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## **Neurocognitive and Psychosocial Effects of Repeated Concussions in Children and Adolescents**

Shina Halavi

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LOMA LINDA UNIVERSITY  
School of Behavioral Health  
in conjunction with the  
Faculty of Graduate Studies

---

Neurocognitive and Psychosocial Effects of Repeated Concussions in Children and  
Adolescents

by

Shina Halavi

---

A Dissertation submitted in partial satisfaction of  
the requirements for the degree  
Doctor of Philosophy in Clinical Psychology

---

June 2018

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Each person whose signature appears below certifies that this dissertation in his/her opinion is adequate, in scope and quality, as a dissertation for the degree Doctor of Philosophy.

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## ABBREVIATIONS

TBI	Traumatic brain injury
mTBI	Mild traumatic brain injury
CSF	Cerebral spinal fluid
MRI	Magnetic resonance imaging
NFL	National Football League
DAI	Diffuse axonal injury
Na <sup>+</sup> /K <sup>+</sup>	Sodium-potassium
ATP	Adenosine triphosphate
LOC	Loss of consciousness
ADD	Attention-deficit disorder
CT	Computerized tomography
NP	Neuropsychology
RTP	Return-to-play
CTE	Chronic traumatic encephalopathy
AD	Alzheimer's disease
SIS	Second impact syndrome
PCS	Post-concussion syndrome
GCS	Glasgow Coma Scale
dpi	Days post injury
ADHD	Attention deficit/hyperactivity disorder
MANOVA	Multivariate analysis of variance
ANOVA	Analysis of variance

IV	Independent variable
DV	Dependent variable
WNL	Within normal limits
Ln	Natural log

### **Neurocognitive Measures (alphabetical order)**

BASC-2	Behavioral Assessment System for Children – 2 <sup>nd</sup> Edition
BESS	Balance Error Scoring System
BRIEF	Behavior Rating Inventory of Executive Function
BVMT-R	Brief Visuospatial Memory Test-Revised
CVLT-C	California Verbal Learning Test, Children’s Version
CVLT-II	California Verbal Learning Test, Second Edition
DKEFS	Delis-Kaplan Executive Function System
HVLTR	Hopkins Verbal Learning Test-Revised
ImPACT	Immediate Post-Concussion Assessment and Cognitive Testing
MR	Matrix Reasoning
MSVT	Green’s Medical Symptom Validity Test
NEPSY	A Developmental Neuropsychological Assessment
PCSC	Postconcussion Symptom Checklist
Rey-O	Rey-Osterrieth Complex Figure
SAC	Standardized Assessment of Concussion
SCAT3	Sport Concussion Assessment Tool 3
SDMT	Symbol Digit Modalities Test

TOMM	Test of Memory Malingering
WAIS-IV	Wechsler Adult Intelligence Scale, Fourth Edition
WASI-II	Wechsler Abbreviated Scale of Intelligence, Second Edition
WISC-IV	Wechsler Intelligence Scale for Children, Fourth Edition

## ABSTRACT OF THE DISSERTATION

### Neurocognitive and Psychosocial Effects of Repeated Concussions in Children and Adolescents

by

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Doctor of Philosophy, Graduate Program in Clinical Psychology

Loma Linda University, June 2018

Dr. Richard E. Hartman, Chairperson

Dr. Anita H. Hamilton, Co-Chairperson

In the United States, an estimated 1.7 million people sustain a traumatic brain injury (TBI) annually. About 75% of these TBIs are mild, which are referred to as “concussions.” This study assessed the neurocognitive and psychosocial effects of repeated concussions in children and adolescents and their interactions with age and gender. It also assessed the correlation between psychosocial functioning and neurocognitive functioning. Given the paucity of research on the effects of concussion in the developing brain, the current study characterized the neurocognitive and psychosocial effects of concussion in young populations.

The overarching hypothesis stated that repeated concussions would induce more severe neurocognitive and psychosocial deficits than a single concussion. Concussion-induced effects were hypothesized to be worse in females and adolescents. Furthermore, it was hypothesized that pre- and post-morbid impairment would be negatively correlated with post-morbid neurocognitive functioning.

The results showed that those who performed worse on tasks of executive function also experienced more post-morbid depression. Additionally, data trends



suggested that repeated concussions induced more anxiety and depression than a single concussion. In addition, children performed worse on tasks of executive function and demonstrated more hyperactivity following concussion than adolescents. Females performed better on the spatial Rey-O Copy and verbal WASI-II Vocabulary tasks than males following concussion, and males endorsed a greater increase in depression and hyperactivity following concussion.

Since some of the subjects' recovery from concussion was atypical (i.e., experienced persistent concussion-induced effects past the typical range of recovery), these findings may not translate to typically recovering individuals. Nevertheless, these findings clarify understanding and increase awareness of the specific complications associated with concussion in young people and can be used as a baseline of reference as to how repeated concussion-induced effects compare to those following single concussion in the younger aged population. These findings may lead to modifications in the return-to-play guidelines and safety measures of physical activities, with the hopes of diminishing the prevalence of repeated concussions and mitigating the resulting adverse effects.

# **CHAPTER ONE**

## **LITERATURE REVIEW**

### **Demographics**

In the United States, an estimated 1.7 million people sustain a traumatic brain injury (TBI) annually, contributing to about a third of all injury-related deaths (Faul, Xu, Wald, & Coronado, 2010). The term “TBI” refers to a myriad of brain injuries of different types and severity (i.e., mild, moderate severe) that may result from varied causes (Graham, R., Rivara, F. P., Ford, M. A., Spicer, 2013). About 75% of these TBIs are mild (i.e., “concussion”), and the consequences of repeated mild TBI (mTBI) can be greater than the sum of the individual TBIs. Concussion is a common injury in individuals of all ages, including children and adolescents. Almost half a million emergency department visits for TBI are made annually by children between the ages of 0 and 14. Among the more commonly played high school sports, football and ice hockey have the highest incidence of concussion (Kirkwood, 2006). By the time adolescents reach high school, 53% report a history of concussion, and in the college populations, 36% report a history of repeated concussions (Field, Collins, Lovell, & Maroon, 2003). In every age group, TBI rates are higher for males than for females. Males aged zero to four years have the highest rates for TBI-related emergency department visits, hospitalizations, and deaths combined (Faul et al., 2010).

Presenting this data is critical to understanding the impact of this important public health problem in the United States. This information provides the building blocks to inform concussion prevention strategies, identify research and education priorities, and support the need for services among those living with a concussion.

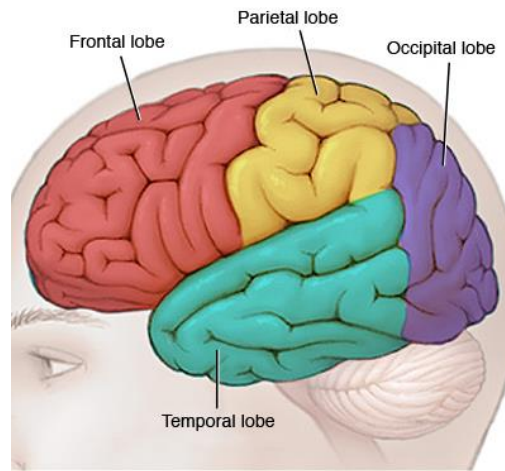
## **Definition**

A concussion, such as that sustained in sports (e.g., football, baseball, volleyball...) or combat, is the mildest and most common form of TBI and may be associated with functional, but usually not structural, changes in the brain. The word “concussion” comes from the Latin verb, *concutere*, meaning “to shake violently” (Bey & Ostick, 2009). The 2012 Zurich Consensus statement included four major features into the definition of concussion: 1. “Concussion may be caused either by a direct blow to the head, face, neck or elsewhere on the body with an ‘impulsive’ force transmitted to the head.” 2. “Concussion typically results in the rapid onset of short-lived impairment of neurologic function that resolves spontaneously. However in some cases, symptoms and signs may evolve over a number of minutes to hours.” 3. “Concussion may result in neuropathological changes, but the acute clinical symptoms largely reflect a functional disturbance rather than a structural injury and, as such, no abnormality is seen on standard structural neuroimaging studies.” 4. “Concussion results in a graded set of clinical symptoms that may or may not involve loss of consciousness. Resolution of the clinical and cognitive symptoms typically follows a sequential course. However, it is important to note that in some cases symptoms may be prolonged” (Paul McCrory, Meeuwisse, Aubry, et al., 2013).

## **Neuroanatomy**

The brain is comprised of four lobes: frontal lobe, parietal lobe, temporal lobe, and occipital lobe (Figure 1). The frontal lobe is located in the front of the brain, which is concerned for our reasoning, planning, parts of speech and movement, emotions and

problem-solving. The frontal lobe governs executive function, which entails planning and organizing and problem-solving. The parietal lobe is concerned with perception of stimuli such as touch, pressure, temperature and pain. The temporal lobe governs our perception and recognition of auditory stimuli (hearing) and memory. The occipital lobe governs our vision.



**Figure 1.** The four lobes of the brain. (<http://www.mayoclinic.org/brain-lobes/img-20008887>)

The brain is protected by the skull, meninges (membranes covering the brain and spinal cord), and cerebral spinal fluid (CSF). The three layers of the meninges include the pia mater (delicate innermost membrane), arachnoid (middle membrane), and dura mater (tough outermost membrane). The CSF protects the brain inside the skull. It is a clear, colorless body fluid that acts as a cushion or buffer for the brain's cortex (outermost layer of neural tissue).

### **Normal Brain Development**

Until recently, very little was known about brain development during

adolescence. The notion that the brain continues to develop after childhood is relatively new. Development of brain and cognitive process occur during adolescence (Blakemore & Choudhury, 2006).

Research on post-mortem human brains revealed that some brain areas (i.e., prefrontal cortex) continue to develop well beyond early childhood. Studies found that structural changes occur in the prefrontal cortex during puberty and adolescence. The two main changes revealed in the brain before and after puberty include the formation of myelin and altered synaptic density (Blakemore & Choudhury, 2006).

As neurons develop, a layer of myelin (an insulating sheath) is formed around the axon (long part of the neuron that sends electrical impulses to other neurons). Myelin acts as an insulator and increases the speed of transmission of electrical impulses from neuron to neuron up to 100 fold. In the first few years of life, sensory and motor brain regions become fully myelination. However, axons in the frontal cortex continue myelination well into adolescence. This suggests that the transmission speed of neural information in the frontal cortex should increase throughout childhood and adolescence.

Altered synaptic density marks another sign of brain development. An adult brain has about 100 billion neurons. This number is slightly fewer at birth (Pakkenberg & Gundersen, 1997). Although neurons grow during development, what accounts for the most significant change are the synapses (the junction between two neurons, which impulses pass by diffusion of a neurotransmitter). During postnatal development, the brain begins to form new synapses, so that the synaptic density (the number of synapses per unit volume of brain tissue) exceeds that of an adult's. This process is called synaptogenesis, which lasts up to a few months depending on the species of animal and

brain region. The brain then goes through synaptic pruning, or the strengthening of frequently used synapses and the elimination of infrequently used connections. This process, which occurs over years, reduces the overall synaptic density to adult levels.

Synaptogenesis and synaptic pruning occur at different stages of life depending on the species of animal and brain region. In studies with monkeys and humans, synaptogenesis in the prefrontal cortex took place during childhood and again at puberty, followed by a plateau phase and subsequent synaptic pruning after puberty (Bourgeois, Goldman-Rakic, & Rakic, 1994; Huttenlocher, 1979; Woo, Pucak, Kye, Matus, & Lewis, 1997; Zecevic & Rakic, 2001). These findings suggest synaptic pruning occurs throughout adolescence, resulting in a net decrease in synaptic density in the frontal lobes during this time. As such, development of cognitive processes associated with the frontal lobes may continue throughout adolescence (Blakemore & Choudhury, 2006).

Synaptic pruning is essential for the fine-tuning of functional networks of brain tissue. For example, it is thought to underlie sound categorization (Blakemore & Choudhury, 2006). Newborn babies have the ability to distinguish between all kinds of speech sounds. However, by the end of their first year of life, following synaptic pruning in sensory brain areas involved in processing sound, they lose the ability to distinguish between sounds to which they are not exposed (Kuhl, 2004).

During childhood and adolescent years, a critical increase in gray and white matter occurs. Grey matter is the dark tissue of the brain and spinal cord, consisting mainly of nerve cell bodies and branching dendrites (region of the nerve cell, or neuron, that receives information, or electrical nerve pulses, from other neurons). White matter is the “white” tissue of the brain and spinal cord, consisting mainly of axons (the part of the

neuron that sends information, or electrical nerve pulses, to other neurons) covered with myelin (an insulating sheath that increases the speed at which impulses are conducted).

In a study of children (average age of 9 years) and adolescents (average age of 14 years), results suggested that adolescents had a higher volume of white matter in the frontal and parietal cortices than children, and children had a higher volume of grey matter in the same brain regions than adolescents (Sowell et al., 1999). These findings have been supported in other studies as well (Barnea-Goraly et al., 2005; Giedd et al., 1999; Sowell et al., 2003; Sowell, Thompson, Tessner, & Toga, 2001).

As white matter development follows a linear course, grey matter development is non-linear (Blakemore & Choudhury, 2006). In a longitudinal magnetic resonance imaging (MRI) study on individuals ranging from four to 22 years old, results suggested the volume of grey matter in the frontal and parietal lobes increased during pre-adolescence followed by a decline during post-adolescence. In the temporal lobes, grey matter development increased until about 17 years of age, at which point, it declined. In the occipital lobes, grey matter continued to increase through age 20 (Giedd et al., 1999). This increase in grey matter at puberty reflects an increase in the number of synapses. Synaptic pruning then occurs after puberty, resulting in a decline in grey matter density continuing until early adulthood.

Initially, areas involved in primary senses and motor skills are developed by age four. Areas for language develop through age 10 with further development of specific areas involved in complex thinking (e.g., parietal lobe) and fine motor skills. The frontal lobes, which control abstract processes, reasoning, judgment, emotion, and impulsivity, remain less developed through the teenage years and into the early 20's (Toledo, E.,

Lebel, A., Becerra, L., Minster, A., Linnman, C., Maleki, N., Dodick & Borsook, 2012).

### **Biomechanics of Concussion**

There are two types of forces that can lead to concussion during an impact: linear and rotational. The linear force is what occurs during a car accident where the car hits an object, stopping suddenly. In this scenario, the person's head moves forward and rapidly hits the steering wheel with his/her forehead. Since the brain is floating within the CSF in the skull, as the skull accelerates forward and comes to a sudden stop, so does the brain. The brain moves forward and suddenly stops when it hits the skull. This acceleration leads to what is known as a coup injury. This acceleration is followed by deceleration, where the brain bounces back within the skull, resulting in the rear portion of the brain hitting the cranium, which is known as the contrecoup injury. Coup-contrecoup injuries result in contusions (i.e., bruise) that are both at the site of impact and on the complete opposite side of the brain. These injuries are mainly the result of moderate and severe TBI, referring to more focal brain injuries, which occur in a particular spot in the brain.

Rotational injury is the result of nonlinear forces that twist the brain within the skull. In this type of injury, the inertial forces are imparted to the skull and brain so that an angular acceleration occurs around the mid-line axis. The dangers of rotational force injuries are why the National Football League (NFL) made helmet-to-helmet hits illegal. This type of injury can result in shearing/tearing of brain tissue and stretching of brain tissue. These injuries result in concussions and are often associated with diffuse injuries, occurring over a more widespread area.

Diffuse axonal injury (DAI) refers to damage to axons as a result of TBI, which is



likely to be the primary damage that occurs in concussion. DAI is a brain injury in which the damage occurs in widespread areas across the brain. Given that children are going through rapid white matter development, DAI following severe head injury may account for worse neurobehavioral functioning in young children relative to older children and adolescents (Thompson, Francis, Stuebing, & Fletcher, 1994).

### **Neurometabolic Cascade of Concussion**

The movement of the brain within the skull (i.e., concussion) results in damage to brain tissue, which initiates a cascade of molecular events that disrupt normal nerve function (Graham, R., Rivara, F. P., Ford, M. A., Spicer, 2013). A concussion injury can be thought of as a two-part process: the primary insult and a secondary inflammatory response (Grady, 2010). The primary insult results in a release of glutamate, an excitatory amino acid. This release of glutamate, in addition to the efflux of potassium and the influx of calcium, results in the depolarization (the moment at which the negative internal charge of the cell becomes positive) and suppression of neuronal activity.

To restore the ion balance, the sodium-potassium ( $\text{Na}^+/\text{K}^+$ ) pump, which moves sodium and potassium ions in opposite directions across the plasma membrane, works overtime. This pump requires increasing amounts of adenosine triphosphate consumption (ATP; energy carrier) and glucose (important energy source) metabolism. This results in decreased cerebral blood flow and an “energy crisis” (due to the difference between glucose supply and demand). This energy crisis is likely the mechanism for post-concussive vulnerability, making the brain less able to respond adequately to a second injury (Giza & Hovda, 2001). The actual pathophysiology of repeated concussions over a

subacute time period and the mechanisms responsible for the clinical manifestations remain poorly understood (DeRoss et al., 2002).

Following a concussion, the brain also produces an inflammatory response (Patterson & Holahan, 2012). However, the role of the neuroinflammatory response following concussion remains unclear. The neuroinflammatory response involves the recruitment of certain types of white blood cells, neutrophils and monocytes, to the site of injury. These white blood cells secrete cytokines and other signaling molecules. Regarding the role of this response, on one hand, prolonged exposure to inflammatory cytokines is ultimately harmful. On the other hand, it has been suggested that neuroinflammation contributes to the neuroprotective regenerating efforts of the brain. In addition, the absence of neuroinflammation following concussion has been known to cause cumulative damage (Patterson & Holahan, 2012).

### **Concussion in the Younger Versus Older Athlete**

There exist many commonalities in the biomechanical properties of concussion across age groups. Across age groups, all concussions primarily involve rotational acceleration and/or deceleration forces that stress or strain the brain tissue, vasculature, and other neural elements (Barth, Freeman, Broshek, & Varney, 2001). Certain developmental factors differ between developing and mature organisms such as brain water content, cerebral blood volume, level of myelination (substance that surrounds axon to increase speed of conduction), and skull geometry (Kirkwood, 2006). Experimental studies suggest that the smaller size of immature brains could require increased force to produce actual cerebral injury (Ommaya, A. K., Goldsmith, W.,

Thibault, 2002). McCrory et al. (2004) followed up on that, suggesting that young children may require increased force when compared with adults to become symptomatic after head injury. However, once actual injury has occurred, the immature brain is likely to respond less well overall.

Concussions in the pediatric athlete differ from that in the adult athlete. Children are not “little adults,” but are actively developing organisms who respond differently to injury than fully-developed individuals (Kirkwood, 2006). However, it remains unclear as to whether children or adults suffer worse head injuries. On one hand, children have less well-developed neck and shoulder musculature than adults. As a result, they will not be able to transfer energy directed at the head throughout the body, increasing their risk of concussive injury in certain circumstances. On the other hand, they have smaller in size and have less strength than adults, and their lower force/mass ratios may result in decreased injury rates in most situations. (Kirkwood, 2006).

### **Severity of Concussion**

As stated in the Third Consensus Statement on Concussion in Sport (Zurich, 2008), grading systems of concussion severity have been abandoned due to their non-specificity (P. McCrory et al., 2009). This statement was made following the Second Consensus Statement on Concussion in Sport (Prague, 2004), where they introduced the classification of concussions into simple and complex groups (Paul McCrory et al., 2005). Prior to the abandonment of the grading system, a “simple” concussion was defined as an injury that progressively resolves without complication over 7 to 10 days, and a “complex” concussion was defined as an injury where the athlete suffers persistent

symptoms such as specific sequelae (e.g., convulsive convulsions), prolonged loss of consciousness (more than one minute), or prolonged cognitive impairment after the injury.

### **Signs and Symptoms**

Clinically, the immediate signs and symptoms of a sport-related concussion are similar in younger and older athlete, which can include a change in playing ability, vacant stare, fogginess, confusion, slowing, memory disturbance, loss of consciousness (LOC), increased emotionality, incoordination, headache, dizziness, and vomiting (Kirkwood, 2006). The Fourth Consensus Statement on Concussion in Sport in 2012 (Paul McCrory, Meeuwisse, Aubry, et al., 2013) described the signs and symptoms of acute concussion (period shortly after injury) as a presence of one or more components from the five stated clinical domains. The clinical domains include: “symptoms (somatic [e.g., headache], cognitive [e.g., feeling in a fog], and/or emotional [e.g., lability]), physical signs (e.g., loss of consciousness, amnesia), behavioral changes (e.g., irritability), cognitive impairment (e.g., slowed reaction times), sleep disturbance (e.g., insomnia).”

Signs and symptoms following a concussion can be variable and may not occur for a few hours about the initial trauma. They should be seen as an evolving injury. Persistent symptoms (>10 days) are generally reported in 10-15% of concussions. This may be higher in certain sports (e.g., elite ice hockey) and populations (e.g., children). Occasionally, symptoms are not recognized until cognitive stress, such as school work, makes the attention or memory deficits more noticeable (Grady, 2010). Headache is the most frequently reported symptom, and LOC only occurs in less than 10% of concussions

(Halstead & Walter, 2010). Prolonged LOC (> 1 minute duration) would be considered as a factor that may modify management (Paul McCrory, Meeuwisse, Aubry, et al., 2013). Dick (2009) suggested that females are more honest in reporting their concussion symptoms than males, leading to a higher reported rate (Dick, 2009). In patients with preexisting mental health disorders, concussion may exacerbate those symptoms and make them more difficult to control. It is important to monitor this population carefully and consider altering existing care plans.

Concussions may rarely result in immediate motor phenomena (Paul McCrory, Meeuwisse, Aubry, et al., 2013), such as tonic posturing (muscle stiffening) or convulsive movements (i.e., seizure). If these responses occur, they are generally benign and require no specific treatment beyond the standard management of the underlying concussion.

Poor understanding of a concussion and its symptoms may complicate the recognition of a concussion. As such, it is important to have a clear understanding of the signs and symptoms associated with a concussion.

### **Evaluation and Diagnosis**

It is important to note that concussion symptoms often overlap with other medical conditions (Grady, 2010). For instance, migraine headaches and dehydration can both present as headaches after exercise. Also, anemia (medical condition of blood deficiency), overtraining, or inadequate sleep can present as fatigue. Further, attention-deficit disorder (ADD), learning disabilities, absence seizures (brief seizure involving staring spells), and mood disorders can all present as concentration problems or poor

school functioning. The diagnosis of a concussion should be suspected in any individual who presents with signs or symptoms of a concussion shortly after a traumatic blow to the head or body (Grady, 2010). If a concussion has been diagnosed, it is assumed that there is not another reason for altered brain function, such as intoxication, infection, anatomic brain problem, or mass lesion (i.e., tumor).

A range of investigations may be utilized to assist in the diagnosis and/or exclusion of injury. When a player shows any features of a concussion, an on-field evaluation must be administered (Paul McCrory, Meeuwisse, Aubry, et al., 2013). This consists of an onsite licensed healthcare provider using standard emergency management principles to evaluate the player. Once the first-aid issues are addressed, an assessment of the concussive injury should be made using a sideline assessment tool. A player with diagnosed concussion should not be allowed to return to play on the day of injury.

### ***Sideline Evaluation***

Sideline evaluation consists of brief neuropsychological test batteries that assess cognitive function (i.e., attention and memory). It is an essential component in the assessment of a concussion, and they have been shown to be practical and effective (Paul McCrory, Meeuwisse, Aubry, et al., 2013). However, it is important to note that these evaluations are designed for rapid concussion screening on the sidelines and are not meant to replace comprehensive neuropsychological testing. Examples of sideline evaluations include the Sport Concussion Assessment Tool 3 (SCAT3) and the Standardized Assessment of Concussion (SAC). The SCAT3 is concussion evaluation tool designed for individuals 13 years and older. The SAC is a brief cognitive screening

tool (takes about five to seven minutes to administer) to evaluate athletes with possible concussion.

### *Neuroimaging*

The need for imaging and diagnosis of a concussion remains a clinical decision, as there is no test to “prove” that an individual has sustained a concussion (Grady, 2010). Disturbance of brain function following concussion is related to neurometabolic dysfunction, rather than structural brain injury. Hence, concussions are typically associated with normal structural imaging findings such as computerized tomography (CT) and MRI (Paul McCrory, Meeuwisse, Aubry, et al., 2013). Currently, there is insufficient evidence to recommend routine clinical use of advanced neuroimaging techniques (Paul McCrory, Meeuwisse, Aubry, et al., 2013). However, brain CT and MRI should be employed when there are suspicions of structural lesions (e.g., skull fracture), LOC for more than one minute, prolonged impairment of the conscious state, dramatic worsening of symptoms, or seizure.

### *Neuropsychology*

Neuropsychology (NP) is the study of brain-behavioral relationships. Traditional NP testing has been the gold standard in documenting deficits in cognitive function (Grady, 2010). NP testing in concussion has been shown to be of clinical value as it contributes significant information in concussion evaluation (Paul McCrory, Meeuwisse, Aubry, et al., 2013). Comprehensive NP testing should be performed by a trained neuropsychologist, as they must be sensitive to the subtle deficits that may exist beyond

the acute episode. Of note, NP testing should not be the sole basis of management decisions. Rather, it should be used as an aid to the clinical decision-making process.

NP testing can objectively identify cognitive, psychosocial, and achievement difficulties and assist with differential diagnosis and clinical management through the use of various measures (Kirkwood, 2006). Typical cognitive domains that are measured via NP testing include intelligence, language, fine and gross motor skills, verbal and nonverbal memory, executive functioning (i.e., planning and organization, attention, working memory, mental shifting), and visuoperception. Among a number of psychosocial domains that are measured, some include hyperactivity, aggression, anxiety, and depression. Achievement difficulties are measured by assessing certain skills that are acquired in school, such as reading, writing, and comprehension.

