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RELATIONSHIP BETWEEN POST-CONCUSSION SYMPTOM FACTORS AND NEUROPSYCHOLOGICAL OUTCOMES IN COLLEGIATE ATHLETES

A Thesis in

Psychology

by

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Abstract

Objective: Research indicates that symptoms following a concussion are related to cognitive dysfunction, however, less is known about how different types of symptoms may be related to cognitive outcomes or how specific domains of cognition are affected. The present study aims to explore the relationship between specific types of symptoms and these various cognitive outcomes following a concussion. Participants and Methods: One hundred and twenty-two student-athletes with sports-related concussion were tested with a neuropsychological battery that included a symptom report measure and various cognitive tests. Symptoms were separated into five factors: Physical, Sleep, Cognitive, Affective and Headache. Participants were grouped into “symptom” and “no symptom” groups for each factor. Cognitive outcomes included both overall performance as well as impairment scores in which individuals were grouped into impaired and not impaired based on a cut-off of 2 or more tests at the impaired level (<80 in Standard scores). These cognitive outcomes were examined for all the tests combined and then specifically for the memory tests and attention/processing speed tests. Results: Headache symptoms were related to overall cognitive impairment as well as memory and attention/processing speed impairment. Physical symptoms were related to impairment in attention/processing while sleep symptoms were related to memory impairments. Conclusion: Given that certain symptoms show a specific relationship to cognitive outcomes, this may provide important information for guiding treatment and accommodations for athletes following a concussion.

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Introduction

Epidemiology of Sports-Related Concussion

According to a recent consensus statement (McCrory et al., 2013), a concussion is "…a brain injury and is defined as a complex pathophysiological process affecting the brain, induced by biomechanical forces." Although there is no current consensus regarding the terminology of concussion versus mild Traumatic Brain Injury (mTBI), in this document these terms will be used interchangeably.

Early estimates of the incidence rate of sports-related concussion by the Center for Disease Control (CDC) approximated the prevalence at 300,000 cases per year in the United States (Guskiewicz, Weaver, Padua, & Garrett, 2000). However, this figure is based on only sports-related concussions that resulted in a reported loss of consciousness, which only account for between approximately 8-20% of all cases of sports-related concussion (Langlois, Rutland-Brown, & Wald, 2006). Given this information, a more appropriate estimate for the rate of sports-related concussions is 1.6 million to 3.8 million cases annually (Langlois et al. 2006). Approximately 134,000 cases of sports or recreation-related concussion result in emergency room visits each year (Laker, 2011). There was also a documented 62% increase in the number of hospital visits for sports concussion from 2001 to 2009 for individuals 19 and under (Clay, Glover, & Lowe, 2013). This increase could be due to increased awareness about sports-related concussion. By 2012, 38 states had legislation that requires coaches to be trained in how to monitor concussions in their players (Clay et al., 2013).

Football accounts for both the highest number and percentage of concussions in both high school and college athletes (Laker, 2011). Among females, soccer accounts for the highest rates of concussion, accounting for about half of all cases. When examining rates of concussion across comparable sports, there is a marked gender difference, with females experiencing twice the rate of males. There are multiple proposed mechanisms behind this difference, including social pressures and biological discrepancies. There may be more stigma for males to report concussion symptoms or there could be biomechanical factors such as head-to-ball ratios or weaker neck muscles that contribute to this difference. Despite this potential vulnerability in females for sustaining concussions, due to the bulk of injuries being from football, most of the individuals who experience sports-related concussion are males (Laker, 2011).

One difficulty with assessing the prevalence rates for concussions is the non-uniform nature of concussion; however, with increased awareness, there has also been a movement towards the development of guidelines for identifying symptoms of a concussion that distinguishes it from other more severe forms of traumatic brain injury, as well as what distinguishes it from a non-pathological reaction after a blow to the head (McCrory et al., 2013).

Classification of Concussion

There are some discrepancies among sources with regard to what qualifies as a concussion or how concussions should be graded on severity (Lovell, Echemendia, Barth, & Collins, 2004). Currently there are three widely used grading systems for concussion, all of which focus on the presence or absence of loss of consciousness (LOC) or post traumatic amnesia (PTA). One of the drawbacks of these common grading systems is the lack of emphasis on post-concussion symptoms, something that can vary greatly in presentation and duration. While concussions can be characterized by LOC, this is not required for the diagnosis. A variety of other symptoms can be present following a concussion, including confusion, headache, dizziness, loss of balance, memory dysfunction, sleep disturbance, and visual disturbances (Lovell, Echemendia, Barth, & Collins, 2004).

Even without LOC at time of injury or a short duration of LOC after the trauma, individuals may still experience severe and prolonged expression of post-concussion symptoms. This raises the issue of how useful grading systems are without greater consideration of symptoms. This conflict resulted in an update of the commonly-used Cantu Grading System for Concussion to include post-concussion symptoms at every level of the three-tier grading scale (Lovell, Echemendia, Barth, & Collins, 2004).

Biology and Pathophysiology of Concussion

A concussion is defined as a temporary state of neurological dysfunction resulting from trauma to the head (Giza & Hovda, 2001). Post-concussion symptoms often occur with very little detectable pathology in the brain and often resolve over time, and this likely indicates neural dysfunction rather than permanent cell damage or death (Giza & Hovda, 2001). Earlier animal models and more recent human studies have demonstrated that the underlying pathology of concussion appears to be "a neurometabolic cascade of events that involves bioenergetic challenges, cytoskeletal and axonal alterations, impairments in neurotransmission and vulnerability to delayed cell death and chronic dysfunction" (Giza & Hovda, 2014).

Bioenergetic changes appear to be characterized by changes in ionic influx and alteration in glutamate release at the cellular level (Giza & Hovda, 2014). In order to counteract these abnormal influxes, ionic pumps begin working in overdrive, resulting in energy depletion. It is possible that this instability at the cellular metabolic level may cause long-term changes and damage that can put an individual at greater vulnerability for repeated injury (Giza & Hovda, 2014). Another potential mechanism is inflammation, which has also been primarily studied in more severe TBI cases, but in rat models there is evidence for an upregulation of inflammatory genes following mild TBI (Giza & Hovda, 2014).

A third potential mechanism of impairment is at the structural level, with axonal damage and disconnections linked to cognitive impairments in animal models. With concussion in humans, there has previously been little data to show pathological changes in anatomy. However, with the use of Diffusion Tensor Imaging (DTI), changes in water diffusivity serve as a marker of axonal damage, with higher values of fractional anisotropy (FA) indicating greater diffusivity. An earlier study on DTI found that average FA values were decreased in mTBI individuals compared to healthy controls and this predicted poorer performance on neuropsychological tests at a 6-month follow up (Miles et al., 2008). Another study found increased FA values for adolescents in the acute phase following concussion, but this was not related to cognitive functioning (Giza & Hovda, 2014). A more recent meta-analysis on DTI findings in cases of mTBI in the semi-acute phase (3 months or less) revealed that approximately an equal number of studies reported increased and decreased FA findings, and a number of other studies that have shown both increased and decreased FA having a relationship to poorer cognitive functioning (Dodd, Epstein, Ling, & Mayer, 2014). Despite the current lack of consensus in more mild cases, the relationship between decreased FA in major fiber tracts and cognitive functioning is evident in more severe cases of TBI (Giza & Hovda, 2014).

