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To cite this article: Mark L. Ettenhofer, Jamie N. Hershaw, James R. Engle & Lars D. Hungerford (2018) Saccadic impairment in chronic traumatic brain injury: examining the influence of cognitive load and injury severity, Brain Injury, 32:13-14, 1740-1748, DOI: 10.1080/02699052.2018.1511067

To link to this article: https://doi.org/10.1080/02699052.2018.1511067
Saccadic impairment in chronic traumatic brain injury: examining the influence of cognitive load and injury severity

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ABSTRACT
Objective: Previous research suggests that saccadic eye movements can be uniquely sensitive to impairment in chronic traumatic brain injury (TBI). This study was conducted to examine saccadic eye movements across varying levels of cognitive load and TBI history/severity. We hypothesized that saccadic impairment in chronic mild and moderate-severe TBI would be most pronounced under conditions of high cognitive load.

Methods: In total, 61 participants (including \( n = 20 \) with chronic mild TBI, \( n = 15 \) with chronic moderate-severe TBI, and \( 26 \) uninjured controls) completed a battery of conventional neuropsychological tests and the Fusion n-Back Test, which measures manual and saccadic response time (RT) across varying cognitive load and cueing conditions.

Results: Consistent with our hypotheses, chronic mild and moderate-severe TBI were associated with substantial saccadic impairment under conditions of high cognitive load. Participants with moderate-severe TBI also demonstrated saccadic impairment at low levels of cognitive load. TBI groups and uninjured controls did not differ significantly on manual metrics or conventional neuropsychological measures.

Conclusions: This study provides additional support for the value of eye tracking for enhanced assessment of TBI. Additionally, findings suggest that TBI is associated with greatest susceptibility to oculomotor interference under high levels of cognitive load.

Introduction

After traumatic brain injury (TBI), many experience a positive recovery and resume regular activities without the need for long-term care; however, a substantial proportion continues to experience clinically significant difficulties into the chronic phase of recovery (1–6). Considering the wide range of potential outcomes, cognitive assessment can be invaluable to the process of developing plans for treatment and graded return to activity. In mild TBI, a number of cognitive deficits are detectable in the acute stage, but findings on common clinical tests typically resolve within a week to 3 months (7,8). In moderate-severe TBI, cognitive deficits are more likely to persist long-term (9).

These general trends, however, obscure important forms of heterogeneity within the TBI population, and cognitive performance can be impacted by many factors (10–16). Using conventional assessment tools, it can be very difficult to objectively distinguish between neurological and non-neurological sources of impairment. For example, button presses, verbal responses, and other forms of somatomotor output can be strongly influenced by factors unrelated to injury—such as intelligence or level of education—that can complicate interpretation of clinical results (17–19). Because post-injury cognitive performance is typically interpreted in comparison with ‘best estimates’ of pre-injury functioning, it can be especially challenging to identify cognitive changes among those patients whose pre-injury intellectual functioning falls outside of the average range (20,21). In particular, patients who were functioning at a high intellectual level prior to injury may demonstrate ‘average’ or ‘normal’ cognitive performance after injury, despite having experienced a significant decline from pre-injury levels of function.

Eye tracking technology may provide a means to circumvent some of the limitations of conventional assessment methods. Our group has shown that saccadic metrics—variables representing the speed and accuracy of eye movements in response to targets and cues—can serve as reliable and unique measures of cognitive and neuromotor function (19). Unlike many conventional metrics, saccadic response time (RT) appears to be minimally impacted by education or intelligence (19,22,23). In terms of clinical applications, eye tracking has demonstrated particular value for TBI assessment, with a growing body of evidence indicating that acute and chronic TBI are associated with slower and less accurate acquisition (e.g. planning and execution of saccadic eye movements) and tracking (e.g. smooth pursuit) of visual targets (24–38). For example, in a recent study using a cued saccadic RT paradigm to compare participants with remote mild TBI to uninjured controls, we found evidence for persistent saccadic impairment among those with multiple previous...
injuries and/or chronic symptoms, whereas asymptomatic participants with a single mild TBI performed similarly to controls (35). Impaired eye movements have also been found to relate to TBI clinical characteristics such as severity of symptoms and extent of diffuse axonal injury (as measured by diffusion tensor imaging) (22,36–38).

