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Implications of Race on Post-Concussion Neurocognitive Performance and Symptom Presentation

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Supervisor: Christie, Anita D., The University of Western Ontario A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Kinesiology © Taia B.B. MacEachern 2022

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Abstract

The objective of this thesis was to examine the impact of race on post-concussion symptoms and neurocognitive performance. This was achieved through a systematic review and metaanalysis (Chapter 2), and a retrospective study (Chapter 3). From 15 published studies, it was found that Whites (70.11%) reported a higher prevalence of concussion then Black/African American (13.65%). A small effect $(g = 0.3)$ of race was found on neurocognitive measures, indicating that Whites performed better. Using a database of concussion outcomes, it was found that Black/African American reported significantly higher symptom severities (*p <*0.05), but this was dependent on the scale used. Significant differences were found on some, but not all, neurocognitive outcomes (*p <*0.05). This highlights the complex relationship between race and concussion presentation and outcomes and suggests racial differences should be considered when selecting assessment methods.

Keywords

Concussion; mTBI; race; neurocognitive performance; symptom presentation; racial disparities

Summary for Lay Audience

Concussions have the potential to cause a wide variety of symptoms. One of the numerous possible symptoms post-concussion is a decline in neurocognitive performance. Previously, studies have shown that Black/African Americans, when compared to their White counterparts, are more likely to present with high symptom scores and greater cognitive decline post-concussion. Both White and Black/African Americans use the same cognitive assessment tools and currently it is unknown if performance on these assessments is similar. Therefore, the purpose of this thesis was to determine race-based differences in concussion prevalence, symptom presentation, and neurocognitive performance. The results indicated that race played a significant role in symptom presentation, though it was dependent on the scale that was used. In general, Black/African Americans tended to report a higher severity of symptoms and had lower performance on neurocognitive measures post-concussion. In summary, this thesis suggests that post-concussion symptom presentation and neurocognitive performance is different between races. This thesis highlights the complex relationship between race and concussion presentation and outcomes and provides several suggestions for future research.

Co-Authorship Statement

Taia MacEachern is the primary author of all chapters contained in this thesis. Dr. Anita Christie is a co-author and provided guidance and feedback on the entire manuscript, along with overall study design and data analysis.

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Table of Contents

List of Tables

List of Figures

Chapter 1

1 General Introduction

1.1 General Introduction

A Concussion, defined by a panel of experts at the *4 th International Conference on Concussions in Sports* as: "a complex pathophysiological process that affects the brain and is induced by biomechanical forces" (McPherson et al., 2019), is often used in the medical literature interchangeably with a mild traumatic brain injury (mTBI). A concussion can be caused by any biomechanical injury that results in transient neurological dysfunction or leads to cerebral dysfunction without significant cell death. The Centres for Disease Control and Prevention (CDC; (*TBI Data*, 2021) estimated in 2018 that Traumatic Brain Injuries (TBI) accounted for 223,050 emergency department visits in the USA, most of which were later classified as mTBIs. Over recent years the topic of concussion has gained traction within the literature and media leading to an increase in diagnosis. This increase in attention has led concussions to become a major health concern, costing individuals on average \$13,564 in healthcare over a 12-month follow-up period (Pavlov et al., 2019).

1.2 Pathophysiology (Brief Review)

When a biomechanical force acts on neurons and glia it can damage microstructural components such as dendritic arbors, axons, and astrocytes. Axons appear to be particularly vulnerable to biomechanical stretch forces, which are commonly the cause of concussions (Giza et al., 2018). Axonal stretching can lead to microtubule disruption and intra-axonal calcium (Ca^{2+}) flux which has been linked to changes in axonal integrity and function. As early as five minutes after the biomechanical injury has occurred, decreased compaction and stability of the neurofilament structures can be detected. This destabilization of axons can last anywhere from 6-24 hours post injury (Giza & Hovda, 2014; MacFarlane & Glenn, 2015). Unmyelinated axons are particularly vulnerable to these forces and show greater subsequent impairment of electrophysiological function (Giza & Hovda, 2014). Recent MRI work by Li et al., (2021) has also shown changes in

macro- and micro-structural white matter integrity, connectivity alterations and functional networks of concussion patients (Li et al., 2021). However, a concussion generally shows little, if any, cellular death, even in the presentation of measurable functional impairment (MacFarlane & Glenn, 2015).

The structural destabilization of neurons is associated with chemical and metabolic alterations that also contribute to neurological dysfunction. Initially, at the point of injury there is an efflux of potassium (K^+) , an indiscriminate release of glutamate, and an influx of Ca^{2+} that becomes sequestered in the mitochondria and inhibits the oxidative metabolism of the mitochondria and impairs axonal function (Giza & Hovda, 2014). In an attempt to regain homeostasis, there is an increase in the productivity of the sodiumpotassium ATPase ionic pumps, leading to a state of hyper glycolysis due to the increased energy demand for these pumps to function. During this phase of hypermetabolism there is a simultaneous uncoupling of autoregulation which results in a decrease in cerebral blood flow (CBF; MacFarlane & Glenn, 2015). This creates a scenario of dysregulation where there is an increased demand for ATP due to the hypermetabolism, with a decreased energy supply caused by the decreased CBF, leading to an energy crisis and a prolonged period of decreased glucose metabolism (MacFarlane & Glenn, 2015). After the initial hypermetabolic phase, the hypometabolic period has the potential to last 7-10 days (Giza et al., 2018). This disruption of cellular homeostasis is thought to cause the signs and symptoms of a concussion, which typically last 1-2 weeks and are more severe in the acute phase but improve over time (Giza et al., 2018).

1.3 Post-Concussion Symptoms

Within the first 72 hours following a concussive injury, 80-100% of patients report one or more symptoms (Junn et al., 2015). Due to the wide variety of possible symptom presentation Clinicians have created symptom subtypes, denoted as; physical signs, sleep disturbances, social or emotional changes and cognitive impairment (Bauer & Jaffee, 2021; McPherson et al., 2019; *CDC Injury Center*, 2021). The highest rates of concussion symptoms are often reported within the first month post-injury and may take anywhere from three months to a year to resolve (Barker-Collo et al., 2015; Bauer & Jaffee, 2021; Junn et al., 2015).

1.3.1 Physical Symptoms

The most commonly reported physical symptoms of a concussion is headaches (Junn et al., 2015; *CDC Injury Center*, 2021). Post-concussion headaches are classified as secondary headaches which are further classified by subtypes based on characteristics that fit within primary headache categories; migraine, tension-type headache, cluster headache/other trigeminal autonomic cephalalgias, and other primary headaches (Harmon et al., 2013; Junn et al., 2015; Lipton et al., 2004). Depending on the severity of the headache, it can lead to nauseas and vomiting as well as sensitivity to light and noise (Bauer & Jaffee, 2021).

The second most commonly reported post-concussion symptom is dizziness which is often accompanied by a lack of postural stability and control (Harmon et al., 2013). Dizziness may be caused by central or peripheral dysfunction. One aspect that distinguishes the two is that peripheral dysfunction can cause sudden vertigo, whereas a central dysfunction has a slow onset of standing and walking imbalances ("Central Vestibular Disorders," n.d.). Deficiency to postural control generally begins immediately following a concussive event, though it can take up to 14 days to manifest (Kelly et al., 2019). Once these symptoms manifest, they are not long lasting with symptoms affecting motor function, movement, and balance typically resolving within 3-5 days post-injury (Broglio & Puetz, 2008; McPherson et al., 2019).

Other physical symptoms of a concussion can include neck pain and changes in vision. Neck pain occurring up to 28% of the time and can occur with or without concomitant headaches, as it may arise from many anatomical sites including occipital nerve compression, facet dysfunction and soft tissue damage (Junn et al., 2015). Changes in vision, which may be reported anywhere from 16-21% of the time. Visual changes may be due to an accommodative insufficiency leading to an inability to sustain near vision for extended periods of time (Junn et al., 2015). Often when individuals report these deficiencies they report blurred vision, photosensitivity, and reduced screen tolerance, as well as eye fatigue (Bauer & Jaffee, 2021).

Not all post-concussive symptoms that manifest are physical in nature. Fatigue and general feelings of malaise are reported 40-43% of the time as a post-concussion symptom. Such fatigue is often described as mental fatigue, weariness or "pathological fatigue" which is unrelated to exertion and does not resolve with rest. Such fatigue is often reported acutely but has been shown to impact approximately 28% of individuals with mTBIs, up to 3-months post-injury (Junn et al., 2015).

1.3.2 Sleep Disturbances

Non-restorative sleep has been cited as a potential cause of fatigue as well as cause of exacerbation of depression, headache, and cognitive symptoms (Junn et al., 2015). Up to 60% of individuals with mTBIs report difficulty sleeping (Junn et al., 2015). The CDC defines sleep disturbances as either sleeping less than usual, sleeping more than usual or general trouble sleeping (*CDC Injury Center*, 2021). Often individuals cite problems with initiation and poor maintenance of sleep, middle of the night awakenings and excessive daytime sleepiness as a post-concussion symptom (Bauer & Jaffee, 2021).

1.3.3 Social or Emotional Changes

Social and emotional changes are another subtype of concussion symptoms. Anxiety, irritability, feeling more emotional as well as increased sadness or depression are some of the symptoms that individuals have reported post-injury (*CDC Injury Center*, 2021). Anxiety is commonly understood as nervousness, feeling overwhelmed or hypervigilance (Bauer & Jaffee, 2021) and is reported post-injury in 26-29% of cases (Junn et al., 2015). Anxiety has been shown to continue to increase up to six months post injury and has been found to predict a worse outcome after a concussion (Barker-Collo et al., 2015; Junn et al., 2015). Depression is commonly understood as feelings of severe despondency and dejection, irritability, loss of energy, fatigue, and poor motivation (Bauer & Jaffee, 2021). Depression or depression-like symptoms are reported in 15-52% of individuals with mTBI, with 53% of individuals with mild-severe TBI meeting the criteria for at least one major depressive episode within the first year (Junn et al., 2015).

1.4 Symptom Scales

Though it is reported that 1.7 million mTBIs occur annually in the United States, concussion remains a clinical diagnosis based on connecting traumatic events to symptom presentation. Clinical symptoms are assessed through an interview with a clinician or through a symptom checklist where the respondent indicates if they are experiencing a specific symptom and rate its severity on a scale (Bauer $\&$ Jaffee, 2021). As it stands, there is several scales that are used clinically and in research. Two of the commonly used scales that are the focus of the work in this thesis are the Brief Symptom Inventory-18 (BSI-18) and Glasgow Outcome Scale Extended (GOS-E).

1.4.1 Brief Symptom Inventory (BSI-18)

The Brief symptom inventory-18 (BSI-18; Derogatis, 2000) is a patient reported tool used to assess psychological distress and psychiatric disorders (Asner-Self et al., 2006). It was created using a community sample of 1,134 individuals and consists of 18-items taken from the 53-item Brief Symptom Inventory (BSI; Derogatis, 1993), which itself is a condensed form of the long form 90-item Symptom Checklist-90-Revised (SCL-90-R; Derogatis, 1994). The BSI-18 has also proven reliable in psychotherapy research as well as in quality assurance for psychotherapeutic long-term effects (Franke et al., 2017).

The BSI-18 is divided equally amongst three dimensions: somatization (SOMA) – distress caused by the perception of bodily dysfunction; anxiety (ANX) – symptoms of nervousness, tension, motor restlessness, panic states and apprehension; and depression (DEPR) - symptoms of disaffection and dysphoric mood (Andreu et al., 2008). Each dimension is comprised of six items, and scores range from 0 to 24 as each item is rated on a five-point Likert scale. Respondents are asked how much they have been affected by their symptoms in the prior seven days, from 0 (*not at all)* to 4 (*extremely)*. Results from these dimensions are summarized in the Global Severity Index (GSI) of distress. GSI is calculated by the sum of the three-dimensions and ranges from 0-72 with higher scores indicating higher levels of psychological distress (Asner-Self et al., 2006). According to Derogatis (2000), it is recommended that a T-score ≥ 63 on two of the three-dimension

scales or a T-score ≥ 63 on GSI should be classified as having clinically significant distress.