Computerized tests have been increasingly used, as they are thought to have a number of potential advantages over paper-and-pencil measures (Kirkwood, 2006). However, there currently exist both advantages and disadvantages to paper-and-pencil and computerized testing. Traditional paper-and-pencil NP testing has less test-to-test variability than computerized testing, making it easier to detect minor differences (Echemendia, Putukian, Mackin, Julian, & Shoss, 2001). However, they can also be more time-consuming and labor intensive than computerized NP testing. On the other hand, computerized NP testing is easily administered and takes a shorter duration to complete (Grady, 2010), but as mentioned, makes it more difficult to detect minor differences (Echemendia et al., 2001). As such, the type of NP measure used must be selected with caution depending on the individual case.



## **Management**

Sideline management of a concussion begins as soon as an individual exhibits signs and symptoms of a concussion. Following signs and symptoms of a concussion, the individual should be removed from the game or situation and evaluated on the sideline. In the high school athlete, it is never appropriate to return the player back to play the same day as the injury regardless of the resolution of symptoms while on the sideline (Paul McCrory, Meeuwisse, Aubry, et al., 2013).

The most effective intervention for a concussion is cognitive and physical rest (Grady, 2010). Activities that exacerbate signs and symptoms include, but are not limited to, schoolwork, video games, and physical exertion. Cognitive and physical rest must take place soon after the concussion, as animal models have suggested that early activity may worsen or prolong the initial injury (Grace S Griesbach, Gómez-Pinilla, & Hovda, 2007). The student may start to transition back to school once the symptoms are minimal at home (Grady, 2010).

Following the acute recovery phase of concussion (three to four weeks), studies suggest it's effective to engage in low-intensity exercising during the subacute phase (between the acute and chronic phases) while still symptomatic to promote neuroplasticity (Dick, 2009; G. S. Griesbach, Hovda, Gomez-Pinilla, & Sutton, 2008; G. S. Griesbach, Hovda, Molteni, Wu, & Gomez-Pinilla, 2004). One study assessed pediatric and adolescent-aged patients with symptoms of concussion longer than one month (Sarmiento, Mitchko, Klein, & Wong, 2010). They found that the individuals who gradually engaged in increased amounts of cognitive and physical work without further exacerbating their symptoms resolved their symptoms quicker than expected.

For preadolescent and adolescent age groups who attend school, the concept of brain rest must be balanced with the academic demands of school. Individuals with mild symptoms are generally able to return to school after a few days of rest at home. However, returning to school is generally not recommended until the symptoms are mild or absent at rest (Grady, 2010).

Students with severe symptoms must return to school gradually (Grady, 2010). Certain barriers exist if the student returns to school while severe symptoms are still present. Firstly, for those with severe symptoms, trying to concentrate can exacerbate symptoms. Also, severe headaches, impaired memory, or impaired attention span significantly impedes new learning. Further, since concussed individuals look normal, teachers often expect them to function normally. A student with a leg cast will be excused from running in gym without a second thought, but a concussed student will often be accused of malingering (faking an illness) if they cannot keep up with the academic load.

### **Return to Play**

The return-to-play (RTP) stepwise process published in the Fourth Consensus Statement on Concussion in Sport is widely accepted as the standard of care in management of RTP following sport-related concussions. The process is illustrated in Table 1 (Paul McCrory, Meeuwisse, Aubry, et al., 2013).

**Table 1.** Graduated Return to Play

Rehabilitation Stage	Functional Exercise at Each Stage of Rehabilitation	Objective of Each Stage
1. No activity	Symptom limited physical and cognitive rest.	Recovery
2. Light aerobic exercise	Walking, swimming, or stationary cycling keeping intensity < 70% maximum permitted heart rate.	Increase heart rate
3. Sport-specific exercise	Skating drills in ice hockey, running drills in soccer. No head impact activities	Add movement
4. Noncontact training drills	Progression to more complex training drills (e.g., passing drills in football and ice hockey)	Exercise, coordination, and cognitive load
5. Full contact practice	Following medical clearance, participate in normal training activities.	Restore confidence and assess functional skills by coaching staff
6. Return to play	Normal game play.	

Within this process, an athlete should proceed to the next level if asymptomatic at the current level. Generally, each step should take about 24 hours to complete, taking about one week to proceed through the full rehabilitation protocol once they are asymptomatic at rest and when engaging in rigorous exercise. If any post-concussion symptoms occurs while in the program, then the patient should go back to the previous asymptomatic level and try to progress again after a further 24-hour period of rest has passed (Paul McCrory, Meeuwisse, Aubry, et al., 2013). The consensus unanimously agreed that no RTP on the day of concussive injury should occur. Research suggests that, at the collegiate and high school levels, returning to play on the same day as the concussive injury leads to delayed onset of symptoms (Michael W Collins et al., 1999;

MW W Collins et al., 2002; K. Guskiewicz et al., 2003; M. R. Lovell, 2004; McCrea et al., 2003).

### **Recovery**

The majority (80-90%) of concussions resolve in about seven to 10 days, but that recovery time frame may be longer in children and adolescents (Paul McCrory, Meeuwisse, Aubry, et al., 2013). Traditionally, it was believed that young age at the time of brain injury has protective benefits, such that the young brain's plasticity would allow for more recovery after insult (Kennard, 1935; Kirkwood, 2006). However, a growing literature suggests that the immature brain is more vulnerable, not more plastic, to diffuse injury, or concussion (V Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2000; Vicki Anderson & Moore, 1995; Brookshire, Chapman, Song, & Levin, 2000; Levin, Song, Ewing-Cobbs, Chapman, & Mendelsohn, 2001). This increased vulnerability may be due to the fact that skills that are not yet well established at the time of insult could be more susceptible to disruption than well-established ones, the brain systems responsible for learning the skill could be affected directly by the concussion, recovery may be restricted by the injured child's smaller repertoire of existing skills, and an injury to the immature brain could interfere neurobiologically with the intricate sequence of chemical and anatomic events necessary for normal development (Ewing-Cobbs, Barnes, & Fletcher, 2003; Giza & Hovda, 2001; Levin, 2003).

For an effective recovery process to take place, individuals must modify their environment by limiting their level of cognitive and physical exertion. Adults have already learned and mastered much of their knowledge and many of the skills they need

to function successfully in everyday settings. On the other hand, children are still acquiring new information and skills (especially in school). They are expected to use a set of neurobehavioral skills that are vulnerable to concussion, such as ability to focus and sustain attention, rapidly processing information, executive function (Mittenberg, Wittner, & Miller, 1997; Yeates et al., 1999). This stands as a barrier to the path of recovery for children following concussion. As such, clinical management of pediatric concussion requires an understanding of the contextual demands that children face across development to allow for the provision of suitable assistance (Kirkwood, 2006).

Another distinguishing factor that children face when recovering from a concussion compared to adults is that the individuals involved in the decision-making and care will differ (Kirkwood, 2006). Children have parents or guardians who are legally responsible for their medical decisions. Depending on the individual case, this may or may not account as a barrier, but is a difference in the recovery process between the two age populations.

## **Repeated Concussions**

### ***Complications***

Long-term consequences have been associated with repeated concussion. In a study of high school athletes, findings suggested that those with two or more concussions who had not been concussed in the previous six months performed similarly on NP testing, as did athletes who were concussed within the previous week (Moser, Schatz, & Jordan, 2005).

## **Chronic Traumatic Encephalopathy**

A proportion of individuals who sustained repeated concussion may develop a progressive neurodegenerative condition referred to as chronic traumatic encephalopathy, or CTE (McKee et al., 2009). This condition is associated with chronic depression, insomnia, paranoia, impaired memory, and suicide (Omalu, Hamilton, Kamboh, DeKosky, & Bailes, 2010). CTE shares similar histopathological changes with other neurodegenerative disorders, particularly Alzheimer's disease (AD). Specifically, it involves hyperphosphorylation of the tau protein (multiple phosphates attach to the tau protein [proteins that stabilize microtubules, a component of the cytoskeleton]) in neurofibrillary tangles (neuropathological hallmark of AD). In some cases (Roberts, Allsop, & Bruton, 1990), it leads to the deposition of amyloid  $\beta$  ( $A\beta$ ; an abnormal protein derived from a larger precursor protein and is the primary component of plaques characteristic of AD) in diffuse plaques (aggregation of soluble peptides). CTE diagnosis can only be made post mortem (Baugh et al., 2012; Goldstein et al., 2013).

The first neuropathological report discussing the long-term effects of contact sport was written by Brandenburg and Hallervorden in 1954. In this study, a 51-year-old retired boxer who manifested delayed posttraumatic dementia (chronic disorder of mental processes caused by brain disease or injury and marked by memory impairment, personality changes, and impaired reasoning) with AD pathological changes (Omalu et al., 2005). Subsequent reports (Roberts, 1988; Roberts et al., 1990) described the characteristic neuropathological findings of CTE, especially in boxers, which comprise of neocortical (part of the cerebral cortex associated with sight and hearing in mammals, which is regarded as the most recently evolved part of the cortex) neurofibrillary tangles,

neocortical neuropil threads (composed of unmyelinated axons, dendrites [part of the neuron that receives electrical impulses from other cells], and glial cells [provide support to neurons]), and neocortical diffuse amyloid plaques.

The first documented case of long-term neurodegenerative changes in a retired professional NFL player consistent with CTE was published in 2005 (Omalu et al., 2005). In this study, a complete autopsy with a comprehensive neuropathological examination was performed on a retired NFL player approximately 12 years after retirement. He died suddenly as a result of coronary atherosclerotic disease (blockage of one or more arteries that supply blood to the heart). The case highlighted potential long-term neurodegenerative outcomes in retired professional NFL players subject to repeated concussion. Omalu et al. (2005) reported that possible symptoms of CTE may include recurrent headaches, irritability, dizziness, lack of concentration, impaired memory, mental slowing, mood disorders, explosive behavior, morbid jealousy, paranoia, tremor, dysarthria (unclear articulation of speech), and parkinsonian movement disorder.

Although many studies have suggested the association between repeated concussion and CTE, the speculation that repeated concussion causes CTE remains unproven (Paul McCrory, Meeuwisse, Aubry, et al., 2013). The evidence supporting the link between repeated concussion and CTE consists of case reports, case series and retrospective analyses (Hazrati et al., 2013; Paul McCrory, Meeuwisse, Kutcher, Jordan, & Gardner, 2013; Tartaglia et al., 2014) and have not yet controlled for the potential contribution of confounding variables (eg., alcohol abuse, drug abuse, psychiatric illness).

## **Second Impact Syndrome**

Second impact syndrome (SIS; also known as acute cerebral edema) refers to the rapid cerebral swelling that occurs when a second head injury is sustained before the brain has recovered from the initial insult (Bey & Ostick, 2009). The majority of SIS cases involve athletes under the age of 18, but it can also be seen in college athletes (Mori, Katayama, & Kawamata, 2006). This condition is very rare that even the frequency of its occurrence is in question (Bey & Ostick, 2009), but must be taken seriously as the consequences could be grave.

Typically, the individual will sustain an initial head injury, which will be followed by post-concussion symptoms. Before the symptoms resolve, which may take days or weeks, the individual receives a second head injury. The second injury may be relatively minor compared to the first, but the repercussions are much worse given the brain is more vulnerable at this point. In this next 15 seconds to one minute, the individual may appear stunned (i.e., in a dazed state), but remains on their feet. What happens in the next few seconds to several minutes is what sets aside this syndrome apart from a concussion (Cantu & Gean, 2010). During this period, the individual “collapses to the ground, semi-comatose with rapidly dilating pupils, loss of eye movement, and respiratory failure” (Cantu & Gean, 2010).

SIS is believed to be caused by a loss of auto regulation of the cerebrovasculature (Cantu & Gean, 2010). Following a single concussion, an individual may develop cerebral edema (Bey & Ostick, 2009), which refers to swelling in the brain caused by a presence of excessive fluid. The brain normally has an auto regulation mechanism of limiting that cerebral blood flow to protect against the massive swelling. However, as



Fisher and Vaca (2004) concluded, when an individual sustains a “second impact,” the brain loses its ability to auto regulate intracranial and cerebral perfusion pressures (Fisher & Vaca, 2004).

This dysregulation leads to hyperemic brain swelling within the cranium (an increased amount of blood flow in the brain), which leads to intracranial pressure, leading to herniation (condition where an organ protrudes through the wall of the cavity containing it) of the temporal lobes, herniation of the cerebellar tonsils through the foramen magnum (the hole in the base of the skull where the spinal cord passes), and brainstem (region of the brain that controls reflexes and essential internal mechanisms, such as respiration and heartbeat) compression (Cantu & Gean, 2010). It usually takes about two to five minutes from the time of second impact to brainstem failure, resulting in death.

There exist age-related differences in SIS, such that the immature brain is a risk factor for cerebral swelling and edema (Bruce et al., 1981; Kirkwood, 2006). This phenomenon has been described as “malignant brain edema.” More research is necessary to determine if malignant brain edema and SIS are related, or if they occur by the same process (Bey & Ostick, 2009).

### **Post-Concussion Syndrome**

There currently exists no clear definition of post-concussion syndrome (PCS). However, a recently proposed definition is that PCS is a complex constellation of cognitive, physical, or emotional symptoms that persist for an extended period of time (from one to six weeks) following an initial concussion (Jotwani & Harmon, 2010).

Given the high prevalence of concussion, a considerable number of athletes each year in the United States may experience PCS.

Among the existing definitions, the World Health Organization (WHO) defined PCS in 1992 as the presence of three or more of the following symptoms after a head injury: “headache; dizziness; fatigue; irritability; difficulty with concentrating and performing mental tasks; impairment of memory; insomnia; and reduced tolerance to stress, emotional excitement, or alcohol” (“The ICD-10 classification of mental and behavioural disorders,” 1992) In 2007, this was updated to include any number of symptoms rather than a specific amount. However, this definition was criticized for being non-specific, as it was not able to distinguish those with PCS from those with chronic pain (Jotwani & Harmon, 2010).

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) included a history of head injury in the definition (Brown, Fann, & Grant, 1994). They defined a PCS as a history of head injury that includes two of the following “loss of consciousness for five minutes or more, posttraumatic amnesia of 12 hours or more, or onset of seizures within six months of injury.” There must also be three months’ duration of three or more of the following symptoms: “fatigue; disordered sleep; headache; vertigo/dizziness; irritability or aggressiveness; anxiety or depression; personality changes; and/or apathy.” However, this definition was criticized of being too strict (Jotwani & Harmon, 2010).

There exists a lot of ambiguity regarding PCS. The ambiguity of when the normal course of symptom resolution in a concussion should end and PCS begins leads to imprecision and variability in interpretation of the literature (Jotwani & Harmon, 2010).

Also, the terms, post-concussive *symptoms* and post-concussive *syndrome* are often incorrectly used interchangeably. The distinguishing factor between post-concussive *symptoms* and post-concussive *syndrome* is the duration of symptoms (Jotwani & Harmon, 2010).

The clinical features of PCS include a persistence of acute concussion symptoms as well as other physical, cognitive, and emotional symptoms. Physical symptoms of PCS include headache, fatigue and low energy, sleep disturbance, nausea, vision changes, tinnitus (buzzing or ringing in the ears), photophobia (extreme sensitivity to light), and dizziness (Kirkwood, 2006). Just as post-concussive symptoms, headache is the most common complaint of PCS.

Cognitive symptoms include slowed thinking or response speed, mental foginess, poor concentration, distractibility, trouble with learning and memory, disorganization, and problem solving difficulties (Kirkwood, 2006). As such, PCS often leads to a significant decline in school performance. NP testing usually demonstrates difficulty in attention or memory (Halstead & Walter, 2010).

Finally, emotional symptoms of PCS include lowered frustration tolerance, irritability, increased emotionality, depression, anxiety, clinginess, and personality changes (Kirkwood, 2006). Previous studies of retired professional football players found that a history of one concussion did not raise the likelihood of depress in life, but those with a history of three or more concussions were three times more likely to be diagnosed with depression. In a study assessing retired NFL players who were diagnosed with post-concussion related depression, 87% continued to have lifelong symptoms (K. M. Guskiewicz et al., 2007).

## **CHAPTER TWO**

### **DISSERTATION AIMS**

#### **Aim 1**

The first aim of the current study was to determine whether concussion history (single concussion vs. repeated concussion), age (children [ $<12$  years] vs. adolescents [ $\geq 12$  years]), and/or gender (male vs. female) affect performance on tasks of neurocognitive functioning (i.e., processing speed, executive function, verbal/nonverbal reasoning, motor skills, verbal/visual memory, visuoperceptual skills). However, certain domains were not further explored due to low sample size. As a result, only processing speed and executive functioning were explored as a factor of concussion history, age, and gender. Additional neurocognitive tasks measuring nonverbal reasoning, word knowledge, and verbal learning and memory were explored as a factor of gender in Aim 1c. The age group classification (i.e., children [ $<12$  years old], adolescents [ $\geq 12$  years old]) was broken down with a cut-off of age 12 so that it could stay consistent with the age group classification used in the BASC-2, the psychosocial measure used for the current study.

Aim 1 was broken down into four sub-aims. The first three sub-aims each had their own specific hypothesis, and the final sub-aim was comprised of four hypotheses. The sub-aims and hypotheses are discussed below.

#### ***Aim 1a/Hypothesis 1a***

Aim 1a assessed how the number of concussions affects neurocognitive functioning. Hypothesis 1a stated that children and adolescents who have sustained

repeated concussions would perform worse on tasks of executive function and processing speed, based on age-related norms, compared to those who have sustained a single concussion. Neurologist Amy McKee examined a former football player's brain and found "tremendous abnormalities" throughout the frontal cortex, which showed longstanding neural atrophy related to repeated concussion (Roehr, 2012). The frontal cortex is the part of the brain that controls executive function, which is dependent on processing speed. This was supported by another study, which suggested that executive functions are the most sensitive to multiple concussion (Karr, Areshenkoff, & Garcia-Barrera, 2014).

### **Single Concussion**

Concussions can lead to immediate impairments in multiple cognitive domains, including executive function, attention, processing speed, and memory (Baillargeon, Lassonde, Leclerc, & Ellemberg, 2012; Belanger & Vanderploeg, 2005; Echemendia et al., 2001). These acute cognitive deficits resulting from concussion were found to resolve in about seven to 10 days (Aubry et al., 2002; Baillargeon et al., 2012; Echemendia et al., 2001; Grant L Iverson, Brooks, Collins, & Lovell, 2006).

One study found long-term deficits in executive function following childhood TBI by assessing the Behavior Rating Inventory of Executive Function (BRIEF) and several neuropsychological measures of executive functions (Mangeot, Armstrong, Colvin, Yeates, & Taylor, 2002). The BRIEF is a standardized rating scale used to assess children's executive functions in home and school environments. Participants were six to 12 years old when they sustained a TBI and assessed five years post injury at 10 to 19

years of age. Individuals had sustained a severe TBI, moderate TBI, or orthopedic injury (not involving brain insult). Severe TBI was defined by the lowest Glasgow Coma Scale (GCS) score of eight or less. Moderate TBI was defined as a GCS score of nine to 12 out of 15 (lower scores accounting for greater deficits). The GCS is a common scoring system used to describe the level of consciousness in a person following TBI (Teasdale & Jennett, 1974). Findings suggested that children with TBI displayed long-term deficits in executive function, as rated by parents on the BRIEF. Further, they found that the largest deficits in executive function occurred in children with more severe TBI.

In another study assessing other cognitive deficits following concussion, it was found that those who had sustained a concussion had deficits in processing speed, verbal and visual memory, and reaction time (Grant L Iverson et al., 2006). This study assessed the cognitive performance of middle school, high school, and collegiate athletes at three time intervals following concussion: 1-2 days post injury (dpi), 3-7 dpi, and 1-2 weeks post injury. Athletes were administered version 2.0 of Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT), a brief computerized neuropsychological test battery that consists of six individual test models that measure aspects of cognitive functioning. Further findings suggested that as time continued, the severity of deficits decreased. Specifically, compared to their baseline performance, 90% of athletes had worse cognitive functioning in two or more domains (processing speed, verbal memory, visual memory, reaction time) at one dpi, which decreased to 37% at 10 dpi. Increased repeated concussion tended to slow down recovery (Grant L Iverson et al., 2006; DeRoss et al., 2002; M R Lovell & Fazio, 2008; McClincy, Lovell, Pardini, Collins, & Spore, 2006).

Johansson et al. (2009) found persistent executive function and processing speed deficits in adults six months following their concussion. The cognitive domains assessed in the study included processing speed, attention, working memory, verbal fluency and reading speed, which are common problems following concussion (Johansson, Berglund, & Rönnbäck, 2009).

Other studies assessed cognitive deficits in only male athletes who sustained concussion (Baillargeon et al., 2012; Warden, D. L., Bleiberg, J., Cameron, K., L., Ecklund, J., Walter, J., Sparling, M. B., Reeves, D., Reynolds, K. Y., Arciero, 2001) and found deficits in executive function and reaction time. Baillargeon et al. (2012) studied male athletes following concussion, ranging from age nine to adulthood. Specifically, the study included three age groups (9-12 years old, 13-16 years old, and adults) of male athletes in soccer, hockey, rugby, and football. Results suggested deficits in working memory, an aspect of executive function.

Cognitive function was assessed using an adaptation of the battery used by the National Hockey League (Mark R Lovell & Collins, 1998). The tasks administered included the Symbol Digit Modalities Test (SDMT; measures visuo-motor speed), Hopkins Verbal Learning Test-Revised (HVLTR; measures verbal memory and learning), Brief Visuospatial Memory Test-Revised (BVMTR; measures visuospatial memory and learning), Color Trails (measures speed of attention, sequencing, and mental flexibility), Pennsylvania State University Cancellation Task (PSU; measures processing speed and selective visual attention), Brown-Peterson test (measures mental manipulation of content held within short-term memory [i.e., working memory]), and Controlled Oral Word Association Test (COWAT; measures word retrieval and word fluency, an aspect

of frontal lobe functioning). Findings suggested that individuals who sustained a concussion had significantly worse working memory than those who had not sustained a concussion.

Warden et al. (2001) found that individuals who sustained a concussion had slower reaction time and worse performance on continuous performance tests than their baseline performance (prior to injury). The researchers administered baseline testing to incoming male cadets (prior to injury) and again after having experienced a concussion. These individuals were in their first year of education after high school and had a mean age of 19 years.

Cognitive function was assessed using Automated Neuropsychological Assessment Metrics, or ANAM (Bleiberg, Kane, Reeves, Garmoe, & Halpern, 2000). ANAM is a computerized neuropsychological assessment. Warden et al. (2001) administered the following subtests in their study: Simple Reaction Time (SRT; measures reaction time), Continuous Performance Test (CPT; assessment of attention-related problems), Mathematical Processing (MTH; measures math performance); Sternberg Procedure (STN; measures short-term memory), Matching to Sample (MSP; measures visual memory), and Code Substitution Delayed Memory (CDD; delayed memory). Findings suggested that individuals who sustained a concussion had slower reaction time and performed slower on tasks of attention and concentration, which are abilities governed by the frontal lobe.

The studies mentioned above focus on the cognitive deficits resulting from a single concussion. Although factors vary across studies (e.g., gender, age, sample size, neuropsychological battery), executive function appears to be the domain that is most



commonly impaired following concussion. The next section describes previous studies that explore neurocognitive impairments following repeated concussion, which is the focus of the current study.

### **Repeated Concussion**

One study found that those with a history of concussion (single and multiple) had impaired attention (aspect of executive function) and motor function (Alexander Collie, Makdissi, Maruff, Bennell, & McCrory, 2006). Male Australian footballers (mean age of 23 years old) received a neuropsychological assessment at baseline (prior to concussion) and within 11 days following their injury. Cognitive functioning was assessed via the computerized CogSport (A Collie et al., 2003) neuropsychological battery as well as paper and pencil cognitive tasks. The CogSport battery took 15-18 minutes to complete and assessed for the following cognitive domains: motor function, decision making, attention, divided attention, working memory, complex attention, and learning and memory. The paper and pencil tasks that were administered assessed for information processing.

Within 11 days of injury, concussed athletes, who still experienced post-concussions symptoms, displayed impaired attention and motor function. Memory and learning were preserved. History of concussion ranged from zero to 10 concussions, with an average of 2.7 (Alexander Collie et al., 2006). Further, asymptomatic athletes who endured concussion were only impaired in attention, not motor function. These findings suggest that certain cognitive abilities may be differentially sensitive to early and later

stages of recovery following single or repeated concussion. Nevertheless, attention (i.e., an aspect of executive function) seems to be impaired by repeated concussion.

Wall et al. (2006) found that jockeys who sustained repeated concussion had worse executive function (i.e., response inhibition and attention) compared to those who sustained single concussion. These differences existed even after three months following injury. College athletes were found to have worse executive function following repeated concussion in another study as well (McAllister et al., 2012), which included the administration of the ImPACT neuropsychological battery.

The ImPACT battery differs from the neurocognitive measures administered in the current study in multiple ways. Firstly, ImPACT is strictly focused on computerized tasks, whereas the current study uses a combination of computerized and paper-and-pencil tasks. Also, ImPACT has not been shown to be reliable for children younger than high-school age (M R Lovell & Fazio, 2008), whereas the current study included neurocognitive measures that have been specifically designed to include this age population.

Finally, in a study assessing male footballers, the cumulative effects of concussion were examined (Michael W Collins et al., 1999). In this study, a 30-minute long neuropsychological battery was administered, which assessed verbal learning, delayed memory, visual scanning, executive function, attention and concentration, processing speed, fine motor speed, and word fluency. Findings suggested that those who sustained greater than or equal to two concussions performed worse on tasks of executive function and processing speed.

From the study mentioned above, Collins et al. (1999) found that performance on the Trails B task was impaired (i.e., measure of executive function). In this task, individuals were timed to see how quickly they could draw a line, alternating from number to letter, in chronological order. This task was administered in the current study and incorporated into the executive function domain created in the current study. Collins et al. (1999) also found that performance on the SDMT was impaired (i.e., measure of processing speed). In this task, individuals were given 90 seconds to pair specific numbers with given geometric figures. A task similar to this was administered in the current study and incorporated into the processing speed domain created in the current study. The current study expanded on the findings suggested by Collins et al. (1999) by including additional measures into the executive function and processing speed domains. In addition, the current study will assess the young age population.

