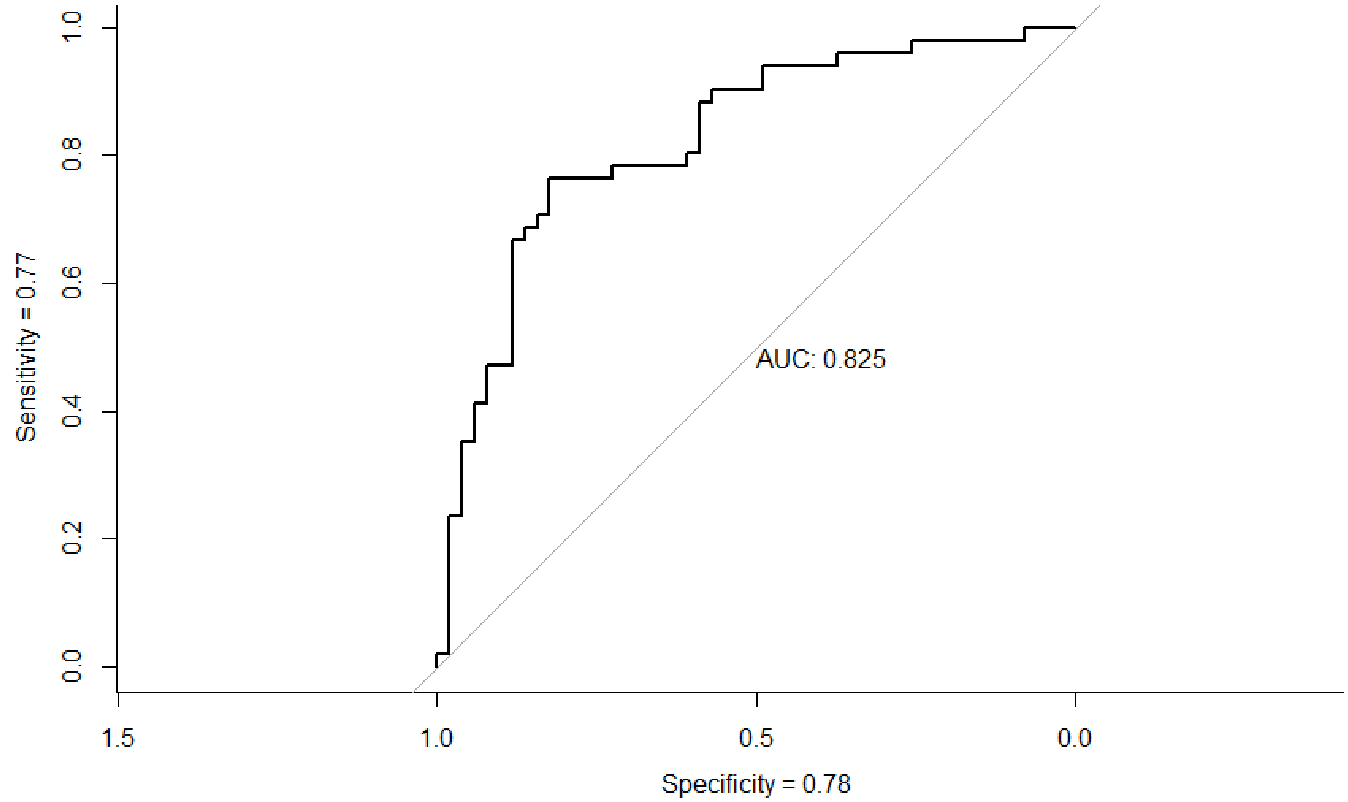

Figure 4: ROC for Horizontal Saccades (Fixation # and S/A Ratio) – No-TBI Vs TBI

Vertical Saccades

The ANOVA for targeting metrics revealed significant differences between the groups. Targeting metrics resulted in a significant main effect, F (3, 191) = 5.17; $p < 0.01$ (See Figure 1). In addition, the pairwise t-test demonstrated a significant difference between each TBI Group and the no-TBI group (see Figure 5).