The BSI-18 is a quick, simple tool for the assessment of psychological distress. It has proven reliable when assessing psychological distress in the general population (Franke et al., 2017) as well as in clinical samples, including cancer patients (Calderon et al., 2020; Recklitis et al., 2017), Parkinson Disease patients (Abraham et al., 2017) and both patients with Mild Traumatic Brain Injuries (Lancaster et al., 2016) and Traumatic Brain Injuries (Meachen et al., 2008). In a general adult population, the BSI-18 has demonstrated good internal consistency estimates (Cronbach α) for all dimensions; 0.82 for SOM, 0.84 for ANX, 0.87 for DEPR and 0.93 for GSI (Franke et al., 2017). The GSI has also been shown to demonstrate high internal consistency (α range = 0.84-0.91) and moderate test-retest reliability (Pearson product moment correlation $= 0.66$) in adults with mild to severe traumatic brain injuries (Meachen et al., 2008).

1.4.2 Glasgow Outcome Scale Extended (GOS-E)

The Glasgow Outcome Scale Extended (GOS-E) is an extension from the five-point Glasgow Outcome Scale (GOS; Jennett & Bond, 1974) to an eight-point scale. GOS was designed to assess level of consciousness and an overview of outcome after brain injury (McMillan et al., 2016). The GOS is scored on five-levels; 1 – Death, 2 – Vegetative State, 3 – Severely Disabled, 4 – Moderately Disabled and 5 – Good Recovery. The GOS-E was designed to address the limitations of the GOS, which include the lack of specification and of a structured interview, as well as limited categories (Moin et al., 2011). In the GOS-E, the Moderately Disabled, Severely Disabled and Good Recovery categories have each been divided into two additional categories. Data is collected through a structured interview with both the patient and caretaker and scored on the following levels; 1 – Dead, 2 – Vegetative State: condition of unawareness with only reflex responses, 3- Low Severe Disability: unable to be left alone for eight hours at home and is dependent on frequent daily support for mental or physical disability, 4 -Upper Severe Disability: able to be left along for more than 8 hours but less then 24 hours and is dependent on others for shopping, travel and regular daily support, $5 - Low$

Moderate Disability: dependent on support for shopping, travel and activities outside of the home and cannot resume previous social activity, 6 – Upper Moderate Disability: able to return to work with adaptations but not to prior level and can resume modified previous social activity, 7 – Low Good Recovery: resumption of normal life but preinjury status is not achieved, 8 – Upper Good Recovery: full recovery or minor symptoms that does not affect daily living (*Glasgow Outcome Scale - Extended*, 2019; Olsen, 2014)

The GOS-E has been designed as an outcome measurement to assess level-ofconsciousness and as an early indicator of the index of severity after an mTBI and TBI (Yeatts et al., 2020). Among 163 outcome measures included in the Common Data Elements recommendations for TBI, which was developed as a recommendation for coding of clinical and demographic variables for a broad spectrum of studies, the GOS-E outcome is classified as a core element indicating that its GOS-E score is essential and relevant to all TBI studies (Maas et al., 2010; Yeatts et al., 2020)

Previous work has identified the high level of reliability of both the GOS and GOS-E but also considerable interrater variation in rankings and systematic differences. This variability arises due to assessor experience and background (McMillan et al., 2016). The interview included in the GOS-E is designed to reduce interrater variations by standardizing the questions relative to the assessment and to assist the interpretation of recording certain classifications (Lu et al., 2010).

1.5 Cognitive and Functional Impairment

Cognitive function is an overarching term used to describe a variety of mental functions including memory, attention, perception, decision making, and language comprehension. Cognitive dysfunction may arise after a brain injury such as a concussion and symptoms may include difficulties with attention or concentration, feeling slowed down, fogginess, and memory problems (*CDC Injury Center*, 2021). Concussions may also lead to a reduction in reaction time, processing speed, working memory and executive function (Bauer & Jaffee, 2021). These post-concussion symptoms can be identified through cognitive testing, for which many measures exist. Those of focus in this thesis include the Controlled Oral Word Association test, Grooved Pegboard Test, and the Trail Making Test.

Following a concussion, impaired attention is reported 25-38% of the time and memory impairment is reported 26-44% of the time (Junn et al., 2015). Working memory in particular is affected by concussion. Working memory is the ability to temporarily store and manipulate information and is closely associated with executive function due to the need for integration and ongoing control of information. These working-memory deficiencies post-injury may be caused by a slowed processing speed post injury, though it is understood that this system may be disturbed by any damage to the frontal lobe (Junn et al., 2015).

Deficits in reaction time and processing speed are common indications of cognitive impairment. A common mechanism thought to underlie all these deficits after a concussion is a diffuse axonal injury. Barker-Collo et al., (2015) reported that neuroradiological and neuro-pathological investigations linked deficits in information processing to diffuse brain damage in the frontal and temporal lobes, corpus callosum and fornices in those with mTBI (Barker-Collo et al., 2015). Giza & Hovda (2014) also found that damage to white matter has a strong correlation to the level of neurocognitive impairment. Alterations in protein expression as well as axonal dysfunction, caused by physiological changes to the brain at the time of concussion, also contribute to the severity of neurocognitive impairment (Giza & Hovda, 2014).

Cognitive dysfunction is accepted as a common consequence of concussion and contributes to both an economic and personal burden (Barker-Collo et al., 2015). A 2021 study found that within the first two days post-injury, 32% of concussion patients reported experiencing cognitive disturbances, 40% within the first three days, 47% within the first month and 39% within the first three months post-injury (Bauer & Jaffee, 2021). Memory, processing speed, executive function, psycho-motor speed, reaction time, and complex attention have all shown to improve over a one-year follow up period, yet complex attention shows the slowest recovery with over 20% of people still experiencing difficulties at the 12-month mark (Barker-Collo et al., 2015).

1.5.1 Controlled Oral Word Association Test (COWAT)

The Controlled Oral Word Association Test (COWAT) has been used since its inception by Benton & Hamsher in 1976, as a test of neurocognitive function through the testing of word fluency (Loonstra et al., 2001). Verbal communication deficits are compared between neurologically impaired participants and healthy controls by evaluating the spontaneous production of words within a given time frame (Ross et al., 2007). Participants are given a specific letter of the alphabet (e.g., FAS or CFL) and told to say as many words as they can that begin with the letter in one minute. Evaluators record the words that participants produce in the order that they are said. The participants final score is the sum of all words produced for the three letters, excluding; proper nouns, repeating words, repeating words in a different tense, plurality or grammar usage and words that start with the wrong letter (Loonstra et al., 2001; Ross et al., 2007).

Since its development the COWAT has been used to detect deficits in verbal communication after a brain lesion, and to monitor delays in a child's language development (Loonstra et al., 2001). In addition to the sensitivity to motor and cognitive speed, the COWAT is also an indicator of sufficient executive functions such as suppression of interference and response inhibition, cognitive flexibility, regulation of attention, working memory process and strategy utilization (Ross et al., 2007). It has been recommended by the Clinical Data Interchange Standards Consortium for assessments in TBI and Neuropsychological impairment.

Though the COWAT is one of most commonly used measures of verbal fluency, previous studies have revealed that performance on the COWAT can be affected by other variables such as; age, where an improvement is seen until about 30 years of age and a decline is seen after 60 years of age (Rodriguez-Aranda & Martinussen, 2006); sex where women tend to perform slightly better than men (Barr, 2003); ethnicity where White individuals tend to perform better than identified minorities (Johnson-Selfridge et al., 1998); and education where a higher education is correlated with a higher score on the COWAT (Loonstra et al., 2001). Despite the possible effect of cofounding variables, the COWAT has shown to have both high internal consistency of 0.83 and significant test-retest reliability ($r=0.74$, $p<0.001$) (Ruff et al., 1996). Ruff et al. in 1996 reported a set of

updated norms based on a sample of 360 community volunteers that is more commonly used in the literature.

1.5.2 Grooved Pegboard Test (GPT)

The Grooved Pegboard Test (GPT; Køve, 1963) is one of the most commonly used measures of motor performance and is included in the Wisconsin Neuropsychological Test Battery, the Repeatable Cognitive-Perceptual-Motor Battery, and the Halstead-Reitan Battery (Bryden & Roy, 2005). The GPT consists of slotting 25 one-inch pegs with a ridge running along one side, into a 5x5-inch metal surface. The holes, which the pegs are to be slotted into, are identical with varying orientations so the subject must rotate the peg to align the ridge before slotting the peg in. Causby et al., (2014) determined the GPT to have sufficient reliability with correlations ranging from 0.84 to 0.86 and has demonstrated high test-retest reliability ($r=0.91$, $p<0.001$) (Wang et al., 2011). The GPT has also shown convergent reliability with other tests of motor performance such as the Finger Tapping Test (Halstead, 1947), O'Connor Tweezer Dexterity Test (O'Connor, 1926), and Purdue Pegboard Test (Tiffin, 1948) in addition to a significant correlation with other dexterity-related criteria (Causby et al., 2014; Wang et al., 2011).

The 25 grooved holes are arranged in a 5x5 pattern, and subjects must insert the pegs in a fixed pattern from side to side and top to bottom. An individual's score is the total amount of time it takes to insert all 25 pegs (Ruff & Parker, 1993). The rotation of the pegs in the GPT adds a layer of complexity that allows it to be sensitive to general cognitive decline due to medication or disease progression in various populations (Bryden & Roy, 2005). Previous literature has shown a practice effect (Schmidt et al., 2000), where an individual is able to perform faster on repeated trials; a sex effect (Bornstein, 1985; Bryden & Roy, 2005; Ruff & Parker, 1993) where females performed faster than males; an education effect (Ferrett et al., 2014; Ruff & Parker, 1993), where increased education was associated with a faster completion; and an age effect (Bornstein, 1985; Ferrett et al., 2014; Ruff & Parker, 1993; Wang et al., 2011), where improved performance is seen with an increase in age in a pediatric and adolescent population and a decreased performance with an increased age in adult population. In a

comparison of pegboard scores the effect of handedness has been both affirmative (Bryden & Roy, 2005) and negative (Ruff & Parker, 1993). The GPT has been used in studies looking at motor deficits post-concussion in adolescents (Servatius et al., 2018), and athletes (Tarazi et al., 2018). It has been cited as a tool that has promise in detecting persistent motor and cognitive deficits in the subacute period after a concussion (Servatius et al., 2018).

1.5.3 Trail Making Test

The Trail Making Test (TMT) is a popular neuropsychological instrument used to screen for neurological impairment and detect neurological disease (Bowie & Harvey, 2006). TMT has also been identified as a significant predictor of anxiety disorder following TBI (de Guise et al., 2016). The TMT consists of two test that measure different areas of cognition. Trail A (TMT A) is generally understood to look at visual searching, processing speed and motor speed, while Trail B (TMT B) is generally understood to assess higher-level cognitive skills such as visuospatial understanding, divided attention, working memory, mental flexibility, and executive functioning (Bowie & Harvey, 2006; Bracken et al., 2019; de Guise et al., 2016).

Both TMT A and TMT B consist of connecting 25 circles distributed over a white sheet of paper. In TMT A, the circles are numbered 1 to 25, and participants are asked to connect each circle in numerical order (Bowie & Harvey, 2006). TMT B consists of both numbers from 1 to 13 and letters A to L. Participants are asked to connect all 25 numbers and letters in ascending order, alternating between the numbers and letters. For example: participants would start at "1" and then must connect it to the encircled "A", followed by the second number "2", then the second letter "B". Encircled numbers and letters are organized in a semi-random way, guaranteeing that the participant does not draw any overlapping lines. Both tests are scored based on the total amount of time it takes the participant to complete connecting all 25 letters and numbers in the appropriate order. Typically test administration is discontinued at 300 seconds (Bowie & Harvey, 2006; Reitan, 1958).

TMT has been shown to be a reliable testing measure in general community population (Tombaugh, 2004), as well as a reliable indicator of brain impairment associated with various lesions on the brain (Reitan, 1958). Both TMT A and TMT B have demonstrated to have a main effect of IQ (Bowie & Harvey, 2006; Diaz-Asper et al., 2004), age (Bornstein, 1985; Bowie & Harvey, 2006; de Guise et al., 2016; Tombaugh, 2004), and education (Bornstein, 1985; Bowie & Harvey, 2006; de Guise et al., 2016; Tombaugh, 2004). In general, a better score was associated with a younger age and higher education (Bornstein, 1985; Tombaugh, 2004). The TMT has been shown to be sensitive to typical age-related differences as a higher age was associated with a longer time to complete part A and B in the absence of motor or sensory deficits (Bornstein, 1985). TMT is commonly employed as a measure of cognition post-concussion (Collie et al., 2006).