Enduring a single concussion increases one's vulnerability for sustaining a repeated concussion (Graham, R., Rivara, F. P., Ford, M. A., Spicer, 2013). Prior head injury leads to worse cognitive outcome, and repeated concussion increases the effect size associated with the current sport-related concussion (Belanger & Vanderploeg, 2005). Given how prevalent concussion is and how distressing its repercussions can be for an individual, it is that much more important to study repeated concussion. The current study addressed the stated hypothesis by expanding on the findings of the previous literature. The current study assessed a younger age population than the studies cited above and incorporated additional neurocognitive measures into the neurocognitive domains (i.e., processing speed, executive function). This will allow for a broader and detailed understanding of the influence of repeated concussion on the developing brain.

### *Aim 1b/Hypothesis 1b*

Aim 1b assessed how age affects neurocognitive functioning after concussion. Hypothesis 1b stated that, in general, adolescents with a history of concussion would perform worse on neurocognitive tasks than children with a history of concussion, based on age-related norms.

There are many hormonal and physical changes that occur during adolescence (Coleman, 2011), which set that developmental period apart from childhood. One of these changes includes the brain's maturation process, which consists of two main processes. These processes include myelination (i.e., the increase in white matter) and synaptic pruning. During brain development in adolescents, white matter increases in the frontal cortex and then pruning begins post adolescence (Blakemore & Choudhury, 2006). White matter is the tissue of the brain and spinal cord that consists of nerve fibers (i.e., myelin sheaths). It provides connectivity in the brain, uniting different regions into networks that perform various mental operations. Myelin is the insulating sheath surrounding axons (the portion of the neuron that sends electrical impulses to other neurons) that increases the speed of transmission (up to 100-fold) of electrical impulses from neuron to neuron. Maturation of white matter is an important factor in cognitive development, as well as behavioral, emotional, and motor development (Barnea-Goraly et al., 2005). Synaptic pruning refers to the strengthening of frequently used synapses and the elimination of infrequently used connections.

The increase of white matter in the frontal cortex during adolescence suggests that executive function might be expected to improve during this time, given that executive function is one of the main roles of the frontal cortex. Executive function allows us the

ability to control our thoughts and behaviors (Blakemore & Choudhury, 2006). Executive functions include planning and organizing, attention, decision-making, impulse control, and working memory. Each aspect of executive function plays a role in cognitive control (e.g., filtering out unimportant information). Improved executive function during adolescence may lead to the improvement of other cognitive abilities during this period as well, as many cognitive abilities overlap with one another. For example, although memory and attention fall in separate cognitive abilities from one another, improvement in attention is likely to lead to improvement in memory.

As a result of this maturation process, brain regions are more developed in adolescents than in children (Blakemore & Choudhury, 2006). Specifically, adolescents experience dramatic changes in cognitive abilities including cognitive flexibility. Cognitive flexibility, which is a component of executive function, refers to the mental ability to switch between thinking about two different concepts.

However, adolescents also appear to be more susceptible to disruptions during this critical period of brain development (Wall et al., 2006). Such disruptions may include repeated concussion. Previous research has assessed the age-related effects following concussion in individuals of different ages (i.e., children, adolescents, adults). In multiple studies, the age-related effects following concussion in high school and college athletes have found that high school athletes are more vulnerable to cognitive impairment than college athlete (Baillargeon et al., 2012; T. Covassin, Elbin, Harris, Parker, & Kontos, 2012; Field et al., 2003; M. R. Lovell, 2004). Covassin et al. (2012) assessed concussion in high school and college athletes at baseline (before sustaining concussion) and again at two, seven, and 14 days following concussion. Individuals were assessed via the

ImPACT computerized neuropsychological battery. Results suggested that high school athletes performed worse than college athletes on verbal and visual memory at two dpi (T. Covassin et al., 2012).

These findings were consistent with Field et al. (2003), who found that high school athletes performed significantly worse on neuropsychological measures than college athletes at seven dpi. Interestingly, these findings existed despite the fact that the college athletes experienced more post-concussive symptoms (i.e., loss of consciousness) than the high school athletes. Additionally, the gender distribution of this study was worth noting, such that the high school sample consisted of all male athletes (male football and male soccer players), and the college sample consisted of both males and females (male football and female soccer players). This may have impacted the high school athletes performing worse than the college athletes. In the current study, there was a relatively even distribution of males and females in each age group. In Field et al. (2003), the athletes were administered a 25-minute battery of neuropsychological tests, assessing verbal learning and memory, attention/concentration, visual scanning, executive function, word fluency, and visual memory. The current study planned to assess additional cognitive domains than that assessed in Field et al., 2003, such as, verbal and nonverbal reasoning, motor skills, processing speed, and psychosocial functioning. However, due to reasons explained in the Method section, the current study explored executive function, processing speed, verbal and nonverbal reasoning, and psychosocial functioning.

In the aforementioned studies, high school athletes were also found to have recovered more slowly than college athletes. Specifically, that high school athletes were

still impaired on verbal memory seven days after concussion compared to college athletes (T. Covassin et al., 2012). This finding was consistent with previous research that suggests that high school athletes take longer to recover from concussion than do college athletes (Field et al., 2003; Grant L Iverson et al., 2006; M. R. Lovell, 2004; McClincy et al., 2006).

Next, Baillargeon et al. (2012) hypothesized that the younger age groups would always perform worse on neuropsychological measures than the older age groups following concussions, since high school athletes performed worse than college athletes in previous studies. Baillargeon et al. (2012) assessed processing speed, verbal and visual learning and memory, and attention and executive function.

Baillargeon et al. (2012) found their hypothesis to be unsupported. In their study assessing age-related neuropsychological differences following concussion across three age groups (i.e., children, adolescents, and adults), adolescents performed worse than children and adults. Specifically, adolescents showed the most persistent deficits in working memory (Baillargeon et al., 2012) than other age groups.

These findings could be explained by the fact that the frontal lobe, which is responsible for working memory and other executive functions, undergoes its final stages of maturation during adolescents (Baillargeon et al., 2012; Luna et al., 2011; O'Hare, Lu, Houston, Bookheimer, & Sowell, 2008). During this critical period of development, adolescents are most vulnerable to disruptions in the brain, including those caused by repeated concussion.

The current study assessed the age-related differences on neurocognitive performance in children and adolescents. We measured individuals' performance in

processing speed, executive function, psychosocial functioning, nonverbal reasoning, word knowledge, and verbal learning and memory.

### ***Aim 1c/Hypothesis 1c***

Aim 1c assessed how gender affects neurocognitive functioning after concussion. Hypothesis 1c stated that, with a history of concussion, males would perform better on spatial tasks (i.e., mental rotation, spatial perception) and females better on verbal tasks (i.e., verbal learning and memory, verbal concept formation). Males have significantly larger volumes of parietal lobe grey matter, white matter, and cortical surface area compared to females (Koscik et al., 2009). This greater surface area in male parietal lobes may allow for more neurons in the parietal lobe than females, leading to improved performance on spatial tasks, such as mental rotation, in males versus females.

Gender differences in memory performance have seldom been examined explicitly (Herlitz, Nilsson, & Bäckman, 1997). Many studies have found a relationship between gender and memory performance (Albus et al., 1997; Bolla- Wilson & Bleecker, 1986; Geffen, Moar, O’hanlon, Clark, & Geffen, 1990; McGivern et al., 1998; Ruff, Light, & Quayhagen, 1989), while others have not (Freides & Avery, 1991). However, Lowe et al. (2003) examined gender differences in memory amongst children and adolescents. Lowe et al. (2003) used a comprehensive memory battery (Test of Memory and Learning [TOMAL]), which previous studies did not use, to measure performance. The TOMAL emphasizes broad-based and narrow-band aspects of memory (Reynolds & Bigler, 1994) rather than only narrow-band aspects. This helps provide a clearer understanding of the relationship between gender and memory.



Lowe et al. (2003) assessed 1,279 children (637 males, 642 females) ranging from 5 to 19 years old. Findings suggested that males performed better on spatial memory tasks than females, which was consistent with studies of intelligence in which males outperformed females on spatial tasks (Kaufman, Kaufman-Packer, McLean, & Reynolds, 1991). Lowe et al. (2003) also found that females performed better on verbal memory tasks than males, which was consistent with studies of intelligence where females outperformed males on verbal tasks (Born, Bleichrodt, & Flier, 1987). These findings are supported by another study, which suggests that males rely on a spatial strategy for mental rotation whereas females rely on a more verbal strategy for mental rotation (Pezaris & Casey, 1991).

The current study assessed the gender differences in spatial- and verbal-related tasks amongst children and adolescents. It was hypothesized that, following concussion, males would outperform females on spatial tasks, and females would outperform males on verbal tasks.

### ***Aim 1d***

Aim 1d assessed how the above factors (i.e., concussion history, age, gender) interact to affect neurocognitive functioning after concussion. This aim is comprised of four hypotheses, which are described below.

#### **Hypothesis 1d<sub>1</sub>**

Hypothesis 1d<sub>1</sub> stated that there would be no interaction between age and concussion history on neurocognitive functioning following concussion. Specifically, it

was hypothesized that adolescents would always perform worse on neurocognitive tasks than children, irrelevant of having undergone single or repeated concussion. As described earlier, the adolescent brain is going through a critical stage of the maturation process (i.e., myelination, pruning). As such, the adolescent brain is more susceptible to disruptions in the brain. Such disruptions include concussions. It is hypothesized that adolescents will always perform worse on neurocognitive tasks than children, irrelevant of having undergone single or repeated concussion.

The current study assessed the age-related neuropsychological impairments following repeated concussion in children and adolescents. The current study used a combination of computerized and paper-and-pencil neuropsychological tests, which allowed for a more comprehensive assessment of cognitive abilities.

### **Hypothesis 1d<sub>2</sub>**

Hypothesis 1d<sub>2</sub> stated that there would be no interaction between gender and concussion history on neurocognitive functioning following concussion. Specifically, it was hypothesized that females would always perform worse on neurocognitive tasks than males, irrelevant of having undergone single or repeated concussion. Previous research suggests that females are more likely to be cognitively impaired following concussion than males (Broshek D.K. et al., 2005; T. Covassin et al., 2012; Tracey Covassin, Schatz, & Swanik, 2007). There are multiple explanations that may support this hypothesis. From a physiological perspective, blood flow, glucose metabolism, and musculature may partially explain these findings (Broshek D.K. et al., 2005; Dougan, Horswill, & Geffen, 2014). Blood flow rates are greater in females than in males (Esposito, Van Horn,

Weinberger, & Berman, 1996), and females exhibit a greater basal rate of glucose metabolism (Andreason, Zametkin, Guo, Baldwin, & Cohen, 1994). These differences may lead to an increased ionic flux across the membrane following concussion in females compared to males (Broshek D.K. et al., 2005), exacerbating their neurocognitive impairment following concussion. Regarding musculature, females have weaker head and neck muscles compared to males, allowing for more severe injury, resulting in more severe cognitive outcome (Broshek D.K. et al., 2005; T. Covassin et al., 2012; Tracey Covassin et al., 2007)

Broshek et al. (2005) assessed the gender-related cognitive impairment in high school and college athletes following concussion. Neuropsychological functioning was assessed via the Concussion Resolution Index (CRI), a brief, web-based computerized neurocognitive assessment tool. The CRI assessed three speed factors, including simple reaction time, complex reaction time, and processing speed. Simple reaction time refers to reaction time when only one stimulus is presented, and one response is required. Complex reaction time refers to reaction time when a response is required to only one of two or more stimuli. Findings suggested that females had worse cognitive outcome following concussion. Specifically, they exhibited slower simple and complex reaction time following concussion compared to males (Broshek D.K. et al., 2005). Females were also cognitively impaired 1.7 times more frequently than males following concussion. Also, a meta-analysis assessing the gender-related cognitive sequelae of concussion found that females produced larger effect sizes than males, suggesting they experienced greater cognitive impairment following concussion than males (Karr et al., 2014).

Another possible explanation for these gender-related cognitive differences following concussion may be related to the style of play or level of aggressiveness in different sports. Sports played by males are typically assumed to be more aggressive. This is partly why helmets are often required for males, but not for females, even though the same sport is played. An example of such a sport is lacrosse (Broshek D.K. et al., 2005). However, this is only a theory and may not substantially account for that gender-related cognitive difference.

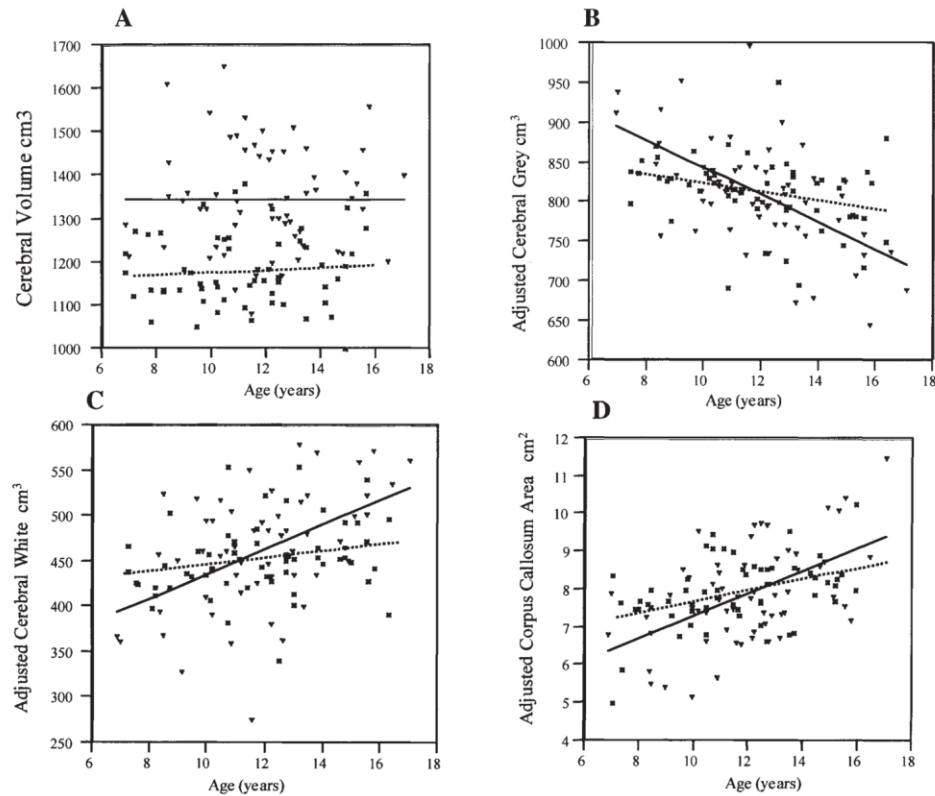
The current study assessed the neurocognitive impairments following repeated concussion. As previous findings suggested, females have weaker musculature than males, such that each injury will have cumulative adverse effects. This hypothesis was tested in the younger age population, which assessed neurocognitive impairment in children and adolescents following repeated concussion.

### **Hypothesis 1d<sub>3</sub>**

Hypothesis 1d<sub>3</sub> stated that, with a history of concussion, female children would perform better than male children, and male adolescents would perform better than female adolescents, on neurocognitive performance. Males and females' brains work very differently. Given that they develop at different rates, it is likely that their performance on neurocognitive measures will differ based on their age.

Bellis et al. (2001) assessed sex differences in brain maturation during childhood and adolescence. The individuals ranged from six to 17 years old. Magnetic resonance imaging (MRI) was performed to assess the total cerebral gray and white matter volumes as well as the corpus callosum area (band of nerve fibers that connect the two

hemispheres of the brain together). Findings suggested a significant age by sex interaction for cerebral grey and white matter volumes and corpus callosum area (Figure 2). Females showed significant changes with age, but at a slower rate than boys. Specifically, males experienced a ~19.1% reduction in grey matter volume between ages six and 18, whereas females experienced a 4.7% reduction. On the other hand, males experienced a 45.1% increase in white matter and a 58.5% increase in corpus callosum area, whereas females experienced a 17.1 and 27.4% increase, respectively (Bellis et al., 2001). The reduction in grey matter volume is likely due to dendritic pruning, and the white matter increase is likely due to increases in myelination.



**Figure 2.** Scatterplots of cerebral volume (A), cerebral grey matter (B) and cerebral white matter (C) volumes, and corpus callosum areas (D) by age and gender in healthy male (solid line) and female (dashed line) children and adolescents (Bellis et al., 2001). Males had an ~19.1% reduction in grey matter volume between six and 18 years of age compared with a 4.7% reduction in females. On the other hand, males had a 45.1% increase in white matter and a 58.5% increase in corpus callosum area compared with 17.1 and 27.4% increases, respectively, in females.

Given this age by gender interaction, it is likely that children and adolescents will perform differently on neurocognitive measures as a function of their gender. As such, given that female children have a greater volume of white matter compared to male children, female children will likely perform better on neurocognitive measures than male children. However, given females' slower rate of brain development than males, female adolescents will have less white matter than male adolescents. Hence, it is hypothesized that female children will perform better on neurocognitive measures than male children,

and male adolescents will perform better than female adolescents on neurocognitive measures.

Another study assessed the age and gender differences in high school and college athletes (T. Covassin et al., 2012). This study found there to be an age by gender interaction on the Balance Error Scoring System (BESS), which assesses for postural stability defects. The interaction suggested that high school male athletes demonstrated worse overall performance on the BESS than college male athletes, and college female athletes demonstrated worse overall performance on the BESS than high school female athletes. They found no age by sex interaction on neurocognitive performance including visual memory, verbal memory, processing speed, or reaction time. Given the developmental changes that exist during that developmental transition, it is expected that the age by gender interactions will be found in younger children, following a history of concussion.

The current study assessed sex differences as a function of age in children and adolescents with a history of concussion. This study expanded on the findings of Bellis et al. (2001) by exploring whether the structural developmental differences determined by the MRI scans translate to neurocognitive differences following concussion.

### **Hypothesis 1d<sub>4</sub>**

Hypothesis 1d<sub>4</sub> stated that there would be no interaction between age, gender, and concussion history on neurocognitive functioning following concussion. No evidence was found to suggest or rule out an interaction between these three factors. The hypothesized

age-by-gender interaction on neurocognitive performance described above is likely to occur in the presence of a single concussion as well as following a repeated concussion.

## **Aim 2**

The second aim of the current study was to determine whether concussion history (1 concussion vs. >1 concussion), age (children [<12 years] vs. adolescents [ $\geq$ 12 years]), and/or gender (male vs. female) affect psychosocial functioning (i.e., anxiety, depression, hyperactivity). Aim 2 was broken down into four sub-aims. The first three sub-aims each had their own specific hypothesis, and the final sub-aim was comprised of four hypotheses. The sub-aims and hypotheses are discussed below.

### ***Aim 2a/Hypothesis 2a***

Aim 2a assessed how the number of concussions affects psychosocial functioning. Hypothesis 2a stated that children and adolescents who have sustained repeated concussion would exhibit a greater increase of psychosocial impairment (i.e., anxiety, depression, hyperactivity), based on age-related norms, compared to those who have sustained a single concussion.

A study assessing long-term executive function in children who have sustained TBI found that the resulting impairments in executive function following TBI are related to more general measures of psychosocial and adaptive functioning (Mangeot et al., 2002). These children were found to display deficits in executive function (e.g., behavioral regulation), which interfered with their social relationships and caused problems at home. These social and personal issues are likely to lead to other



psychosocial difficulties, such as depression (e.g., loss of a relationship or difficulty coping with unpleasant situations), anxiety (e.g., struggling to make friends), and hyperactivity (e.g., engaging in behavioral dysregulation due to frustration, anger, or loneliness).

A mouse model of TBI to the immature brain was developed to understand the psychosocial effects following TBI in children (Pullela et al., 2006). To assess these effects, mice were subjected to TBI to the frontoparietal cortex at postnatal day 21, the time point approximate to that of a toddler-aged child. The frontoparietal cortex, which includes regions of the frontal and parietal cortices, has been hypothesized to control the allocation of spatial attention to environmental stimuli (Capotosto, Babiloni, Romani, & Corbetta, 2009). As a result of this injury, the mice exhibited hyperactivity, which was evident two weeks after injury. Specifically, the mice were more active in a novel environment following TBI compared to age-matched controls. Clinical studies demonstrate similar findings. Specifically, attention deficit/hyperactivity disorder (ADHD) is found to be the most common psychiatric disorders following pediatric TBI (Bloom et al., 2001; Konrad, Gauggel, & Schurek, 2003).

In another study, Bajwa et al., 2016 looked into the long-term affective and behavioral deficits after repeated injury in which mice received either a single mild CHI (mCHI), a repeated mild CHI (rmCHI) consisting of one impact to each hemisphere separated by three days, or a moderate controlled cortical impact injury (CCI). Findings suggested that depression-like behaviors were observed in rmCHI animals at 90 dpi.

Disturbances to the prefrontal cortex may be integral to the pathogenesis of hyperactivity and anxiety disorders. Anatomical and functional alterations in the

frontostriatal circuits (neural pathways that connect the frontal lobe regions with the basal ganglia, which is associated with voluntary motor skills) have been implicated in the pathogenesis of ADHD (Solanto, 2002).

Depression is the most cited psychological disturbance after TBI (K. M. Guskiewicz et al., 2007). Anxiety and depression are well recognized to occur after TBI (Kutcher & Eckner, 2010). Recently, TBI has been identified as a risk factor for chronic depression, which was evidenced by a prospective cohort of retired World War II veterans that were assessed for prevalence of depression several decades after the initial injury (K. M. Guskiewicz et al., 2007). A study assessing about 50-year-old retired professional football players suggested a link between recurrent sport-related concussion and increased risk for clinical depression (K. M. Guskiewicz et al., 2007). These findings emphasize the importance of understanding potential neurological consequences of recurrent concussion.

The current study addressed the psychosocial functions that were addressed in these studies. However, what set the current study apart from the studies illustrated above was that the current study focused on the younger aged population (children and adolescents). The previous research suggests that mood instability is a consequence of TBI (Jorge & Arciniegas, 2014). The current study assessed how certain psychosocial functions (i.e., anxiety, depression, hyperactivity) are affected following concussion, which is a mild TBI.

### ***Aim 2b/Hypothesis 2b***

Aim 2b assessed how age affects psychosocial functioning after concussion.

Hypothesis 2b stated that, with a history of concussion, adolescents would exhibit a greater increase of psychosocial impairment (i.e., depression, anxiety, hyperactivity), based on age-related norms, compared to children.

Adolescence is a time of greater emotional reactivity and a period where symptoms of many psychiatric disorders manifest (Casey, Jones, & Hare, 2008). During brain development, white matter increases in the frontal and parietal cortices and then pruning begins post adolescence (Blakemore & Choudhury, 2006). As such, adolescents have more developed frontal and parietal cortices compared to children. These cortices are associated with perspective-taking, such as making the distinction between awareness of one's own mental state and another person's mental state at the emotional, conceptual, motor, and visuospatial levels (Blakemore & Choudhury, 2006). Therefore, adolescents have improved social cognition (ability to process and apply information about other people and social situations) than children. This can be taken one step further as to say that as a result of improved social cognition, adolescents are hyperaware of others and how others can affect them, making them more susceptible to vulnerability and getting hurt from others. Without proper and effective coping skills, this hyperawareness and vulnerability may lead to the development of poor psychosocial functioning, such as depression or anxiety. In addition, the increased social stressors that adolescents experience in comparison to children may exacerbate these symptoms.

It was hypothesized that adolescents would exhibit a greater increase of hyperactivity following concussion than children. The evidence behind this is that the frontal cortex, specifically the prefrontal cortex, is one of the last brain structures to mature. This region of the brain is associated with behavioral regulation. As such, the

brain is going through critical stages of development during adolescence, and brain injury is likely to interfere with that process, affecting the individual's ability to regulate their behavior.

These phenomena were explored in the current study via parent rating scales on the BASC-2. The frontal lobe is the one region of the brain most affected by sport-related concussion (Baillargeon et al., 2012). As a result, abilities governed by that brain region are likely to be compromised. As such, it was hypothesized that there would be age-related psychosocial effects of individuals with a history of concussion.

### ***Aim 2c/Hypothesis 2c***

Aim 2c assessed how gender affects psychosocial functioning after concussion. Hypothesis 2c stated that, with a history of concussion, females would endorse a greater increase of psychosocial impairment (i.e., depression, anxiety, hyperactivity) than males. One explanation for this hypothesis is that females tend to be more emotionally perceptive than males (Whittle, Yucel, Yap, & Allen, 2011), so it is hypothesized that they would experience their psychosocial and affective difficulties more significantly than males do.

One study found that women reported more lingering mood disorders and anxiety symptoms following concussion than males (Santa Maria, Pinkston, Miller, & Gouvier, 2001). This study assessed the post-concussion symptomology of undergraduates who sustained a concussion (Santa Maria et al., 2001). Participants were administered the Postconcussion Symptom Checklist (PCSC), an instrument assessing self-reported post-concussion symptoms. Females reported higher levels of post-concussion symptomology

compared to males, including symptoms of depression and anxiety (Santa Maria et al., 2001). These findings are supported by other studies suggesting higher base rates of depressive disorders (Compas et al., 1997; Frank, Carpenter, & Kupfer, 1988; Gater et al., 1998) and anxiety disorders (Gater et al., 1998) in women than in men. These findings have been supported in the adolescent population (age 11 to 18) as well, suggesting females have higher mood and anxiety levels than males (Compas et al., 1997).

The current study assessed whether there are gender-related psychosocial differences in children and adolescents with a history of concussion. The previous studies suggested women reported more mood-related symptoms compared to males following concussion. The current study assessed these differences via parent-rated scores on the BASC-2. This allowed for an objective analysis of gender-related differences of psychosocial functioning.

### ***Aim 2d***

Aim 2d assessed how the above factors (i.e., concussion history, age, gender) interact to affect psychosocial functioning after concussion. This aim was comprised of four hypotheses, which are described below.

#### **Hypothesis 2d<sub>1</sub>**

Hypothesis 2d<sub>1</sub> stated that there would be no interaction between age and concussion history on psychosocial impairment following concussion. Specifically, it was hypothesized that adolescents would always exhibit a greater increase in psychosocial

difficulties following concussion, irrelevant of having endured single or repeated concussion, compared to children. The explanation behind this hypothesis is that the adolescent brain is going through a critical stage of development and any injury, including single or repeated concussion, would interfere with that process.