Decreased cerebral blood flow (CBF) post-injury compared to controls has also been reported in cases of mild TBI, but this appears to resolve within a one-month period for most individuals (Barkhoudarian, Giza, & Hovda, 2016). However, a study by Meier and colleagues (2015) found that individuals who were still symptomatic between 3 and 12 months following injury still showed decreased CBF. Results from animal models have been mixed and there is still relatively limited evidence for the role of reduced CBF in concussion (Barkhoudarian et al., 2016). Overall, there has been increased knowledge of the potential underlying biological mechanisms of concussion over the last decade. Still, more research needs to be conducted to explore how the proposed mechanisms factor into the presentation and outcomes of concussion.

Symptomatology of Concussion

One method of assessing symptomatology following concussion is the Post-Concussion Symptoms Scale (PCSS), a self-report measure that has the examinee rate 22 symptoms on a severity scale of zero to six (Lovell et al., 2006). Often the total sum of the scale is used as an outcome measure following concussion, but given the heterogeneity of presentation, the individual symptom items from the scale may provide unique information. Factor analyses have been performed on the PCSS, both in individuals at baseline and post-concussion, and these have revealed that items from the PCSS cluster together into 4 distinct factors (Pardini et al., 2004; Merritt & Arnett, 2014). Pardini and colleagues (2004) found cognitive, sleep, emotional, and somatic factors when examining symptoms post-concussion. Similarly, symptoms reported at baseline followed a four-factor structure, with cognitive, sleep, affective, and physical factors identified (Merritt & Arnett, 2014). Interestingly, the headache symptom did not load onto any of the four factors, despite its intuitive relationship with other symptoms encompassed by the physical factor, including dizziness and sensitivity to light.

Headache appears to be a symptom of particular significance following concussion. It is one of the most common symptoms post-concussion, and individuals who report immediate headache symptoms following injury also have more symptom reporting in the first week following concussion (Guskiewicz, Weaver, Padua, & Garrett, 2000; Merritt, Rabinowitz, & Arnett, 2015). Other research has shown that headache lasting more than 60 hours following injury is related to delayed return-to-play (Makdissi et al., 2010). While the research specifically linking post-concussion headache to neurocognitive performance seems limited, one study on high school athletes did that headache was related to poorer reaction time and memory scores on the ImPACT (Collins et al., 2003).

Cognitive Impairment Following Concussion

The research on cognitive functioning has been somewhat variable, but does indicate a clear pattern of cognitive impairment following concussion. In fact, cognitive evaluations have been shown to provide critical information to clinicians post-injury, and are often part of return-to-play decisions (McCrory et al., 2005; Grindel, Lovell, & Collins, 2001). A meta-analysis by Broglio and Puetz (2008) found that sports-related concussion showed a large negative effect on general cognitive performance. A review of meta-analyses explored the specific domains of cognition that appear to be affected by concussion (Karr et al., 2014). These analyses show differences between domains, with one meta-analysis examining various types of mTBI showing the greatest effects for verbal fluency and delayed memory, and the smallest effects for global abilities and memory generally (Karr et al., 2014). Another meta-analysis examining sports concussion specifically found the largest effects for global abilities and memory. Karr and colleagues (2014) posit that these discrepancies may be related to how the authors operationalized the cognitive domains, particularly executive functioning, which was variable across the different meta-analyses. For example, some studies include measures of verbal fluency in the executive functioning category and some do not (Karr et al., 2014). Despite the variability among cognitive domains explored, overall neurocognitive performance appears to be negatively affected by concussion (McCrory et al., 2005; Grindel, Lovell, & Collins, 2001; Broglio & Puetz, 2008; Karr et al., 2014).

Present Study

Research has also shown a link between the symptoms following concussion and neurocognitive impairments. A study by Collie and colleagues (2006) examined the cognitive performance of concussed athletes compared with non-injured athlete controls. They further explored the differences between injured athletes who were symptomatic versus asymptomatic. Compared to baseline performance, symptomatic athletes showed cognitive declines in multiple domains while asymptomatic athletes remained mostly stable, except for declines on divided attention measures. The non-injured controls showed no significant changes from baseline. More specifically, symptomatic athletes showed large and significant declines on attention and motor functioning tasks. A similar result was replicated with Fazio and colleagues (2007) who found that, compared with asymptomatic concussed athletes, symptomatic athletes performed worse on computerized measures of cognitive functioning. These findings support the idea that the symptoms following concussion are related to neurocognitive functioning. While there is evidence for the effect of general symptomatology on cognitive performance, there have been mixed results for the domains of cognition that are most strongly affected. Also, less work has explored how differences in the type of symptoms may result in different levels of impairment of cognition.

Specific Aim 1a: Examine the distinct relationship between each of the different post-concussion symptom factors (Cognitive, Physical, Affect, Sleep, and Headache) and neurocognitive performance globally.

Specific Aim 1b: Examine the distinct relationship between each of the different post-concussion symptom factors (Cognitive, Physical, Affect, Sleep, and Headache) and neurocognitive performance in different domains of cognition, specifically memory and attention/processing speed.

Specific Aim 2a: Examine the distinct relationship between each of the different post-concussion symptom factors and neurocognitive *impairment*.

Specific Aim 2b: Examine the distinct relationship between each of the different post-concussion symptom factors and impairment in different domains of cognition, specifically memory and attention/processing speed.

Hypotheses: Given the importance and salience of headache as a post-concussion symptom, headache will show a significant relationship with neurocognitive performance and impairment, such that individuals reporting headache symptoms would have poorer overall neurocognitive performance and would be more likely to be impaired compared to those individuals not reporting headache.