However, not all eye movements are equally sensitive to the effects of TBI. In a survey of the literature on oculomotor assessment of TBI, including studies of smooth pursuit, accommodation, pupillary light reflex, saccades and vergence, Barker et al. (39) suggested that saccadic metrics demonstrate the greatest sensitivity to impairment—particularly those that require significant cognitive processing. While saccadic responses are routinely influenced by attentional processing (40,41), the neurocognitive contributions to saccadic responses can also be modulated or magnified through the design of the cognitive task in which they are embedded (19).

In a recent demonstration of the potential value of this approach for clinical assessment, our group found that sensitivity of saccadic RT to remote mild TBI was strongest in the presence of cognitive cues that increase executive and attentional processing demands (35).

These findings are consistent with an established body of research showing that performance is most likely to be compromised when cognitive demand exceeds available cognitive resources (42,43). A number of previous studies have found that increased cognitive load can disproportionately affect cognitive and motor performance in those with a history of TBI (44–48). A ‘threshold’ model focusing on availability of cognitive resources in low- versus high-load situations may help to explain the experiences of those individuals with TBI who are able to perform normally on highly structured or overlearned tasks (including many forms of cognitive testing), but who are easily flustered or overwhelmed by the multiplexed demands of everyday life. Potentially, this model of cognitive load interference might also be leveraged to further enhance the sensitivity of eye tracking for assessment of TBI.

In summary, previous research suggests that saccadic eye movements may provide unique value in assessment of TBI-related impairment and that cognitive and motor deficits in TBI may be most apparent under conditions of high cognitive load. Little is known, however, about how cognitive load may impact saccadic performance after TBI. The current study was conducted to investigate methods for further enhancement of eye tracking for TBI assessment by probing performance across multiple levels of cognitive load. We hypothesized that chronic TBI would be associated with impaired saccadic RT and that these effects would be most pronounced under conditions of high cognitive load.

**Methods**

**Participants and procedures**

A community sample of participants with and without a history of TBI was recruited via advertisements posted within the Washington, D.C. metro area. The TBI group consisted of adults (> 18 years old) with a history of mild, moderate or severe TBI (defined according to American Congress of Rehabilitation Medicine criteria) sustained 3 months to 10 years prior to enrollment, whereas the control group consisted of adults without a history of concussion/TBI or other neurological conditions. Participants with medical conditions other than TBI that would be expected to impact performance, uncorrected visual impairment, failure on two or more measures of response validity/effort, or failure to follow task instructions were excluded from analysis. Out of 67 participants enrolled based upon initial screening, 61 (n = 26 Control; n = 35 TBI) met full eligibility requirements and were included in the study. All procedures were approved by the local Institutional Review Board. Training and supervision for all study procedures was provided by a licensed clinical neuropsychologist. Testing took place in a non-clinical setting, and participants were informed that data would be used only for research purposes. After written informed consent, participants provided demographic information and medical history. TBI history, including mechanism of injury, loss of consciousness (LOC), post-traumatic amnesia (PTA) and alteration of consciousness (AOC), was assessed using the Ohio State University TBI Identification Method (OSU TBI-ID (49,50)) and confirmed using available medical records. Participants then completed a fixed battery of standardized neuropsychological measures and the Fusion n-Back Test, described below.

**Measures**

**Neuropsychological assessment**

Standardized neuropsychological tests included the Wechsler Test of Adult Reading (WTAR), a measure of premorbid IQ (51); Trail Making Test (TMT) Parts A and B (52), measures of psychomotor speed and executive functions; Hopkins Verbal Learning Test-Revised (HVLT-R (53)), a measure of learning and memory; and the following subtests of the Wechsler Adult Intelligence Scale-IV (WAIS-IV (54,55)): Digit Span, a measure of working memory; Symbol Search, a measure of visual scanning and processing speed; and Coding, a measure of processing speed and working memory. Additionally, embedded metrics from WAIS-IV Digit Span and TMT were used to evaluate performance validity (i.e. test-taking effort) using previously validated cut-offs for each measure (56,57). The Glasgow Outcome Scale-Extended (GOS-E (58)) was administered as an index of functional outcome. Post-concussive symptoms were measured using the Neurobehavioral Symptom Inventory (NSI) (59).