One study assessed a mouse model of TBI to the immature brain to understand psychosocial effects following TBI (Pullela et al., 2006). The mice were subjected to TBI to the frontoparietal cortex at postnatal day 21, an age approximate to that of a toddler-aged child (Pullela et al., 2006). Findings suggested age-dependent decreases in measures of anxiety. Specifically, reduced measures of anxiety were apparent in the juvenile cohort, relative to controls, but were not evident in the older-aged cohort. The older cohort exhibited worse anxiety-like symptoms following TBI compared to the younger-aged cohort.

As stated earlier, given that adolescents are going through a critical period of brain development (i.e., white matter increases and synaptic pruning), it was hypothesized that brain injury would have more severe effects during that stage of development (Wall et al., 2006). Their frontal and parietal lobes are going through maturation, which play a role in executive functioning, behavioral regulation, and psychosocial functioning. Additionally, deficits in behavioral manifestations of executive functions are related to psychosocial functioning (Mangeot et al., 2002).

The current study assessed the age-specific psychosocial effects following single and repeated concussion in children and adolescents. The current study differed from the previous studies in the instrument that was used to assess psychosocial functioning, as well as the age population that was examined. The current study measured psychosocial

functioning using parent-rated scores on the BASC-2, and the current study assessed children and adolescents.

### **Hypothesis 2d<sub>2</sub>**

Hypothesis 2d<sub>2</sub> stated that there would be no interaction between gender and concussion history on psychosocial impairment following concussion. Specifically, it was hypothesized that females would always exhibit a greater increase in psychosocial difficulties following concussion, irrelevant of having endured single or repeated concussion, compared to males.

As described earlier, women are known to report more lingering mood disorders and anxiety symptoms following concussion than males (Santa Maria et al., 2001). As such, given that TBI is known to result in psychosocial difficulties, such as depression, anxiety, and hyperactivity (Santa Maria et al., 2001), that repeated concussions' adverse effects are cumulative (Michael W Collins et al., 1999), and that females are affected more severely to concussion than males (Broshek D.K. et al., 2005; T. Covassin et al., 2012; Tracey Covassin et al., 2007), then it is likely that females will endorse worse psychosocial effects than males following concussion.

In the current study, the gender-specific psychosocial effects were assessed in children and adolescents following single and repeated concussion via parent-rated scales on the BASC-2. The current study differed from the studies described above, in that the psychosocial outcome in the current study was assessed via parent-rating scales on the BASC-2.

### **Hypothesis 2d<sub>3</sub>**

Hypothesis 2d<sub>3</sub> states that, with a history of concussion, male children would have a greater increase of psychosocial difficulties than female children, and female adolescents would have a greater increase of psychosocial difficulties than male adolescents.

Although the brain reaches approximately 90% of its adult size by the age of six, the gray and white matter components undergo dynamic changes throughout adolescence (Casey et al., 2008). As described earlier, males and females' brains work very differently. As their brains develop at different rates and stages of life, it is likely that their psychosocial functions will be affected differently in the presence of a history of concussion. In a study assessing sex differences in brain maturation during childhood and adolescents (Bellis et al., 2001), findings suggested a significant age by sex interaction of white matter volumes (Figure 2). The findings suggested that females showed significant changes with age, but at a slower rate than males.

A decreased amount of white matter in the brain is associated with psychosocial difficulties, such as depression (Westlye, Bjørnebekk, Grydeland, Fjell, & Walhovd, 2011), anxiety (Cooper, Thapar, & Jones, 2015; Westlye et al., 2011) and hyperactivity (Cooper et al., 2015). As such, since male children have less white matter volume than female children (Bellis et al., 2001), it is hypothesized that male children would endorse greater increases in psychosocial difficulties (depression, anxiety, hyperactivity) than female children. Also, since female adolescents have less white matter volume than male adolescents (Bellis et al., 2001), it is hypothesized that female adolescents would endorse



greater increases in psychosocial difficulties (depression, anxiety, hyperactivity) than male adolescents.

The current study explored the age by gender interaction in children and adolescents with a history of concussion. The current study expanded on the findings from Bellis et al. (2001), Westlye et al. (2011) and Cooper et al. (2015) by assessing the link between white matter differences in young people (i.e., children and adolescent) and psychosocial functioning across gender.

#### **Hypothesis 2d<sub>4</sub>**

Hypothesis 2d<sub>4</sub> stated that there would be no interaction between concussion history, age, and gender on psychosocial impairment following concussion. No evidence was found to suggest or rule out an interaction between these three factors.

#### **Aim 3**

The third aim of the current study was to determine whether psychosocial functioning in young people is correlated with neurocognitive functioning following concussion in young people. This aim was broken down into two hypotheses. Hypothesis 3a stated that, in young people, there would be a negative correlation between premorbid psychosocial impairment (i.e., anxiety, depression, hyperactivity) and neurocognitive functioning following concussion. Specifically, higher premorbid anxiety, depression, and hyperactivity would be associated with worse post-concussive neurocognitive functioning in young people. Hypothesis 3b stated that, in young people, there would be a negative correlation between post-morbid psychosocial impairment (i.e., anxiety,

depression, hyperactivity) and neurocognitive functioning following concussion.

Specifically, higher post-concussive anxiety, depression, and hyperactivity would be associated with worse post-concussive neurocognitive functioning in young people.

Aim 3 was intended to bridge Aims 1 and 2 together. Specifically, these findings could help suggest the implications of psychosocial functioning in young people.

Additionally, if these hypotheses were found to be supported, it would provide additional attention and importance on psychosocial functioning in young people and possibly lead to the discussion of helpful treatment recommendations for improving psychosocial functioning in young people.

Cromer, Stevens, DePrince, and Pears, 2006 were the first to investigate the specificity of cognitive functions related to dissociation in children. Dissociation was defined as a disruption in the usually integrated functions of consciousness, identity, and perception (American Psychiatric Association, 2000). Cromer et al., 2006 asked twenty-four 5- to 8-year-old foster children to complete several subtests from A Developmental Neuropsychological Assessment (NEPSY) in the executive function/attention domain. The foster caregivers also completed the Child Dissociative Checklist. Findings suggested that higher levels of childhood dissociation were associated with deficits in tasks requiring inhibition, but not with tasks requiring primarily planning, strategy, or multiple rule sets. Cromer et al. (2006) is related to the current study, in that dissociation may also include psychosocial difficulties (i.e., anxiety, depression, hyperactivity). As a result, the finding that childhood dissociation is related to executive function (Cromer et al., 2006) may support Hypothesis 3. The current study expands on Cromer et al. (2006) by specifically addressing this correlation in the event of having undergone a concussion.

In a later study, DePrince, Weinzierl, and Combs, 2009 examined executive functions amongst children exposed to familial trauma (e.g., sexual abuse, physical abuse, witnessing domestic violence). The contribution of trauma exposure to executive functioning took into account symptoms of trauma (i.e., anxiety and dissociation), socio-economic status, and possible TBI exposure. Findings suggested that executive functioning deficits might provide one route via which maltreated children become at risk for peer, academic, and behavior problems relative to their peers.

The current study expands on the previous literature by exploring whether premorbid or post-morbid psychosocial impairment (i.e., anxiety, depression, hyperactivity) is associated with post-morbid neurocognitive impairment in young people. These findings may help stir up discussions regarding the implications of psychosocial functioning in young people.

## CHAPTER THREE

### SPECIFIC AIMS

The purpose of the current study was to determine the neurocognitive and psychosocial effects of repeated concussions on children and adolescents and interactions with age and gender. The overarching hypothesis was that repeated concussions would induce more severe neurocognitive (i.e., executive function, processing speed) and psychosocial (i.e., anxiety, depression, hyperactivity) deficits than a single concussion, and that these deficits would be worse in females and adolescents. The objective was met by addressing the following three aims.

#### Aim 1

Aim 1 was to determine whether concussion history (single concussion vs. repeated concussion), age (children [ $<12$  years] vs. adolescents [ $\geq 12$  years]), and/or gender (male vs. female) affect performance on tasks of neurocognitive functioning (i.e., processing speed, executive function). Neurocognitive tasks that were a measure of nonverbal reasoning, motor control, word knowledge, and verbal learning and memory were only explored as a factor of gender, in Aim 1c. Main Effects: **Hypothesis 1a:** Children and adolescents who have sustained repeated concussions would perform worse on tasks of executive function and processing speed, based on age-related norms, compared to those who have sustained a single concussion. *Rationale:* Repeated concussions result in substantial abnormalities (neural atrophy) in the frontal cortex, which governs executive function (which is dependent on processing speed; Karr, Areshenkoff, & Garcia-Barrera, 2014). **Hypothesis 1b:** In general, adolescents with a

history of concussion would perform worse on neurocognitive tasks than children with a history of concussion, based on age-related norms. *Rationale:* Adolescents are more susceptible to disruptions in the brain during their critical period of brain development (Wall et al., 2006). ***Hypothesis 1c:*** With a history of concussion, males would perform better on spatial tasks (i.e., mental rotation, spatial perception) and females better on verbal tasks (i.e., verbal learning and memory, verbal concept formation). *Rationale:* Males' parietal lobe, which governs visuospatial ability, has a larger surface area than that of females (Koscik et al., 2009). Previous studies have found that males outperform females on spatial tasks (Lowe, Mayfield, & Reynolds, 2003; Huang, 1993; Robinson et al., 1996), and females outperform males on verbal tasks (Lowe et al., 2003; Huang, 1993; Temple & Cornish, 1993). Interactions: ***Hypothesis 1d<sub>1</sub>:*** There would be no interaction between age and concussion history on neurocognitive functioning following concussion. *Rationale:* Adolescents would always perform worse on neurocognitive tasks than children, following concussion, due to frontal lobe functions being more susceptible to disruption during adolescence. Specifically, the frontal lobe region is going through its final maturation process (Baillargeon et al., 2012; Wall et al., 2006). ***Hypothesis 1d<sub>2</sub>:*** There would be no interaction between gender and concussion history on neurocognitive functioning following concussion. *Rationale:* Females would always perform worse on neurocognitive tasks than males, irrelevant of having undergone single or repeated concussion, due to their generally weaker musculature compared to males. ***Hypothesis 1d<sub>3</sub>:*** With a history of concussion, female children would perform better than male children, and male adolescents would perform better than female adolescents, on

neurocognitive performance. *Rationale:* Girls' brains mature at a slower rate than boys' (Bellis et al., 2001).

## **Aim 2**

Aim 2 was to determine whether concussion history (1 concussion vs. >1 concussion), age (children [ $<12$  years] vs. adolescents [ $\geq 12$  years]), and/or gender (male vs. female) affect psychosocial functioning (i.e., anxiety, depression, hyperactivity). Main Effects: **Hypothesis 2a:** Children and adolescents who have sustained repeated concussion would exhibit a greater increase of psychosocial impairment (i.e., anxiety, depression, hyperactivity), based on age-related norms, compared to those who have sustained a single concussion. *Rationale:* TBI results in long-term psychosocial difficulties in children (Mangeot et al., 2002), and repeated concussions' adverse effects are cumulative (Michael W Collins et al., 1999). **Hypothesis 2b:** With a history of concussion, adolescents would exhibit a greater increase of psychosocial impairment (i.e., depression, anxiety, hyperactivity), based on age-related norms, compared to children. *Rationale:* More developed parietal and frontal cortices allow individuals to distinguish awareness of their own and others' mental state and emotional levels (Blakemore & Choudhury, 2006). **Hypothesis 2c:** With a history of concussion, females would endorse a greater increase of psychosocial impairment (i.e., depression, anxiety, hyperactivity) than males. *Rationale:* Females are more aware of their emotions. Interactions: **Hypothesis 2d<sub>1</sub>:** There would be no interaction between age and concussion history on psychosocial impairment following concussion. *Rationale:* Adolescents would always exhibit a greater increase in psychosocial difficulties following concussion, irrelevant of

having endured single or repeated concussion, compared to children. ***Hypothesis 2d<sub>2</sub>***: There would be no interaction between gender and concussion history on psychosocial impairment following concussion. *Rationale*: Females would always exhibit a greater increase in psychosocial difficulties following concussion, irrelevant of having endured single or repeated concussion, compared to males. ***Hypothesis 2d<sub>3</sub>***: With a history of concussion, male children would have a greater increase of psychosocial difficulties than female children, and female adolescents would have a greater increase of psychosocial difficulties than male adolescents. *Rationale*: Females' brains mature at a slower rate than males' (Bellis et al., 2001).

### **Aim 3**

Aim 3 was to determine whether psychosocial functioning in young people is correlated with neurocognitive functioning following concussion in young people.

Correlation effects: ***Hypothesis 3a***: In young people, there would be a negative correlation between premorbid psychosocial impairment (i.e., anxiety, depression, hyperactivity) and neurocognitive functioning following concussion. *Rationale*: Childhood dissociation is related to executive dysfunction (Cromer et al., 2006). Maltreated children experience executive dysfunction, leading to higher risk for peer, academic, and behavior problems (DePrince et al., 2009). ***Hypothesis 3b***: In young people, there would be a negative correlation between post-morbid psychosocial impairment (i.e., anxiety, depression, hyperactivity) and neurocognitive functioning following concussion. *Rationale*: Same as Hypothesis 3a.

## **CHAPTER FOUR**

### **SIGNIFICANCE**

Each year, an estimated 38 million children and adolescents participate in organized sports in the United States (Daneshvar, Nowinski, Mckee, & Cantu, 2011). Many of these activities are associated with increased risk of traumatic brain injury (TBI). One study found that concussion injury in children between the ages of six and 16 is six times more likely to have resulted from an organized sport than from other leisure physical activities (Browne & Lam, 2006). Another study found head injury to be the most frequent cause of death in the pediatric population, comprising between 50 and 80% of all trauma-related deaths each year (Ommaya, A. K., Goldsmith, W., Thibault, 2002).

A concussion, such as that sustained in sports (e.g., football, baseball, volleyball...) or combat, is the mildest and most common form of TBI and may be associated with functional, but usually not structural, changes in the brain. It is a common injury in individuals of all ages, including children and adolescents. A concussion has been estimated to occur in 1.6 to 3.6 million young athletes per year (M R Lovell & Fazio, 2008). By the time adolescents reach high school, 53% report a history of concussion, and in the college populations, 36% report a history of repeated concussions (Field et al., 2003).

Concussions are known to lead to neurocognitive and psychosocial difficulties as well as an increased risk for sustaining future concussions (MW W Collins et al., 2002; Graham, R., Rivara, F. P., Ford, M. A., Spicer, 2013). Moreover, after sustaining a concussion, many athletes tend to hide it for fear of being removed from the game or being seen as weak (Schwarz, 2008). The current study aims to assess to what extent



repeated concussions exacerbate neurocognitive and psychosocial functioning compared to single concussion.

Successful completion of the current study's aims will lead to a clearer understanding and increased awareness of the outcomes and dangers of repeated concussion. Understanding the neurocognitive and psychosocial difficulties followed by concussion is an essential step in normalizing the situation to illustrate that sustaining a concussion is not a sign of weakness. It is also an essential step in creating protective devices to reduce the incidence of sports-related concussion, developing rule changes aimed at reducing individuals' exposure to hazardous conditions, and developing stricter return-to-play guidelines.

Currently, return-to-play guidelines do not take gender and other individual differences into account (Broshek D.K. et al., 2005). Understanding the age and gender specific outcomes of repeated concussion will expand the knowledge in this field. These findings will provide more knowledge to individuals who sustained the concussion, their parents, and doctors.

The current study will improve the methods of intervention approaches by addressing limitations in the previous literature, including small sample size (Michael W Collins et al., 1999; T Covassin, Elbin, & Nakayama, 2010; Tracey Covassin et al., 2007; Graham, R., Rivara, F. P., Ford, M. A., Spicer, 2013; G L Iverson, Lovell, & Collins, 2003; Warden, D. L., Bleiberg, J., Cameron, K., L., Ecklund, J., Walter, J., Sparling, M. B., Reeves, D., Reynolds, K. Y., Arciero, 2001). The current study included children and adolescents between the ages of four and 19. The current study measured neurocognitive performance in multiple cognitive domains (i.e., processing speed, executive function,

verbal and non-verbal reasoning, and verbal learning and memory) and psychosocial functioning via parent-ratings on the Behavioral Assessment Scale for Children, Second Edition (BASC-2). Finally, the current study bridged these findings by exploring the relationship between pre- and post-morbid psychosocial and post-morbid neurocognitive functioning.

## **CHAPTER FIVE**

### **INNOVATION**

Previous studies have assessed the neurocognitive and psychosocial effects of individuals who have sustained repeated concussions compared to single concussions. This has been extensively studied in professional athletes, but there remains a dearth of literature with regard to children and adolescents and repeated concussions (MW W Collins et al., 2002; M R Lovell & Fazio, 2008). Studying the younger aged population is important to explore, given the increasing participation of the younger age ranges in sports over the past decade (M R Lovell & Fazio, 2008).

The current study aimed to determine in what ways repeated concussions further exacerbate neurocognitive and psychosocial effects in children and adolescents compared to single concussion. Neurocognitive outcomes were measured by way of neuropsychological measures, and psychosocial outcomes were measured by way of parent-rating scales.

Previous studies have found that repeated concussions further exacerbate neurocognitive (Belanger & Vanderploeg, 2005; Michael W Collins et al., 1999; Graham, R., Rivara, F. P., Ford, M. A., Spicer, 2013; Karr et al., 2014; Wall et al., 2006) and psychosocial (Daneshvar, Riley, et al., 2011; K. M. Guskiewicz et al., 2007; Schatz, Moser, Covassin, & Karpf, 2011; Schwarz, 2008) outcomes. However, these studies vary in age population, sample size, and the neuropsychological and psychosocial measures used. The current study addressed certain challenges that the previous literature faced in their studies.

Belanger and Vanderploeg's (2005) meta-analysis represented one of the most recent syntheses of findings on multiple concussions. They found that the effect sizes inflated with prior history of concussion. They concluded that acute effects (within 1 day of injury) of concussion were greatest for delayed memory, memory acquisition, and global cognitive functioning, whose effect sizes inflated with prior history of concussion. However, when assessing the neuropsychological outcomes of individuals in sports that involve contact with the head (e.g., soccer heading, boxing), they utilized a different set of tests that relied more heavily upon executive functioning and concluded that executive function represented one of the largest effect sizes. To address this variability in results, the current study involved a broader set of tests to measure different cognitive domains (i.e., processing speed, executive function, verbal and non-verbal reasoning, and verbal learning and memory).

Karr et al. (2014) also conducted a meta-analysis of neuropsychological outcomes following concussion. They concluded that executive function was the most sensitive cognitive domain following repeated concussion. They also found that females and high school athletes (when comparing high school athletes to adults) suffered the largest deficits.

The studies listed previously only included high school, collegiate, and adult age groups. The current study involved the younger age population, including individuals between the ages of four and 19. Also, the previous studies failed to assess certain cognitive domains such as processing speed, and verbal and non-verbal reasoning, which are addressed in the current study.

In regards to psychosocial functioning, Daneshvar et al. (2011) concluded that prior concussions might have lasting effects on behavior. They found these effects are more common in children because they are more likely to have symptoms of mood or conduct disorders reported by parents and teachers after injury. These changes include depression (K. M. Guskiewicz et al., 2007), anxiety (Kutcher & Eckner, 2010), and hyperactivity (Daneshvar, Riley, et al., 2011) and are more likely to occur in females (Santa Maria et al., 2001). Rather than using a general health questionnaire, the current study utilized a more accurate measure of psychosocial functioning by way of the Behavioral Assessment System for Children, Second Edition (BASC-2). The current study addressed the limitations of the previous literature to develop a more extensive exploration of the neurocognitive and psychosocial outcomes following repetitive concussion.

## **CHAPTER SIX**

### **METHOD**

#### **Patients**

Patients included in the current study were children and adolescents who were diagnosed with a concussion and sought neuropsychological evaluation at Children's Hospital Los Angeles (CHLA), Children's Orthopaedic Center, under the supervision of Anita Hamilton, Ph.D., ABPP-CN. Some of the patients had a history of multiple concussions (repeated concussion group), while others have had only one concussion (single concussion group).

Data collected from patients who were assessed during the years of 2012 to 2016 were included in the analysis. Patients ranged between the ages of four and 19 years old. It was projected that a total of about 160 patients would be included in the analysis, with 50% of them being male. Additionally, it was projected that about 70% of the patients would have only sustained a single concussion, while the remained 30% sustained repeated concussion (more than one concussion). The patients who sustained a repeated concussion were the "experimental group," while those who sustained a single concussion were the "controls."

However, after conducting the analyses, the actual sample sizes differed slightly from the projected sample sizes. Firstly, neuropsychological data was collected for a total of 118 patients, not 160. Secondly, not each and every one of the 118 patients was administered every measure. As a result, when conducting the multivariate analysis of variance (MANOVA), the total sample size included the common number of subjects

whose data existed under each factor. Tables 2-5 illustrate the sample sizes used in each aim.

**Table 2.** Sample Sizes (n) of Each Condition in Aim 1

<u>Single Concussion</u>	<u>&lt;12 years old</u>	<u>≥12 years old</u>	<u>Total</u>
Male	6	12	18
Female	7	8	15
Total	13	20	33
<u>Repeated Concussion</u>			
Male	6	8	14
Female	3	5	8
Total	9	13	22
<u>Grand Total</u>	22	33	55

**Table 3.** Sample Sizes (n) of Hypothesis 1c Conditions Amongst Spatial and Verbal Tasks

<b>Male</b>	<u>&lt;12 years old</u>	<u>≥12 years old</u>	<u>Total</u>
<u>Concussion History</u>			
Single Concussion	2	5	7
Repeated Concussion	4	9	13
≥1 concussion	1	4	5
Total	7	18	25
<b>Female</b>			
<u>Concussion History</u>			
Single Concussion	0	2	2
Repeated Concussion	0	4	4
≥1 concussion	1	8	9
Total	1	14	15

**Table 4.** Sample Sizes (n) of Aim 2's Main Effect and Interaction Conditions

<u>Single Concussion</u>	<u>&lt;12 years old</u>	<u>≥12 years old</u>	<u>Total</u>
Male	3	8	11
Female	0	1	1
Total	3	9	12
<u>Repeated Concussion</u>			
Male	4	2	6
Female	1	5	6
Total	5	7	12

**Table 5.** Sample Sizes (n) of Aim 2's Main Effect Conditions Only

<u>Age</u>	<u>n</u>
<12 years old	8
≥12 years old	16
<u>Gender</u>	
Male	17
Female	7
<u>Concussion History</u>	
Single	12
Repeated	12

### Measures

Patients were administered a neuropsychological evaluation from a battery compiled by CHLA. The battery included measures assessing neurocognitive and psychosocial functioning. When necessary, tests were used that had versions that were specifically adapted to age. In other instances, the tests that were used were appropriate for all age groups tested. The measures assessing neurocognitive functioning were administered in a quiet environment, and the procedure lasted about four hours. The neurocognitive domains that were assessed included processing speed, executive function, verbal and non-verbal reasoning, and verbal learning and memory. Psychosocial domains that were assessed via the Behavioral Assessment System for Children – 2<sup>nd</sup> Edition (BASC-2) included anxiety, depression, and hyperactivity. These measures are described in detail below.

#### ***Behavioral Assessment System for Children, 2<sup>nd</sup> Edition (BASC-2)***

The BASC-2 was a norm-referenced diagnostic tool designed to assess the psychosocial functioning (relating to the interrelation of social factors and individual



thought and behavior) of children and young adults ages two to 21 years.

The current study analyzed psychosocial data that was collected from the parent-rating scale (BASC-2-Parent Rating Scales [BASC-2 PRS]). The BASC-2 PRS is a parent-rating scale that takes about 10 to 20 minutes to complete. This measure was separated into three forms: preschool (ages two to five; BASC-2 PRS-P), child (ages six to 11; BASC-2 PRS-C), and adolescent (ages 12 to 21; BASC-2 PRS-A). When given these measures, parents were asked to fill out the form to reflect their child's psychosocial functioning before and after the concussion (premorbid and post-morbid psychosocial functioning, respectively).

#### ***Modified Balance Error Scoring System (Modified BESS)***

This task measured balance. The task consisted of patients putting their hands on their iliac crest and closing their eyes for twenty seconds in each of the following position, double leg stance, single leg stance, and tandem stance. The examiner recorded the number of errors to determine their performance (i.e., hands lifted off iliac crest, opening eyes, stepping, stumbling, falling, moving hips into greater than 30 degrees abduction, lifting forefoot or heel, or remaining out of test position for more than five seconds). For reasons described in the Operational Definitions section below, this measure was not incorporated into the current study.

#### ***California Verbal Learning Test***

These tasks assessed verbal learning and memory and were explored in Hypothesis 1c.

### **California Verbal Learning Test, Children's Version (CVLT-C)**

This task is designed for individuals between the ages of five years and 16 years, 11 months. It takes about 15 to 20 minutes to administer plus 20 to 30 minutes of delay. The task begins with the examiner reading a "Monday shopping list" five times. The individual is asked to recall as many items as possible following each presentation. The list consists of 15 items and three semantic categories (fruit, clothing, and toys). The sixth trial is an interference task or the "Tuesday shopping list" consisting of 15 new items. Patients are asked to recall as many items as possible from this list. The individual is then asked to recall as many items as possible from the original list. Next, the examiner provides list categories as cues to elicit recall from the original list. Following a 20-minute delay, the individual is asked to recall as many items from the original list as possible, asked to recall items from the original list after being provided with the categorical cues, and finally read a 45-item list aloud and asked to indicate whether or not each word was on the list. After a 10-minute delay, the forced-choice recognition task is administered. In this task, the examiner reads two words and asks the patient which word was on the original list.

### **California Verbal Learning Test, Second Edition (CVLT-II)**

This task is designed for individuals between the ages of 16 and 89 years. It takes about 30 minutes to administer plus 30 minutes of delay. The task follows the same protocol as the CVLT-C, except that the lists in the CVLT-II consist of 16 items rather than 15 and the original list includes four semantic categories (furniture, vegetables, ways of traveling, and animals).

### ***Delis-Kaplan Executive Function System (D-KEFS)***

#### **Trails Test**

This task included five conditions, but only the fourth condition was incorporated into the current study. In Condition Four, the patient was given two pages with many numbers and letters on it. In this condition (Number-Letter Sequencing), the patient was to draw lines alternating between number and letter (e.g., “1” to “A” to “2” to “B” etc. in order until the end, “P”). This task measured executive functioning and was incorporated into the Executive Function domain in the current study.