1.6 Racial Differences

It is estimated that while approximately 13.4% of the population of the United States identified as Black/African American, this population makes up approximately 31% of athletes participating in high school athletics. Black/African Americans have a strong representation within high-risk sports as they make up 30% of youth participants in American Football, far higher than their presence in the general population (Wallace, Moran, et al., 2020). Though Black/African American athletes are overrepresented in concussion-risk sports, they are less likely to be diagnosed with a concussion in an emergency department when compared to White/non-Hispanics (Wallace, Moran, et al., 2020). This underrepresentation is possibly due to the fact that non-white minorities are significantly more likely to be seen by a resident rather than an emergency medical technician, staff physician or other provider and less likely to be referred to a physician after discharge (Bazarian et al., 2000). As a concussion is a complex injury, residents and clinicians may overlook sociodemographic factors that may affect clinical diagnosis, treatment, and outcomes (Wallace, Worts, et al., 2020).

One such factor is socioeconomic status (SES), also known as sociodemographic characteristics, sociocultural factors, or socioeconomic position. SES has influenced clinical outcomes dating as far back as the Pellagra epidemic in the 1900s (Goldberger et al., 1920). It has been found that community poverty and health disparities in the Unites

States are more common amongst racial and ethnic minorities and that African Americans comprise the majority of underserved, low-income student athletes (Wagner et al., 2020; Wallace, Worts, et al., 2020). SES has been directly linked to poor performance on cognitive testing, specifically those with outcomes that measure processing speed, memory, and reaction time (Houck et al., 2018; Wallace, Worts, et al., 2020). Houck et al., (2017) suggested that this poor performance may be due to environmental factors associated with low SES, as it has been shown that SES plays a large role in an individual's access to education and is significantly associated with cumulative reading time (Houck et al., 2018; Wallace, Worts, et al., 2020).

Though SES plays a large role in how an individual scores on a neurocognitive test, race, independent of SES has been shown to be significantly associated with neurocognitive test performance (Wallace, Moran, et al., 2020). Black/African American individuals are 2.4 times more likely than White individuals to experience clinically significant declines in at least one neurocognitive measurement by seven days post-concussion (Kontos et al., 2010). Amongst collegiate athletes, White/non-Hispanic's perform significantly better than Black/African American athletes on measures of verbal memory, visual memory, reaction time and visual motor processing speed (Wallace, Moran, et al., 2020). Though the prevalence of concussion diagnosis amongst Black/African Americans is lower than their White counterparts, they have repeatedly demonstrated poorer performance postconcussion on neurocognitive measures.

Symptom presentation has also been shown to differ by race. Black student-athletes reported higher symptoms post-concussion and more frequently reported loss of consciousness at the time of injury when compared to White student-athletes (Wallace, Worts, et al., 2020; Wallace, Hou, et al., 2021). However, in direct contradiction with a more severe symptom presentation, it has been reported that Black/African American athletes reach an asymptomatic status earlier and return to school sooner than their White counterparts (Yengo-Kahn et al., 2021). It was suggested that the observed shorter symptom duration amongst Black/African American athletes may be due to a complex interplay amongst race, attitudes towards concussions, reporting behaviour, SES and concussion knowledge (Yengo-Kahn et al., 2021). Previous research has shown that

Black/African American athletes and parents have less knowledge regarding concussion symptoms and management (Wagner et al., 2020; Wallace, Affagato, et al., 2020; Wallace, Beidler, et al., 2021), indicating that the faster return to asymptomatic status is not an accurate representation of the injury progression.

1.7 Purpose and Hypothesis

Currently the research surrounding the impact of race on concussion presentation and outcomes is extremely limited. Therefore, the overall objective of this thesis was to examine race-related differences in concussion presentation in individuals who identify as Black/African American compared with those who identify as White.

The purpose of chapter two was to examine race-based differences in concussion prevalence and outcomes currently documented in the literature. The first aim was to systematically review the reported prevalence rates of concussion in Black/African American and White Individuals. The second aim was to systematically review differences between races in post-concussive neurocognitive function and symptom presentation and perform a meta-analysis of the included studies. It was hypothesized that White individuals would have a higher prevalence of concussion when compared with Black/African American individuals and that White individuals would perform better on neurocognitive testing measurements and report lower symptom scores.

The purpose of chapter three was to determine whether there are race-based differences in symptom severity and cognitive outcomes in the acute phase post-concussion in young adults (18-25 years old). Specifically, we aimed to determine differences in symptom severity and cognitive performance in concussed White and Black/African American individuals across a one-month post-injury time frame and compared with published normative values. It was hypothesized that performance on cognitive testing would be lower for Black/African American individuals when compared to their White counterparts and normative scores. It was also hypothesized that Black/African American individuals would report a greater severity of concussive symptoms when compared to their White counterparts.

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Chapter 2

2 The Prevalence and Effects of Race on Symptom and Neurocognitive Performance in a Concussed Population: A Systematic-Review and Meta-Analysis

2.1 Introduction

It is estimated that 38 million children and 170 million adults participate in physical activity and sport annually (*National Council of Youth Sports Report on Trends,* 2018). Many of these activities have been found to have an increased risk of mild traumatic brain injury (mTBI) (Daneshvar et al., 2011). Information collected in the Injury Surveillance System (ISS), used by the National Collegiate Athletic Association (NCAA) to collect data pertaining to injury presence across 16 sport activities, found that from 1988-2004 the rate of concussion doubled from 0.17 to 0.34 of 1000 athlete-exposures (Daneshvar et al., 2011). Over this period more than 9000 concussions were reported, with an average of 563 per year (Hootman et al., 2007). Some of the identified risks that increase the chances of sustaining a sport related concussion (SRC) include: Sport type which includes allowance of bodily contact, match vs. practice and use of protective equipment (Abrahams et al., 2014; Hootman et al., 2007; Zuckerman et al., 2015), presence of previous concussion (Abrahams et al., 2014; Zuckerman et al., 2015), female sex (Abrahams et al., 2014; Hootman et al., 2007; Zuckerman et al., 2015), and increased age (Abrahams et al., 2014; Zuckerman et al., 2015). In 2021 it was reported that the NCAA student-athlete population was comprised of approximately 35% racial or ethnic minorities (*NCAA Demographics Database*, n.d.). Within the high-risk, revenue producing sports (e.g. football, men's and women's basketball) nearly 50% of collegiate participants identify as Black (Wallace, Bretzin, Beidler, et al., 2021). Due to this over representation in high risk sports the interaction between race and concussion has been highlighted as an area in need of further exploration (Wallace et al., 2018).

As there is currently no widely accepted objective test, concussions are diagnosed based on the presence of symptoms. These symptoms are characterized by transient neurological changes and can include many different symptoms such as: confusion,

disorientation, headache, nausea, balance problems, irritability, and depression (Currie et al., 2017; Junn et al., 2015). Due to the extreme variance in concussion symptom presentation clinicians often group symptoms into categories; cognitive disturbance, physical symptoms, emotional/mood disturbance (Currie et al., 2017; MacFarlane & Glenn, 2015). On concussion grading scales symptoms of amnesia and loss of consciousness (LOC) are often reported as being indicative of a more severe concussion (Currie et al., 2017). Recently it was found that Black/African American individuals tend to report a higher total number (Holmes et al., 2016; Wallace, Beidler, Covassin, et al., 2021; Wallace, Bretzin, Beidler, et al., 2021) and severity (Wallace, Hou, Hajdu, et al., 2021) of symptoms post-concussion. Specifically higher scores have been observed in symptoms categorized as physical and sleep domains (Wallace, Beidler, Covassin, et al., 2021). Additionally, in their analysis of adolescent athletes, Wallace, et al., (2021) found that Black athletes more frequently reported LOC (21.9%) when compared with White athletes (11.8%) (Wallace, Hou, Hajdu, et al., 2021).

One common post-concussion symptom is cognitive dysfunction. Cognitive dysfunction may cause a reduction in different areas of memory, reaction time, processing speed, and executive function (Lam et al., 2014). On symptom measures patients may report feelings of "fogginess", feeling run down, difficulty remembering (Bauer & Jaffee, 2021). As cognitive function/dysfunction is a term that encompasses many different aspects of cognition, different scales have been developed to assess different cognitive domains. It has generally been found that compared with White, Black/African American individuals tend to have lower neurocognitive performance at baseline (Caccese et al., 2020; Norheim et al., 2018;. Wallace et al., 2018; Wallace, Moran, Beidler, et al., 2020; Wallace, Worts, Moran, et al., 2020) and post-concussion (Alosco et al., 2019; Kontos et al., 2010; Wallace, Beidler, Covassin, et al., 2021). Specifically, decreased performance has been seen in measures of visual memory (Wallace, Moran, Beidler, et al., 2020; Wallace, Bretzin, Beidler, et al., 2021), visual motor processing speed (Wallace, Moran, Beidler, et al., 2020; Wallace, Bretzin, Beidler, et al., 2021), verbal memory (Holmes et al., 2016; Wallace, Moran, Beidler, et al., 2020) and reaction time (Caccese et al., 2020; Wallace, Moran, Beidler, et al., 2020).

Though racial differences in concussion prevalence and outcomes have been identified, there is limited literature in this area. To this author's knowledge, to date no systematic review has been completed regarding the relationship between identifying as Black/African American and concussion outcomes. Therefore, there are two primary objectives of this paper: 1) to provide a systematic review of the literature pertaining to the prevalence of concussed Black/African American and White individuals; and 2) to provide a systematic review and meta-analysis of the differences between races in neurocognitive function and concussion symptom presentation. It was hypothesized that there would be a lower prevalence of concussed Black/African American individuals when compared with White individuals. It was also hypothesized that Black/African American individuals would score worse on neurocognitive assessments and report higher (worse) symptom scores.

2.2 Methods

2.2.1 Literature Search and Data Extraction

This review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Moher et al., 2009). An electronic search of the literature was conducted via PubMed, Medline (OVID), Scopus and Web of Science. The search was performed on articles up to and including articles published until January 5, 2022. To identify these articles the following search terms were used: (Black OR "African American") AND (concussion OR "brain concussion" OR "mild traumatic brain injury" OR mTBI) and the following MeSH terms: ("blackness"[All Fields] OR "blacks"[MeSH Terms] OR "blacks"[All Fields] OR "black"[All Fields] OR "African American"[All Fields]) AND ("brain concussion"[MeSH Terms] OR ("brain"[All Fields] AND "concussion"[All Fields]) OR "brain concussion"[All Fields] OR "concussion"[All Fields] OR "concussions"[All Fields] OR "concussed"[All Fields] OR "concussive"[All Fields] OR "brain concussion"[All Fields] OR "mild traumatic brain injury"[All Fields] OR "mTBI"[All Fields]).

After completing the initial search all articles were run through Covidence software where duplicate items were removed. To be considered for inclusion in this review articles had to; 1) be original research (including randomized clinical trials (RCT), quasiexperimental designs, case studies and series, prospective and retrospective studies, cohort studies, and pilot studies), 2) include human participants who have sustained a concussion or mild traumatic brain injury, 3) include results that compare study outcomes between Black/African American and White/Caucasian.

Articles published in English, with any sample size were included. There were no limitations to the age of participants, mechanism of injury, or time of assessment. Review articles and articles published in only abstract form were excluded. In addition, articles that contained only baseline measures of concussive measurements (i.e., no postconcussion measures) were excluded.

Stage 1 consisted of a screening of the titles and abstracts performed by one author (TM). Stage 2 consisted of a full text review of the articles included in Stage 1. If at any stage the above criteria were not met, the study was excluded. Studies were then categorized by the type of information that was explored. The following were extracted; study information (type of study, location of study, study duration, study funding sources), population characteristics (population type, sample size, race, age, sex), concussion assessment(s) and key findings on outcome measures related to prevalence, neurocognitive assessments, and/or symptom scales.

The meta-analysis was conducted in reference to the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) protocol (Stroup et al., 2000). Data extracted from the included studies consisted of information on the design, participants (sample size, racial profile), details of the assessment(s) and findings on prevalence rates as well as neurocognitive and symptom outcome measures associated with concussion.

2.2.2 Prevalence Calculations

The percentage of Black/African American, White, and individuals of other races, termed as "Other", was calculated in the studies that addressed the primary outcome of
prevalence. This percentage was calculated based on each racial groups reported number of concussed individuals divided by the total study population. These percentages were used to calculate the average percentage of concussion in each racial group across all included studies and the magnitude of the difference across groups was determined using Cohen's *d* effect sizes.