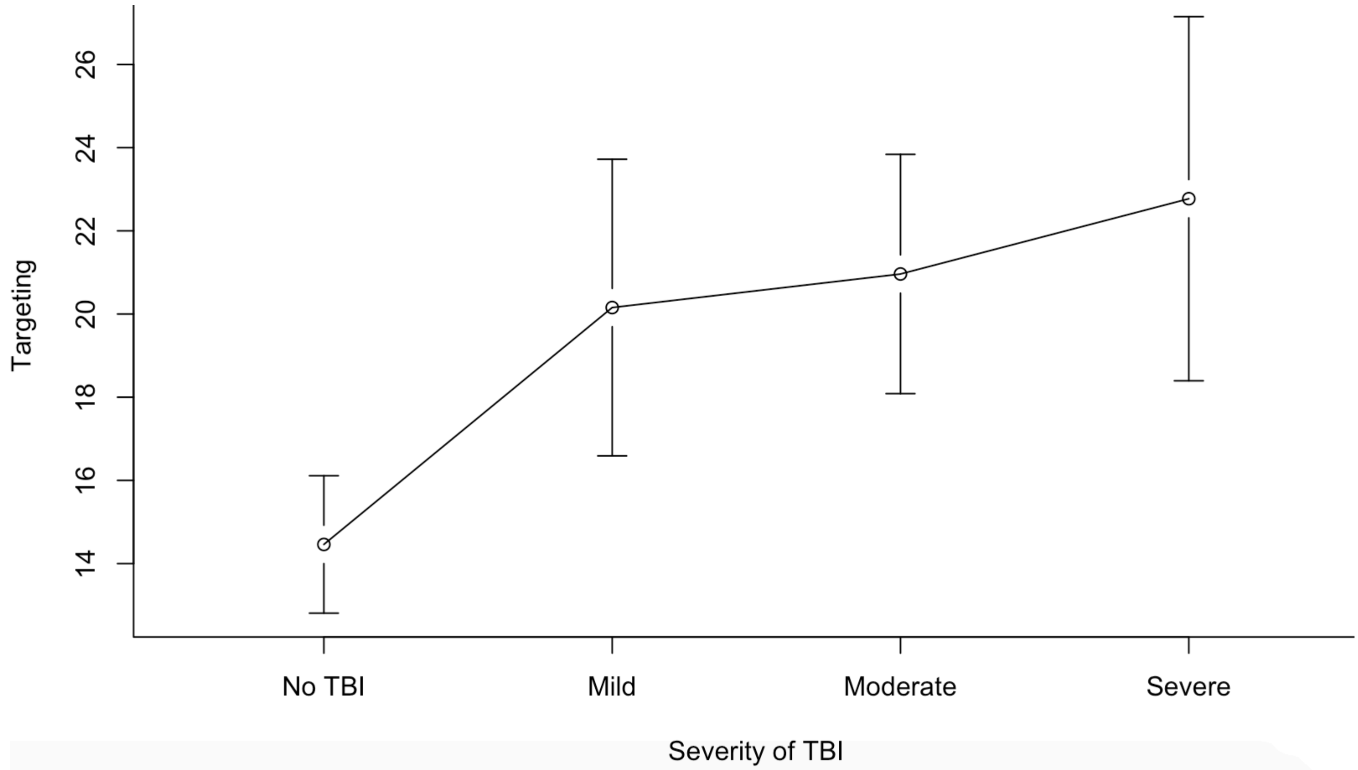

Figure 5: Mean Plot with 95% Confidence Interval

The ANOVA for S/A ratio metrics revealed significant differences between the groups. S/A ratio metrics resulted in a significant main effect, F (3, 88) = 5.64; p = < 0.001 (See Table 2). In addition, the pairwise t-test demonstrated a significant difference between each TBI Group and the no-TBI group (see Figure 6).