#### ***Grooved Pegboard***

This task measured bilateral manipulative dexterity and visuomotor coordination. The task was designed for “kiddies” (ages five years to eight years, 12 months), adolescents (ages nine years to 14 years, 12 months), and adults (ages 15 years and above). The task consisted of 25 holes with randomly positioned slots. The pegs, which had a key along one side, had to be rotated to match the hole before they could be inserted. For reasons described in the Operational Definitions section below, this measure was not incorporated into the current study.

#### ***Green’s Medical Symptom Validity Test (MSVT)***

This computerized task assessed effort and motivation. In the learning trial, a list of semantically associated word pairs was presented on a computer screen (e.g., “soccer ball” and “jet plane”). In the immediate recognition (IR) trial, individuals had to select the target words that were recently presented to them (e.g., “soccer”) from pairs of words

(e.g., “soccer” vs. “basketball”). The delayed recognition (DR) trial is administered 15 minutes later and follows the same protocol as the IR trial, but different sham words were used. In the following paired associates (PA) trial, the first word of each pair was given (e.g., “soccer”), and the matching target word had to be recalled (e.g., “ball”). Finally, in the free recall (FR) trial, the individual was asked to name as many words as they could remember from the initial learning trial. A consistency score from the IR and DR trials was computed. For reasons described in the Operational Definitions section below, this measure was not incorporated into the current study.

### ***Rey-Osterrieth Complex Figure (Rey-O) Copy***

In the Copy trial, the patient was to copy a complicated abstract design as best they could. This trial measured visuoperceptual skills and was explored into Hypothesis 1c.

### ***Test of Memory Malingering (TOMM)***

The TOMM was a 50-question visual memory recognition test that discriminated between true memory impairment and malingering, with two learning trials and an optional retention trial following a delay. For reasons described in the Operational Definitions section below, this measure was not incorporated into the current study.

### ***Wechsler Abbreviated Scale of Intelligence, Second Edition (WASI-II)***

The WASI-II was designed for individuals between the ages of 16 and 90 years, 11 months. The Vocabulary and Matrix Reasoning subtests were administered, which are

described below. These measures were explored in Hypothesis 1c.

### **Vocabulary**

In this task, the patient defined words that were presented visually and orally by the examiner. This task measured word knowledge, verbal concept formation, and verbal reasoning

### **Matrix Reasoning**

In this task, individuals viewed an incomplete matrix made up of three abstract designs and selected one of the five response options that completed the matrix. The task measured non-verbal reasoning.

### ***Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV) and Wechsler Adult Intelligence Scale, Fourth Edition (WAIS-IV)***

The WISC-IV was designed for children between the ages of six years and 16 years, 11 months. The WAIS-IV is designed for individuals between the ages of 16 and 90 years, 11 months. The following WISC-IV and WAIS-IV subtests were administered.

### **Coding**

This task measured processing speed. In the WISC-IV version, a string of digits (i.e., digits one through nine) were displayed on the page with a key provided above it, illustrating a special mark (e.g., “+” or concave curves facing the left and the right) associated with each digit. The child was given two minutes to fill in as many special

marks as possible. The child was told to work as quickly as possible and to not skip any. The WAIS-IV version of Coding differs with slightly different special marks and more special marks for the individual to fill in. The WISC-IV and WAIS-IV Coding scores were combined, yielding one Total Coding score per subject. The Total Coding score was averaged with the Total Symbol Search score per subject, yielding the Processing Speed domain score for each subject.

### **Symbol Search**

This task also measured processing speed. In the WISC-IV version, the child was shown two target items (i.e., abstract items) followed by five more patterns. If either of the two target items matched any of the five following patterns, the child was to mark the “yes” box. If not, the child was to mark the “no” box. The child was given two minutes to fill out as many as possible. The child was told to work as quickly as possible and to not skip any.

The WAIS-IV version of Symbol Search differed slightly. If either of the two target items matched any of the five following patterns, the individual was to mark that item that matched that target item. If there was no match, the individual would mark the “no” box. Again, the individual is given two minutes to complete as much as possible.

Similarly to the Total Coding score, the WISC-IV and WAIS-IV Symbol Search scores were combined, yielding one Total Symbol Search score per subject. The Total Coding score was averaged with the Total Symbol Search score per subject, yielding the Processing Speed domain score for each subject.

## **Digit Span**

This task measured executive function (i.e., attention and working memory) and was incorporated in the Executive Function domain in the current study. The WISC-IV and WAIS-IV versions of Digit Span consisted of the forward trial and the backwards trial. In the forward trial, the examiner read a string of digits and the child was to repeat the digits in the same order as read by the examiner. This subtask assessed attention. In the backwards trial, the child was to repeat the digits in the backwards order. This subtask assessed working memory.

In the WAIS-IV version of Digit Span, the individual was administered a sequencing trial in addition to the forward and backward trials. In the sequencing trial, the individual was to mentally rearrange the string of digits in chronological order from smallest to largest. This task assessed working memory.

The WISC-IV and WAIS-IV Digit Span scores were combined, yielding one Total Digit Span score per subject. The score from the D-KEFS Trails Test Condition Four was averaged with the Total Digit Span score to yield an Executive Function composite score.

## **Operational Definitions**

The current study had three independent variables (IV) with two levels each: concussion history (control group [1 concussion] vs. experimental group [ $>1$  concussion]), age at injury (children [ $<12$  years] vs. adolescents [ $\geq 12$  years]), and gender (male vs. female). The dependent variables (DV) from Aim 1 were the neurocognitive outcomes, which included processing speed and executive function. The dependent

variables from the Aim 2 included the psychosocial factors, such as depression, anxiety, and hyperactivity. Aim 3 assessed the correlation between premorbid and post-morbid psychosocial functioning with neurocognitive functioning following concussion.

Prior to analyses, the plan was to assess more neurocognitive domains than were actually assessed. Specifically, in addition to processing speed and executive function, the plan was to also assess how concussion history, age, and gender affected intelligence, motor skills, verbal and nonverbal reasoning, and verbal and visual memory. The reason for not including intelligence as a dependent variable was because previous literature suggested that intelligence is quite resistant to concussion, as intelligence is a stable trait. Specifically, a longitudinal study of intelligence found that mental ability differences showed substantial stability from childhood to late life, across a span of 77 years (Deary, Whalley, Lemmon, Crawford, & Starr, 2000). Given that there were plenty of subtests scores to assess motor skills (i.e., Modified BESS, Grooved Pegboard) and many aspects of motor skills to assess within those measures (i.e., balance, motor speed, dexterity, coordination), it was decided that its complexity would be best suited for further exploration in a future study.

Regarding the other domains previously mentioned, they had to be calculated, as composite scores were not recorded from the data. Manually creating neurocognitive domains entailed combining or averaging scores from subtests that measure similar domains. Given that not every subject in the study was administered every subtest, some subtests had too low of a sample size to be included into a domain variable. Processing speed and executive function were the only domains that had a sufficient number of



subtests and sample size within each subtest to qualify into a domain. The Results section describes how the processing speed and executive function domains were created.

Hypothesis 1c explored the following measures to determine how performance on spatial and verbal tasks differs as a factor of gender: WASI-II MR, Rey-O Copy, WASI-II Vocab., and CVLT-II/C. These subtests measure nonverbal reasoning, visuospatial skills and motor control, verbal comprehension, and verbal learning and memory, respectively. These measures were selected, as they measure spatial (i.e., WASI-II MR, Rey-O Copy) and verbal (i.e., WASI-II Vocab., and CVLT-II/C) abilities.

In Aim 2, psychosocial functioning scores were analyzed by assessing the change in parental reports of psychosocial functioning from premorbid (i.e., pre-concussive) to post-morbid (i.e., post-concussive) status, which was referred to as the Psychosocial Ratio. See the Results section for a detailed description of how this calculation was carried out.

### **Statistical Analysis**

Aims 1 and 2 were analyzed by a three-way multivariate analysis of variance (MANOVA; 2x2x2). Specifically, the three independent variables had two levels each. The MANOVA conducted for Aim 1 assessed for three main effects (Hypotheses 1a through 1c) and four interactions (Hypotheses 1d<sub>1</sub> through 1d<sub>4</sub>). However, the MANOVA conducted for Aim 2 only assessed for three main effects (Hypotheses 2a through 2c) since there was not a large enough sample size in each condition to carry out the interaction analyses (Hypothesis 2d<sub>1</sub> through 2d<sub>4</sub>). Bivariate correlational analyses were conducted in Aim 3. Statistical analyses used an  $\alpha$ -level of 0.05 for tests of significance

(IBM SPSS Statistics 20.0). Power analyses were conducted using G\*Power, Version 3.1.9.2.

*A priori* power analyses were conducted to determine the sample sizes necessary to obtain an effect size of 0.25 and power of 0.8. Results suggested that a sample size of 42 was required for Aim 1 (three IVs with two levels each; two DVs) and 30 for Aim 2 (three IVs with two levels each; three DVs). *A priori* power analyses for Aim 3 suggested that a sample size of 82 would be required to achieve an effect size of 0.3 and a power of 0.8. Given that the study had a projected sample size of 160 patients, the effective results were likely to be achieved. However, certain subjects in these analyses were missing certain sets of data, so including all sets of data in the mix yielded cell sizes with too few subjects to have sufficient statistical power. This led there to be fewer subjects for each aim. As a result, *post-hoc* analyses had to be conducted to ensure the analyses had sufficient statistical power, given the sample size.

*Post-hoc* power analyses were conducted to assess whether the findings from the current study produced effective results. As illustrated in Table 2, the total sample size in Aim 1 equaled to 55. This sample size was higher than what was necessary to obtain an effect size of 0.8, based on *a priori* analyses, suggesting effective results. Table 4 illustrates the initial sample sizes detected in each condition from Aim 2 (including main effects and interactions). However, due to low sample sizes in the interaction cells, interaction effects were excluded from interpretation. As a result, Table 5 illustrates the sample sizes of only the main effects from Aim 2. With a total sample size of 24, *post-hoc* power analyses suggested Aim 2 yielded a power of 0.7.

Two correlational analyses were conducted in Aim 3. Each hypothesis (i.e., Hypothesis 3a and 3b) included six neurocognitive factors (i.e., processing speed, executive function, WASI-II MR, Rey-O Copy, WASI-II Vocab., CVLT-II/C) and three psychosocial factors. Hypothesis 3a's psychosocial factors included premorbid anxiety, depression, and hyperactivity, and Hypothesis 3b's included post-morbid anxiety, depression, and hyperactivity.

Since certain subjects in this analysis were missing certain sets of data, including all sets of data in the mix yielded cell sizes with too few subjects to have sufficient statistical power (Hypothesis 3a,  $N = 15$ ; Hypothesis 3b,  $N = 19$ ). As a result, factors for which there was insufficient sample size were removed. Specifically, the factors that had sample sizes below 82 (sample size required to yield power of 0.8 and effect size of 0.3) were removed initially. Such factors included Rey-O Copy ( $n = 41$ ), premorbid anxiety ( $n = 47$ ), premorbid depression ( $n = 47$ ), and premorbid hyperactivity ( $n = 47$ ). Removing those factors provided a sample size of 68 for the correlational analysis, yielding a power of 0.7. To increase the statistical power some more, processing speed ( $n = 83$ ) was removed as a factor from the correlational analysis, yielding a total sample size of 92. Finally, *post-hoc* power analysis for a sample size of 92 and an effect size of 0.3 yielded a statistical power of 0.8.

## CHAPTER SEVEN

### RESULTS

The current study determined the main effects and interactions among concussion history (single vs. repeated), age (<12 years old vs.  $\geq 12$  years old), and gender (male vs. female) on neurocognitive (i.e., processing speed, executive function) and psychosocial (i.e., anxiety, depression, hyperactivity) scores in a sample of youths being evaluated at Children's Hospital Los Angeles for traumatic brain injury (TBI). Our overarching hypothesis suggested that individuals with repeated concussions would exhibit more severe neurocognitive and psychosocial deficits than those with a single concussion. Furthermore, we hypothesized that concussion-induced deficits would be worse in females compared to males and in adolescents compared to younger children. We also hypothesized that males would perform better on spatial tasks, and that females would perform better on verbal tasks. Finally, we hypothesized that pre- and post-morbid psychosocial impairment would be negatively correlated with post-morbid neurocognitive functioning.

*Processing speed* was determined by averaging the Coding and Symbol Search scaled scores from the WISC-IV battery. *Executive function* was determined by averaging Digit Span scaled scores from the WISC-IV and WAIS-IV batteries and Trail Making Test Condition Four scaled scores from the DKEFS. Scaled scores were a representation of raw score performance that have been converted into a consistent standardized scale using norms. Norms accounted for the individual's age and gender. Scaled scores have a mean of 10 and standard deviation of 3. Specifically, scaled scores of 8 to 12 are considered to be in the Average range.

The psychosocial functioning scores were analyzed by assessing the change in parental reports of psychosocial functioning from premorbid (i.e., pre-concussive) to post-morbid (i.e., post-concussive) status, which was referred to as the Psychosocial Ratio. Specifically, caregivers filled out premorbid and post-morbid anxiety, depression, and hyperactivity ratings for their child or adolescent after the concussion/concussions had taken place. These ratings were then calculated into T-scores obtained using norms. T-scores less than 60 are considered to be within normal limits (WNL), between 60-69 are considered to be “at-risk” for becoming clinically significant, and  $\geq 70$  are considered to be clinically significant. Clinically significant T-scores suggest a high level of maladjustment.

The Psychosocial Ratio focused on each individual’s percentage of change in psychosocial functioning from premorbid to post-morbid status. This ratio was calculated by dividing a subject’s post-morbid psychosocial T-score by that same subject’s premorbid psychosocial T-score. A Psychosocial Ratio of one would indicate no change in psychosocial functioning (i.e., anxiety, depression, hyperactivity) from premorbid to post-morbid status. A Psychosocial Ratio of less than one would indicate a decrease in anxiety, depression, or hyperactivity from premorbid to post-morbid status. Finally, a Psychosocial Ratio of greater than one would indicate an increase in anxiety, depression, or hyperactivity from premorbid to post-morbid status.

*Spatial tasks* included the WASI-II Matrix Reasoning subtask (WASI-II MR) and the Rey-O Copy task. *Verbal tasks* included the WASI-II Vocabulary subtask (WASI-II Vocab.) and the CVLT-II and CVLT-C. The CVLT scores were analyzed by combining the Total T-scores from both versions of the measure (i.e., CVLT-II and CVLT-C). The

Total CVLT T-scores were calculated from the Total CVLT raw scores using norms (sum of all the words immediately recalled across trials). The current study combined the Total CVLT-II and Total CVLT-C T-scores to one variable, which will be referred to as, CVLT-II/C.

One of the assumptions of a MANOVA is the absence of multivariate outliers. To detect outliers, the Mahalanobis distance (a measure of the distance between a point and a distribution or mean, which is the gold standard method for detecting multivariate outliers), was used, but no outliers were detected in any of the analyses.

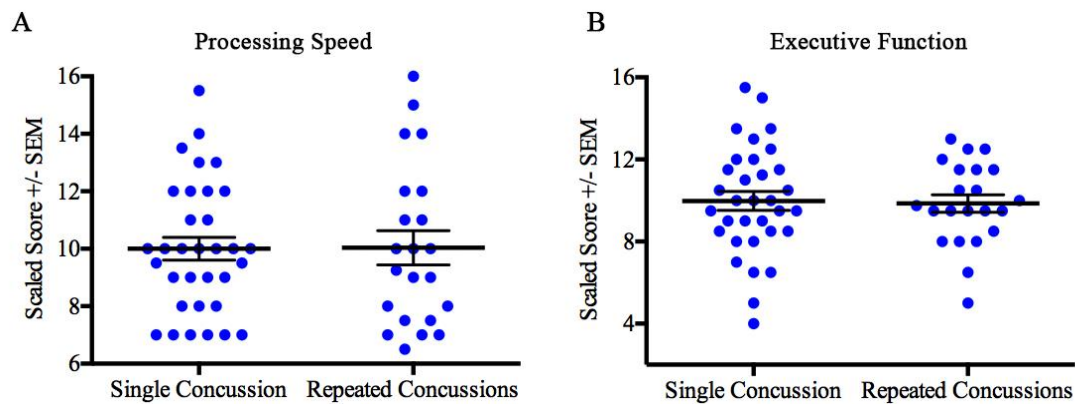
### **Aim 1**

The first aim of the current study was to assess the neurocognitive effects of concussion in young people. This aim was broken down into four sub-aims. The first three sub-aims each had their own specific hypothesis, and the final sub-aim was comprised of four hypotheses. The sub-aims and hypotheses are discussed below. Table 2 illustrates the sample sizes of each condition in Aim 1.

For the MANOVA analyses that indicated no significant differences, subsequent three-way analyses of variance (ANOVA) were conducted. Each ANOVA entailed three IVs (i.e., age, gender, concussion history) and one DV each (i.e., processing speed or executive function). These analyses were conducted to further seek for significant differences.

**Aim 1a** assessed how concussion history (i.e., single vs. repeated) affected neurocognitive functioning in young people. **Hypothesis 1a** stated that children and adolescents with repeated concussions would perform worse on tasks of processing speed

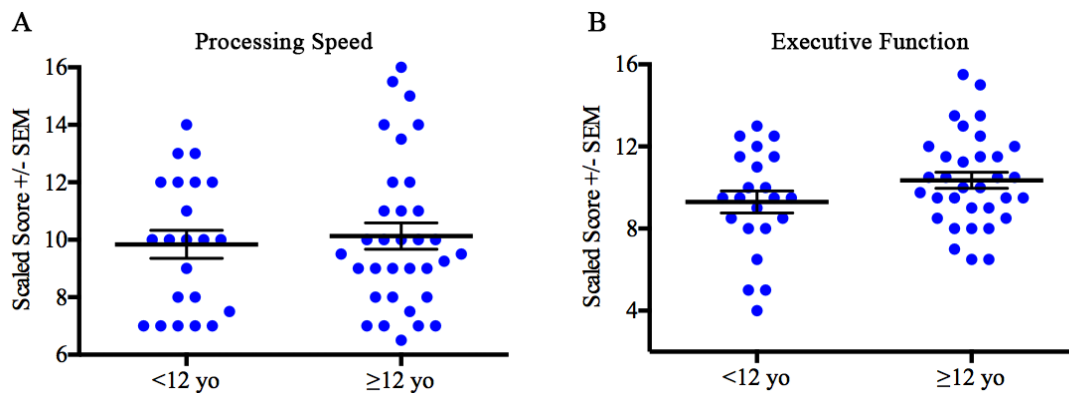
and executive function, based on age-related norms, compared to those with a single concussion. However, the data showed that concussion history did not affect performance on tasks of processing speed or executive function (Figure 3). Additionally, individuals generally appeared to perform in the Average range on task of processing speed ( $M[\text{single concussion}] = 9.97$ ,  $M[\text{repeated concussion}] = 10.17$ , Figure 3a) and executive function ( $M[\text{single concussion}] = 9.92$ ,  $M[\text{repeated concussion}] = 9.82$ , Figure 3b), suggesting their performance was similar to those who did not undergo concussion. The two three-way ANOVAs corroborated these findings, indicating that concussion history did not affect performance on tasks of processing speed or executive function.



**Figure 3.** How concussion history (single concussion vs. repeated concussion) affects processing speed and executive function performance. Contrary to what was hypothesized, concussion history, on average, did not affect performance on tasks of **A.** processing speed or **B.** executive function in young people.

**Aim 1b** assessed how age (i.e., <12 years old vs. ≥12 years old) affected post-concussion neurocognitive functioning in young people. **Hypothesis 1b** stated that adolescents would perform worse on tasks of processing speed and executive function, based on age-related norms, than children. The data showed that age did not affect

processing speed performance (Figure 4a) and that children scored slightly worse on tasks of executive function than adolescents (Figure 4b), but that difference was not significant. Additionally, individuals generally appeared to perform in the Average range on task of processing speed ( $M[<12 \text{ years old}] = 9.90$ ,  $M[\geq 12 \text{ years old}] = 10.24$ , Figure 4a) and executive function ( $M[<12 \text{ years old}] = 9.37$ ,  $M[\geq 12 \text{ years old}] = 10.38$ , Figure 4b), suggesting their performance was similar to those who did not undergo concussion. The two three-way ANOVAs corroborated these findings, indicating that age did not significantly affect performance on tasks of processing speed or executive function.



**Figure 4.** How age (children <12 years old vs. adolescents ≥12 years old) affects processing speed and executive function performance. **A.** This plot illustrates that age does not affect average processing speed performance. **B.** This plot illustrates that on average, contrary to what was hypothesized, children <12 years of age scored slightly worse on tasks of executive function than adolescents ≥12 years of age. However, that difference was not significant.

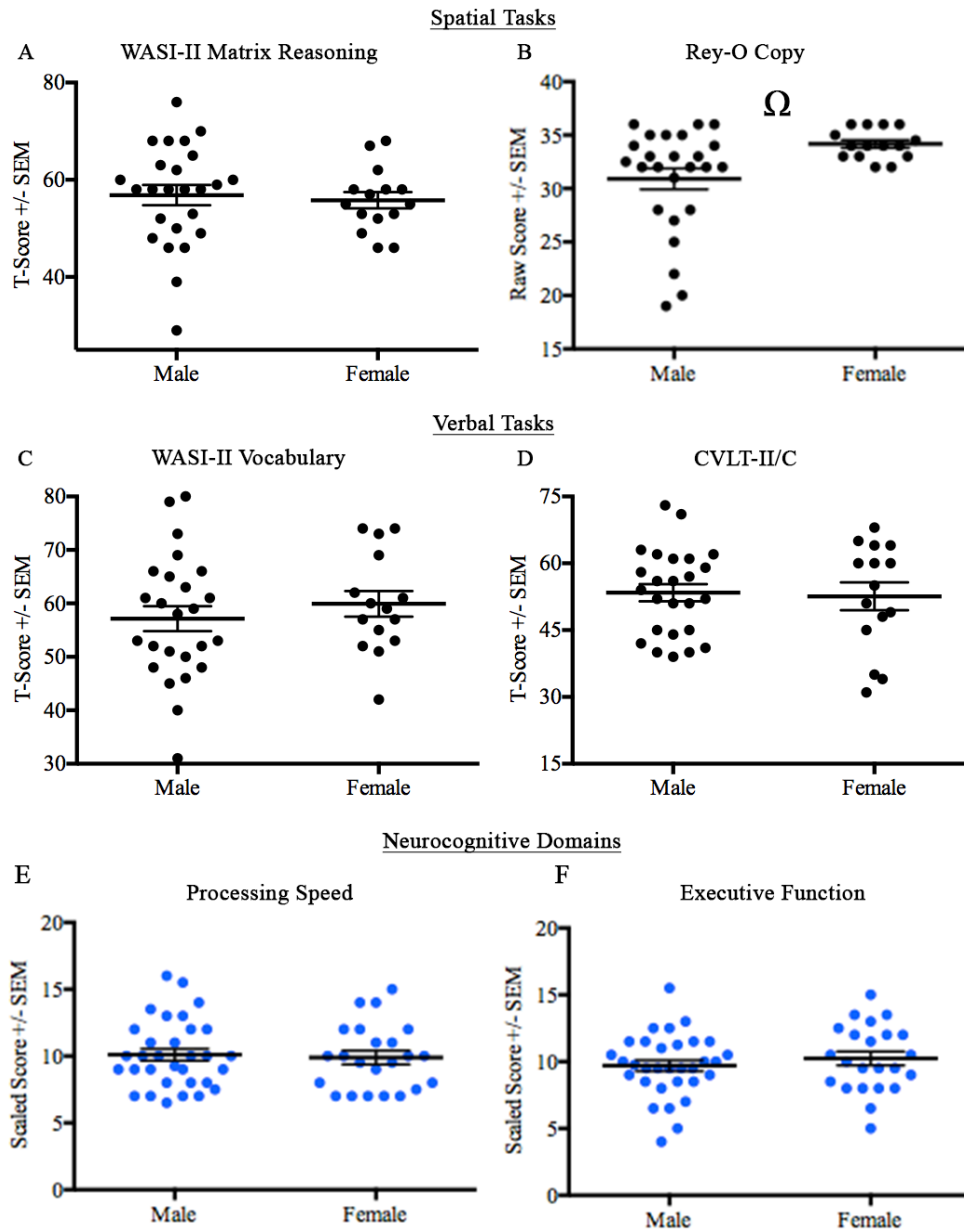
**Aim 1c** assessed how gender affected post-concussion neurocognitive functioning in young people. **Hypothesis 1c** stated that males would perform better on spatial reasoning tasks than females and that females would perform better on verbal memory and concept formation tasks than males. Table 3 illustrates the sample sizes of each



condition in Hypothesis 1c. A one-way MANOVA was conducted for this analysis, including one IV (gender). All subjects whose gender was recorded in the data were included in the analysis. This included subjects whose concussion history was unknown (i.e., single vs. repeated concussion). As a result, the concussion history for these subjects was labeled as “ $\geq 1$  concussion” in Table 3. The initial analysis for this hypothesis included four dependent variables. These variables included tasks assessing spatial reasoning (i.e., WASI-II MR [*non-verbal reasoning*], Rey-O Copy [*visuospatial skills and motor control*]) and verbal memory (i.e., WASI-II Vocab. [*word knowledge and verbal concept formation*], CVLT-II/C [*verbal learning and memory*]). However, the Rey-O Copy data did not pass Levene’s test (suggesting unequal variance). Additionally, the WASI-II MR and Rey-O Copy variables did not pass the Shapiro-Wilk test for normal distribution.