**Fusion n-Back Test**

The Fusion n-Back Test was designed to systematically measure the effects of cognitive load (attentional demands and memory) and predictive cues (valid or invalid) on saccadic and manual RT (60) (see Figure 1). This test adds the working memory demands of the classic ‘n-back’ continuous performance task (61) to the alerting, orienting and interference cues used to modulate saccadic and manual RT in the Bethesda Eye and Attention Measure (BEAM) (19) (please see (62) for previous use of similar cues with manual RT in the Attention Network Task [ANT]). Across each of three separate cognitive load conditions, participants completed a series of test trials in...
which circular targets appeared to the left or the right of a central fixation cross. Participants were instructed to respond as quickly as possible by moving their eyes towards each target and pressing the appropriate button. After each target, participants returned their gaze to the central fixation cross and awaited the next target. To increase the attentional demands of the task, directional (valid) and misdirectional (invalid) visual cues (left- or rightward facing arrows) or no cue were presented centrally for 200 ms immediately prior to the appearance of the target. Whereas directional cues pointed towards the impending target, providing an opportunity to reduce RT latency through anticipatory spatial orienting, misdirectional cues pointed away from the impending target, diverting spatial orientation and provoking attentional conflict. At the ‘Low’ level of cognitive load (‘Simple RT’), participants were instructed to press a single button as quickly as possible in response to all targets (white circles). At the ‘Moderate’ level of cognitive load (‘0-Back’/colour discrimination), participants were instructed to press buttons labelled ‘Green’ or ‘Blue’ in response to green or blue targets. Relative to the ‘Simple RT’ condition, the ‘0-Back’ condition added the momentary cognitive demand of discriminating between green and blue targets and selecting the correct versus incorrect response. At the ‘High’ level of cognitive load (‘1-Back’/working memory), participants were instructed to press buttons labelled ‘Same’ or ‘Different’, depending on whether the target circle was the same colour or a different colour relative to the previous target. Compared with the ‘0-Back’ condition, the ‘1-Back’ condition added the continuous cognitive demand of maintaining the representation of the previous target colour in working memory. Cognitive load condition was randomized across test blocks, and cue type was randomized on a trial-by-trial basis within each test block.

### Eye tracking

Saccadic eye movement data were acquired at 120 Hz using an Applied Science Laboratories (ASL) D6 High-Speed Desktop Eye Tracker. Eye tracking calibration was performed at the beginning of each testing session using a 9-point rectangular calibration screen. Manual responses were recorded with a Cedrus RB-530 response pad. While completing the Fusion n-Back Test, participants wore a Lycra cap for EEG acquisition; these data will be reported elsewhere. Stimuli were presented using Presentation software (Neurobehavioral Systems) at 1920 × 1080 resolution on a 19” LCD monitor with 60 Hz refresh rate. Head movements were minimized with a chin rest. Participants were seated with eyes positionned 24” from the stimulus display. Gaze data and manual responses were synchronized with task event markers during data acquisition.

### Analysis

Gaze data were processed using ASL Results (Version 2.4.3; ASL, 2011) to identify fixations and saccades. Custom scoring software was then used to remove invalid trials and aggregate RTs across trials as median scores. Raw scores from the conventional neuropsychological battery were converted to Z-scores based on published age-corrected normative data and aggregated to represent ‘Global Cognition’, with better performance yielding higher scores. Statistical analyses were conducted using the SPSS 24.0 statistical package. Missing data (4.9% of all primary metrics) were imputed using expectation maximization. A one-way ANOVA was used to compare neuropsychological test results between groups. Primary analyses of Fusion n-Back results were performed using 3 (load) x 3(cue) x 3(group) mixed model ANCOVAs for manual and saccadic RT, controlling for age.

### Results

#### Participant characteristics

Table 1 presents participant characteristics. There was a non-significant trend towards a higher proportion of females in the control (73.1%) versus mild TBI (50.0%) and moderate-severe TBI (40.0%) groups, $p = 0.09$. However, gender was not statistically significant for the control versus mild TBI groups, $p = 0.09$.