Method

Participants

This is an archival study involving 122 college students (100 men and 22 women) from the Pennsylvania State University who were involved in college athletics at the time of testing. The sports included football, soccer, wrestling, lacrosse, ice hockey, basketball, baseball, softball, rugby, swimming and diving, and golf. The mean age of the participants was 18.7 years (SD = 1.04) with a range from 17 to 22 years old, and the majority of the participants were Caucasian (67.2%). Participants were involved in the concussion program at the university and were referred to testing after experiencing an mTBI/concussion as determined by posttraumatic amnesia lasting less than 24 hours, a loss of consciousness lasting 30 min or less, or any change in mental status and/or post-concussion symptoms following the injury (Ruff et al., 2009). Following the concussion, the student athletes were referred to our program for testing by an athletic trainer or physician, and they completed a series of questionnaires and neuropsychological tests. The participant sample will be restricted to those individuals who were tested less than 30 days post-concussion. A majority of the individuals were tested within four days of sustaining their concussion (N = 78) and almost all were tested within the first two weeks (N = 109). The average number of days between concussion and the testing was 5.67 (SD = 5.56). While research has shown that individuals who sustain mTBI often recover from their symptoms within 1-2 weeks, this broader sample was used to allow for a range of recovered and non-recovered athletes. Some participants were missing measures and thus, in some analyses, there may be a reduction in the size of sample due to missing data. See Table 1 for more information on participant demographics.

Table 1. Participant characteristics

	Mean (SD)
Age (years)	18.7 (1.04)
Time since Concussion (days)	5.67 (5.56)
	N (%)
Sex	
Male	100 (82%)
Female	22 (18%)
Ethnicity	
Caucasian	82 (67.2%)
African American	32 (26.2%)
Other	8 (6.5%)
Sport	
Football	42 (34.4%)
Men's Lacrosse	17 (13.9%)
Men's Basketball	15 (12.3%)
Other	48 (39.4%)

Measures

The participants completed an extensive neuropsychological battery of tests that assessed various domains of cognitive functioning including memory, attention, and processing speed. The participants also completed questionnaires assessing their symptomatology following their concussion. The neuropsychological battery consisted of the Brief Visuospatial Memory Test–Revised (BVMT–R; Benedict, 1997) and the Hopkins Verbal Learning Test–Revised (HVLT–R; Brandt & Benedict, 2001), which test visual and verbal memory, respectively. The Symbol Digit Modalities Test (SDMT; Smith, 1991), the Vigil/W Continuous Performance Test (Cegalis & Cegalis, 1994), and the Stroop Color–Word Test (SCWT; Trenerry, Crosson, DeBoe, & Leber, 1989) were all used as measures of attention and processing speed. Additionally, the ImPACT (Immediate Post-Concussion Assessment and Cognitive Testing; Lovell, Collins, Podell, Powell, & Maroon, 2000), a test with multiple modules designed to measure outcomes following concussion, was also administered for measures of verbal memory, visual memory, attention and processing speed. The Wechsler Test of Adult Reading (WTAR; Psychological Corporation, 2001) was given to athletes at their baseline assessment (pre-concussion) as a measure of premorbid IQ. The BDI-FS (Beck Depression Inventory – Fast Screen; Beck, Steer, & Brown, 2000) is an abbreviated 7-item depression questionnaire given to athletes at both baseline and post-concussion assessments. The participants also completed the Post-Concussion Symptom Scale (PCSS), rating their experience of 22 common post-concussion symptoms on a scale of 0 (None) to 6 (Severe) (Lovell & Collins, 1998).

Procedures

The Pennsylvania State University's Sports-Concussion Program is based on the "Sports as a Laboratory Assessment Model (SLAM)" model (Bailey, Barth, & Bender, 2009). All participants were referred to our program from their team physician following a sports-related concussion and were administered the neuropsychological measures, as well as the background information and neurobehavioral questionnaires. The neuropsychological tests were administered by clinical psychology graduate students and well-trained undergraduate research assistants, all under the supervision of a clinical neuropsychologist. This study was approved by the University's Institutional Review Board and informed consent was collected from all participants.

Analyses

Approach to Data Analysis

All analyses were conducted with the Statistical Package for the Social Sciences (SPSS), Version 19.0 (IBM Corp., 2010), and significance levels were set at .05.

Main Data Analyses

The aim of this study is to explore the relationship between specific post-concussion symptoms and cognitive outcomes. Previous research using factor analysis has shown that the items on the PCSS group fall out into four main factors: Cognitive, Physical, Affective, and Sleep. These clusters do not include the items assessing headache, sleeping more than usual, or numbness/tingling, because these items did not make the cut off for the rotated component loadings (Merritt & Arnett, 2014). New variables were created using the sum of the participants' scores from the questions that comprise the various Symptom Factors. Higher values on these factor variables indicate more symptoms. Given the evidence that headache is an important symptom following concussion, this variable was also examined in the same manner as other symptom factors.

In order to determine the best approach for analyzing the data, exploratory analyses of these factor variables were conducted. The distribution of total sleep symptom scores was positively skewed with 56 of participants reporting 0 (See Figure 1) and a range of scores from 0 to 16. The distribution of total physical symptom scores was also positively skewed, with 83 of participants reporting 0 (See Figure 2) and a range of scores from 0 to 14. The distribution of total cognitive symptom scores was additionally positively skewed, with 58 of participants reporting 0 (See Figure 3) and a range of scores from 0 to 18. The distribution of total affective symptom scores was positively skewed, with 86 of participants reporting 0 (See Figure 4) and a range of scores from 0 to 14. Finally, the distribution of headache symptom scores was positively skewed, with 66 of participants reporting 0 (See Figure 5) and a range of scores from 0 to 5. Due to these skewed distributions, each factor variable and the headache variable was dichotomized. Given the large number of individuals who were reporting no symptoms at the time of testing following their concussion, “no symptoms” and “symptoms” groups were used which separated the individuals into a group with scores of 0 and a group with scores of 1 or more.

Ideally, it would be optimal to analyze the data by groups that include individuals with no symptoms, individuals with symptoms of just one factor, and individuals with just symptoms from the other factors. However, preliminary analyses revealed that very few individuals experienced symptoms from just one factor alone, and in fact, there were no individuals who experienced only sleep or physical symptoms. Only two individuals experienced only cognitive symptoms, two individuals experienced only affective symptoms, and five individuals experienced only headache symptoms. Therefore, it would not be feasible to group individuals in this manner in any meaningful way. Instead, the data were analyzed in two ways. First, the aforementioned groups of “symptoms” and “no symptoms” were compared. For these analyses, the “symptoms” group for each factor did include individuals with symptoms from other factors, but the individuals with “no symptoms” for a specific factor may also be experiencing symptoms from any of the other factors. Second, in order to explore the more distinct influence of one symptom factor (e.g. headache) over and above the other factors, I created three distinct groups: a no symptoms group, a group of individuals with symptoms from any other factor except headache, and a group of individuals with any other symptoms plus headache (this group included the five individuals who only had headache symptoms). Orthogonal contrasts were created for two planned comparisons. The first contrast compared the neurocognitive outcomes of both symptom groups (combined) against the no symptom group. The second contrast compared the two symptom groups against one another on the different neurocognitive outcome measures. The first contrast just reiterates the general effect of symptoms of neurocognitive performance, while the second contrast helps to elucidate whether having headache *in addition* to other symptoms was meaningful for neurocognitive outcomes. Linear and logistic regression analyses were conducted with the two contrast codes as predictors of the different neurocognitive outcomes.