2.2.3 Meta-Analysis Effect Size Calculations

Using Comprehensive Meta-Analysis (CMA), Version 3.0 (Biostat, Engelwood, NJ), Hedge's g was calculated and used to compute the standardized effect size for each study as the difference in Black/African American and White scores, divided by the pooled standard deviation (SD).

Across studies a random-effect model was used, which assumes that participants are sampled from different populations and that the true effect varies across studies. The overall effect size was calculated through the weighted means across studies of the sample effect size estimates. The weights of each effect sizes were determined by its sample error which is based on sample size and variability. Therefore, more weight is given to studies with larger sample sizes and low sample errors (Hedges & Vevea, 1998).

For the meta-analyses, the scales were categorically coded as Neurocognitive or Symptom scales. Neurocognitive scales consisted of two scales, each with four subscales; Principal Component Analysis subscales: Psychomotor speed/executive function, Verbal Episodic Memory, Visual Episodic Memory, Behaviour/mood; Immediate Post-Concussion Assessment and Cognitive Test (ImPACT) subscales: Verbal Memory, Visual Memory, Visual Motor Processing Speed, and Reaction Time. Symptom scales consisted of 25 subscales across six scales. ImPACT subscales: Total Symptoms; ImPACT Concussion Symptom Cluster Score subscales: Physical Score Endorsement, Cognitive Score Endorsement, Emotional Score Endorsement, Sleep Score Endorsement; Glasgow Coma Scale Subscale: Mild, Moderate, Severe; Activity and Sport Behaviour Following Injury subscale: Any Activity Change, Slept More, Slept Less, More Television, Less Television, More Schoolwork, Less Schoolwork, More Video Games, Less Video Games, Any Sport Behaviour Changes, Less Reckless, Changed Protective

Equipment, Stopped Playing offending Sport; and On Field Interview domains: Loss of consciousness, and Amnesia.

Effect sizes were coded as "positive" when studies reported White individuals performed better on neurocognitive assessments or reported fewer symptoms, and "negative" when Black/African American individuals performed better on neurocognitive assessments or reported fewer symptoms. A higher score represented better performance/outcome on: Principle Component Analysis subscales (Psychomotor Speed/Executive function, Verbal Episodic Memory, Visual Episodic Memory, Behaviour Mood) which was represented by a z-score across a series of assessments, as well as the ImPACT subscales (Verbal Memory, Visual Memory, Visual Motor Processing Speed). A lower score represented better performance/outcome on: ImPACT subscales (Reaction time, Total Symptoms, Physical Score Endorsement, Cognitive Score Endorsement, Emotional Score Endorsement, Sleep Score Endorsement), Glasgow Coma Scale, or a lower reporting on the Activity and Sport Behaviour Following Injury, On-field interview (Loss of Consciousness and Amnesia), and Cognitive Related Symptoms.

2.2.4 Heterogeneity and Publication Bias

If all studies on concussion and race differences produce the same results the standardized effect will be homogenous. If different designs/methodologies produce different results across studies the standardized effect will be heterogeneous (Hedges & Pigott, 2001). Publication bias was assessed through a funnel plot of standard error versus Hedge's g effect size. The plot may be assessed visually and if bias is present, the funnel plot will be skewed and asymmetrical, whereas if there is an absence of bias the plot will represent a symmetrical inverted funnel (Egger et al., 1997).

2.3 Results

A total of 447 articles were identified via the electronic search. Of these 447, 234 were duplicates and removed, leaving 213 articles to be screeded for eligibility. 49 articles were retrieved for the full text detailed evaluation. Within these 49 reviewed articles, 17 where included, though two studies (Alosco et al., 2019; Brown et al., 2004) were identified that compared other aspects of health between Black/African American and

White individuals post-concussion. There were not enough studies with consistent outcomes on these factors to do a meta-analysis, and therefore were excluded, resulting in a total of 15 studies being included. 10 met the inclusion criteria for the systematic review on prevalence (see Methods for criteria). Seven articles met the inclusion criteria for the Meta-Analysis of neurocognitive and symptom outcomes. Two of these articles (Wallace, Hou, Hajdu, et al., 2021; Wallace, Moran, Beidler, et al., 2020) were included in both the prevalence systematic review and symptom meta-analysis. A PRISMA diagram of the screening process is shown in Figure 1.

Figure 1. PRISMA Flow Diagram. PRISMA flow diagram as follows: Records after duplicates removed 213; Records screened 213, and Records excluded 34. The inclusion/exclusion criteria of each step are outlined in the methods.

2.3.1 Participant Characteristics

The 15 articles included a total of 2,051,392 participants with 733,512 concussed participants (69,621 Black/African American and 384,909 White). One study did not report the number of White participants (Ganti et al., 2015). In total two studies included children and adolescents participants (\leq 18 years) (Haarbauer-Krupa et al., 2021; Lyons et

al., 2019), one included adults $(>18$ years) (Rhame et al., 2021), 10 included both child and adult participants (Aggarwal et al., 2020; Bazarian et al., 2000; Bazarian et al., 2003; Holmes et al., 2016; Kontos et al., 2010; Lemme et al., 2020; Troyanskaya et al., 2021; Wallace, Hou, Hajdu, et al., 2021; Wallace, Moran, Bretzin, et al., 2020; Wallace & Mannix, 2021) and two did not report participant age ranges (Ganti et al., 2015; Wallace, Beidler, Covassin, et al., 2021)

2.3.2 Prevalence

Ten studies were identified that examined prevalence of concussed individuals in different racial groups (Black/African American, White, and Other) (Table 1). Where a single study had more than one population (Haarbauer-Krupa et al., 2021) a separate percentage was calculated for each population. The majority of these studies took place in a population based on Hospital Admissions with one (Wallace, Hou, et al., 2021) taking place in a student-athlete population. Across these studies, the majority of the concussed population identified as White (70.11%), followed by those that identified as Other (16.55%) while Black/African American individuals made up the smallest percentage (13.65%) of those diagnosed with a concussion. There is a large effect size (*d =* 5.81) for the difference in prevalence between Black/African American and White.

Table 1 Summary of Systematic Review of Prevalence Studies

NR = not reported

2.3.3 Meta-Analysis

Three articles were identified that contained at neurocognitive assessments (Table 2) and six that contained symptom assessments (Table 3). Two studies (Kontos et al., 2010; Wallace, Beidler et al., 2021) contained assessments of both neurocognitive performance and symptom presentation. Where a single study had more than one scale or time point used, an effect size was calculated for each assessment.

A total of 20 standardized effect sizes were calculated for neurocognitive assessment scales (Figure 2). Alosco et al., (2019), Wallace, Beidler et al., (2021) and Kontos et al., had more than one measure of neurocognitive function, and therefore produced multiple effect sizes. Most neurocognitive scales had a positive effect, meaning that White individuals performed better on these assessments then Black/African American. However, the overall effect size was $g=0.3$ ($p<0.001$) indicating a small effect.

A total of 31 effect sizes were calculated for symptom scores (Figure 3). Kontos et al., (2010), Wallace, Beidler et al., (2021), Wallace, Hou et al., (2021), Wallace, Moran, Bretzin et al., (2020) and Yengo-Kahn et al., (2021) had more than one measure of symptom presentation, and therefore produced multiple effect sizes. Just over half of the effect sizes were positive, indicating White participants reported lower symptoms. However, the overall effect size was $g=0.1$ indicating there was no effect of race on symptom presentation post-concussion.

Study	Study	Sample		Scale	Time of	Subscale	Black/African	White Score	
	Design	N	Age (yrs	Pop.		Collection		American Score	
			$± sd$ or	Type					
			range)						
(Alosco et	Case	68	54.69 \pm	Athlete	Principal	After	Psychomotor	z-score Mean $= -0.47$	z-score Mean $= 0.29$
al., 2019)	Control	B: 27	8.16		Component Analysis (PCA)	Career Retirement	speed/executive	$Sd = 0.78$	$Sd = 0.72$
		W: 41					function		
		O:0					Verbal Episodic	z -score Mean = -0.24	z-score Mean $= 0.03$
							Memory	$Sd = 0.58$	$Sd = 0.99$
							Visual Episodic	z-score Mean = 0.13	z-score Mean = 0.06
							Memory	$Sd = 0.91$	$Sd = 0.94$
							Behaviour/Mood	z-score Mean $= 0.25$	z-score Mean $= 0.32$
								$Sd = 0.87$	$Sd = 0.09$
(Kontos et	Case	96	$19.33 \pm$	Athlete	ImPACT	2 Days	Verbal Memory	$Mean = 0.77$	$Mean = 0.81$
al., 2010)	Control	B: 48	2.08		version 2.0	Post-Injury		$Sd = 0.13$	$Sd = 0.12$
		W: 48			(NeuroHealth		Visual Memory	$Mean = 0.68$	$Mean = 0.69$
		O:0			System)			$Sd = 0.15$	$Sd = 0.14$
							Reaction Time	$Mean = 0.61$	$Mean = 0.57$
								$Sd = 0.19$	$Sd = 0.13$
						7 Days Post-Injury	Motor Processing	$Mean = 34.02$	Mean = 37.57
							Speed	$Sd = 8.90$	$Sd = 8.71$
							Verbal Memory	$Mean = 0.82$	$Mean = 0.85$
								$Sd = 0.11$	$Sd. = 0.11$
							Visual Memory	$Mean = 0.72$	$Mean = 0.75$
								$Sd = 0.13$	$Sd = 0.12$
							Reaction Time	$Mean = 0.58$	$Mean = 0.55$
								$Sd = 0.11$	$Sd = 0.1$
							Motor Processing	$Mean = 36.54$	$Mean = 40.7$
							Speed	$Sd = 8.46$	$Sd = 7.82$
(Wallace,	Cohort	235	B.M.	Athlete	Immediate	Within 14	Verbal Memory	M. Mean = 79.30	M. Mean = 81.03
Beidler,		B : 81	$19.48 \pm$		Post-	days of		$M. Sd = 12.18$	M. $Sd = 13.90$
Covassin,		W:154	1.2		Concussion	injury		F. Mean = 83.81	F. Mean = 83.20
et al.,		O:0			Assessment			$F. Sd = 13.74$	$F. Sd = 11.63$

Table 2 Summary of Systematic Review of Studies with Neurocognitive Assessments

B = Black/African American; W = White; O = Other; M = Male; F = Female

Study	Study		Sample		Scale	Time of	Subscale	Black/African	White Score
	Design	${\bf N}$	Age (yrs $±$ sd or	Pop. Type		Collection		American Score	
			range)						
(Holmes et al., 2016)	Case series	1429 B : 170 W: 1146 O: 113	$2-19$	Hospital Admission	Cognitive related symptoms	7.6 ± 4.3 days post- Injury	Present	$N = 130$ % 76.5%	$N = 899$ $% = 78.4%$
(Kontos et al.,	Case Control	96 B: 48	$19.33 \pm$ 2.08	Athlete	ImPACT version 2.0	2 Days Post-Injury	Total Symptoms	Mean = 16.42 $Sd = 20.25$	$Mean = 18.67$ $Sd = 19.78$
2010)		W: 48 O: 0			(Neuro Health System)	7 Days Post-Injury	Total Symptoms	$Mean = 9.0$ $Sd = 13.33$	$Mean = 12.31$ $Sd = 14.06$
(Wallace, Beidler, Covassin, et al., 2021)	Cohort	235 B: 81 W: 154 O:0	B.M.: $19.48 \pm 1.$ $\overline{2}$ B.F. $19.63 \pm 1.$ $\overline{4}$ W.M.: $19.85 \pm 1.$ $\overline{2}$ $W.F.$: $19.48 \pm 1.$ $\overline{2}$	Athlete	Immediate Post- Concussion Assessment and Cognitive Testing (ImPACT)	Within 14 days of injury	Total Symptoms	M. Mean $= 12.41$ $M. Sd = 13.95$ F. Mean = 18.43 $F. Sd = 15.73$	M. Mean $= 11.12$ $M. Sd = 12.40$ $F. Mean = 12.14$ $F. Sd = 13.05$
(Wallace, Hou,	Cohort	582 B: 96	$12 - 23$	Athlete	Interview	On-field interview	Loss of Consciousness	$N = 21$ $% = 21.9%$	$N = 57$ $% = 11.8%$
Hajdu, et al., 2021)		W: 486 O: N/R					Amnesia	$N = 14$ $% = 14.6%$	$N = 94$ $% = 19.3%$
(Wallace, Moran,	Cross Sectional	2857 B: 459	$16.41 \pm$ 1.90	Hospital Admission	Glasgow Coma Scale	N/R	Mild (score 13- 15)	$N = 324$	$N = 1615$
Bretzin,		W: 2329					Moderate (score	$N = 3$	$N = 7$

Table 3 Summary of Systematic Review of Studies with Symptom Assessments

B = Black/African American; W = White; O = Other; M = Male; F = Female

Figure 2. Effect sizes for Neurocognitive Assessments. Twenty effect sizes were calculated from three studies. *Outcomes:* 1a, Principle Component Analysis – Psychomotor speed/executive function; 1b, Principle Component Analysis – Verbal Episodic Memory; 1c, Principle Component Analysis – Visual episodic memory; 1d, Principle Component Analysis – Behaviour/mood; 3a, ImPACT – Verbal Memory; 3b, ImPACT – Visual memory; 3c – ImPACT Visual Motor Processing; 3d, ImPACT – Reaction Time. *Time Points:* A, <1 week; B, 1 weeks – 1 Month; $C \geq 3$ Months.