### Table 1. Participant characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Mild TBI</th>
<th>Moderate-Severe TBI</th>
<th>$\rho^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>26</td>
<td>20</td>
<td>15</td>
<td>–</td>
</tr>
<tr>
<td>Female, # (%)</td>
<td>19 (73.1%)</td>
<td>10 (50.0%)</td>
<td>6 (40.0%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Age in years, Mean (SD)</td>
<td>33.46 (9.45)</td>
<td>37.05 (10.26)</td>
<td>37.07 (12.96)</td>
<td>0.43</td>
</tr>
<tr>
<td>Years education, Mean (SD)</td>
<td>16.68 (1.93)</td>
<td>15.75 (3.91)</td>
<td>15.20 (2.14)</td>
<td>0.15</td>
</tr>
<tr>
<td>Estimated premorbid IQ, Mean (SD)</td>
<td>107.00 (11.07)</td>
<td>112.27 (8.64)</td>
<td>108.60 (9.80)</td>
<td>0.28</td>
</tr>
<tr>
<td>Neurobehavioral Symptom Inventory score, Mean (SD)</td>
<td>8.81 (10.06)</td>
<td>28.35 (14.82)</td>
<td>27.47 (11.48)</td>
<td>&lt; 0.001 (C &lt; M,MS)</td>
</tr>
<tr>
<td>Glasgow Outcome Scale-Extended, Mean (SD)</td>
<td>7.81 (0.49)</td>
<td>6.65 (1.27)</td>
<td>6.21 (1.42)</td>
<td>&lt; 0.001 (C &lt; M,MS)</td>
</tr>
<tr>
<td>Months Since Injury, Mean (SD)</td>
<td>–</td>
<td>39.30 (33.24)</td>
<td>57.27 (42.44)</td>
<td>0.17</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td>–</td>
<td>10 (38.5%)</td>
<td>3 (15.0%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Black, # (%)</td>
<td>–</td>
<td>3 (15.0%)</td>
<td>1 (6.7%)</td>
<td>0.58</td>
</tr>
<tr>
<td>White, # (%)</td>
<td>–</td>
<td>11 (42.3%)</td>
<td>12 (60.0%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Hispanic/Latino, # (%)</td>
<td>–</td>
<td>2 (7.7%)</td>
<td>2 (10.0%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Asian, # (%)</td>
<td>2 (7.7%)</td>
<td>3 (15.0%)</td>
<td>0 (0.0%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Other, # (%)</td>
<td>1 (3.8%)</td>
<td>0 (0.0%)</td>
<td>1 (6.7%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Cause of Injury</td>
<td>–</td>
<td>9 (45.0%)</td>
<td>8 (53.3%)</td>
<td>0.58</td>
</tr>
<tr>
<td>Motor vehicle accident, # (%)</td>
<td>–</td>
<td>3 (15.0%)</td>
<td>4 (26.7%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Sports participation, # (%)</td>
<td>–</td>
<td>3 (15.0%)</td>
<td>2 (13.3%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Fall, # (%)</td>
<td>–</td>
<td>3 (15.0%)</td>
<td>0 (0.0%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Assault/Combat, # (%)</td>
<td>–</td>
<td>1 (5.0%)</td>
<td>1 (6.7%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Military Training, # (%)</td>
<td>–</td>
<td>1 (5.0%)</td>
<td>0 (0.0%)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Note: C = Control Group. M = Mild TBI Group. MS = Moderate-Severe TBI Group.

* Statistical significance of ANOVA or chi-square, as appropriate.
significantly associated with primary outcomes in any of the participant groups; therefore, results from male and female participants were pooled for analyses. Participant groups did not differ significantly in age ($p = 0.43$), education ($p = 0.15$), estimated premorbid IQ ($p = 0.28$), or race/ethnicity ($p = 0.11$). Participants in the control group reported significantly fewer post-concussive symptoms (NSI total $M = 8.81$, $SD = 10.06$) than those in the mild TBI ($M = 28.35$, $SD = 14.82$) and the moderate-severe TBI ($M = 27.47$, $SD = 11.48$) groups, $p < 0.001$. Participants in the control group also had significantly higher functional outcome scores on the GOS-E ($M = 7.81$, $SD = 0.49$) than those in the mild TBI ($M = 6.65$, $SD = 1.27$) and moderate-severe TBI ($M = 6.20$, $SD = 1.42$) groups, $p < 0.001$. Time since injury did not differ significantly between the mild TBI ($M = 39.30$ months, $SD = 33.24$) and moderate-severe TBI ($M = 57.27$ months, $SD = 42.44$) groups, $p = 0.17$. Primary injury mechanisms related to TBI included motor vehicle accidents, sports participation and accidental falls; mechanism did not differ between mild and moderate-severe TBI groups, $p = 0.58$.