Figure 1. Histogram of Total Sleep Symptom Scores

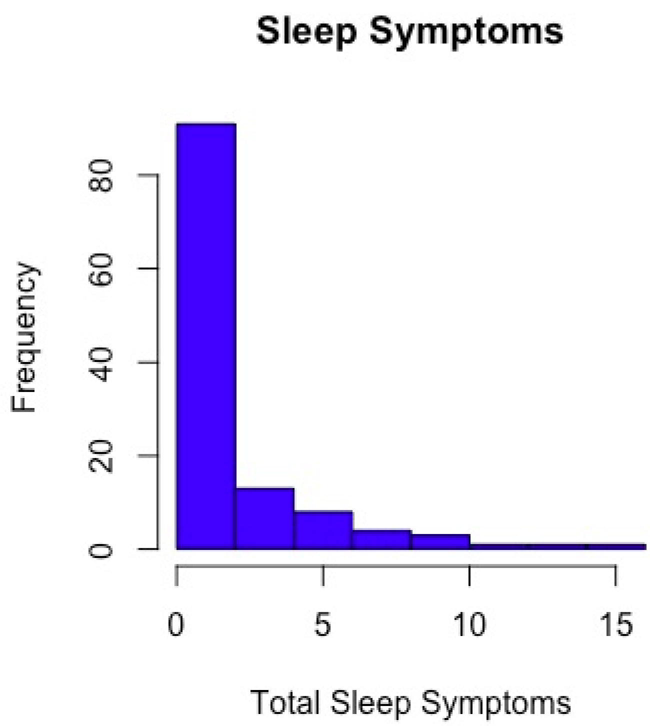


Figure 2. Histogram of Total Physical Symptom Scores

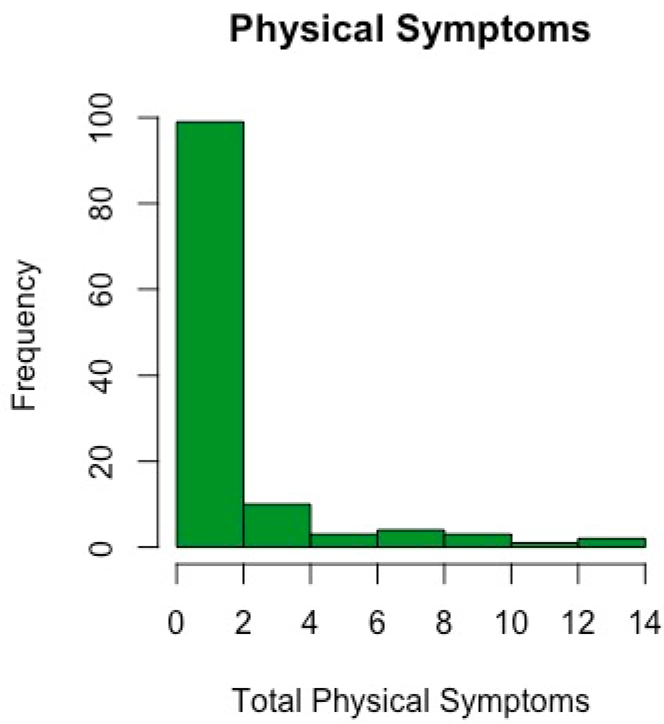


Figure 3. Histogram of Total Cognitive Symptom Scores

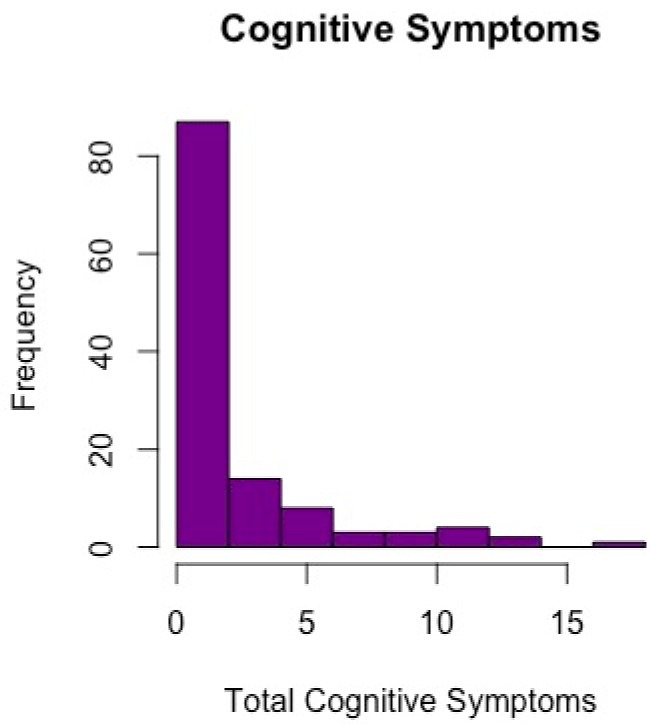


Figure 4. Histogram of Total Affective Symptom Scores

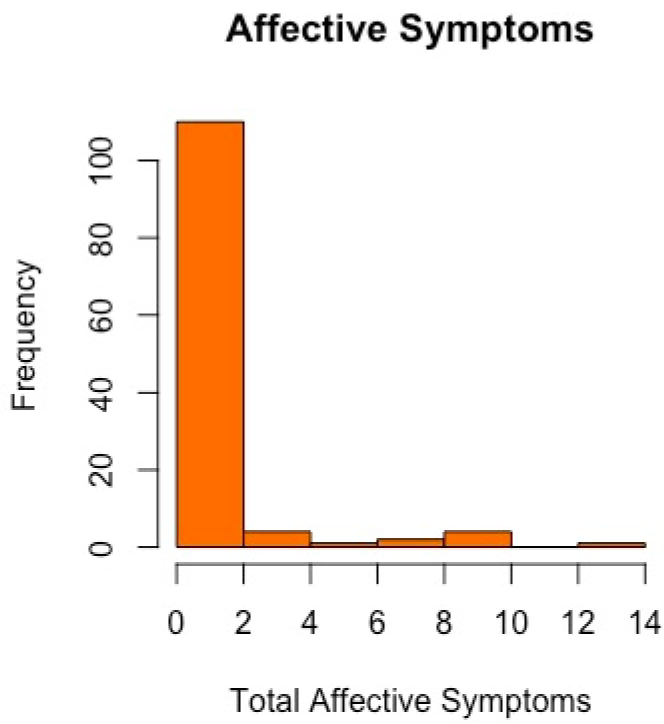
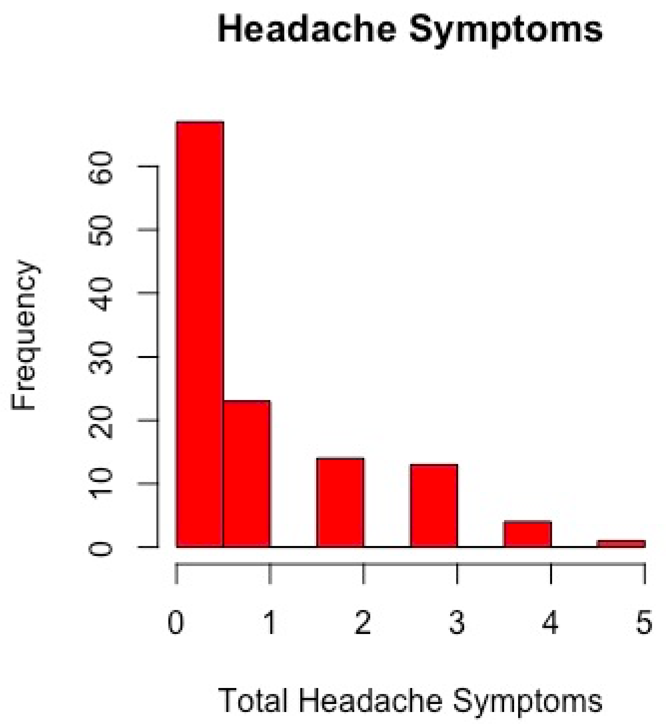