Favours Black

Favours White

39

Figure 3. Effect sizes for Symptoms Assessments. Thirty-one effect sizes were calculated from five studies. *Outcomes*: 3f, ImPACT – Total Symptoms; 3ga, ImPACT Concussion Symptom Cluster – Physical Score Endorsement; 3gb, ImPACT Concussion Symptom Cluster – Cognitive Score Endorsement; 3gc, ImPACT Concussion Symptom Cluster – Emotional Score Endorsement; 3ga, ImPACT Concussion Symptom Cluster – Sleep Score Endorsement; 4, Cognitive Related Symptoms; 5a, Glasgow coma scale – mild; 5b, Glasgow coma scale – moderate; 5c, Glasgow coma scale – severe; 6a, Activity and Sport Behaviour Following Injury – Any activity change; 6b, Activity and Sport Behaviour Following Injury – Slept more; 6c, Activity and Sport Behaviour Following Injury – Slept less; 6d, Activity and Sport Behaviour Following Injury – more television; 6f, Activity and Sport Behaviour Following Injury – Less television; 6g, Activity and Sport Behaviour Following Injury – More schoolwork; 6h, Activity and Sport Behaviour Following Injury – Less schoolwork; 6i, Activity and Sport Behaviour Following Injury – more video games; 6j, Activity and Sport Behaviour Following Injury – less video games; 6k, Activity and Sport Behaviour Following Injury – any sport behaviour changes; 6l, Activity and Sport Behaviour Following Injury – less reckless; 6m Activity and Sport Behaviour Following Injury – changed protective equipment; 6n, Activity and Sport Behaviour Following Injury – stopped playing offending sport; 7a, Loss of Consciousness; 7b, Amnesia. *Time Points*: Time Point: A, <1 week; B, 1 weeks – 1 Month; C, ≥ 3 Months

2.3.4 Risk of Bias

Symmetry was observed in all the funnel plots (Figure 4, Figure 5), indicating an absence of publication bias.

Funnel Plot of Standard Error by Hedges's g

Figure 4. Funnel plot of standard error by standard difference in means for

Neurocognitive Assessment. Effect sizes calculated from included studies is represented by open circles. The 95% confidence interval (CI) is represented by the two angled lines and Hedges' g mean is represented by the central vertical line. Studies that do not follow the expected results have open circles that fall outside the 95% CI lines, which translates to a weak or low publication bias.

Funnel Plot of Standard Error by Hedges's g

Figure 5. Funnel plot of standard error by standard difference in means for Symptom Assessments. Effect sizes calculated from included studies is represented by open circles. The 95% confidence interval (CI) is represented by the two angled lines and Hedges' g mean is represented by the central vertical line. Studies that do not follow the expected results have open circles that fall outside the 95% CI lines, which translates to a weak or low publication bias.

2.4 Discussion

The influence of race on concussion presentation and outcomes is an emerging topic within the literature. The first objective of this study was to provide a systematic review of the literature pertaining to prevalence of concussion amongst Black/African American in relation to White individuals. As hypothesized Black/African American individuals reported a lower rate of concussion when compared to their White counterparts (*d =* 5.81). The second objective was to provide a systematic review and meta-analysis of the differences between races on neurocognitive performance and symptom presentation post-concussion. As hypothesized race influenced cognitive performance post-concussion with White individuals ($g = 0.3$) performing better post-concussion. It was found in this Meta-Analysis that there was no effect of race on symptom presentation $(g = 0.1)$ though

the findings did point to a trend that White individuals reported more favourable symptom outcomes post-concussion. The 15 studies included in this systematic review and meta-analysis, therefore provide evidence to support the idea that race is an important consideration in interpreting concussion prevalence and outcomes.

2.4.1 Prevalence

To this author's knowledge this is the first systematic review addressing racial differences in concussion prevalence. The findings of this study indicate that there is a lower prevalence of Black/African Americans (13.65%) versus White (70.11%) individuals diagnosed with a concussion.

The non-specific nature of concussion symptoms has the potential to lead to misdiagnosis as many of the symptoms may arise from other health complications (Currie et al., 2021). As a concussion is diagnosed based on symptom presentation it is essential that a patient or caregiver have a strong understanding of the symptoms and seek out the appropriate medical care. Previous literature has suggested there is a disparity in concussion symptom knowledge between Black/African American and White individuals. Work by Wallace et al., (2020) found that Black/African American parents/guardians of athletes, had below average understanding of concussion symptoms. White parents/guardians were able to identify 8% more symptoms than Black/African American parents/guardians (Wallace, Affagato, Brooke, et al., 2020). Further work by Wallace, Beidler et al., (2021) found that amongst collegiate athletes, Black athletes reported lower recognition of concussion symptoms specifically; dizziness, memory loss, being in a "fog," difficulty concentrating, and drowsiness (Wallace, Beidler, Kerr, et al., 2021). These demographic differences suggest inequalities in concussion education that may impact the likelihood of seeking medical attention. Such disparities may therefore account for the large difference in concussion prevalence revealed in the current systematic review. As all but one study (Wallace, Hou, et al., 2021) was based on a hospital population, it is likely Black/African American individuals are underrepresented in this cohort, as they would be less likely to recognize concussive symptoms and therefore seek medical treatment.

When treatment for concussion is sought, potential issues with medical jargon on symptom checklists may inhibit individuals from properly identifying symptoms. The symptoms "fatigue" and "nausea" are terms that those less familiar with medical terminology may have difficulty identifying (Wallace, Beidler, Kerr, et al., 2021). Previous literature has shown that Black/African Americans have lower health literacy when compared to White individuals (Kelly & Haidet, 2007; Shea et al., 2004). Lower health literacy has been linked to poor health outcomes, poorer health status and less satisfaction with healthcare (Shea et al., 2004). Such misunderstandings may lead to misdiagnosis of concussion and therefore also contribute to the large discrepancy in prevalence between races, as reported in this systematic review.

There is also evidence to suggest that Black communities do not receive the same quality and standard of care afforded to White communities (Wallace, Beidler, Kerr, et al., 2021). Implicit bias of practitioners towards minorities is a topic that has been widely explored in the literature (Blair et al., 2013; FitzGerald & Hurst, 2017; Fyffe et al., 2011; Williams & Wyatt, 2015). It has been found that clinicians have moderate to strong implicit bias against Black patients (Blair et al., 2013), which have been directly linked to biased treatment recommendations in the care of Black patients (Williams & Wyatt, 2015). Feelings of distrust of healthcare practitioners, as well as reduction in comfort experienced by Black/African American individuals leads to delays in seeking medical care, (Blair et al., 2013; Feagin & Bennefield, 2014), which due to the nature of concussion diagnosis may contribute to an under-reporting and underdiagnosis of concussions in Black/African American individuals.

Another factor that may contribute to the large differences in concussion prevalence observed in this study is the fact that Black/African American individuals are not typically provided equal access to healthcare resources (Wallace, Beidler, Kerr, et al., 2021). All of the studies included in the systematic review were conducted in the USA, where many patients often forgo the medical care they need, as they cannot afford it (Dickman et al., 2017). In 2020 it was reported that 19.5% of Black individuals living in USA were below the poverty line, well above the percentage of the total population living in poverty (11.4%) and more than double that of White individuals (8.2%) (Shrider et al., 2021). In 2019 Pavlov et al., reported that on average over a three-month period an individual may spend \$6,859 (SD=\$26,721) in concussion related healthcare costs (Pavlov et al., 2019). This cost may act as a deterrent to seeking appropriate medical care, particularly for Black/African American individuals, resulting in concussions going under reported.

2.4.2 Neurocognitive Outcomes

The results from this meta-analysis indicated there was a difference between Black and White individuals on post-concussion neurocognitive measures. These results indicated that across three studies and eight different measurement subscales, White individuals generally performed better on neurocognitive assessments when compared to Black/African American individuals, indicating better outcomes, however, the overall effect was small $(g = 0.3)$. Of the 20 different effect sizes calculated in the meta-analysis for neurocognitive outcomes, Black/African American individuals performed better on three (1c, Alosco et al., 2019; Female, 3a Wallace, Beidler et al., 2021; Female, 3b, Wallace, Beidler et al), though all effects were small at best $(g < 0.2)$. White individuals performed better on the majority of scales, with small effect sizes in nine assessments (1b, Alosco et al., 2019; Female, 3c, Wallace, Beidler et al., 2021; Male 3d, Wallace, Beidler et al., 2021; 3a, A, Kontos et al., 2010; 3a, B, Kontos et al., 2010; 3b, B, Kontos et al., 2010; 3c, A, Kontos et al., 2010; 3d, A, Kontos et al., 2010; 3d, B, Kontos et al., 2010) medium effect sizes in three assessments (Male, 3b, Wallace, Beidler et al., 2021; Male, 3c, Wallace, Beidler et al., 2021; 3c, B, Kontos et al., 2010) and a large effect size in one (1a, Alosco et al., 2019). Although the overall effect was small, the varied effects across studies indicate there may be meaningful differences between concussed Black/African American and White individuals on some, but not all neurocognitive domains.

One of the studies (Alosco et al., 2019), which included four subscales, combined a battery of neurological assessments to produce a general composite score for groupings of neurophysiological behaviour. Psychomotor speed and executive function produced a large effect size when reported as a combination of scores across Trail Making test – Trail A and B, Wechsler Adult Intelligence Scale-Revised (WAIS-R) - digital symbol,

Delis-Kaplan Executive Function System Color Word Interference Test (DKEFS) – Word Inhibition/Switching and the Controlled Oral Word Association test (COWAT). The majority of these assessments contain components that measure working memory and visual motor processing speed (Bowie & Harvey, 2006; Climie & Rostad, 2011; Heaton et al., 2004; Loonstra et al., 2001). Therefore, considerations of differences between races in assessments of these cognitive domains post-concussion may be of particular importance.

Working memory is the ability to temporarily store and manipulate information and has been suggested to be greatly impacted by concussion (Junn et al., 2015). Although working memory was not specifically tested in any of the studies in this meta-analysis, it is a component of the visual motor processing and visual memory subscales (X's and O's; Three-Letter module) on the ImPACT (Kontos et al., 2014). A large study (N>900) in a healthy population found that on multiple assessments of attention/working memory, Black/African American individuals scored lower on the total correct score and produced more errors compared with White individuals (Heaton et al., 2004). Therefore, the differences observed between races may be the result of baseline differences, rather than specific to concussion and such assessments of working memory may overestimate the impact of concussion on this cognitive function in Black/African American individuals.

Within this meta-analysis, small to medium effect sizes were reported on all measures of visual motor processing on the ImPACT assessment, with White individuals scoring better (Female, 3c, Wallace Beidler et al., 2021; Male, 3c, Wallace Beidler et al., 2021; 3c, A, Kontos et al., 2010; 3c, B, Kontos et al., 2010). This is consistent with the findings by Wallace, Moran, Beidler et al., (2020), and Wallace et al. (2018), who reported that White high school and collegiate athletes, respectively, performed significantly better than Black athletes on baseline visual motor processing speed (Wallace, Moran, Beidler, et al., 2020). The authors note that these findings were independent of other factors such as sex, history of previous concussion(s) and the presence of ADHD or other learning disabilities (Wallace et al., 2018). As such, these findings indicate that baseline differences between races may play an important role in the interpretation of scoring on measures of visual motor processing following concussion.