### Neuropsychological tests

Neuropsychological tests results are presented in Table 2. As shown, individual neuropsychological tests yielded no significant differences between the control, mild TBI and moderate-severe TBI groups. Global cognition, a composite measure of these neuropsychological tests, also did not differ significantly across groups, $F(2,58) = 0.521$, $p = 0.60$. However, a non-significant trend was observed for poorer performance among the TBI groups relative to the control group on the WAIS-IV Coding test, $p = 0.09$.

### Fusion n-Back: saccadic responses

A mixed model ANCOVA of load*cue*group (controlling for age) on saccadic RT demonstrated main effects for group, $F(2, 57) = 3.51$, $p = 0.037$, $\eta_p^2 = 0.11$, cue ($F(1.62, 92.16) = 3.98$, $p = 0.03$, $\eta_p^2 = 0.07$) and cognitive load ($F(1.55, 88.31) = 7.70$, $p = 0.002$, $\eta_p^2 = 0.12$), as well as an interaction for load*group, $F(3.10, 88.31) = 2.72$, $p = 0.048$, $\eta_p^2 = 0.09$. The main effect of age was non-significant, $F(1, 57) = 0.396$, $p = 0.53$, $\eta_p^2 = 0.01$. Pairwise comparisons for the load*group interaction demonstrated that saccadic RT in the high load (1-back) condition was significantly slower than in the low (simple RT) and moderate (0-back) load conditions for both the mild TBI and moderate-severe TBI groups ($p < 0.03$ for all); the low and moderate load conditions did not differ significantly ($p > .27$ for all). There were no significant pairwise load comparisons for the control group ($p > .52$ for all).

Pairwise analyses controlling for age revealed that saccadic RT was slower in the mild TBI group than the control group for 1-Back/Directional Cue, $F(1, 43) = 4.84$, $p = 0.03$, and 1-Back/Misdirectional Cue, $F(1,43) = 4.72$, $p = 0.04$. Comparison of moderate-severe TBI and control groups demonstrated significant differences for simple RT/Uncued, $F(1, 43) = 6.24$, $p = 0.02$; 0-Back/Uncued, $F(1, 43) = 4.21$, $p = 0.047$; 1-Back/Uncued, $F(1, 43) = 5.39$, $p = 0.03$; 1-Back/Directional Cue, $F(1, 43) = 5.33$, $p = 0.03$; and 1-Back/Misdirectional Cue, $F(1, 43) = 8.97$, $p = 0.005$. An additional non-significant trend was noted for slower performance in the moderate-severe TBI group relative to the mild TBI group for simple RT/Uncued, $F(1, 43) = 3.35$, $p = 0.08$. Saccadic RT by group, load, and cue is presented in Figure 2. Overall saccadic RT by group is presented in Figure 3. Follow-up correlations demonstrated that WAIS-IV Coding test performance was not significantly related to overall Fusion saccadic RT ($r = 0.03$, $p = 0.82$).

### Fusion n-Back: manual responses

A mixed model ANCOVA of load*cue*group (controlling for age) on manual RT demonstrated main effects of cue ($F(2, 114) = 8.32$, $p < 0.001$, $\eta_p^2 = 0.13$), cognitive load ($F(1.95, 110.92) = 11.80$, $p < 0.001$, $\eta_p^2 = 0.17$), and age ($F(1, 57) = 8.60$, $p = 0.005$, $\eta_p^2 = 0.13$). No effect of group was evident, $F(2, 57) = 0.02$, $p = 0.98$, and all interactions were non-significant ($p > .05$). Manual RT by group, load, and cue is presented in Figure 4. Follow-up correlations demonstrated that coding test performance was strongly related to overall Fusion manual RT ($r = -0.33$, $p < 0.001$).

### Discussion

This study evaluated effects of cognitive load and TBI on saccadic and manual performance using a multimodal cognitive task, the Fusion n-Back Test. Consistent with our hypotheses, the chronic TBI groups demonstrated substantial saccadic impairment, particularly under conditions of high cognitive load. In contrast, cognitive load did not significantly impact saccadic performance among uninjured controls. Performance on conventional neuropsychological measures and manual metrics from the Fusion n-Back Test did not differ between those with chronic TBI and uninjured controls. These findings have a number of implications for improved methods of clinical assessment as well as for our understanding of situations or task demands that are most likely to pose problems for those with chronic TBI.