Figure 5. Histogram of Total Headache Symptom Scores



Specific Aim 1a: Examine the distinct relationship between each of the different post-concussion symptom factors (Cognitive, Physical, Affect, Sleep, and Headache) and performance on the overall neurocognitive composite. To examine cognitive functioning, standard score performance on the aforementioned neuropsychological tests was used to create a composite neuropsychological outcome. Each of the symptom factor groups' (i.e. "no symptoms" and "symptoms" for each factor) performance on this neuropsychological composite was compared using an independent samples t-test. Then, a multiple linear regression was conducted with the two aforementioned contrast codes as predictors of the overall neurocognitive performance composite.

Specific Aim 1b: Examine the distinct relationship between each of the different post-concussion symptom factors and each neurocognitive composite subfactor (i.e., Memory and Attention/Processing Speed). Each of the symptom factor groups' (i.e. "no symptoms" and "symptoms") performance on a composite of all the memory tests (Impact Verbal and Visual Memory Composites, HVLT-R Immediate and Delay Trials, and BVMT-R Immediate and Delay Trials) was compared using an independent samples t-test. Then the two groups' performance on a composite of all the attention/processing speed tests (Impact Visuomotor Speed and Reaction Time Composites, SDMT total correct, and Stroop 1 and 2 times) was also compared using an independent samples t-test. A multiple linear regression was also conducted with the two contrast codes as predictors of the memory composite and attention/processing speed composites, respectively.

Specific Aim 2a: Examine the distinct relationship between each of the different post-concussion symptom factors and neurocognitive impairment. Impairment scores were calculated by converting all the neuropsychological scores into standard score units, then any score below 80 (Performance below the 10 percentile) was considered an impaired score. To examine general cognitive impairment, individuals were grouped based on the overall number of impaired scores. An appropriate cut off for this was determined by using the median split score from baseline data (median = 1.00). Thus individuals with 2 or more impaired scores were placed in the impaired groups and individuals with one or no impaired scores were placed in the non-impaired group. Chi-Square analysis on each of the symptom factor groups (i.e. “no symptoms” vs. “symptoms”) and the impairment groups (i.e. “impaired” vs. “not impaired”) was performed to determine if belonging to the “symptoms” group for any particular factor means that an individual is more likely to be in the cognitively “impaired” group.

Specific Aim 2b: *Examine the distinct relationship between each of the different post-concussion symptom factors and impaired vs. unimpaired groups for subcategories of neurocognitive performance (i.e., Memory and Attention/Processing Speed).* A composite variable was created that includes the total number of impairment scores on only memory tests and again the median split score from baseline data was used to create the “memory-impaired” and “not memory-impaired” groups with a cut-off of two or more impaired tests. The same analyses were also conducted with the tests of attention/processing speed and the cut-off was again two tests. A Chi-Square analysis was performed on each of the symptom factors (i.e. “no symptoms” vs. “symptoms”) and the impairment groups (i.e. “memory impaired” vs. “not memory impaired”) to determine if belonging to the “symptoms” group for any particular factor means that an individual is more likely to be in the cognitively “impaired” group for either of these two domains.

Supplementary Data Analyses

Additionally, the amount of time between concussion and neuropsychological testing can have an impact on symptom presentation due to length of recovery time, so supplemental analyses were conducted for each of the symptom groups (some vs. none for each factor) to see if the groups differed on number of days since concussion at time of testing. Independent samples t-tests were used to determine if the symptom groups for each factor were significantly different in time since concussion. Chi-Square analyses were also conducted to determine if being male or female meant that an individual was more likely to be in either symptom group for any particular factor.

Results

Specific Aim 1a: Examine the distinct relationship between each of the different post-concussion symptom factors (Sleep, Physical, Cognitive, Affective, and Headache) and performance on overall neurocognitive composite.

“Symptoms” vs. “No symptoms” T-Test Analyses

There was a significant effect of sleep symptom group, $t(112) = 2.22$, $p = .029$, $d = .43$, with individuals who reported sleep symptoms demonstrating worse performance on the overall neurocognitive composite compared with individuals who were not reporting sleep symptoms. There was also a significant effect of the physical symptom group, $t(53) = 2.15$, $p = .036$, $d = .46$, with individuals who reported physical symptoms demonstrating worse performance on the overall neurocognitive composite compared with individuals who were not reporting physical symptoms. There was no significant effect of cognitive symptom group for the overall neurocognitive composite, *t*(105) = 0.65, *p* = .515, *d = .13,* or of the affective symptom group, *t*(105) = 0.68, *p* = .501, *d = .14.* Finally, individuals who reported headache symptoms had significantly worse performance on the overall neurocognitive composite, *t*(105) = 3.11, *p* = .002, *d = .60*.

<u>Contrast Code Linear Regression Analyses</u>

The first contrast code (which divided the groups into those experiencing symptoms and those who were not) was significantly related to the overall neurocognitive outcome measure in all subsequent analyses such that individuals with symptoms showed worse performance than those without symptoms.