2.4.3 Symptom Outcomes

Across six studies and 24 different measures, with 31 effect sizes, it was indicated that there is no effect of race on symptom score post-concussion, as the effect size was less than small $(g = 0.1)$. In the original reports, the majority of subscales (19/31; 61%) reported that White individuals reported lower symptom scores. Differences in symptom presentation have also been documented at baseline testing (pre-concussion), with Black/African American athletes reporting greater symptoms than White, in both high school (Wallace, Moran, Beidler, et al., 2020) and collegiate athletes (Wallace et al., 2018). Although statistically different in both studies, in collegiate athletes, the effect size was small (Wallace et al., 2018).

It is possible lack of effect observed in this meta-analysis is due to disproportionate sample sizes. In most of the studies, Black/African American individuals accounted for under 20% of the total sample population (Wallace, Beidler et al., 2021; Holmes et al., 2016; Wallace, Hou, et al., 2021; Wallace, Moran, Bretzin et al., 2020; Yengo-Khan et al., 2021). With this relatively small sample size any outlier would have a very strong impact on the overall outcome of the study. Only one study (Kontos et al., 2010) contained sample sizes with \approx 50% Black/African American participants. Therefore, studies regarding symptom presentation post-concussion are potentially bias due to sample sizing, warranting further exploration. Future studies should strive to include a more equal sample size within both races to accurately compare the effects of race on post-concussion symptom presentation.

2.4.4 Other Factors

Additional factors not examined in this meta-analysis may also contribute to differences in concussion outcomes across races. Sex, age, socioeconomic status, general health perceptions and depression may influence race-based differences in concussion outcomes. However, there were not enough studies with consistent outcomes to include these factors in our analysis.

Within this meta-analysis four small to medium effect sizes were calculated for neurocognitive outcomes, with three out of the four being within the male subgroup

(Wallace, Beidler et al., 2021), suggesting sex may be a moderating factor for racial differences in neurocognitive outcomes, consistent with a previous report (Houck et al., 2020). Compared with White individuals, Black/African Americans also tend to have worse perceptions of health following a concussion (Brown et al., 2004). This along, with the risk of discrimination and in particular self-perceived racial discrimination has been associated with worse mental and physical health (Bailey et al., 2019). Indeed, although the rate of depression appears to be lower in Black/African American individuals, when Black/African Americans are diagnosed they tend to be more severely impaired as well as report a more persistently illness (Williams et al., 2007; Woodward et al., 2013). An increase in depressive symptoms post-concussion may contribute to the lower performance on neurocognitive testing seen in this meta-analysis by Black/African American individuals as depression has been linked to significant deficits in cognitive function (Rock et al., 2014). Due to the subjective nature of concussion symptom reporting, these concepts of health perception and depression may contribute to Black/African Americans reporting a higher number and severity of concussion symptoms and worse neurocognitive performance (Holmes et al., 2016; Wallace, Beidler, et al., 2021; Wallace, Hou, et al., 2021). Future research should look to explore the interaction between race, depression, symptoms, and neurocognitive performance postconcussion.

2.5 Limitations

It is important to note that studies in this systematic review had several limitations. The included studies used different assessments to evaluate post-concussion deficits, which makes it difficult to truly synthesize results across studies. Other limitations include variable sample compositions (i.e., athletes vs. hospital admission; variable age compositions), lack of baseline scores and the retrospective nature of some of the studies. Additionally, many studies did not control for confounding variables such as SES and sex which have been shown to influence concussion outcomes (Abrahams et al., 2014; Hootman et al., 2007; Houck et al., 2018).

Due to the nature of the question asked in this meta-analysis only post-injury scoring was included in the meta-analysis. The lack of baseline scoring has the potential to lead to

inaccurate representations of post-concussion differences due to individual variation. As more studies become available, additional meta-analyses that consider the difference of pre- vs. post-concussion symptom and neurocognitive scores in different racial groups should be considered.

A symmetrical funnel plot represents weak publication bias (Egger et al., 1997). A visual analysis of publication bias was employed as Cohen's Q and I^2 have both been reported as being poor in detecting heterogeneity in meta-analysis with small numbers of studies even if heterogeneity exists (Higgins et al., 2003; von Hippel, 2015). For funnel plot of standard error by standard difference in means for Symptom Assessments (Figure 5) a large number of effect sizes are clustered towards the point of the triangle. This cluster may be due to the expected presence in symptoms post-concussion, regardless of racial identity.

2.6 Conclusion

Though race has no scientific classification is has still been linked to several clinical concussion outcomes (Wallace, Moran, Beidler, et al., 2020). This systematic review and meta-analysis demonstrated that there is some current evidence to support the notion that race may play a role in neurocognitive performance on post-concussion assessments. Using assessments and normative data that do not consider social determinants of health, may not be sensitive to cultural differences within minority communities. Racial factors should be considered when interpreting prevalence and symptom score data and when employing neurocognitive measures for post-concussion assessment as race has the potential to influence the utility of the measure. However, despite the growing body of evidence, additional research is needed to determine the effect of race-related differences and potential confounding variables on neurocognitive measures and symptom presentation post-concussion.

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Chapter 3

3 Race-Related Differences in Symptom Presentation and Neurocognitive Performance Post Concussion

3.1 Introduction

In recent decades, the incidence of diagnosed mild traumatic brain injury (mTBI) also known as a concussion, has increased dramatically, creating a major concern and challenge to public health (Pavlov et al., 2019). It is estimated that in the United States, 3.8 million concussions occur annually with up to 50% going unreported or undiagnosed (Harmon et al., 2013). During a concussion, forces imposed on the brain can damage the delicate and complex microstructural components, leading to a widely diverse injury presentation (Giza & Hovda, 2014). Cognitive impairments which can result in changes to an individual's orientation, attention and memory are reported in approximately 15% of individuals who sustain a concussion (Holmes et al., 2016; McInnes et al., 2017). Deficits in reaction time, processing speed and sensory motor planning have also been observed in concussed young adults, which has the potential to be devastating later in life (McPherson et al., 2019).

A population that is generally overlooked in concussion research is Black or African American individuals, despite being over-represented in concussion-risk sports. Racial differences have been identified in some concussion studies relating to awareness (Wallace, Covassin, & Moran, 2018; Wallace, Beidler, Kerr, et al., 2021), incidence (Bazarian et al., 2003; Wallace, Hou, et al., 2021), and outcomes (Alosco et al., 2019; Norheim et al., 2018; Wallace, Beidler, Covassin, et al., 2021). Though White athletes demonstrate higher levels of concussion knowledge, meaning they more readily identify symptoms and therefore seek treatment sooner, Black/African Americans tend to report a higher number of symptoms both pre- and post-concussion. In conjunction with these higher number of symptoms, concussed Black/African Americans also tend to have poorer performances on neurocognitive assessments (Kontos et al., 2010; Wallace, Beidler, Covassin, et al., 2021). Several factors have been suggested to contribute to these poorer performances of Black/African American relative to their White counterparts,

including lower academic aptitude (Houck et al., 2020), lower socioeconomic status (Houck et al., 2018) and the fact that neurocognitive testing is developed by the racial and ethnic majority and may lack the cultural specificity required to accurately assess the cognitive ability of individuals of an ethnic or racial minority (Wallace, Covassin, & Moran, 2018).

Despite acknowledgement of factors that may contribute to differences between races, few studies have specifically examined race-based differences in symptom scores and neurocognitive performance in concussed individuals. Understanding the ways in which different racial groups report concussion symptoms as well as perform on neurocognitive tests post-concussion is an essential first step in accurate interpretation of concussion severity and the tracking of recovery in different racial groups. The purpose of this study was to examine race-based differences in post-concussion symptoms and neurocognitive performance using data from The Federal Interagency Traumatic Brain Injury Research (FITBIR) database. It was hypothesized that Black/African Americans would have a greater number of concussive symptoms and that performance on cognitive testing would be lower for Black/African American young healthy adults when compared to their White counterparts. The results from this study provide novel information on potential racebased differences in cognitive performances post-concussion and have the potential to highlight race as a factor requiring a more in-depth exploration.

3.2 Methods

Prior to beginning the investigation, ethics approval was given by the university's Research Ethics Board. This was a retrospective study that included cross-sectional assessments of data accessed through the Federal Interagency Traumatic Brain Injury Research (FITBIR) database maintained by the National Institute Health Center for Information Technology. FITBIR is an informatic system developed to share data from across the Traumatic Brain Injury (TBI) research field in the USA. Funded projects through the National Institutes of Health and the US Army Medical Research and Development Command that involve TBI are required to upload their raw data to FITBIR.

3.2.1 Screening

Often data input into FITBIR includes General Core Common Data elements (Core CDE), which were used to identify the race of participants for the current study. Core CDE's include categories such as Race USA (RaceUSACat) which is the category that identifies the patient's self-declared racial orientation, independent of ethnic origination and Race (RaceCat) which is the category of race(s) or religion(s) the participant most closely identifies with. Both the RaceUSACat and the RaceCat have pre-defined categories that participants select. RaceUSACat consisting of the seven race categories defined by the Office of Management and Budget (OMB) and RaceCat consisting of 21 race categories. Data included in the current study met the following criteria: i) participants identified as White (RaceUSACat) or White North American (RaceCat), or Black or African American (RaceUSACat) or Black African, Black African American or Black Afro-Caribbean (RaceCat), ii) participants were between the ages of 18 to 25 years old, iii) participants must have sustained a mTBI, iv) participants completed an assessment that is designed to measure cognitive performance or symptom score postconcussion, v) participant completed assessment within the first month (31 days) postinjury, and vi) the assessment scale was used in more than one study.

FITBIR was screened for studies that met the inclusion criteria. Sixty studies were originally identified that identified the race of participants. From these 60 studies, 10 included the appropriate age range (18-25 years old) and appropriate racial categories (Black/African American and White). These 10 studies collected data using many different forms/scales, ranging between 23-31 different measures. Across the 10 studies, 34 scales were identified that measured either neurocognitive function or symptom scores. Nine scales were identified that were used in more than one study, however, 3 were eliminated, as they did not include measures within the first month post-injury. Therefore, six scales across four studies were included in the final results, two that measured symptom presentation: Brief Symptom Inventory 18 (BSI-18) and Glasgow Outcome Scale Extended (GOS-E); and four which measured neurocognitive function: Controlled Oral Word Association Test (COWAT), Grooved Pegboard Test (GPT), Trail Making Test (TMT A and TMT B).

3.2.2 Measures

The BSI-18 is a measure of psychological distress and psychiatric disorders (Asner-Self et al., 2006). The BSI-18 is composed of three dimensions: somatization (SOMA) – distress caused by the perception of bodily dysfunction; anxiety (ANX) – symptoms of nervousness, tension, motor restlessness, panic states and apprehension; and depression (DEPR) - symptoms of disaffection and dysphoric mood (Andreu et al., 2008). Each dimension is composed of six items and participants are asked to rate how much they have been affected by the symptoms over the past week on a five-point Likert scale. Results from all three dimensions are summarized in the Global Severity Index (GSI) of distress, which is scored out of 72, with a higher score indicating a worse performance (Asner-Self et al., 2006).

The GOS-E has been used as a tool used to determine level-of-consciousness and as an early indicator of the index of severity post-injury. The GOS-E is an extension of the five-point Glasgow Outcome Scale (GOS; Jennett & Bond, 1974) to an eight-point scale. Data is collected through an interview between clinicians and patients/caretakers. From this interview clinicians assign a ranking based on the following levels: $1 - Dead$, $2 -$ Vegetative State: condition of unawareness with only reflex responses, 3- Low Severe Disability: unable to be left alone for eight hours at home and is dependent on frequent daily support for mental or physical disability, 4 - Upper Severe Disability: able to be left along for more than 8 hours but less then 24 hours and is dependent on others for shopping, travel and regular daily support, 5 – Low Moderate Disability: dependent on support for shopping, travel and activities outside of the home and cannot resume previous social activity, 6 – Upper Moderate Disability: able to return to work with adaptations but not to prior level and can resume modified previous social activity, $7 -$ Low Good Recovery: resumption of normal life but pre-injury status is not achieved, 8 – Upper Good Recovery: full recovery or minor symptoms that does not affect daily living (*Glasgow Outcome Scale - Extended*, 2019; Olsen, 2014).