Manual and saccadic responses were obtained concurrently in response to the same Fusion n-Back stimuli; however, consistent with previous findings (19,35), these two response modalities represent different forms of cognitive processing, particularly under the moderate and high cognitive load.
conditions. Across load conditions, manual response demands escalate from simple target detection (low load/Simple RT) to discriminating green versus blue targets (moderate load/0-back) to comparing the current target colour to the previous target colour held in working memory (high load/1-back). In this manner, manual RT provides a fairly direct measure of the added cognitive demands across load conditions. In contrast, the saccadic response is constant across cognitive load conditions and does not directly depend upon completion of load-specific cognitive operations—the same saccade is always required regardless of the colour of the current or previous target. Therefore, any saccadic slowing resulting from increased cognitive load on this task represents a shortage of available cognitive resources, or potentially another form of interference between cognitive and oculomotor processes.

Speed of response in this study differed according to group, cognitive load condition, cognitive cue and response modality. As expected, for manual responses, participants across all groups demonstrated increased RT as cognitive load demands increased. For saccadic responses, uninjured controls in this study were able to maintain comparable performance across all cognitive load conditions. However, TBI group participants...
demonstrated saccadic slowing when under high levels of cognitive load. Specifically, both the mild and moderate-severe TBI groups exhibited substantial saccadic slowing associated with the addition of working memory demands (1-back); the saccadic slowing associated with colour discrimination (0-back) relative to simple RT was minimal and non-significant. These findings are sensible in light of the fact that the 0-back colour discrimination relies upon relatively automatic and transient processes that do not necessarily overlap with the time frame in which saccades are executed. In contrast, the 1-back condition requires continuous effort to maintain information in working memory, producing cognitive interference during the preparation and execution of saccadic responses.

This pattern of results is consistent with previous findings suggesting that eye movements provide greater sensitivity to TBI-related impairment under conditions of increased cognitive demand (35,37,63,64). Aside from delivering insights into methods for increasing sensitivity of tools used for assessment of TBI through modulation of cognitive load, these results provide additional evidence for a capacity-constrained model of cognitive processing in TBI. According to such a model, multiple forms of cognitive and motor performance depend upon a more general set of cognitive resources (42,43). Despite reduced cognitive resources, functioning of those with chronic TBI may be intact in many situations due to surplus processing capacity when overall cognitive load is low. However, as shown by previous studies, performance is likely to suffer when cumulative task demands exceed the amount of available cognitive resources (65,66). In the Fusion n-Back Test used in this study, the saccadic response appears to provide an especially valuable means to measure this form of cognitive load interference. A wide range of factors may influence availability of cognitive resources relevant to saccadic performance, including damage to distributed neural systems supporting both working memory and executive control of eye movements (67–69) and individual differences in working memory capacity (70).

The effect of TBI on saccadic performance also appears to vary depending upon cognitive cues. For example, the mild TBI group was only impaired relative to controls in the presence of a valid (directional) or invalid (misdirectional) cue, and not on uncued trials. This finding could be related to difficulties with spatial and executive processing in TBI, or to a more general increase in cognitive demands associated with processing these cues. In either case, this pattern of results highlights the value of pursuing an approach to assessment that systematically manipulates neurocognitive factors influencing eye movements, as opposed to focusing solely on neuromotor forms of impairment.

Whereas the mild TBI group demonstrated saccadic impairment only in the presence of cognitive cues at high cognitive load, the moderate-severe TBI group showed a broader pattern of impairment relative to healthy controls. At high levels of load, the moderate-severe TBI group was impaired across all cue types, whereas at low and moderate levels of load, the moderate-severe TBI group was significantly impaired only on uncued trials.
trials. This pattern may reflect a problem with arousal or sustained attention; whereas participants with moderate-severe TBI may have been ‘caught off guard’ when targets appeared without warning during less demanding (low load) task conditions, the presence of cognitive cues appeared to mitigate this deficit by providing an early warning or by increasing the momentary task demands/stimulation into a range that was more optimal for these individuals. Alternately, consistent with previous research examining saccadic performance after cerebrovascular accident (71), participants with moderate-severe TBI may have experienced a form of disinhibition that accelerated saccadic responses to cues in low-load conditions.