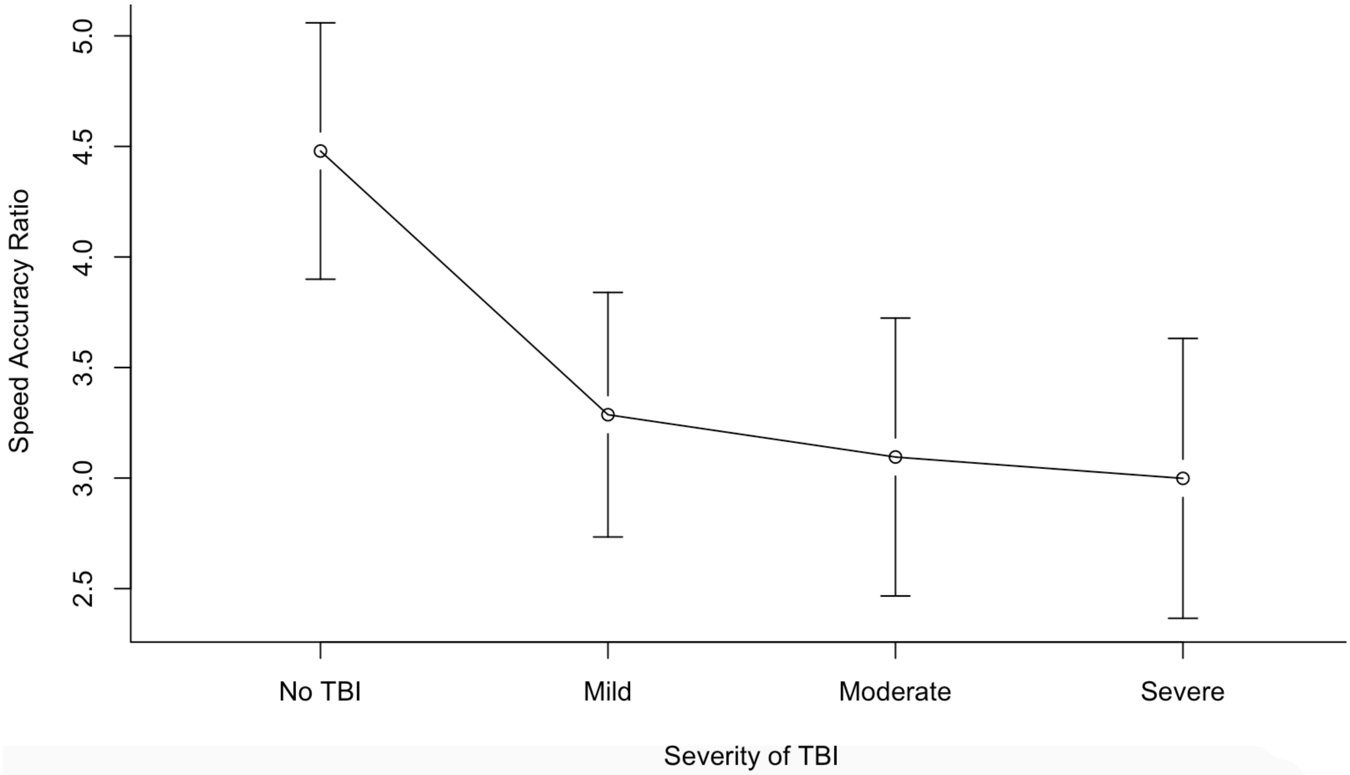

Figure 6: Mean Plot with 95% Confidence Interval

The ANOVA for efficiency metrics did not reveal significant differences between the groups although there was a main effect, F (3, 88) = 0.31; p = 0.81 (see Figure 7).