The second contrast code explored the distinct relationship between specific symptom factors over and above the others in relation to overall neurocognitive performance. There were no significant differences for the groups with the addition of physical or sleep symptoms for overall neurocognitive performance. The group that was experiencing all other symptoms except cognitive symptoms (M = 89.63) had worse overall cognitive performance than the group that was experiencing cognitive symptoms as well (M = 96.00), *t*(2.02), *p* = .046, *d* = .52. The group that was experiencing all other symptoms except affective symptoms (M = 93.69) had worse overall cognitive performance than the group that was experiencing affect symptoms as well (M = 95.51), *t*(2.02), *p* = .046, *d* = .14. There was also no difference in overall neurocognitive performance between the group who was experiencing headache in addition to other symptoms and the group experiencing other symptoms without headache.

Specific Aim 1b: Examine the distinct relationship between each of the different post-concussion *symptom factors and each neurocognitive composite subfactor (i.e., Memory and Attention/Processing Speed).*

"Symptoms" vs. "No symptoms" T-Test Analyses

Individuals reporting physical symptoms also performed significantly worse on the memory composite, $t(112) = 2.21$, $p = .029$, $d = .43$, but not significantly worse on the attention/processing speed composite, $t(47) = 1.79$, $p = .080$, $d = .39$. Individuals reporting sleep symptoms also performed significantly worse on the memory composite, $t(107) = 2.80$, $p = .006$, $d = .53$, but not significantly worse on the attention/processing speed composite, $t(47) = 1.27$, $p = .208$, $d = .25$. There was no significant effect of cognitive symptom group for the memory composite, $t(112) = 1.54$, $p = .127$, $d = .29$, or attention/processing speed composite, $t(107) = 0.35$, $p = .725$, $d = .07$. There was also no significant effect of affective symptom group for the memory composite, $t(112) = 1.18$, $p = .243$, $d = .24$, or attention/processing speed composite, $t(107) = -.015$, $p = .988$, $d = .003$. Individuals who reported headache symptoms, however, had significantly worse performance on both the memory composite, $t(112) = 3.45$, $p = .001$, $d = .64$, and attention/processing speed composite, $t(78) = 2.79$, $p = .007$, $d = .54$.

Contrast Code Linear Regression Analyses

The first contrast code (which divided the groups into those experiencing symptoms and those who were not) was significantly related to both the memory composite and attention/processing speed composite in all subsequent analyses such that individuals with symptoms showed worse performance than those without symptoms.

The second contrast code explored the distinct relationship between specific symptom factors over and above the others in relation to memory and attention/processing speed performance. There were no significant differences for the groups with the addition of physical or sleep symptoms on either the memory or attention/processing speed measures. At a trending level, the group that was experiencing all other symptoms except cognitive symptoms (M = 87.60) had worse performance on the attention/processing speed measure than the group that was experiencing cognitive symptoms as well (M = 95.73), $t(1.86)$, $p = .066$, $d = .47$. There were no significant differences between the cognitive groups for the memory composite. The group that was experiencing all other symptoms except affective symptoms (M = 96.28) had better performance on the attention/processing speed composite than the group that was experiencing affect symptoms as well, but this effect was at a statistical trend, (M = 91.96), $t(1.86)$, $p = .066$, $d = .24$. Also at a trending level, those who were experiencing headache in addition to other symptoms (M = 93.50) had slightly lower memory composite scores than those who were not reporting headache symptoms (M = 98.39), t(-1.82), p = .071, $d = .40$. There was no difference between the headache groups on the attention and processing speed composite.

Specific Aim 2a: Examine the distinct relationship between each of the different post-concussion symptom factors and neurocognitive impairment.

"Symptoms" vs. "No symptoms" Chi-Square Analyses

Regarding overall neurocognitive impairment, the following symptom/no symptom groups were not significantly different: Affective, Somatic, Cognitive, and Sleep (see Table 2 for details). In contrast, the Headache groups differed. In particular, there was a significantly greater proportion of individuals with headache symptoms with overall neurocognitive impairment (64.1%) compared to those without any headache symptoms (35.9%) ($P = .006$, Fisher's exact test).

Table 2. Results from the "Symptoms" Vs. "No Symptoms" Chi-Square for Overall Neurocognitive Impairment

	Impairment		
Factor	**Impaired**	**Not Impaired**	**Fisher's Exact (*P*)**
Physical			
Symptoms	16	23	
No Symptoms	23	60	.151
Sleep			
Symptoms	25	36	
No Symptoms	14	47	.052
Cognitive			
Symptoms	24	40	
No Symptoms	15	43	.180
Affective			
Symptoms	12	24	
No Symptoms	27	59	.834
Headache			
Symptoms	25	31	
No Symptoms	14	52	.007**

** $p < .01$

Contrast Code Logistic Regression Analyses

The first contrast code was significantly related to the overall neurocognitive outcome measure in all subsequent analyses such that individuals with symptoms were more likely to be impaired on the overall neurocognitive composite than those without symptoms.

The second contrast code explored the distinct relationship between specific symptom factors over and above the others in relation to neurocognitive impairment. There were no significant differences in overall neurocognitive impairment between the groups with the addition of physical, sleep, affective, cognitive, or headache symptoms.

Specific Aim 2b: *Examine the distinct relationship between each of the different post-concussion symptom factors and impaired vs. unimpaired groups for subcategories of neurocognitive performance (i.e., Memory and Attention/Processing Speed).*

"Symptoms" vs. "No symptoms" Chi-Square Analyses

Among the individuals demonstrating memory impairment, significantly more reported sleep symptoms (76%) than those who did not (24%) (*P = .006, Fisher's exact test*). However, this did not hold when looking at individuals demonstrating attention/processing speed impairment, where 57.1% reported sleep symptoms compared to 42.9% did not, (*P = .632, Fisher's exact test*). For the memory impaired group, 52% of the individuals reported physical symptoms and 48% reported no physical symptoms, (*P = .090, Fisher's exact test*). However, in the attention/processing speed impaired group, significantly more individuals reported physical symptoms than not, with 54.2% of the individuals reporting physical symptoms and 47.6% reporting no physical symptoms. Among the individuals who were not impaired on attention/processing speed, 72.3% reported no physical symptoms while 27.7% did (*P = .039, Fisher's exact test*). For both memory impaired and attention/processing speed impaired groups, there were no significant differences between the number of people reporting cognitive or affective symptoms. For the individuals in the memory impaired group, significantly more individuals reported headache symptoms than not, with 72% of the individuals reporting headache symptoms and 28% reporting none (*P = .006, Fisher's exact test*). In the attention/processing speed impaired group, significantly more individuals reported headache symptoms than not, with 81% reporting headache symptoms and 19% reporting none (*P = .001, Fisher's exact test)*. See Table 3 and Table 4 for more details.