Similar to previous research (8,9,35,72,73), conventional cognitive measures in this study failed to discriminate between participants with and without chronic mild TBI. In the current study, these measures also failed to identify impairment in the moderate-severe TBI group. However, it is important to consider that our participants may be better-recovered, more resilient and generally higher functioning than the typical patient being evaluated for moderate-severe TBI in real-world clinical settings. Individuals with moderate-severe TBI may experience substantial cognitive recovery over time (9), and our average moderate-severe TBI participant was greater than 57 months post-injury. Additionally, our sample was recruited in a non-clinical setting, and although our control and TBI groups did not differ significantly on demographic characteristics, the overall sample had higher-than-average intelligence and level of education, and the moderate-severe TBI group had a greater than five point estimated IQ advantage over the control group.

Despite a potential sampling bias towards higher functioning individuals, both mild and moderate-severe TBI groups demonstrated impairments on saccadic measures. This finding provides a powerful illustration of the relative sensitivity of different approaches to assessment of TBI-related impairment. The relative underperformance of conventional tests may also be related to many factors known to affect performance other than neural injury. Factors such as age, intelligence and education are known to impact many conventional cognitive tests (17–19), whereas saccadic measures appear to be resistant to these confounds (19,22,23). This relative independence from common confounds may facilitate the detection of useful neural ‘signals’ with less interference from measurement ‘noise’. The one conventional cognitive measure that approached significance in these group comparisons was the Coding test. This test exhibits some similarities to the cognitive and oculomotor demands of the Fusion n-Back Test, in that it requires examinees to quickly execute saccades between test stimuli while retaining information in working memory. However, follow-up analyses demonstrated that Coding test performance was related only to manual RT, and not saccadic RT on the Fusion n-Back Test. These results are consistent with the psychometric divergence that has previously been noted between saccadic and manual approaches to assessment of neurocognitive performance (19), highlighting important differences between direct and indirect measurements of oculomotor function for assessment of chronic TBI.

In summary, this study provides additional evidence that chronic TBI is associated with impaired saccadic performance, even among many individuals who perform normally on conventional neuropsychological tests. Our findings demonstrated that participants with mild and moderate-severe TBI were especially vulnerable to saccadic impairment when placed under conditions of high cognitive load. Participants with moderate-severe TBI also had difficulty with saccadic responses to unexpected (uncued) stimuli at low levels of cognitive load. These results provide additional support for the use of eye tracking in assessment of TBI—particularly for approaches that evaluate eye movements across multiple cognitive load conditions. Additionally, current findings provide additional insights about potential reductions in cognitive bandwidth associated with TBI. However, a number of study limitations must be considered in interpretation of these results. Similar to many previous studies of chronic TBI, this study relied upon structured interviews and review of medical records to identify and characterize injuries retrospectively, without the benefit of standardized evaluations during the acute phase of injury or direct measurements of neural injury. Additionally, sample size in this study was modest, limiting statistical power to detect small effects. Larger scale, prospective studies and additional assessment modalities (such as pupillometry, electroencephalography and magnetic resonance imaging) are needed to replicate and extend current findings.

Acknowledgments

We are greatly appreciative of the assistance that Evelyn Cordero, Ashley Safford, Jessica Kegel and other members of our staff provided in conducting the research on which this manuscript was based. We also wish to thank the many research participants who volunteered for this study, without whom this work would not have been possible.

Declaration of Interests

Support for this research was provided by Congressionally Directed Medical Research Program (CDMRP) Award #W81XWH-13-1-0095 and institutional support from the Defense and Veterans Brain Injury Center (DVBIC) and the Uniformed Services University of the Health Sciences (USUHS). The authors report no conflicts of interest. The technology described in this manuscript is included in US Patent Application No. 61/779,801, US Patent Application No. 14/773,987, European Patent Application No. 14780369.9, and International Patent Application No. PCT/US2014/022468, with rights assigned to the Uniformed Services University of the Health Sciences. Dr. Ettenhofer is listed as an inventor on these patent applications. The views and opinions presented in this manuscript are those of the authors and do not necessarily represent the positions of USUHS, the Department of Defense, the Department of the Navy, or the US government.

Funding

This work was supported by the Medical Research and Materiel Command, Congressionally Directed Medical Research Program [W81XWH-13-1-0095].

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