Nevertheless, an exploratory MANOVA of the raw data with one IV (i.e., Gender) and four DVs (i.e., WASI-II MR, WASI-II Vocab., CVLT-II/C, and Rey-O Copy) was conducted (Figure 5a-d). The analysis revealed a significant main effect ( $F[4, 35] = 2.94, p < .035$ ; Wilks’  $\Delta = 0.749$ ) for Rey-O Copy. Specifically, females performed specifically better on the Rey-O Copy task than males ( $F[1, 38] = 6.296, p < 0.017$ ). Additionally, individuals generally appeared to perform in the Average range on these measures. Specifically, on WASI-II MR ( $M[\text{males}] = 56.84, M[\text{females}] = 55.80$ , Figure 5a), WASI-II Vocab. ( $M[\text{males}] = 57.16, M[\text{females}] = 59.93$ , Figure 5c), and CVLT-II/C ( $M[\text{males}] = 53.40, M[\text{females}] = 52.60$ , Figure 5d). These results suggest that these individuals’ performance was slightly higher than those who did not undergo concussion ( $M = 50$ ), but not significant, as their performance still falls in the Average range. The

Rey-O Copy task was not included in this interpretation, as the Rey-O Copy task includes raw score, not norm-referenced scores (Rey-O copy ( $M[\text{males}] = 30.9$ ,  $M[\text{females}] = 34.17$ , Figure 5b). However, these effects may not be statistically significant due to the violation of MANOVA assumptions (i.e., homogeneity of variance, normal distribution).

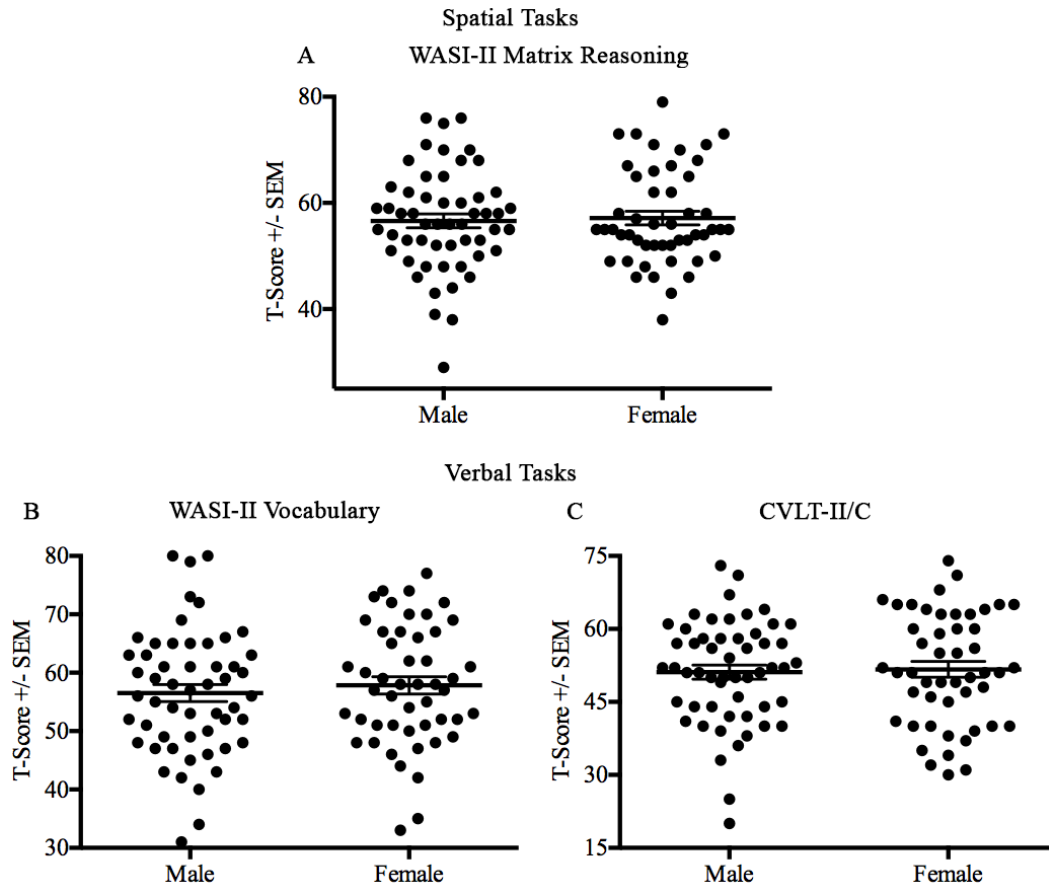


**Figure 5.** Raw data scatter plots illustrate how gender affects neurocognitive functioning (spatial and verbal abilities) after undergoing concussions. Plots **A.** and **B.** illustrate how gender affects performance on tasks assessing spatial abilities. **A.** There were no gender differences on the WASI-II Matrix Reasoning task and, **B.** contrary to the hypothesis, females performed significantly better than males on the Rey-O Copy task [ $F(1, 38) = 6.296, p < 0.017$ ]. Plots **C.** and **D.** illustrate how gender affects performance on verbal ability tasks after undergoing concussions. **C.** As hypothesized, females performed slightly better on the WASI-II Vocabulary task, which assesses word knowledge and verbal concept formation, although the difference was not significant. **D.** There was no difference between males and females on the CVLT-II/C tasks, which assess verbal memory. Plots **E.** and **F.** illustrate that gender does not affect performance in two different neurocognitive domains (i.e., processing speed, executive function). It is important to note that these results are dubious due to the violation of MANOVA assumptions (i.e., homogeneity of variance, normal distribution).

Note: “ $\Omega$ ” indicates that  $p < 0.05$ ; however, the difference could not be defined as statistically significant due to MANOVA assumption violations.

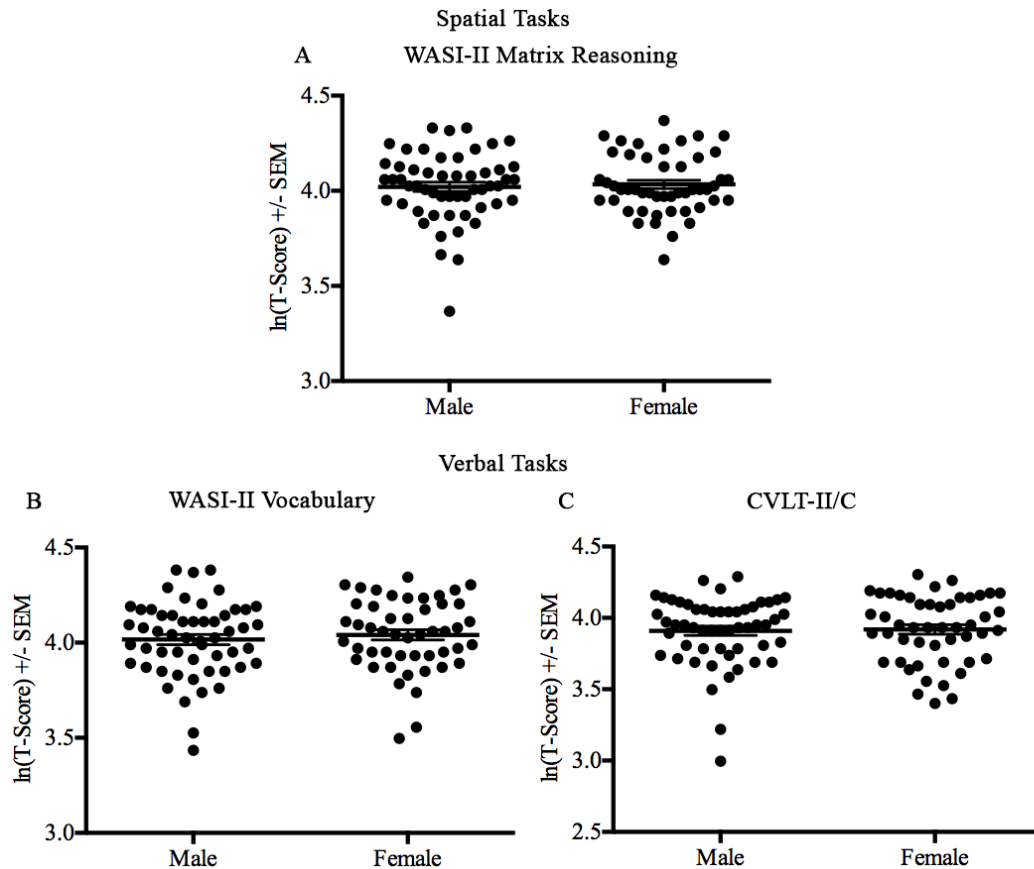
Figure 5 also illustrates how gender affects certain neurocognitive domains, such as processing speed (Figure 5E) and executive function (Figure 5F), following concussion. The data showed that gender did not affect performance on tasks of processing speed or executive function.

Given that the Rey-O Copy violated multiple MANOVA assumptions, the Rey-O Copy was excluded from the MANOVA, and the MANOVA was re-analyzed with the remaining three DVs. WASI-II MR passed Levene's test, but did not pass the Shapiro-Wilk test for normal distribution. Raw data scatter plots for the MANOVA including WASI-II MR, WASI-II Vocab., and CVLT-II/C are shown in Figure 6.



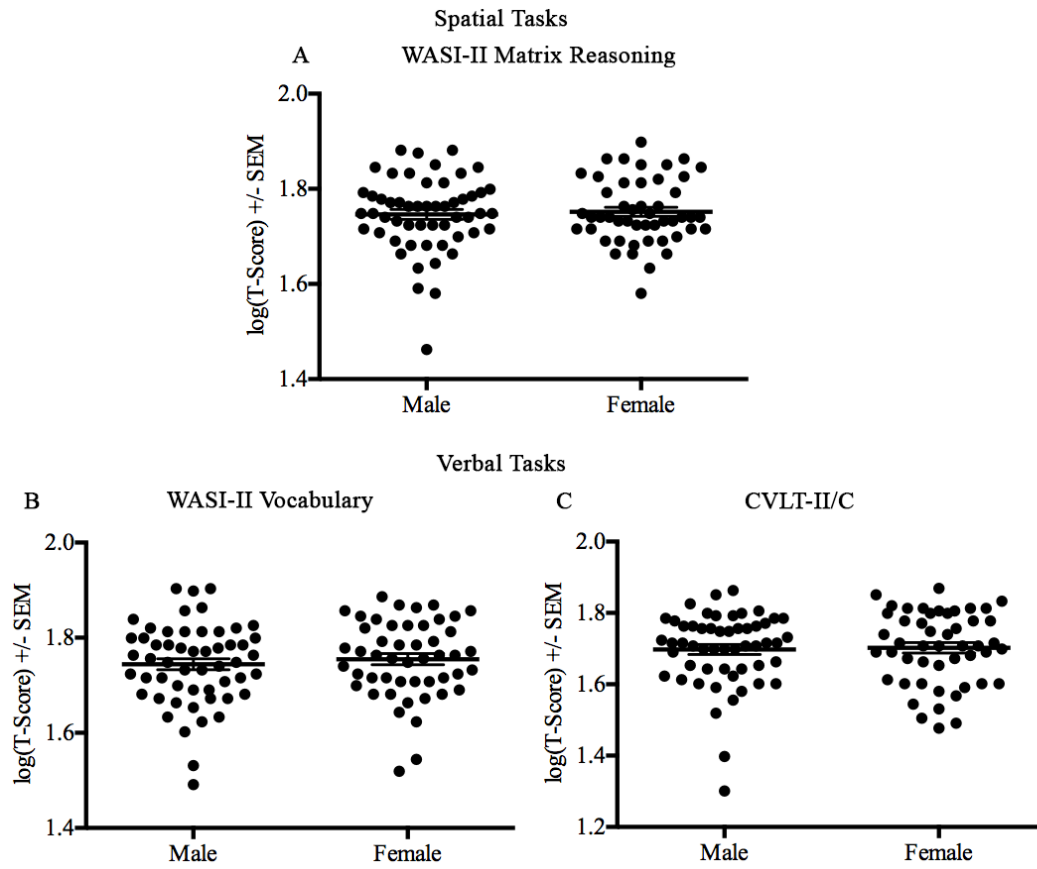
**Figure 6.** Raw data scatter plots illustrate how gender affects neurocognitive functioning (spatial and verbal abilities) after undergoing concussions. Rey-O Copy results were excluded from this analysis, given that it was the only data set that did not pass the Levene's test. Plot **A.** illustrates that there were no gender differences on the WASI-II Matrix Reasoning task (which assesses spatial abilities) after undergoing concussions. Furthermore, there were no gender effects on verbal ability as assessed by the **B.** WASI-II Vocabulary or **C.** CVLT-II/C tasks. However, these results could not be interpreted due to the violation of MANOVA assumptions (i.e., homogeneity of variance, normal distribution).

As mentioned above, the raw data violated multiple MANOVA assumptions (i.e., homogeneity of variance, normal distribution). In hopes of achieving homogeneity and normality, transformation analyses were conducted (i.e., natural log [ln] and base 10 log [log<sub>10</sub>]).



**Figure 7.** Natural log (ln) transformation plots illustrate how gender affects neurocognitive functioning (spatial and verbal abilities) after undergoing concussions. Rey-O Copy results were excluded from this analysis, given that it was the only data set that did not pass the Levene's test. Plot **A.** illustrates that there were no gender differences on the WASI-II Matrix Reasoning task (which assesses spatial abilities) after undergoing concussions. Furthermore, there were no gender effects on verbal ability as assessed by the **B.** WASI-II Vocabulary or **C.** CVLT-II/C tasks. However, these results could not be interpreted due to the violation of MANOVA assumptions (i.e., homogeneity of variance, normal distribution).

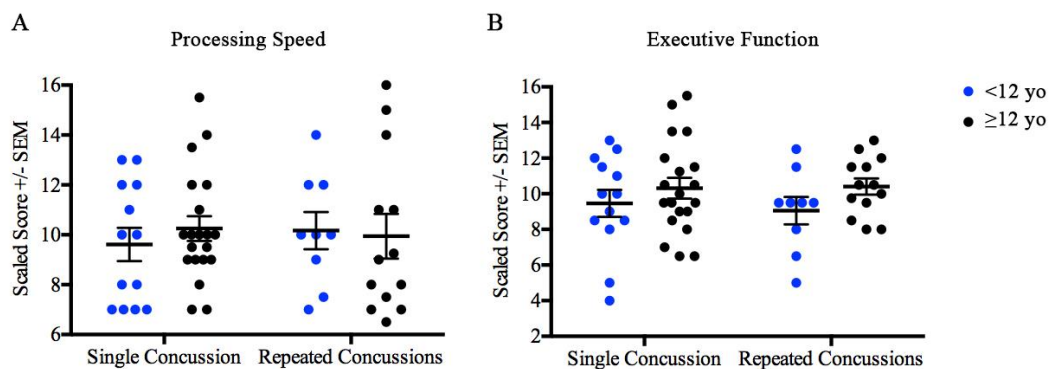
The ln transformation was conducted first, given that it is less aggressive than the  $\log_{10}$  transformation. Specifically, it reduces the raw score to a lesser degree than  $\log_{10}$ . The ln of the DVs was calculated ( $\ln[\text{WASI-II MR}]$ ,  $\ln[\text{WASI-II Vocab.}]$ ,  $\ln[\text{CVLT-II/C}]$ ), excluding Rey-O Copy. However, although the Levene's test passed, this data transformation did not alter the normal distribution violations (see Figure 7). The  $\log_{10}$  data transformation did not alter the normal distributions either (see Figure 8).



**Figure 8.** Log<sub>10</sub> (log) transformation plots illustrate how gender affects neurocognitive functioning (spatial and verbal abilities) after undergoing concussions. Rey-O Copy results were excluded from this analysis, given that it was the only data set that did not pass the Levene's test. Plot **A.** illustrates that there were no gender differences on the WASI-II Matrix Reasoning task (which assesses spatial abilities) after undergoing concussions. Furthermore, there were no gender effects on verbal ability as assessed by the **B.** WASI-II Vocabulary or **C.** CVLT-II/C tasks. However, these results could not be interpreted due to the violation of MANOVA assumptions (i.e., homogeneity of variance, normal distribution).

**Aim 1d** assessed how the above factors (i.e., concussion history, age, gender) interact to affect neurocognitive functioning after concussions. **Hypothesis 1d<sub>1</sub>** stated that there would be no interaction between age and concussion history. Specifically, it was hypothesized that adolescents would always perform worse on neurocognitive tasks than children, irrelevant of having undergone single or repeated concussion. The data show that for processing speed, adolescents who sustained a single concussion performed

slightly better (non-significant) than children who sustained a single concussion (contrary to hypothesis) and the opposite was true for those who sustained repeated concussion (as hypothesized). The data showed that for executive function, concussion history did not affect children and adolescents differently. Specifically, contrary to hypothesis, adolescents always performed slightly better (non-significant) than children, regardless of concussion history (Figure 9).

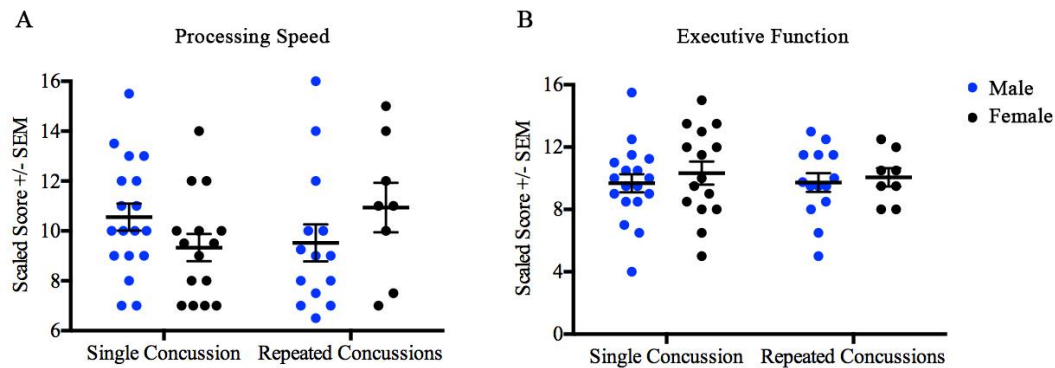


**Figure 9.** How concussion history (single concussion vs. repeated concussion) interacts with age (<12 years old vs. ≥12 years old) to affect neurocognitive functioning (processing speed and executive function) after concussion. **A.** This plot illustrates how concussion history interacts with age to affect processing speed after concussion. For those who underwent single concussion, adolescents performed better than children (contrary to hypothesis), and for those who underwent repeated concussion, adolescents performed worse than children (as hypothesized), although that difference was not significant. **B.** This plot illustrates how concussion history interacts with age to affect executive function after concussion. Contrary to hypothesis, adolescents scored slightly higher on tasks of executive function than children, irrelevant of concussion history, although the difference was not significant.

**Hypothesis 1d<sub>2</sub>** stated that there would be no interaction between gender and concussion history. Specifically, it was hypothesized that females would always perform worse on neurocognitive tasks than males, irrelevant of having undergone single or repeated concussion. The data suggested that females who underwent a single concussion



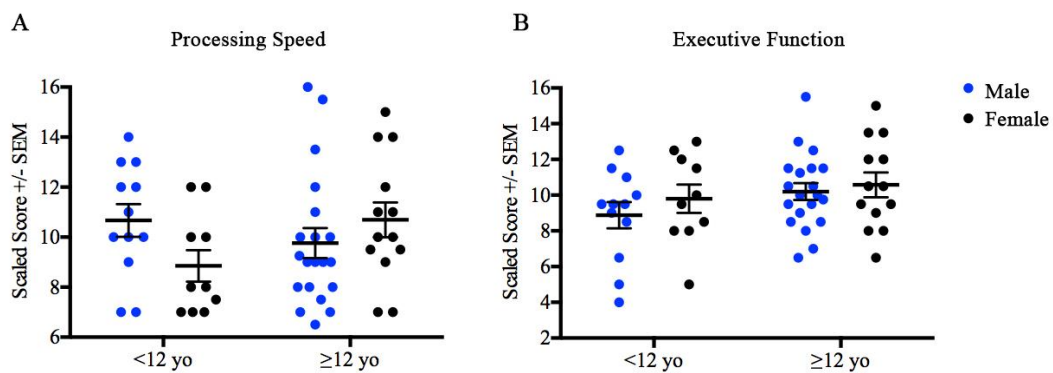
performed slightly worse (non-significant) on processing speed, but better on executive function tasks, than males. Following repeated concussions, females performed slightly better (non-significant) than males on processing speed tasks, but there were no gender differences for executive function tasks (Figure 10). The two three-way ANOVAs supported the hypothesis, indicating no significant interaction between gender and concussion history.



**Figure 10.** How concussion history (single concussion vs. repeated concussion) interacts with gender to affect neurocognitive functioning (processing speed and executive function) after concussion. **A.** This plot illustrates how concussion history interacts with gender to affect processing speed after concussion. As hypothesized, males who underwent a single concussion scored slightly higher on tasks assessing processing speed than females who underwent a single concussion, although not significant. However, the opposite was true for those who underwent a repeated concussion, although not significant. **B.** This plot illustrates how concussion history interacts with gender to affect executive function after concussion. Contrary to what was hypothesized, females who underwent single concussion scored slightly higher on tasks assessing executive function than males who underwent single concussion, although not significant. There were no gender differences for those who underwent repeated concussion.

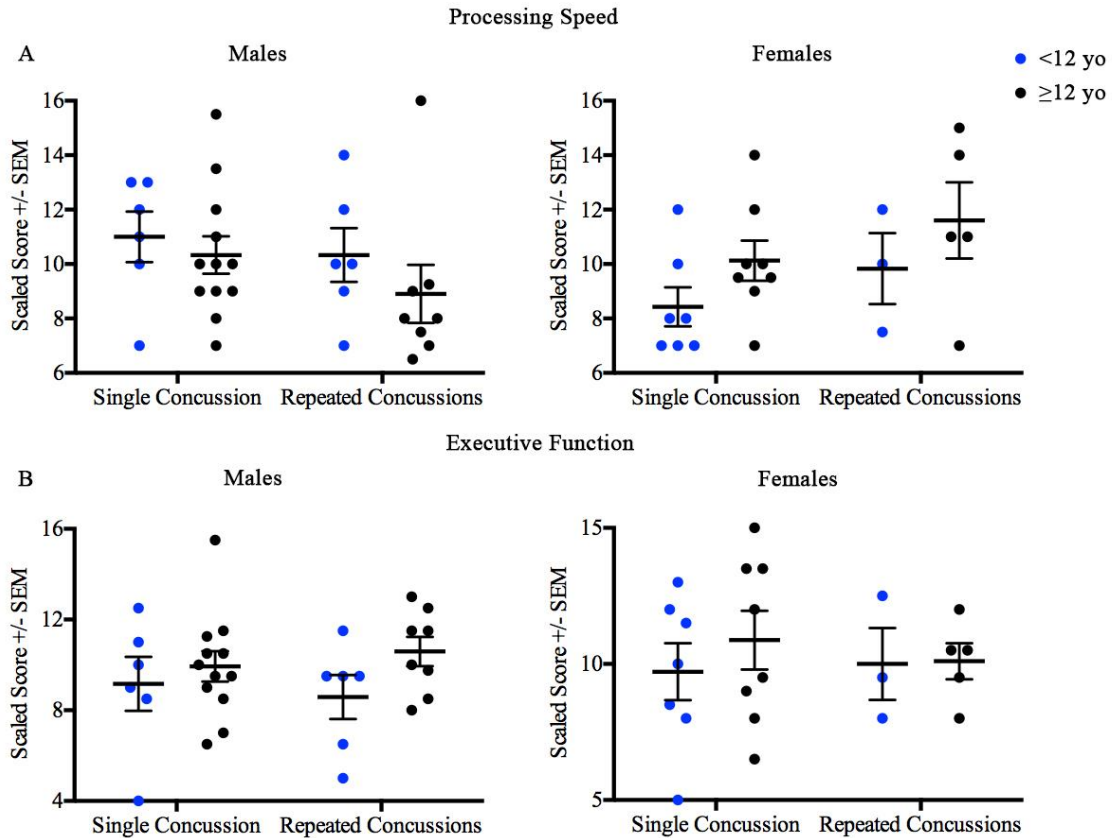
**Hypothesis 1d<sub>3</sub>** stated that, with a history of concussion, female children (younger than 12 years old) would perform better than male children, and male adolescents would perform better than female adolescents, based on age-related norms, on neurocognitive performance. The data showed that in children, females performed

slightly (non-significant) better on executive function tasks than males (as hypothesized), but for tasks of processing speed, they performed slightly (non-significant) worse than males (contrary to hypothesis), although not significant. In adolescents (12 years or older), contrary to what was hypothesized, females actually performed better on processing speed and executive function tasks, although not significant (Figure 11). The gender difference in performance on tasks of processing speed approached significance ( $F[2, 46] = 2.875, p=0.067$ ; Wilks'  $\Delta = 0.889$ ;  $M_{\text{adolescent males}} = 9.620$ ,  $M_{\text{adolescent females}} = 10.863$ ). The two three-way ANOVAs indicated no significant interaction between gender and concussion history.



**Figure 11.** How age (<12 years old vs. ≥12 years old) interacts with gender to affect neurocognitive functioning (processing speed and executive function) after concussion. **A.** This plot illustrates how age interacts with gender to affect processing speed after concussion. Contrary to what was hypothesized, younger males performed slightly better than younger females (non-significant), and older females performed slightly better than older males (approaching significance), on tasks assessing processing speed. **B.** This plot illustrates how age interacts with gender to affect executive function after concussion. Overall, although not significant, females scored slightly higher on tasks of executive functioning than males, irrelevant of age. That difference was slightly larger in younger children. Specifically, as hypothesized, younger females performed slightly better than younger males on tasks of executive functioning, but contrary to the hypothesis, older females also performed slightly better than older males on those tasks.

**Hypothesis 1d<sub>4</sub>** stated that there would be no interaction between repeated concussion, age, and gender. Although the 3-way interaction was not significant (Figure 12), certain trends were observed. On tasks of processing speed, younger males performed slightly better (non-significant) than older males, regardless of whether they underwent single or repeated concussion. The opposite trend was seen in females, where older females performed slightly better (non-significant) than younger females, regardless of whether they underwent single or repeated concussion. In males, a repeated concussion was associated with a worse score than a single concussion for both age classifications, whereas in females, a repeated concussion was associated with a higher score than a single concussion for both age classifications (Figure 12).



**Figure 12.** Three-way interaction to address how concussion history (single concussion vs. repeated concussion), age (<12 years old vs. ≥12 years old), and gender interact with one another to affect neurocognitive functioning (processing speed and executive function). **A.** This plot illustrates how the three factors mentioned above interact with one another to affect processing speed. Although not significant, younger males always performed better than older males on tasks of processing speed, irrelevant of concussion history. Additionally, although not significant, older females always performed better than younger females on tasks of processing speed, irrelevant of concussion history. **B.** This plot illustrates how the three factors mentioned above interact with one another to affect executive function. Results suggested that younger males performed slightly worse than older males, regardless of concussion history, although not significant. For females, younger females who underwent single concussion performed slightly worse than older females who underwent single concussion, but there were no age differences in females who underwent repeated concussion.