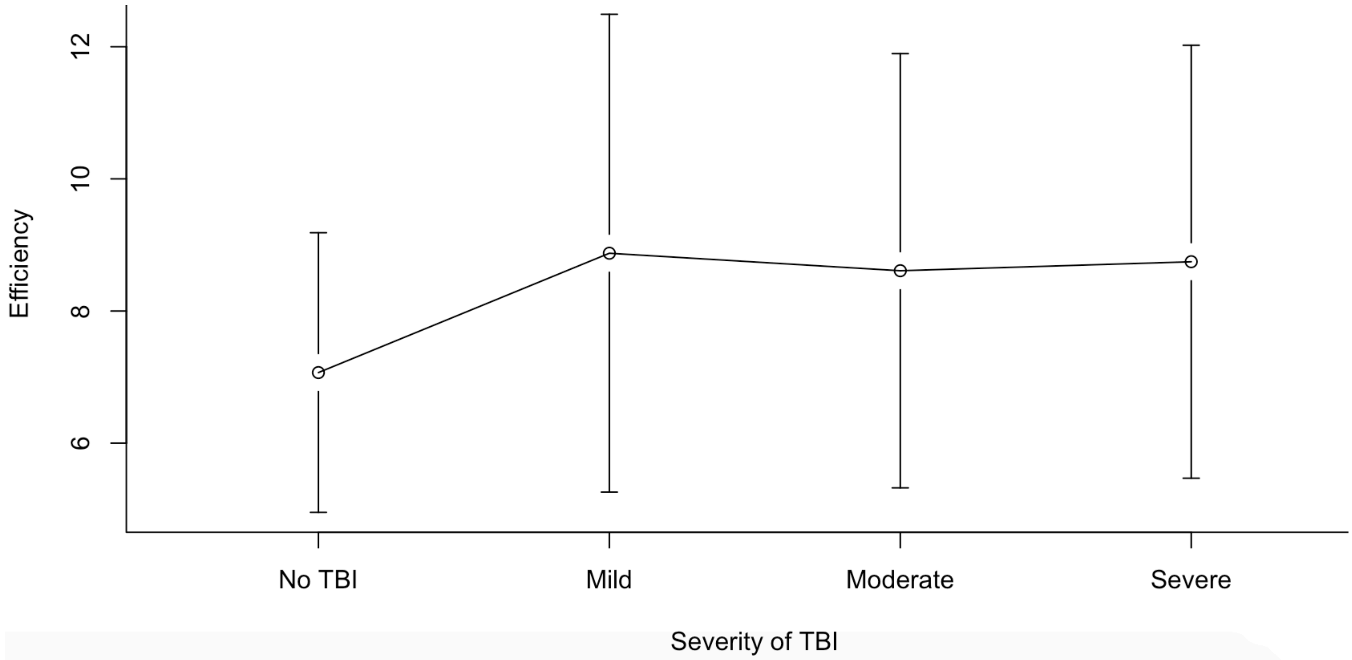

Figure 7: Mean Plot with 95% Confidence Interval

Logistic regression model was built with two metrics, targeting and S/A ratio, which came out as significant in a-priori and post-hoc analysis. Resulting ROC curve produced an Area Under the Curve (AUC) value of 0.772 with sensitivity = 0.64 and specificity = 0.65 (See Figure 8).