The COWAT is a test of word fluency, specifically spontaneous word production (Loonstra et al., 2001). Participants are given a specific letter of the alphabet and asked to produce as many words as they can in one minute that begin with the given letter. This is repeated two more times with different letters. The participants final score is the total number of words produced across the three trials, excluding proper nouns, repeating words, repeating words in a different tense, plurality or grammar usage and words that start with the wrong letter (Loonstra et al., 2001; Ross et al., 2007). Within the literature the normative score for the COWAT was obtained from Ruff et al., 1996.

The GPT is used to assess motor performance (Bryden $\&$ Roy, 2005). In this assessment participants are tasked with slotting 25 grooved pegs into a pegboard in a fixed pattern from left to right and top to bottom. An individual's score is the total amount of time, in seconds, it takes to insert all pegs (Ruff & Parker, 1993). In this assessment a higher score indicates a worse performance as it took participants longer to complete the task. Within the literature the normative scores for the GPT came from Heaton et al., 2004.

The TMT A assesses visual searching, processing speed and motor speed and the TMT B assesses visuospatial understanding, divided attention, working memory, mental flexibility, and executive functioning (Bowie & Harvey, 2006; Bracken et al., 2019; de Guise et al., 2016). Both TMT A and TMT B consist of connecting 25 encircled variables. In the TMT A, the encircled variables are number 1 to 25 which participants are asked to connect in numerical order (Bowie & Harvey, 2006). In the TMT B variables consists of both numbers 1 to 13 and letters A to L. Participants are asked to connect all 25 numbers and letters in ascending order, alternating between the numbers and letters. Both tests are scored based on the total amount of time it takes the participant to complete connecting all 25 variables in the appropriate order. Typically test administration is discontinued at 300 seconds (Bowie & Harvey, 2006; Reitan, 1958). Within the literature the normative score for both the TMT A and TMT B came from Tombaugh, 2004.

3.2.3 Statistical Analysis

Analysis was run using RStudio (R version 4.1.0). Shapiro–Wilk tests were used to assess the normality of all outcome measures. For the Neurocognitive scores, a one-way
analysis of variance (ANOVA) was used to determine if there was a difference between racial groups (Black/AA and White) and normative values. *Post-Hoc* analysis was performed using an independent sample Welch's T-test. A Bonferroni correction was applied where applicable and statistical significance was set at $p \le 0.02$. Both the BSI-18 and GOS-E did not meet the assumptions of normality and therefore were analyzed nonparametrically using the Wilcoxon rank sum test and statistical significance was set at $p \leq$ 0.05. All data were presented as mean ± standard deviation (SD). Effect size (Cohen's *d*) was calculated to determine differences between racial groups, as well as racial groups and normative values. Effect sizes for the difference between groups were also calculated for each measure to address the potentials of low subject numbers on ANOVA results.

3.3 Results

3.3.1 Participant Characteristics

Data from a total of 317 participants across two symptom scores and 313 participants across four neurocognitive measures and were included in this study. Of the symptom scales, 195 participants completed the BSI-18 (27 Black/African American and 168 White); and 122 participants completed the GOS-E (25 Black/African American and 97 White). Of the neurocognitive testing measures, 192 participants completed the COWAT (27 Black/African American and 165 White); 48 participants completed the GPT (7 Black/African American and 41 White); 18 participants completed the TMT A (5 Black/African American and 13 White); and 18 participants completed the TMT A (5 Black/African American and 13 White).

Participant demographics for the symptom measurements are presented in Table 4 and participant demographics for the neurocognitive tests are presented in Table 5.

Table 4 Symptom Score Participant Demographics

3.3.2 Symptom Testing

Brief Symptom Inventory 18 item (BSI-18)

There was a significant difference between Black/African American and White (*p =* 0.004) scores on the BSI-18 (Figure 6). Black/African American individuals reporting a higher number of total symptoms (65 ± 10.47) when compared to White individuals (57.67 ± 11.43) . There was a medium effect size ($d = 0.6$) within this difference.

* Significant p<0.05

Glasgow Outcome Scale Extended (GOS-E)

On the GOS-E (Figure 7) Black/African American (5.56 ± 1.56) reported higher average scores when compared to White (5.29 ± 1.61) individuals, though there was no

significant difference between groups ($p = 0.43$). A small effect size ($d = 0.2$) was reported.

Figure 7. Average score on GOS-E for each racial group. Black/African Americans scored better on this measure, however there was no significant difference between groups ($p = 0.43$) and there was a small effect size ($d = 0.2$)

3.3.3 Neurocognitive Testing

Controlled Oral Word Association Test (COWAT)

On the COWAT the normative group (40.1 \pm 10.5) reported a larger average than both the Black/African American group (27.85 \pm 8.29) and the White group (29.44 \pm 11.59). As indicated by the ANOVA there was differences between groups $(p<0.001)$, such that in a post-hoc comparison Black/African American $(p < 0.001)$ and White $(p < 0.001)$ differed significantly (Figure 8). There was no difference in average score between

Black/African American and White groups $(p = 0.39)$. There was a large effect size between Black/African American and normative (*d* = 1.0), and between White and normative scores $(d = 1.0)$, with the normative scores being better. The effect size between Black/African American and White fell outside of the small range for Cohen's *d* $(d = 0.1)$.

* Significant $p < 0.02$

Figure 8. Average raw score on the COWAT grouped by Black/African American, White participants and Normative values. Both Black/African Americans (p < 0.001) and Whites ($p < 0.001$) scored significantly lower than normative values though they did not report significant differences from each other ($p = 0.39$). A large effect size is seen between Black/African Americans and normative values $(d = 1.0)$, as well as between Whites and normative $(d = 1.0)$.

Grooved Pegboard Test (GPT)

On the GPT the Black/African American group (67.14 \pm 4.95) performed the fastest, followed by the White group (68.07 \pm 12.0) and the normative group (73.17 \pm 20.9) reported the slowest time. As indicated by the ANOVA there was no interaction between groups $(p = 0.2)$. A small effect size was calculated between Black/African American and normative score $(d = 0.3)$ and White and normative scores $(d = 0.3)$, with normative

scores being worse in both instances (Figure 9). The effect size between Black/African American and White fell outside of the small range $(d = 0.08)$.

Figure 9. Average raw score on the GPT grouped by Black/African American, White participants and Normative values. No significant difference was seen between groups ($p = 0.2$) however a small effect size was seen between both Black/African America ($d = 0.3$) and normative and White ($d = 0.3$) and normative, with the normative group performing worse.

Trail Making Test Trail A (TMT A)

On the TMT A the White group (21.08 \pm 4.79) performed the fastest, followed by the normative group (24.4 \pm 8.71) and the Black/African American group (28.8 \pm 15.02) performed the slowest. Results from the ANOVA indicated there was no significant effect between groups ($p = 0.23$). A medium effect size was found between Black/African and normative, with Black/African Americans scoring worse than normative data $(d = 0.5)$ and a small effect size between White and normative, with Whites scoring better $(d = 0.4)$ (Figure 10). A large effect size was found between Black/African Americans and White, with Black/African Americans scoring worse (*d =* 0.9).

Figure 10. Average raw score on the TMT A grouped by Black/African American, White participants and Normative values. No significant difference was seen between groups ($p = 0.23$). A large effect was seen between Black/African American and White individuals $(d = 0.9)$ with White individuals reporting better scores. A medium effect size $(d = 0.5)$ was seen when Black/African Americans were compared to normative, with the normative group performing better. White individuals reported a small effect size $(d =$ 0.4) when compared to normative, with the normative sample performing better.

Trail Making Test Trail B (TMT B)

On the TMT B the normative group (50.68 ± 12.36) reported the fastest score, followed by the White group (52.77 \pm 12.76) and the Black/African American group (80 \pm 45.87) reported the slowest score. Though differences were found between groups (*p =* 0.005), when a post-hoc analysis was employed, no significant differences were found. There was no difference in the average score between Black/African American (*p =* 0.23), White ($p=0.62$) and the normative score; or between Black/African American and White (*p =* 0.26) (Figure 11). However, there was a large effect size between Black/African and normative, with Black/African Americans scoring worse (*d =* 1.5) and Black/African American and White, with Black/African Americans scoring worse $(d = 1.1)$. There is a small effect size between White and normative with White individuals scoring worse (*d* $= 0.2$).

3.4 Summary and Discussion

The purpose of this study was to determine if there were race-related differences between Black/African American and White individuals in their post-concussion symptom

presentation and neurocognitive performance. To the author's knowledge, this is the first study to address race-related differences in multiple symptom and neurocognitive assessments. As hypothesized, Black/African American individuals reported a higher severity of concussion related symptoms. Although concussed individuals differed from normative scores on neurocognitive performance, there was no significant difference between Black/African American and White individuals post-concussion.

3.4.1 Symptom Presentation

This study's findings of Black/African American individuals reporting a higher severity of symptoms post-concussion is consistent with previous studies of concussed individuals within 14-days (Wallace, Beidler, Covassin, et al., 2021) and three months post-injury (Brown et al., 2004). Level of severity was determined by scoring higher on the BSI-18 or lower on the GOS-E. Based on the scoring for the BSI-18, Black/African American individuals meet the criteria to be classified as having clinically significant distress (Derogatis, 2001). The significant differences found in the BSI-18 may be attributed to sociodemographic factors such as lack of concussion education and access to healthcare. Previous work has reported that White individuals more readily recognize concussion symptoms (Wallace, Beidler, Kerr, et al., 2021). This lack of recognition may lead Black/African Americans to not access or delay access when medical care is needed. Even when medical care is sought, it has been shown that Black/African Americans are more likely to have difficulty accessing treatment, and in turn, may not receive the appropriate standard of care (Bazarian et al., 2003; Ortiz et al., 2021). This inability to access the proper resources can lead to the exacerbation of symptoms as they are not addressed or managed in an appropriate, timely manner.

No significant difference was reported on the GOS-E, though Black/African American individuals did report a slightly higher score than White individuals. Based on the GOS-E rating scale, both groups remained at level 5, which is classified as having 'Low Moderate Disability'. The GOS-E score is used as an early indicator of the index of severity and is scored based on the likelihood of an individual's ability to complete daily tasks. In this assessment no significant difference was seen between Black/African American and White performance, and there was a small effect size. This may be

explained by Black/African American's being less likely to report changes to their daily life (Yengo-Kahn et al., 2021). A complex interplay among concussion knowledge, attitude towards concussion, reporting behaviour, race and sociodemographic disparities were cited as reasons why Black/African American individuals are less likely to report changes to daily life (Yengo-Kahn et al., 2021).

The lack of differences between Black/African Americans and White individuals on GOS-E may also be explained by biases in the collection of information. The GOS-E has been cited as having poor interrater reliability, likely due to assessor background and experience (McMillan et al., 2016). Where cultural differences are not considered or controlled for, there exists the potential for inaccurate scoring of racial minorities. Additionally, information for the GOS-E is collected through a structured interview, which allows for interviewer bias. Previous work has shown that individuals with some medical training hold false beliefs about biological differences between Black/African American and White patients and they may use this false belief to inform medical judgments (Hoffman et al., 2016). Due to these reasons, measures that address changes in lifestyle should be interpreted with caution as they may not accurately reflect postconcussive symptoms in Black/African American individuals.

3.4.2 Neurocognitive Outcomes

It was hypothesized that performance on cognitive testing would be lower for Black/African American individuals when compared to their White counterparts, which contradicted what was found in this study. No statistically significant difference was found between racial groups in performance on neurocognitive measures. Although both concussed groups performed more poorly than normative values on the COWAT, there was no racial difference.

The finding that concussed groups differed from the normative values was to be expected as differences from baseline assessments, and normative scores when baseline values are not available, are common indications of cognitive impairment post-concussion (Giza $\&$ Hovda, 2014). However, the finding that there were no racial differences between neurocognitive scores was contradictory to the literature, as racial differences have been

found on neurocognitive measures such as Immediate Post Concussion Assessment and Cognitive Testing (ImPACT) (Houck et al., 2018; Wallace, Covassin, Moran, et al., 2018; Wallace, Moran, et al., 2020; Wallace, Beidler, Covassin, et al., 2021) and the King-Devick (Wallace, Covassin, Moran, et al., 2018; Wallace, Worts, et al., 2020). One possible explanation for the contradictory finding is that the previous studies were able to adjust to baseline scores or limit confounding variables. Wallace, Beidler, Covassin et al. (2021) noted poorer performance in Black/African American individuals in post-injury visual memory, and visual motor speed after covarying for baseline performance (Wallace, Beidler, Covassin, et al., 2021). In Holmes et al., (2016) racial variation was not observed in the initial unadjusted model but once adjusting for potential confounding variables such as insurance, age, sex and length of hospitalization, Black/African American children, relative to White, had a 77% higher risk of experiencing cognitive related symptoms post-concussion (Holmes et al., 2016).