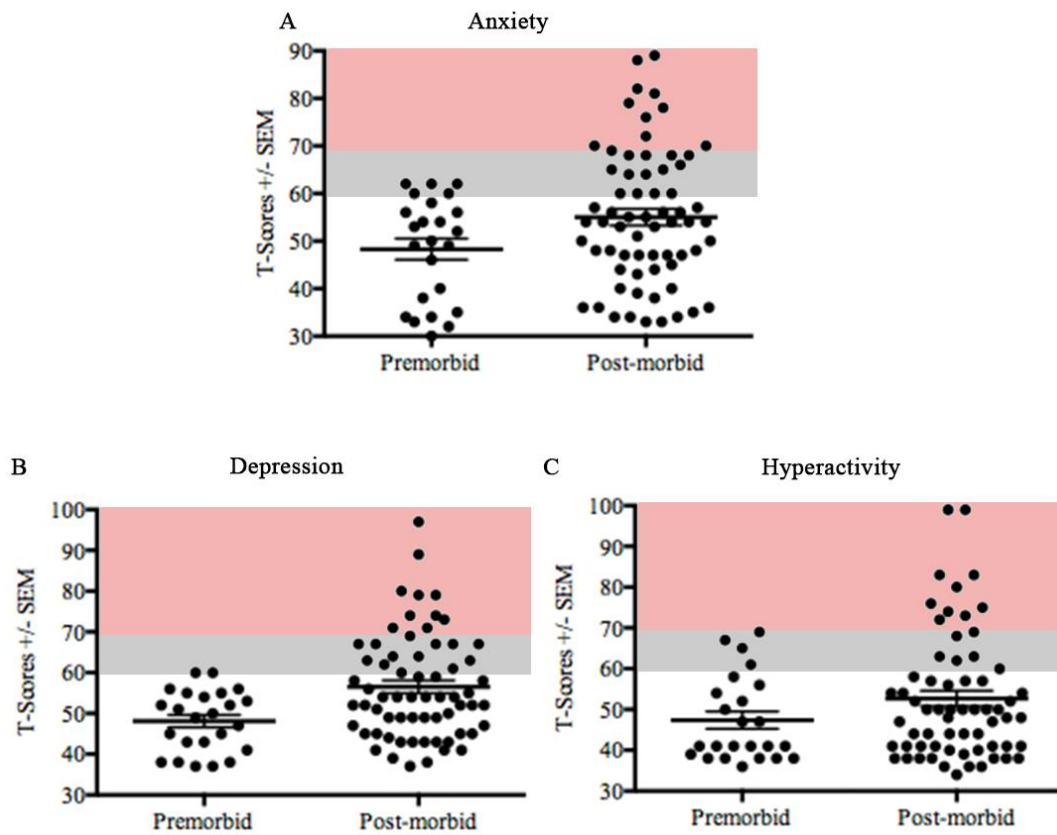
For tasks of executive function, the younger males performed slightly worse (non-significant) than older males, regardless of whether they underwent single or repeated concussion. For females, younger females who underwent single concussion performed slightly worse (non-significant) than older females who underwent single concussion, but

there were no age differences in females who underwent repeated concussion. The two three-way ANOVAs corroborated these findings, indicating no significant interactions.

## **Aim 2**

The second aim of the current study was to assess the psychosocial effects of concussion in young people. The psychosocial effects were quantified by assessing the change in psychosocial functioning from premorbid to post-morbid status. This change was measured by dividing a subject's post-morbid psychosocial T-score by that subject's premorbid psychosocial T-score. This ratio was referred to as the Psychosocial Ratio. An explanation on how to interpret the Psychosocial Ratio (i.e., less than one, equal to one, greater than one) can be found at the beginning of Results.

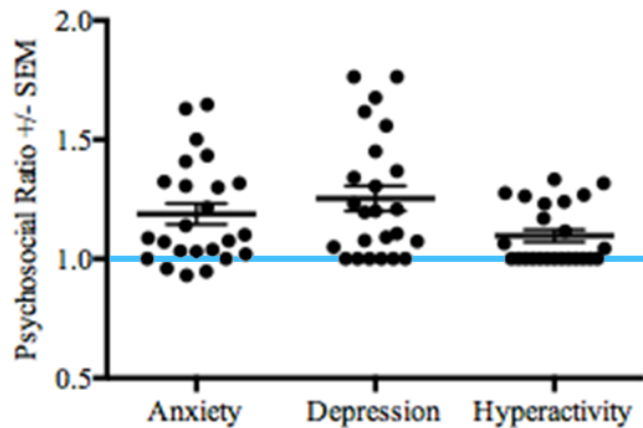
Figure 13 illustrates the premorbid and post-morbid T-scores for each psychosocial domain (i.e., anxiety, depression, hyperactivity). These T-scores were used to calculate the Psychosocial Ratio. As illustrated in Figure 13, many subjects endorsed clinically significant anxiety, depression, and hyperactivity post-morbid (i.e., data points in the red-shaded area), but not premorbid, suggesting a general increase in psychosocial deficits from premorbid to post-morbid across psychosocial domain (i.e., anxiety, depression, hyperactivity).



**Figure 13.** Premorbid and post-morbid T-Scores for psychosocial functioning (i.e., anxiety, depression, hyperactivity). Subjects with T-Scores <60 fall within normal limits (WNL; non-shaded area), T-Scores between 60-69 are at-risk for becoming clinically significant (grey-shaded area), and T-Scores  $\geq 70$  are clinically significant (red-shaded area). These plots illustrate the T-scores for premorbid and post-morbid psychosocial functioning for **A.** anxiety, **B.** depression, and **C.** hyperactivity. Overall, it appears as though youths develop more anxiety, depression, and hyperactivity following concussion. Specifically, there were more subjects who were at-risk and clinically significant for these psychosocial variables post-morbid than premorbid (i.e., data points in the grey-shaded and red-shaded areas). There were no subjects who were clinically significant for these psychosocial variables prior to receiving a concussion, although many became clinically significant following concussion.

The Psychosocial Ratios for anxiety, depression, and hyperactivity are illustrated in Figure 14. The blue line in the figure represents the baseline, indicating no change in psychosocial functioning from premorbid to post-morbid status. As depicted in Figure 14, majority of the data points fell above the baseline (i.e., blue line), suggesting that

majority of subjects exhibited an increase in anxiety, depression, and hyperactivity following concussion. Further analyses were conducted to look into each psychosocial variable under a closer lens.



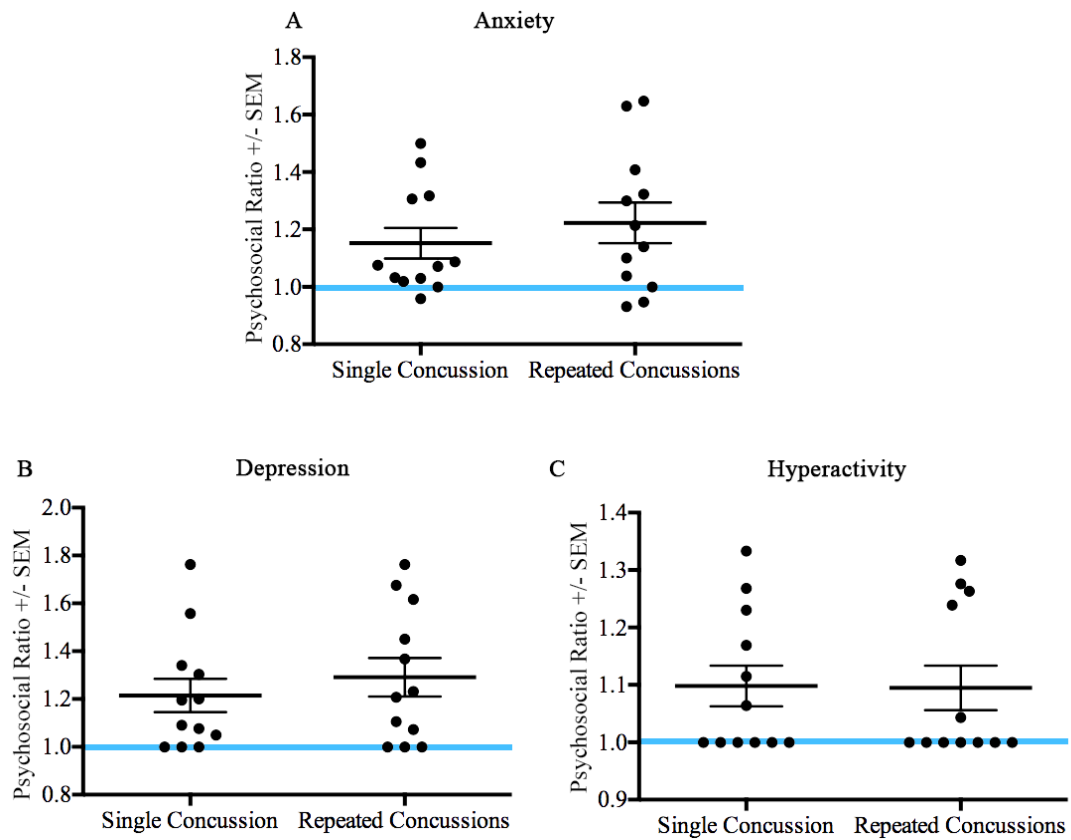
**Figure 14.** Psychosocial Ratio. This plot illustrates the Psychosocial Ratios, which represent the change in psychosocial functioning (i.e., anxiety, depression, hyperactivity) from premorbid to post-morbid status as reported by parents. The blue line represents the baseline, indicating no change in psychosocial functioning. Subjects who fell below the baseline exhibited an increase in that psychosocial variable, and subjects who fell above the baseline exhibited a decrease in that psychosocial variable. As illustrated, the majority of subjects exhibited an increase in anxiety, depression, and hyperactivity following concussion.

Aim 2 was broken down into four sub-aims. The first three sub-aims each had their own specific hypothesis, and the final sub-aim was comprised of four hypotheses. However, a couple of obstacles were encountered during analyses. Firstly, as illustrated in Table 4, one cell had zero subjects (i.e., child females who endured single concussion) and a couple of the cells only had one subject (i.e., female adolescents who underwent single concussion, female children who underwent repeated concussion). Given the low sample size in these interaction cells, interaction effects were excluded from analyses due

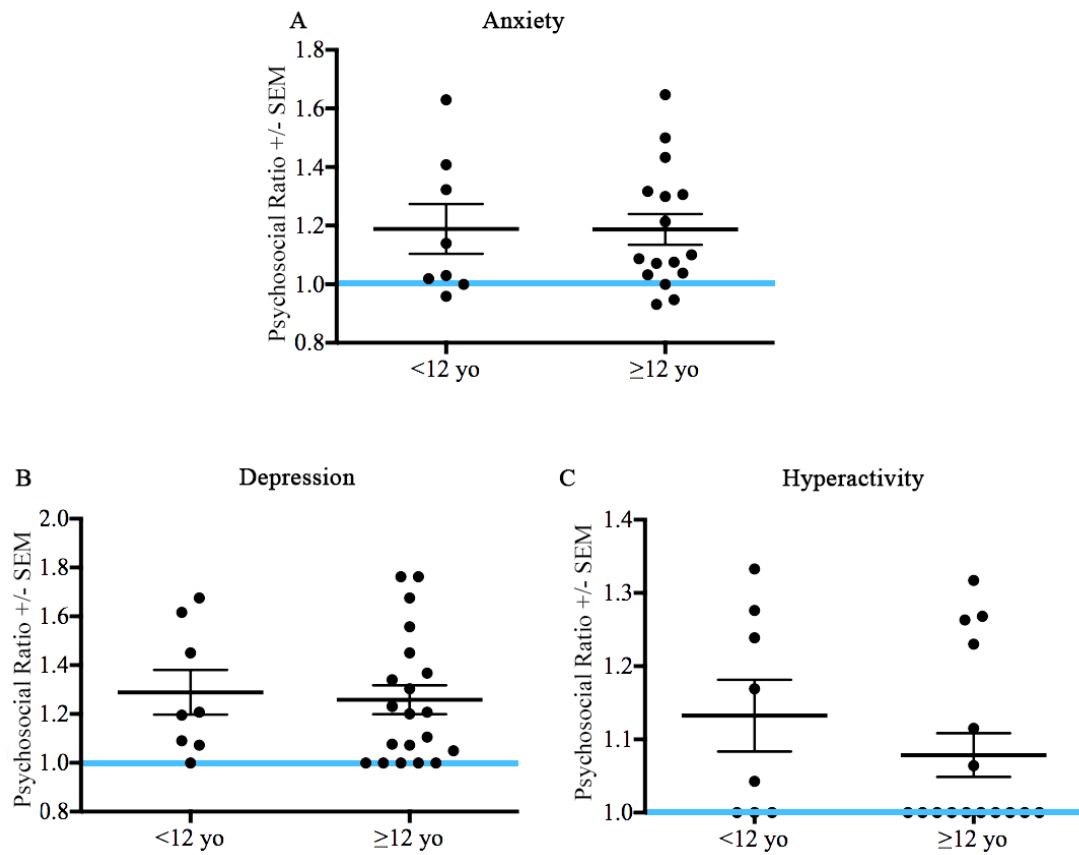
to no variance. In addition, given that the *a priori* power analysis suggested a total sample size of 38 subjects for six conditions (i.e., seven subjects per condition), the data did not have a strong enough power to be interpreted. As a result, the MANOVA was only conducted for main effects (i.e., Hypotheses 2a through 2c; Table 5). Table 5 illustrates the sample sizes of the main effect cells that were analyzed, excluding the interaction cells. The analyses and results are discussed below.

Unfortunately, results suggested that the Anxiety and Hyperactivity data did not pass the Levene's test (suggesting unequal variances) and none of the DVs (i.e., Anxiety, Depression, Hyperactivity) passed the Shapiro-Wilk test for normal distribution. Nevertheless, an exploratory MANOVA of the raw data with all three IVs (i.e., Age, Gender, Concussion History) and three DVs (i.e., Anxiety, Depression, Hyperactivity) was conducted to assess only the main effects. Raw data scatter plots for main effects are illustrated in Figures 15-17. Specifically, these figures illustrate how concussion history (Figure 15), age (Figure 16), and gender (Figure 17) affect anxiety, depression, and, hyperactivity. Interaction effects were not analyzed for reasons described above. The blue bar presented in Figures 15-17 represent the baseline, indicating no change in psychosocial functioning. This bar is equal to a psychosocial ratio of one.

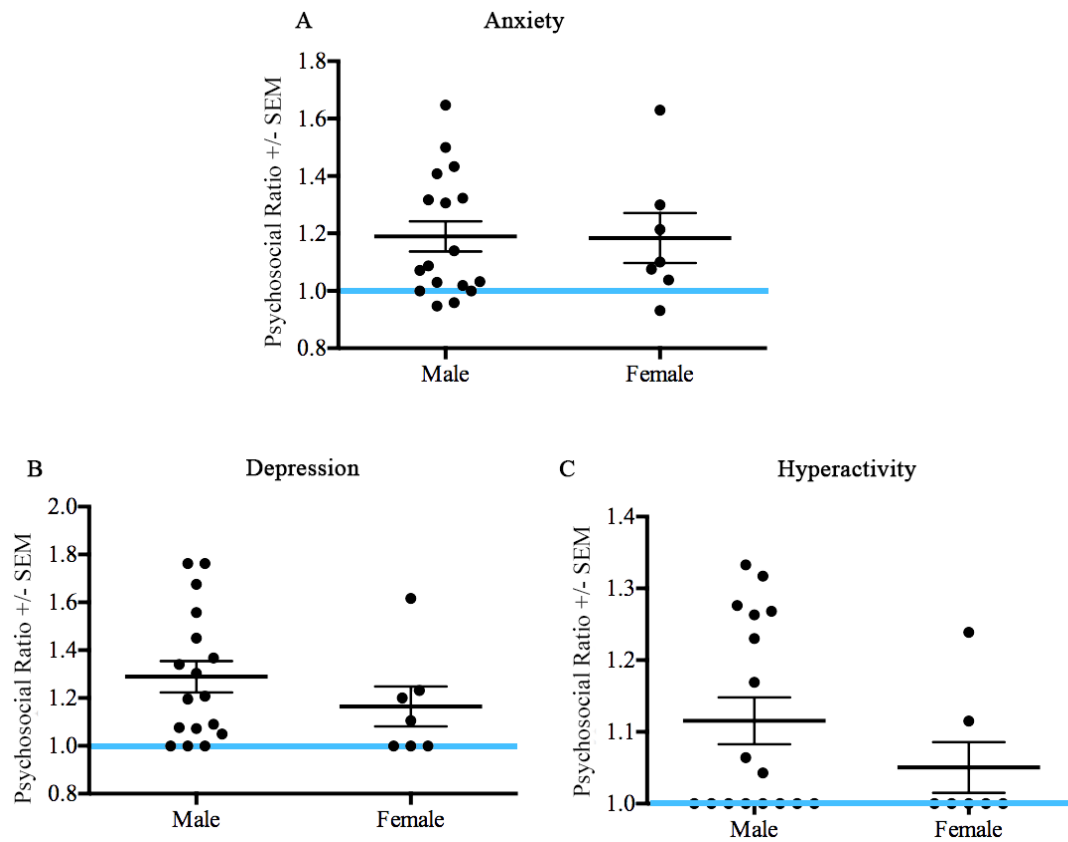




**Figure 15.** Raw data scatter plots of Psychosocial Ratios (i.e., change in psychosocial functioning from pre-morbid to post-morbid status) illustrate how concussion history (single concussion vs. repeated concussion) affects anxiety, depression, and hyperactivity. Those who endured repeated concussion experienced a slightly greater increase in **A.** anxiety and **B.** depression from pre- to post-morbid status compared to those who endured a single concussion, although that difference was not significant. **C.** There was no difference in how concussion history affected hyperactivity in young people. However, these effects could not be interpreted due to the violation of MANOVA assumptions (i.e., homogeneity of variance, normal distribution) and insufficient power.

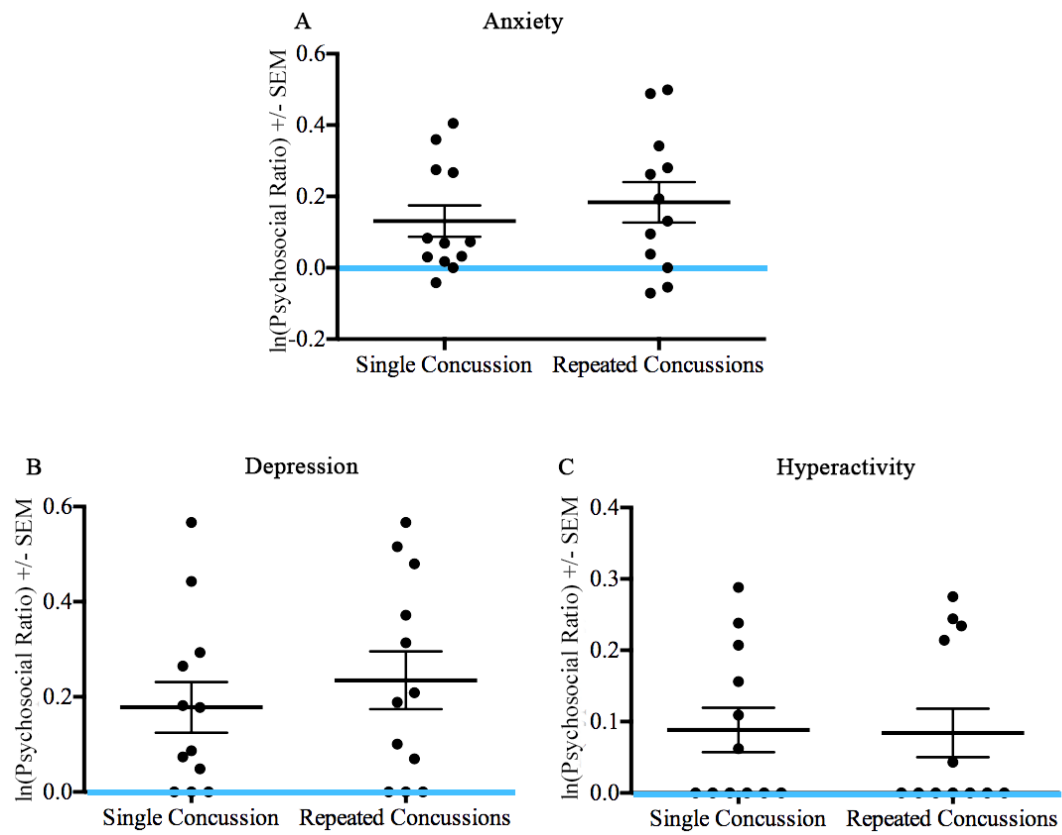


**Figure 16.** Raw data scatter plots of Psychosocial Ratios (i.e., change in psychosocial functioning from premorbid to post-morbid status) illustrate how age (<12 years old vs.  $\geq 12$  years old) affects anxiety, depression, and hyperactivity. There was no difference in how age affected **A.** anxiety and **B.** depression in young people. **C.** Children tended to have a greater increase in hyperactivity than children following concussion, although that difference was not significant. However, these effects could not be interpreted due to the violation of MANOVA assumptions (i.e., homogeneity of variance, normal distribution) and insufficient power.

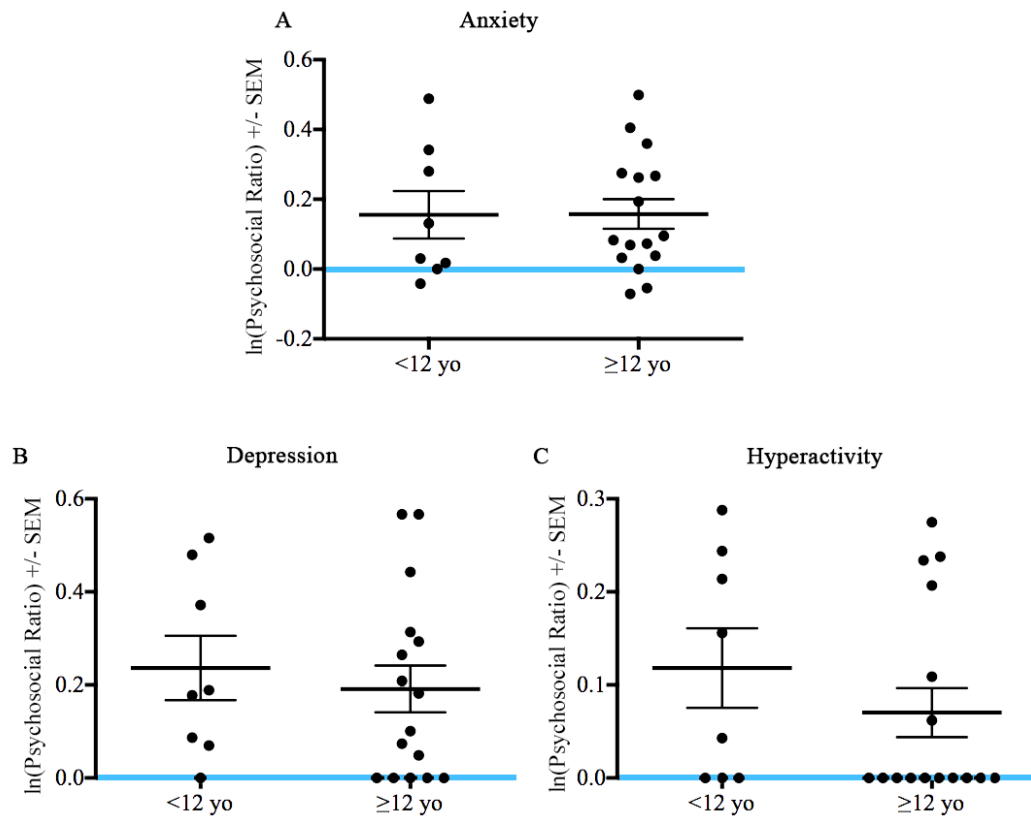


**Figure 17.** Raw data scatter plots of Psychosocial Ratios (i.e., change in psychosocial functioning from premorbid to post-morbid status) illustrate how gender (male vs. female) affects anxiety, depression, and hyperactivity. There were no differences in how **A.** gender affected anxiety in younger children. Findings suggested that males experienced a greater increase in **B.** depression and **C.** hyperactivity than females, following concussion, although that difference was not significant. However, these effects could not be interpreted due to the violation of MANOVA assumptions (i.e., homogeneity of variance, normal distribution) and insufficient power.

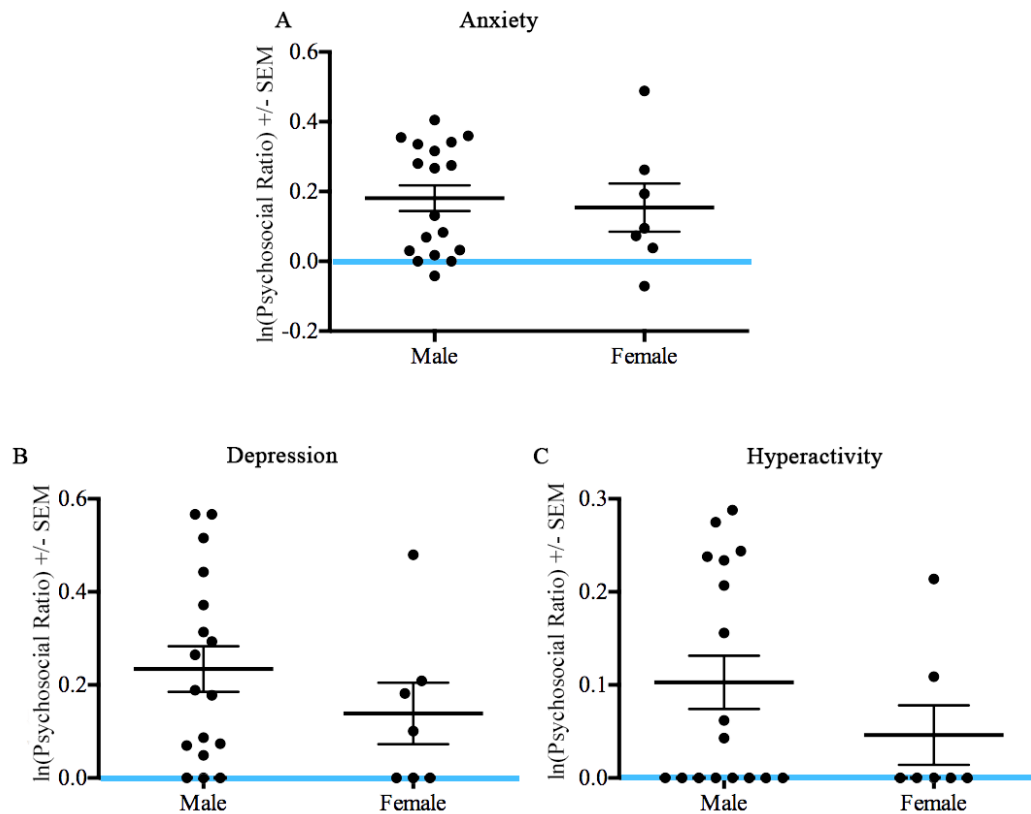
In hopes of achieving homogeneity and normality, transformation analyses were conducted (i.e., natural log [ln] and base 10 log [log<sub>10</sub>]). For the same reasons described in the Aim 1 Results, the ln data transformation was conducted first. Findings suggested that this data transformation did not alter the homogeneity of variance or normal distribution violations (see Figures 18-20).