Table 3. Results from the "Some Symptoms" Vs. "No Symptoms" Chi-Square for Memory Impairment

	Impairment		
Factor	**Impaired**	**Not Impaired**	**Fisher's Exact (*P*)**
Physical			
Symptoms	12	27	
No Symptoms	13	70	.090
Sleep			
Symptoms	19	42	
No Symptoms	6	55	.006**
Cognitive			
Symptoms	16	48	
No Symptoms	9	49	.262
Affective			
Symptoms	10	26	
No Symptoms	15	71	.223
Headache			
Symptoms	18	38	
No Symptoms	7	59	.003**

** $p < .01$

Table 4. Results from the "Some Symptoms" Vs. "No Symptoms" Chi-Square for Attention/Processing Speed Impairment

	Impairment		
Factor	**Impaired**	**Not Impaired**	**Fisher's Exact (*P*)**
Physical			
Symptoms	11	73	
No Symptoms	10	28	.039*
Sleep			
Symptoms	12	49	
No Symptoms	9	52	.632
Cognitive			
Symptoms	12	52	
No Symptoms	9	49	.811
Affective			
Symptoms	6	30	
No Symptoms	15	71	1.00
Headache			
Symptoms	17	39	
No Symptoms	4	62	.001**

* $p < .05$ ** $p < .01$

Contrast Code Logistic Regression Analyses

The first contrast code was significantly related to the overall neurocognitive outcome measure in all subsequent analyses such that having symptoms was associated with impairment on both the memory and attention/processing speed measures.

The second contrast code explored the distinct relationship between specific symptom factors over and above the others in relation to memory and attention/processing speed impairment. There were no significant associations between either memory or attention/processing speed impairment and the addition of physical, sleep, affective, or cognitive symptoms. There were also no significant associations between memory impairment and the addition of headache symptoms. However, reporting headache in addition to all other symptoms was associated with impairment on the attention/processing speed composite, (OR = 0.50 [95% CI, 0.04-0.74], P =.037).

Supplementary Analyses

For each of the five factors, there were no significant differences between the symptom and no symptom groups on days since concussion. An additional analysis also examined whether there was a difference of gender in symptom reporting. There were no significant differences between genders for physical, sleep, cognitive, or affective symptom groups. However, a significantly higher percentage of women reported headache symptoms (77.3%) compared to men (39%) (*P = .002, Fisher's exact test, Phi = 1.00*).

Discussion

Results and Contributions from the Current Study

Symptoms and cognitive impairment are both common outcomes following a concussion and have an impact on an individual's life and daily functioning. Current research has shown a general relationship between symptoms following a concussion and cognitive functioning. However, it has been less clear how specific symptoms may be differentially associated with cognitive outcome generally as well as specific domains of cognition. The current study explored the relationship between different symptom factors and multiple neurocognitive outcomes. First, the neurocognitive outcomes were examined at the mean level and this explored how reporting of symptoms for the five different symptom factors was related to outcomes. Overall, reports of physical, sleep or headache symptoms was related to poorer overall neurocognitive performance. More specifically, reports of sleep symptoms were associated with poorer performance on memory tests while physical symptoms were associated with poorer performance on the attention/processing speed tests. Individuals reporting headache symptoms had significantly worse performance on both the memory and attention/processing tests.

Another way of examining neuropsychological outcomes is through impairment scores which can be more clinically meaningful as they are often used in making return to play decisions. The results of the present study showed that there was no significant relationship between reports of affective, cognitive, physical or sleep symptoms and overall neurocognitive impairment (as defined by two or more impaired scores on any of the neuropsychological tests). However, individuals reporting headache symptoms were more likely to show general neurocognitive impairment than those not reporting headache symptoms. When examining the specific domains of cognition, comparable to the mean level data there was a relationship between sleep and memory, as well as physical symptoms and attention/processing speed. Individuals reporting sleep symptoms were more likely to be impaired on the memory tests than individuals without sleep symptoms, and individuals reporting physical symptoms were more likely to be impaired on the attention/processing speed tests than those without physical symptoms. Again, individuals with headache were more likely to be impaired on both tests of memory and attention/processing speed than those without headache symptoms. Given the importance of cognition in daily functioning, particularly to student-athletes who suffer from concussions, this work could help raise awareness around specific cognitive vulnerabilities that may be associated with distinct symptoms. The knowledge that experiencing sleep symptoms following a concussion could be more related to memory difficulties and physical symptoms more to attention/processing speed difficulties could help clinicians better tailor treatment recommendations and accommodations to suit the needs of the individuals affected. Also, the knowledge that headache appears to be most strongly related to all the aforementioned types of cognitive difficulties could help clinicians more readily identify athletes who may be at particular risk of overall negative cognitive outcomes and make recommendations accordingly.

The supplementary analyses revealed that symptom reporting was not simply a reflection of time since concussion. Additionally, it appears that there may be a gender difference in headache symptom reporting such women reported more headache symptoms than men. Despite the small sample of female participants (n = 22), the effect size was very large (*Phi = 1.00;* Phi is equivalent to the correlation coefficient *r*). This result indicates that women either experience headache symptoms more often than men following a concussion or are more likely to report these symptoms compared to their male counterparts.

Limitations

One of the limitations of the current study is that the grouping method does not fully isolate specific symptoms. For example, individuals who are included in the headache group almost always also reported symptoms from other factors, but the individuals in the no headache group also reported symptoms from other factors. Given the extremely small number of individuals reporting symptoms from only one factor, it was not feasible to create meaningful pure symptom groups. Additionally, given that it is rare for individuals to report only one type of symptom, it may not be clinically meaningful to examine the data in this way because such a conceptualization does not reflect the actual reality of most symptom reports. I attempted to address this issue systematically using the contrast codes to compare the groups in another way, employing both linear and logistic regressions to analyze whether the addition of a specific kind of symptom was related to cognitive outcomes. The results of these analyses showed that having headache symptoms in addition to other symptoms increased the likelihood that an individual would be impaired on attention/processing speed tests. There were also the unexpected findings that having the addition of cognitive or affective symptoms meant that an individual was actually *less* likely to be generally impaired on the neurocognitive tests. This method was most likely limited by small and idiosyncratic sample sizes, with cells of impaired individuals reaching a maximum of 25 individuals and a minimum of 4, which could have reduced the ability to detect differences between the groups.

Other limitations of the study involve the generalizability of the findings given that the sample consisted solely of college athletes who had suffered mild traumatic brain injuries. It is possible that these results might differ in older or more severely injured samples. Our sample also included a majority of male participants (n = 82%), and given that our results indicated a potential increased risk or vulnerability for headache symptoms in women, this could be an important gender difference to study further with a larger sample of female athletes. Another limitation of the current study is the use of self-reported symptoms which may be misrepresented by athletes due to return-to-play motivations. However, the athletes included in this sample all demonstrated sufficient effort and motivation based on clinician ratings and objective neuropsychological testing measures. Given the importance of self-reported symptoms in making return-to-play decisions, it is worthwhile to continue to examine such measures and their relationship to outcomes following concussion.