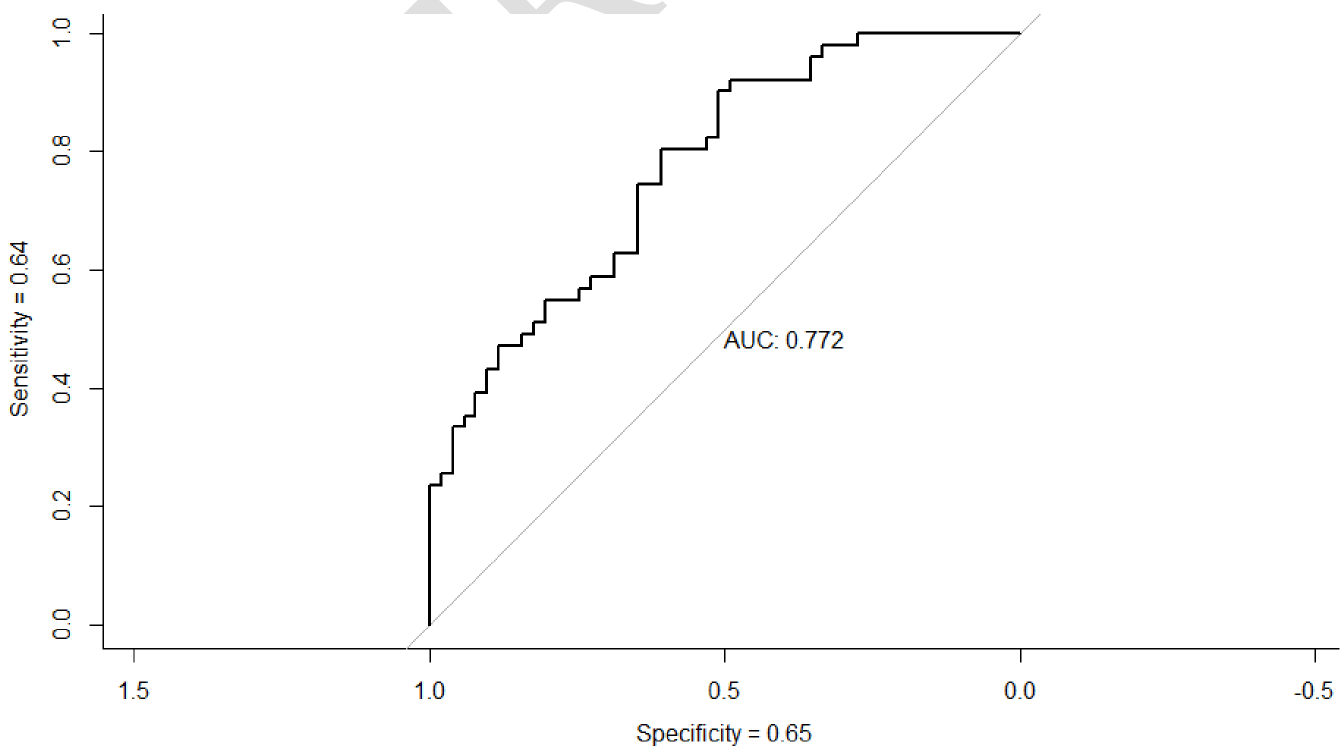

Figure 8: ROC for Vertical Saccades (Targeting and S/A Ratio) – No-TBI Vs TBI

Discussion

This is the first study to systematically examine the use of eye tracking technology to detect symptoms of TBI via the measurement of oculomotor behavior. Given that planning and rapidly producing saccades to targets in the visual field recruits frontoparietal areas vulnerable to damage from TBI, saccadic deficits are important to examine with eye-tracking metrics.[15,25] The technology has been therefore been developed to provide an indication of neural dysfunction via the measurement of eye movements. The tests in the present study measured numbers of fixations, the ratio of saccadic velocity to accuracy (S/A ratio) and targeting metrics alongside efficiency for vertical saccades to quantify the accuracy of the individual's eye movements. For horizontal saccades, the S/A ratio metric was the most sensitive, showing significant differences between each group and the ratio of saccadic velocity to accuracy. Analysis of the numbers of fixations suggested that the tests were able to differentiate between individuals with severe and moderate TBI and those with mild TBI and no-TBI reported. Furthermore, the analysis of the targeting metrics suggest that eye tracking can distinguish between individuals reporting a TBI and those unaffected. Overall, the sensitivity and specificity values for the horizontal saccade metrics are promising in differentiating TBI cases from no-TBI, considering this analysis only accounts for two metrics. Similarly, for the vertical saccades test, the individual metrics were able to detect differences in individuals reporting a TBI and those who did not in both S/A ratio and targeting metrics. The efficiency metric on its own failed to discern any differences between groups, although a main effect was present. Overall, the sensitivity and specificity values for thes vertical saccade test metrics are promising in differentiating TBI cases from No-TBI, considering this analysis only accounts for two metrics.

As the eye tracking tests at the center of this study measure a combination of useful metrics, it is suggested that as a whole this is a useful adjunct to the more established diagnostic tools for TBI symptom detection. Certainly, there is great benefit in testing individuals with suspected TBIs with these eye tracking tests to confirm (or deny) the presence of TBIs given that this is the only method of objectively and accurately recording and analyzing visual behavior. The objectivity and accuracy of eye tracking addresses all of the criticisms of the existing TBI symptom detection methods and therefore addresses problems with subjectivity, under-reporting, and issues with patient motivation. There may also be merit in using such tests to measure progress in rehabilitation from TBI. Given that these tests are simple and quick to administer, investigations into the use in sport settings may prove fruitful, especially for the purposes of 'return-to-play' decisions. However, given the infancy in the use of eye tracking as a means of symptom detection in those with TBIs, it is recommended that further research be conducted to amass a broader sample upon which to compare these results to. Although the sample size (n=287) is relatively small, it was considered adequate for the present study. Clearly, a broader sample of participants from a wider geographical area would ensure enough international diversity upon which to compare results.

Conclusion

TBI is a significant international public health concern, yet the methods currently used for its detection are inconsistent and subject to limitations. This study has demonstrated that specialized eye tracking tests are a useful precise and objective measure of underlying neurological health that indicates the presence of a TBI. Furthermore, particular metrics have been shown to be able to differentiate in the level of severity of the TBI. In conclusion, it is suggested that testing horizontal and vertical saccades using eye tracking technology is a useful adjunct to the more established tests and protocols currently used by clinicians.

Future perspective

It is clear that our knowledge of traumatic brain injury is continually evolving, and with this comes an understanding of how to harness the complexities of the brain and its related systems. Over the next 5-10 years it is predicted that the use of simple user-friendly eye tracking tests such as those analyzed in the present study will become commonplace in the diagnosis of TBI, its severity, and in the monitoring of recovery from this condition.

Executive summary

- Traumatic brain injury is one of the most concerning socio-economic health issues in today's society.
- Although there are a number of tests and protocols to help detect symptoms of TBI, none currently provide objective quantifiable data.
- Oculomotor behavior is a promising neuropsychological endophenotype, as it reflects abnormalities of complex neurocircuitry in an objective examination of neurological health.
- Several studies have revealed deficits on saccade tasks in patients with TBI or Post-Concussion Syndrome (PCS).
- Eye-tracking technology quickly delivers precise, objective eye movement recordings by surveying the eye several times per second.
- This technology can be used to measure horizontal and vertical saccades via a number of discrete metrics.
- The present study shows that using eye-tracking technology to measure horizontal and vertical saccades is a simple, quick and accurate measure that is able to accurately differentiate between individuals with different levels of severity of TBI and those who have not sustained a TBI.

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