A small sample size of Black/African American subjects may also explain the findings in this study. In the COWAT, Black/African Americans accounted for 14% of the sample population; for the GPT Black/African Americans accounted for 15%; and for both TMT A and TMT B, Black/African Americans accounted for 28% of the sample population. The extremely small sample size of Black/African American individuals in this study, may not be an appropriate representation of the population. It should be noted, a smaller sample size of Black/African Americans is often seen in the literature addressing racial differences post-concussion.

This study's use of total scores on assessments may have influenced the findings, where previous studies have looked at independent measures of an assessment. While the overall scale of a study reports on neurocognitive findings, each individual scale within a measure evaluates a different part. Previous work by Wallace et al., (2018) found racial differences pre-injury on certain measures within ImPACT. Specifically, they found that Black athletes reported a greater number of symptoms, had slower reaction times, and scored lower on assessments of visual processing speed (Wallace, Covassin, Moran, et al., 2018). Studies later conducted by Wallace, Beidler, Covassin et al., (2021) found there were racial differences post-concussion with Black athletes reporting a higher

number of symptom and lower scores on verbal memory, visual memory, and visual motor speed (Wallace, Beidler, Covassin, et al., 2021). In the current study, while visual motor processing speed was a component of the GPT, TMT A and TMT B, these tests were not designed to measure this specific area of cognition. Therefore, visual motor processing was measured with other areas of cognition so differences between racial groups may not be evident. It is possible that overall score on neurocognitive assessments is not an accurate representation of neurocognitive performance.

On the COWAT, overall performance is understood to reflect the integrity of the semantic system, the efficiency of retrieval strategies, self-monitoring, and inhibition of inappropriate responses; while errors are indicative of disinhibition or failure of selfmonitoring (Crowe, 1992). GPT consists of multiple scores including hand time duration, hand time duration t-score, hand peg dropped number, and hand pegs placed correctly for both the dominant and non-dominant hand. The primary outcome measured is the hand time duration for the dominant and non-dominant hand. Within all these measures visual motor processing is used, however the GPT is often described as being a test of motor performance, motor speed and hand-eye coordination (Bryden & Roy, 2005; Ruff & Parker, 1993). Though not often assessed, rule violation on the GPT has been shown in individuals with poorer performance on other neuropsychological tests such as the Stroop Color and Word test, Trail Making Test, and the Tower of London test, all which measure different areas of cognition (Tolle et al., 2020). In the TMT A and TMT B, both total time and errors are recorded. Overall time to completion is sited as the best indicator of neuropathology, though it has been suggested that performance errors, in conjunction with inflated time scores, may be useful in the assessment of those with various head injuries (Ruffolo et al., 2000; Stuss et al., 2001). Neurocognitive performance on these tests consists of multiple related but diverse factors such as visual motor performance, processing speed, mental flexibility, and executive functioning (Bowie & Harvey, 2006; Bracken et al., 2019; de Guise et al., 2016; Reitan, 1958). It is possible that overall score on these assessments is not an appropriate way to measure cognitive performance postconcussion and that more specific scoring, such as that done on ImPACT is a more sensitive way to assess neurocognitive performance and the potential impact of race.

3.5 Limitations

This study is not without limitations. Due to COVID-19, I was unable to perform my own data collection. The data presented in this study is from multiple studies that were conducted at an earlier date, at different facilities, and in a different country with different social policies. Although I performed all data and statistical analysis presented, the studies from which the data were collected, were not designed specifically to examine race-based differences. As I did not collect the data myself, this retrospective design may be influenced by selection bias as well as unaccounted confounding variables. The use of pre-existing data precluded data collection of known variables that could provide further explanation regarding the relationship between race, symptom presentations and neurocognitive performance.

Based on the Shapiro-Wilks test for normality TMT A and TMT B did not meet the assumption. A transformation such as a log, square root or cube root transformation could not be applied as a data range was not provided for the normative values used in this analysis. This lack of data range also precluded the use of a Kruskal-Wallis or Wilcoxon rank sum test. When assumptions of normality are not met within an ANOVA, control of the Type I error rate, the probability of erroneously rejecting a true null hypothesis can be jeopardized (Lix et al., 1996). This has been a long-standing topic of discussion in the literature as real data is not often normally distributed (Blanca et al., 2017). Recent work by Balanca et al., (2017) found the *F*-test to be robust against departures from normality amongst various shapes and sample sizes. Due to the limitations caused by not having the data range, and previous literature addressing the robustness of an ANOVA, an ANOVA for the TMT A and TMT B was used. In future, research in this area should aim to include a larger sample size in order to more closely approach normality.

Another possible limitation is that only data for participants 18-25 years old was collected for the concussed group. The scores of the concussed group were compared to normative scores which contained participants of wide age ranges. As age has been shown to be a factor in COWAT, GPT and both TMTs potential differences may have arisen had the normative values been more age specific. These normative values were

selected as they are commonly used in the literature as the normative values for these assessments.

In studies analyzing racial differences post-concussion, there has been a lack of Black/African American representation. Similar to this study, the majority of studies looking at difference in symptoms presentation have less than 25% Black/African American participants (Holmes et al., 2016; Wallace, Hou, et al., 2021; Wallace, Worts, et al., 2020; Yengo-Kahn et al., 2021). The majority of studies that analyze neurocognitive outcomes post-concussion contain subjects that are majority White identifying. More research is required to fully understand the effects of race on symptom presentation and neurocognitive performance post-concussion.

3.6 Conclusion

In this study, I have demonstrated a significant difference in symptom presentation between Black/African Americans and White individuals. Importantly, this difference was specific to the assessment scale employed. I have also demonstrated no significant difference in neurocognitive presentation post-concussion between Black/African American and White individuals but have demonstrated significant difference between each group and a normative data. Although others have found a difference in neurocognitive performance, specifically in visual motor processing and visual memory (Kontos et al., 2010; Wallace, Beidler, Covassin, et al., 2021), the results from this study showed no significant difference between Black/African American and White individuals. However, it was seen that Blacks/African Americans tended to score lower on neurocognitive measures. Further research is required to better understand race-related differences on different cognitive domains as well as the impact of other factors on neurocognitive performance and symptom presentation.

3.7 References

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Chapter 4

4 Overall Discussion

This thesis identified race-based differences in concussion symptom presentation and outcomes in young adults. First, this thesis revealed that Black/African Americans report a lower prevalence of concussions. Race-based differences were also found in symptom presentation as well as neurocognitive performance post-concussion, though it is dependent on the assessment that is used.

The primary hypothesis that there would be a lower prevalence of concussed Black/African American compared with White individuals, was supported by the findings of Study 2. This is similar to the findings from previous studies of the diagnosis and mechanism of concussion in adolescent emergency department visits (Wallace & Mannix, 2021). The results in Chapter 2 were also supported by a previous study that measured the prevalence of sport related injuries in children that lead to Emergency Department visits (Lyons et al., 2019). Unfortunately, the Emergency Department study focused on the presence of head injuries, not concussions specifically. These findings may be explained by a multitude of factors stemming from racial disparities in health care. Racial disparities in health care should be understood in the context of racial inequities embedded within the laws, regulations, and social institutions. Systematic discrimination is not limited to a select few but rather is a widespread societal problem (Williams & Rucker, 2000). The first step to address health care disparities is to create an accurate representation of the problem and the findings of Chapter 2 identify an area of healthcare that is currently going underreported.

This thesis highlights the complex relationship between race and post-concussion outcomes. A novelty of this thesis is the identification of the inconsistencies of the impact of race on different assessments used post-concussion. Within Chapter 2, the difference in symptom presentation of Black/African American and White individuals had an overall effect close to zero $(g=0.1)$. This may be due, in part, to the variety of symptom

scales used across studies, as in Chapter 3, it was identified that race-based differences in symptom reporting are dependent upon the scale used.

For the neurocognitive assessments in Chapter 2, a small effect was observed indicating that White individuals performed better. This was not supported by the findings of Chapter 3, as no differences were found between racial groups on the different neurocognitive assessments. Many clinical neurocognitive measures require the patient outcomes be compared to a normative standard; however, very few measures of cognitive ability have been validated for use amongst racial and ethnic minorities (Manly, 2005; Pedraza & Mungas, 2008). Often the measures are validated within a Non-Hispanic, English speaking White population (Wallace et al., 2018). The research done by the Mayo Clinic on normative studies of neuropsychological test performance among African Americans, shows that diagnostic accuracy improves when norms are applied to an individual that is demographically similar to the normative sample (Lucas et al., 2005). In order to improve neurodiagnostic accuracy, demographic variables that are related to significant test performance such as race, age, education and sex, need to be considered in the normative sample (Heaton et al., 2004). It is possible that the inconsistent results observed in this thesis may be explained by the lack of racial sensitivity in the measures used.

4.1 Limitations

While this thesis provides insight into the potential differences between races in concussion presentation and outcomes, there are limitations. Additional factors not measured in these studies, such as sex (Abrahams et al., 2014; Hootman et al., 2007), age (Aggarwal et al., 2020), socioeconomic status (Wallace et al., 2020), the presence of ADHD (Aggarwal et al., 2020) and prior concussion (Abrahams et al., 2014; Zuckerman et al., 2015), have been shown to influence post-concussion outcomes that were not accounted for in this thesis. Further, the small sample size for Black/African Americans in both the published literature and the FITBIR database may contribute to the inconsistent findings in this thesis. To this author's knowledge, there is currently only one study addressing neurocognitive outcomes that contains a population with 50%

Black/African American individuals (Kontos et al., 2010). Future work requires controls for confounding variables within a more racially equal sample.

Due to COVID-19, original data collection could not occur and instead databases were used. The majority of the studies used in this thesis for the systematic review and metaanalysis, and all of the data in the FITBIR database were completed in the United States of America. In the United States racial categories are defined by the Office of Management and Budget (OMB). In Canada race data is rarely collected, and in terms of research it is suggested that it be an open-ended question for individuals to answer. If individuals do not answer in exactly the same way, it limits researchers' ability to group individuals to perform analysis. As a result, the data in this thesis do not include data from Canada, and this is an area of research that should be pursued in this country.

4.2 Future Direction

This thesis has identified some critical gaps within the literature that may help direct future research. It is paramount that we gain an accurate representation of concussion within Black/African American communities. Future work should strive to identify racially motivated health-discrepancies that prohibit Black/African American individuals from receiving the same standard of care post-injury. While it is suggested that race influences visuomotor processing speed and working memory, this body of literature is very limited. Future work is necessary to better understand the effects of race on different areas of cognition. Although differences in symptom presentation are noted, it is still unknown what causes these differences. Future work is necessary to understand the physiology underlying symptom scores that indicate increased impairment in Black/African American individuals. Studies that draw samples from the wider population and that proportionately represent Black/African Americans are needed. Additionally, research should be pursued to determine if normative standards in assessment tools are appropriate comparison measures in a minority population. These findings highlight the importance of including analysis of racial differences in concussions and more specifically neurocognitive research. This information in its entirety will enhance our understanding of the potential effect that race plays on concussion presentation and post-concussion deficits.

4.3 Conclusion

The overall objective of this thesis was to investigate the impact of race on concussion presentation and outcomes. This thesis identified that Black/African Americans report a lower prevalence of concussions when compared to their White counterparts. It was found that Black/African Americans report a higher number of symptoms and perform worse on neurocognitive assessments post-concussion, though these results are dependent on the type of assessment that was used. These results provide evidence that there are race-based differences in concussion presentation and outcomes. More importantly it highlights the need for racially sensitive assessment measures. Further research is required to identify racial bias within testing measures which would support clinicians and therapists in their selection of patient-appropriate assessments.

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Curriculum Vitae

Presentations

MacEachern, T. "Implications of Race on Cognitive Post-concussion Symptoms and Neurocognitive Performance." Oral presentation at the Exercise Neuroscience Group annual meeting, London, ON, Canada (May 2022)

MacEachern, T. "Implications of Race on Cognitive Post-concussion Symptoms and Neurocognitive Performance." Poster presented at the American College of Sport Medicine annual meeting and word congress, San Diego, CA (June 2022)