Conclusions

When examining the relationship between specific types symptoms and cognitive outcomes following concussion, headache symptoms are related to overall cognitive impairment as well as memory and attention/processing speed impairment. Physical symptoms have a specific relationship to attention/processing speed impairment, while sleep symptoms are specifically related to impairments in memory. As previous research has established, the overall number of reported symptoms is related to outcomes following concussion. However, but the present results highlight the importance of identifying the particular types of symptoms as this could provide more knowledge about specific cognitive impairment and allow for more tailored recommendations for treatment and accommodations following injury.

References

Bailey, C. M., Barth, J. T., & Bender, S. D. (2009). SLAM on the stand: How the sports-related concussion literature can inform the expert witness. The Journal of Head Trauma Rehabilitation, 24(2), 123–130.

Barkhoudarian, G., Hovda, D. A., & Giza, C. C. (2016). The Molecular Pathophysiology of Concussive Brain Injury – an Update. *Phys Med Rehabil Clin N Am*, *27*, 373–393.

Beck, A.T., Steer, R.A., & Brown, G.K (1996). Beck depression inventory-II. San Antonio, TX: Psychological Corp.

Benedict, R. H. B. (1997). Brief Visuospatial Memory Test–Revised: Professional manual. Odessa, FL: Psychological Assessment Resources.

Brandt, J., & Benedict, R. H. B. (2001). Hopkins Verbal Learning Test–Revised. Odessa, FL: Psychological Assessment Resources.

Broglio, S. P., & Puetz, T. W. (2008). The Effect of Sport Concussion on Neurocognitive Function, Self-Report Symptoms and Postural Control A Meta-Analysis. *Sports Med*, *38*(1), 53–67.

Cegalis, J. A., & Cegalis, S. (1994). The Vigil/W Continuous Performance Test (manual). New York, NY: ForThought.

Clay, M. B., Glover, K. L., & Lowe, D. T. (2013). Epidemiology of concussion in sport: A literature review. *Journal of Chiropractic Medicine*, *12*(4), 230–251.

Collins, M. W., Field, M., Lovell, M. R., Iverson, G., Johnston, K. M., Maroon, J., & Fu, F. H. (2003). Relationship between postconcussion headache and neuropsychological test performance in high school athletes. *The American journal of sports medicine*, *31*(2), 168-173.

Dodd, A. B., Epstein, K., Ling, J. M., & Mayer, A. R. (2014). Diffusion tensor imaging findings in semi-acute mild traumatic brain injury. *Journal of neurotrauma*, *31*(14), 1235-1248.

Echemendia, R. J., & Julian, L. J. (2001). Mild traumatic brain injury in sports: Neuropsychology's contribution to a developing field. *Neuropsychology Review*, *11*, 69.

Giza, C. C., & Hovda, D. A. (2014). The new neurometabolic cascade of concussion. *Neurosurgery*, *75 Suppl 4*(0 4), S24-33.

Giza, C. C., & Hovda, D. A. (2001). The neurometabolic cascade of concussion. *Journal of Athletic Training Jul-Sep*, *36*(3).

Grindel, S.H, Lovell, M.R., & Collins, M.W. (2001). The assessment of sport- related concussion: the evidence behind neuropsychological testing and management. Clinical Journal of Sport Medicine, 11 (3), 134-43.

Guskiewicz, K. M., Weaver, N. L., Padua, D. a, & Garrett, W. E. (2000). Epidemiology of Concussion in Collegiate and High School Football Players. *The American Journal of Sports Medicine*, *28*, 643–650.

Karr, J. E., Areshenkoff, C. N., & Garcia-Barrera, M. A. (2014). The Neuropsychological Outcomes of Concussion: A Systematic Review of Meta-Analyses on the Cognitive Sequelae of Mild Traumatic Brain Injury. *Neuropsychology*, *28*(3), 321–336.

Laker, S. R. (2011). Epidemiology of Concussion and Mild Traumatic Brain Injury. *Pm R*, *3*(10), 354–358.

Langlois, J. A., Rutland-brown, W., & Wald, M. M. (2006). The Epidemiology and Impact of Traumatic Brain Injury A Brief Overview. *Journal of Head Trauma Rehabilitation*, 11–14.

Lovell, M.R., Echemendia, R.J., Barth, J.T., & Collins, M.W. (Eds.). (2004). Traumatic Brain Injury in Sports: An International Neuropsychological Perspective. Lisse, The Netherlands: Swets & Zeitlanger.

Lovell, M. R., Collins, M. W., Podell, K., Powell, J., & Maroon, J. (2000). ImPACT: Immediate Post-concussion Assessment and Cognitive Testing. Pittsburgh, PA: NeuroHealth Systems, LLC.

Makdissi, M., Darby, D., Maruff, P., Ugoni, A., Brukner, P., & McCrory, P. R. (2010). Natural History of Concussion in Sport: Markers of Severity and Implications for Management. *The American Journal of Sports Medicine*, *38*(3), 464–471.

McCrory, P., Meeuwisse, W. H., Aubry, M., Cantu, R. C., Dvorák, J., Echemendia, R. J., … Turner, M. (2013). Consensus Statement on Concussion in Sport-The 4th International Conference on Concussion in Sport Held in Zurich, November 2012. *British Journal of Sports Medicine*, *5*(4), 255–279.

McCrory P, Johnston K, Meeuwisse W, et al. (2005). Summary and agreement statement of the second International Conference on Concussion in Sport, Prague 2004. British Journal of Sports Medicine, 39 (4), 196-204.

Meier, T. B., Bellgowan, P. S., Singh, R., Kuplicki, R., Polanski, D. W., & Mayer, A. R. (2015). Recovery of cerebral blood flow following sports-related concussion. *JAMA neurology*, *72*(5), 530-538.

Merritt, V. C., & Arnett, P. A. (2014). Premorbid predictors of postconcussion symptoms in collegiate athletes. *Journal of Clinical and Experimental Neuropsychology*.

Miles, L., Grossman, R. I., Johnson, G., Babb, J. S., Diller, L., & Inglese, M. (2008). Short-term DTI predictors of cognitive dysfunction in mild traumatic brain injury. *Brain Injury*, *22*(2), 115-122.

Ruff, R.M., Iverson, G.L., Barth, J.T., Bush, S.S., Broshek, D.K., & the NAN Policy and Planning Committee (2009). Recommendations for Diagnosing a Mild Traumatic Brain Injury: A National Academy of Neuropsychology Education Paper. *Archives of Clinical Neuropsychology*, 24: 3-10.

Smith, A. (1991). Symbol Digit Modalities Test. Los Angeles, CA: Western Psychological Services.

Trenerry, M. R., Crosson, B., DeBoe, J., & Leber, W. R. (1989). Stroop neuropsychological screening test. Odessa, FL: Psychological Assessment Resources.