**Figure 18.** Natural log (ln) transformational analyses of Psychosocial Ratios (i.e., change in psychosocial functioning from pre-morbid to post-morbid status) illustrate how concussion history (single concussion vs. repeated concussion) affects anxiety, depression, and hyperactivity. Findings suggest that those who endured repeated concussion experienced a slightly greater increase in **A.** anxiety and **B.** depression than those who endured a single concussion, although that difference was not significant. **C.** There was no difference in how concussion history affected hyperactivity. However, these effects could not be interpreted due to the violation of MANOVA assumptions (i.e., homogeneity of variance, normal distribution) and insufficient power.

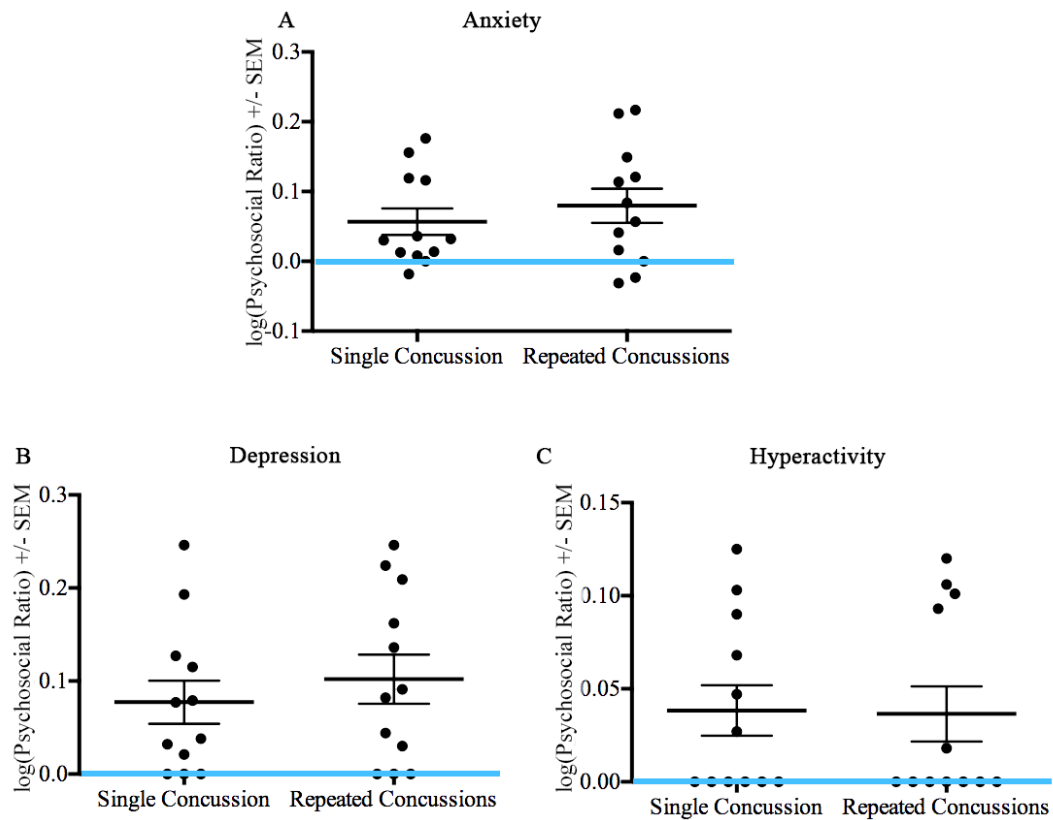


**Figure 19.** Natural log (ln) transformational analyses of Psychosocial Ratios (i.e., change in psychosocial functioning from premorbid to post-morbid status) illustrate how age (<12 years old vs. ≥12 years old) affects anxiety, depression, and hyperactivity. **A.** Findings suggest that there was no difference in how age affected anxiety following concussion. Plots **B.** and **C.** suggest that children (<12 years old) endorsed a greater increase in **B.** depression and **C.** hyperactivity than adolescents (≥12 years old), although that difference was not significant. However, these effects could not be interpreted due to the violation of MANOVA assumptions (i.e., homogeneity of variance, normal distribution) and insufficient power.

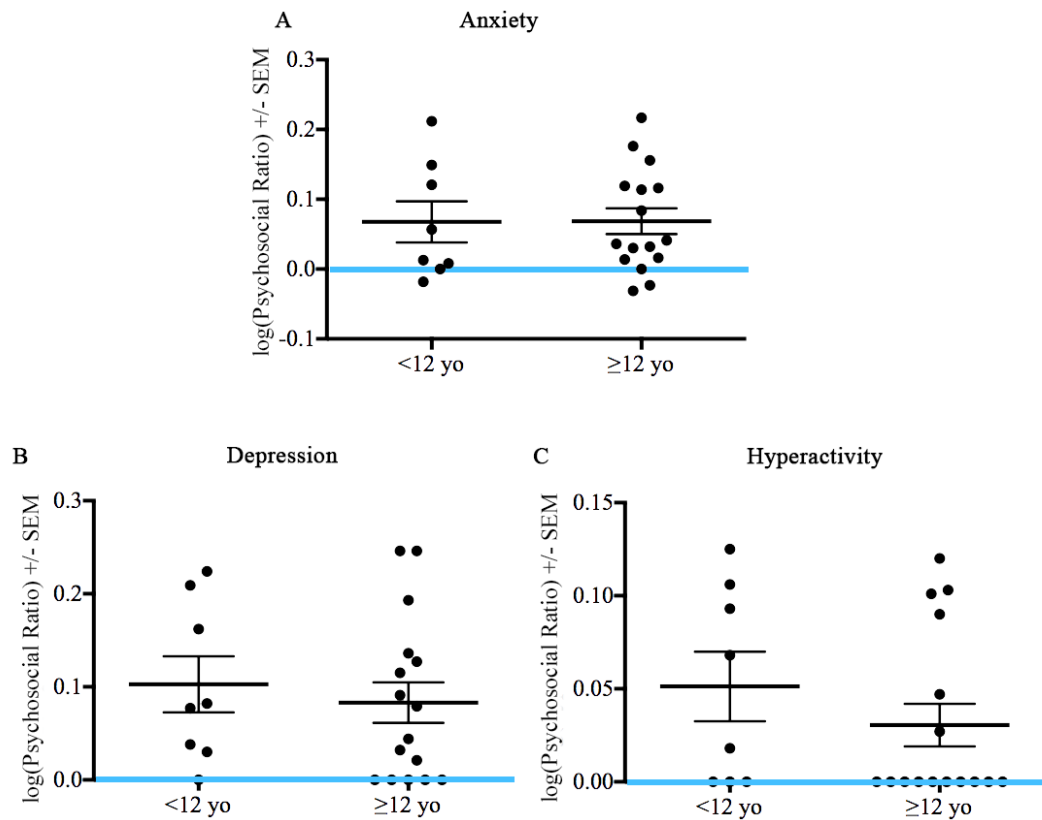


**Figure 20.** Natural log (ln) transformational analyses of Psychosocial Ratios (i.e., change in psychosocial functioning from premorbid to post-morbid status) illustrate how gender (male vs. female) affects anxiety, depression, and hyperactivity. **A.** Findings suggest that there was no difference in how gender affected anxiety following concussion. Plots **B.** and **C.** suggest that males endorsed a greater increase in **B.** depression and **C.** hyperactivity than females, although that difference was not significant. However, these effects could not be interpreted due to the violation of MANOVA assumptions (i.e., homogeneity of variance, normal distribution) and insufficient power.

An even more drastic transformation of the psychosocial ratios ( $\log_{10}$ ) did not alter the homogeneity of variance or normal distribution violations either (see Figures 21-23). For Figures 18-23, the baseline was placed at the 0 mark, given that the  $\ln(1)$  and  $\log(1)$  is equal to 0. This calculation was tested and confirmed, such that, subjects who fell below, on, or above the baseline for the raw data also fell below, on, or above the baseline for the transformed data, respectively.

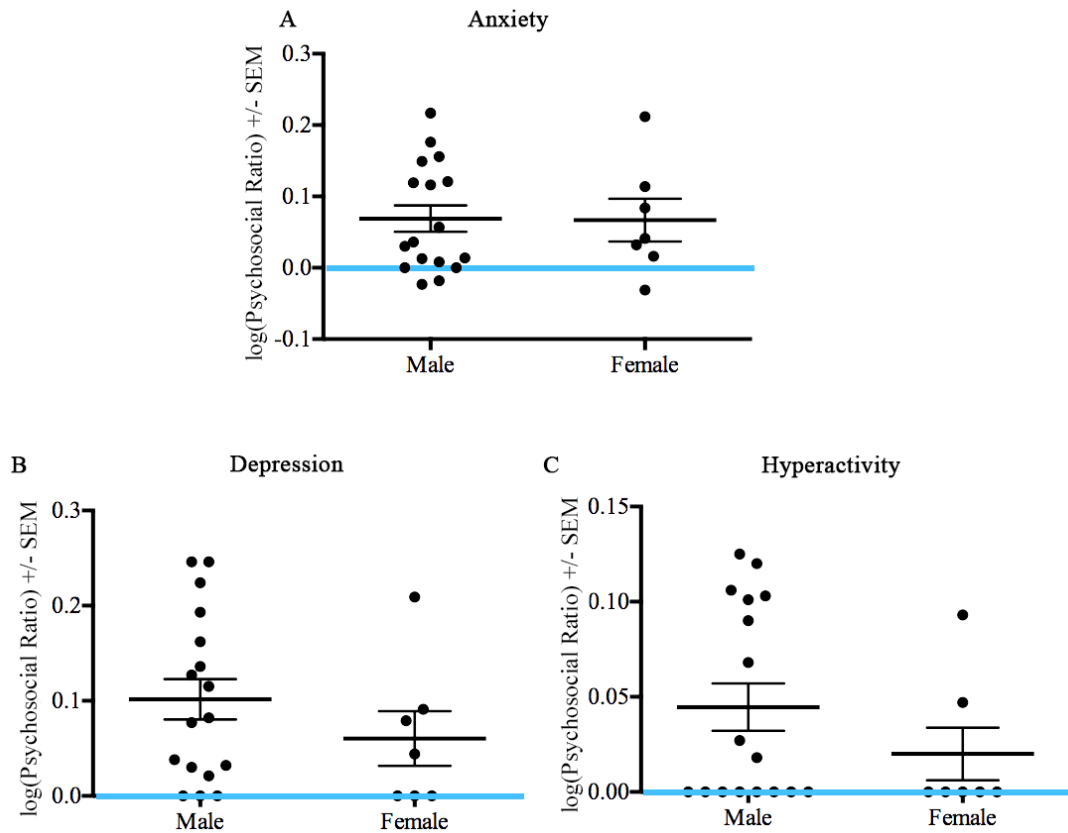


**Figure 21.** Log<sub>10</sub> (log) transformational analyses of Psychosocial Ratios illustrate how concussion history (single concussion vs. repeated concussion) affects anxiety, depression, and hyperactivity. Findings suggest that those who endured repeated concussion experienced a slightly greater increase in **A.** anxiety and **B.** depression than those who endured a single concussion, although that difference was not significant. **C.** There was no difference in how concussion history affected hyperactivity after concussion. However, these effects could not be interpreted due to the violation of MANOVA assumptions (i.e., homogeneity of variance, normal distribution) and insufficient power.



**Figure 22.** Log<sub>10</sub> (log) transformational analyses of Psychosocial Ratios illustrate how age (<12 years old vs.  $\geq 12$  years old) affects anxiety, depression, and hyperactivity. **A.** Findings suggest that there was no difference in how age affected anxiety after concussion. Plots **B.** and **C.** suggest that children (<12 years old) endorsed a greater increase in **B.** depression and **C.** hyperactivity than adolescents ( $\geq 12$  years old) following concussion, although that difference was not significant. However, these effects could not be interpreted due to the violation of MANOVA assumptions (i.e., homogeneity of variance, normal distribution) and insufficient power.





**Figure 23.** Log<sub>10</sub> (log) transformational analyses of Psychosocial Ratios illustrate how gender (male vs. female) affects anxiety, depression, and hyperactivity. **A.** Findings suggest that there was no difference in how gender affected anxiety after concussion. Plots **B.** and **C.** suggest that males endorsed a greater increase in **B.** depression and **C.** hyperactivity than females after concussion, although that difference was not significant. However, these effects could not be interpreted due to the violation of MANOVA assumptions (i.e., homogeneity of variance, normal distribution) and insufficient power.

As done for Aim 1, subsequent three-way ANOVAs were conducted to further seek for significant differences. Each ANOVA entailed three IVs (i.e., age, gender, concussion history) and one DV each (i.e., Anxiety, Depression, or Hyperactivity). Unfortunately, there were no significant main effects in any of the three-way ANOVAs. Tables 6 and 7 illustrate the overall main effect and interaction findings for Aims 1 and 2.

**Table 6.** Review of Main Effect Findings for Aims 1 and 2

	<u>Concussion History</u>		<u>Age</u>		<u>Gender</u>	
	Single	Repeated	Children	Adolescents	Male	Female
Processing Speed	No Difference		No Difference		No Difference	
Executive Function	No Difference		Worse	-	No Difference	
Spatial (WASI-II MR)	n/a		n/a		No Difference	
Spatial (Rey-O Copy)	n/a		n/a		-	Better
Verbal (WASI-II Voc.)	n/a		n/a		No Difference	
Verbal (CVLT-II/C)	n/a		n/a		No Difference	
Increase in Anxiety	-	Greater	No Difference		No Difference	
Increase in Depression	-	Greater	No Difference		Greater	-
	No Difference		Greater	-	Greater	-

**Table 7.** Review of Interaction Findings for Aims 1 and 2

***Concussion History by Age***

<u>Processing Speed</u>	<u>Age</u>	
Concussion History	<u>Children</u>	<u>Adolescents</u>
Single Concussion	-	Better
Repeated Concussion	-	Worse
<u>Executive Function</u>		
Concussion History	<u>Children</u>	<u>Adolescents</u>
Single Concussion	-	Better
Repeated Concussion	-	Better

***Concussion History by Gender***

<u>Processing Speed</u>	<u>Gender</u>	
Concussion History	<u>Male</u>	<u>Female</u>
Single Concussion	Better	-
Repeated Concussion	Worse	-
<u>Executive Function</u>		
Concussion History	<u>Male</u>	<u>Female</u>
Single Concussion	-	Better
Repeated Concussion	No Difference	

***Age by Gender***

<u>Processing Speed</u>	<u>Gender</u>	
Age	<u>Male</u>	<u>Female</u>
Children	Better	-
Adolescents	-	Better
<u>Executive Function</u>		
Age	<u>Male</u>	<u>Female</u>
Children	-	Better
Adolescents	-	Better

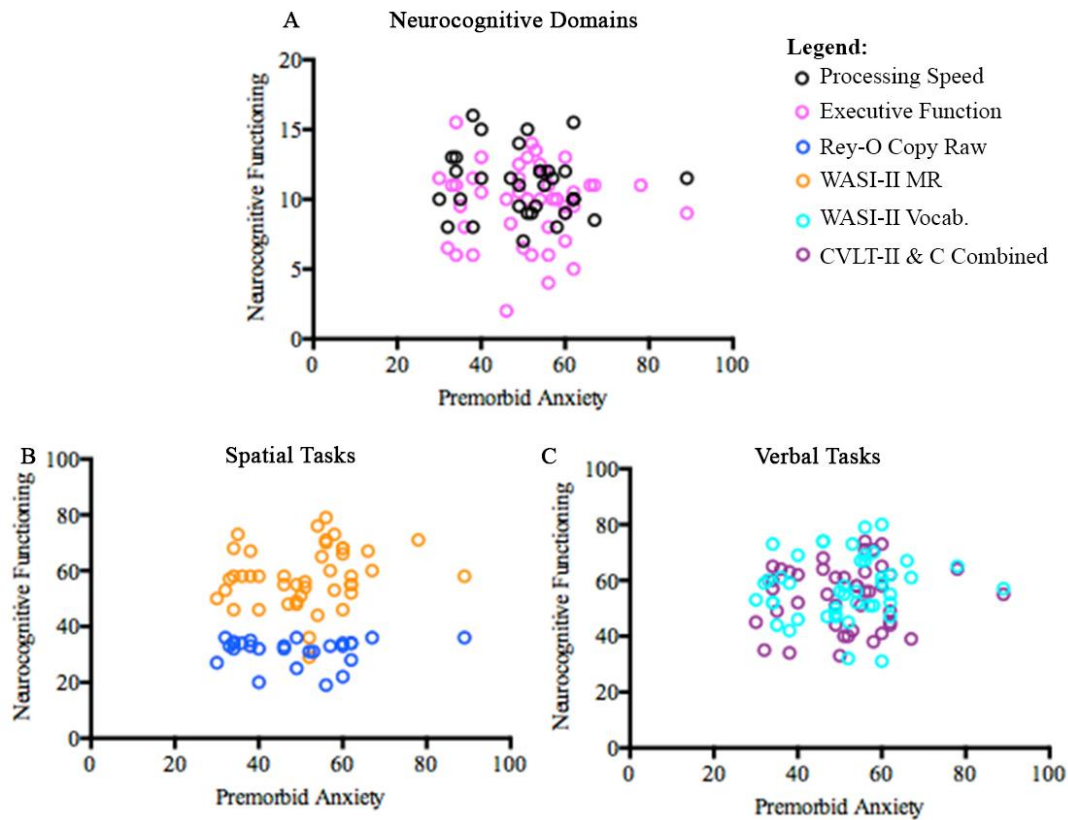
**Aim 3**

The third aim of the current study was to assess how premorbid or post-morbid psychosocial functioning (i.e., anxiety, depression, hyperactivity) is associated with neurocognitive functioning (i.e., processing speed, executive function) following concussion in young people. Aim 3 was broken down into two hypotheses. These results were discussed below.

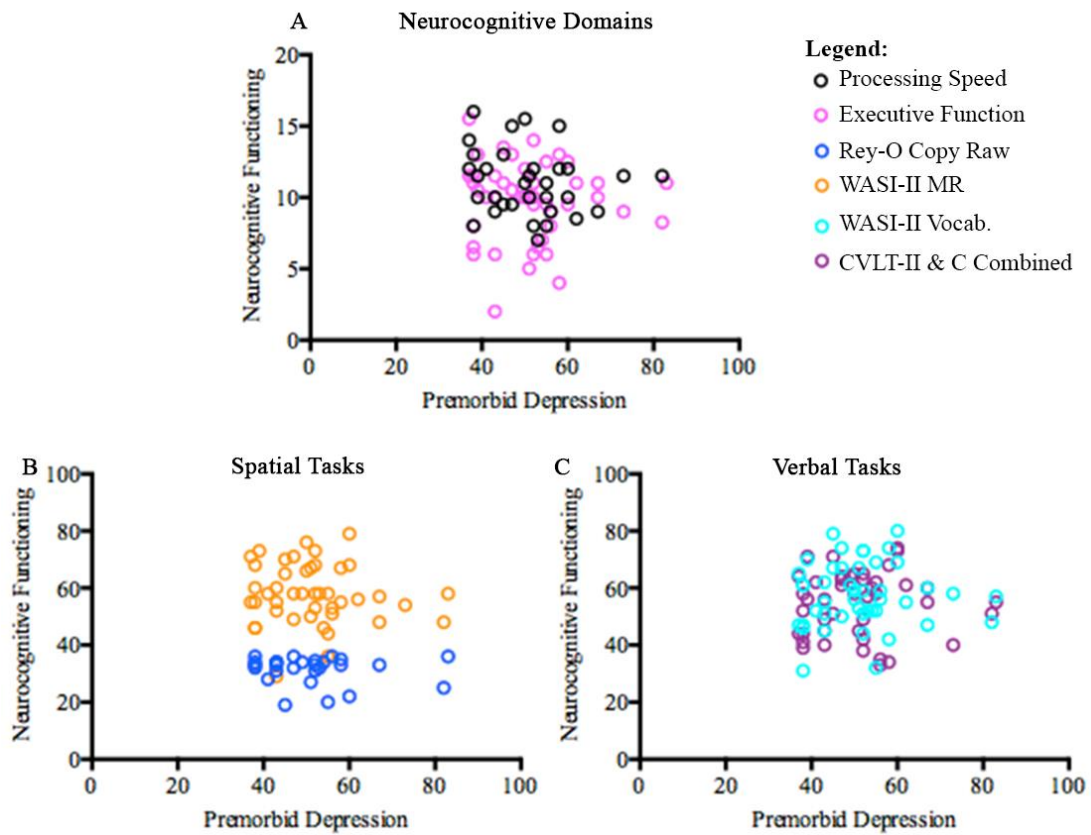
**Hypothesis 3a** stated that, in young people, there would be a negative correlation between premorbid psychosocial functioning and neurocognitive functioning following concussion. Specifically, high premorbid anxiety, depression, and hyperactivity would be correlated with lower neurocognitive functioning following concussion and vice versa. A bivariate correlational analysis was conducted, including premorbid anxiety (Figure 24), depression (Figure 25), and hyperactivity (Figure 26) and performance in certain neurocognitive domains (i.e., processing speed and executive function) and neurocognitive tasks (i.e., Rey-O Copy, WASI-II MR, WASI-II Vocab., CVLT-II and -C Combined). The results did not indicate any significant correlations (Table 8, Figures 24-26). However, given that these premorbid psychosocial factors had a lower sample size ( $n = 47$ ) than what *a priori* power analyses ( $n = 82$ ) suggested were required to obtain effective results, these results yielded weak power.

**Table 8.** Aim 3 Correlation Analysis of Premorbid Psychosocial Functioning

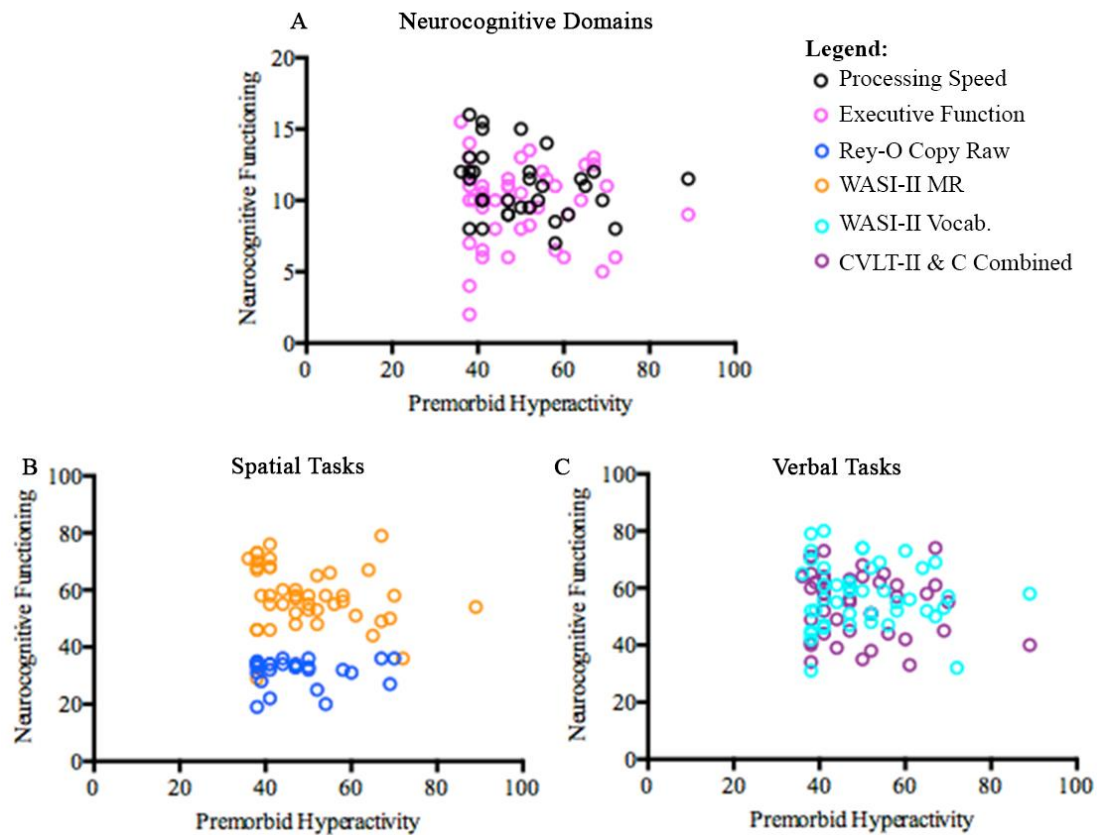
Variables	Premorbid Anxiety	Premorbid Depression	Premorbid Hyperactivity
Processing Speed	$r = -0.10, n = 33$	$r = -0.18, n = 33$	$r = -0.02, n = 33$
Executive Function	$r = -0.02, n = 46$	$r = -0.05, n = 46$	$r = -0.03, n = 46$
Rey-O Copy	$r = 0.23, n = 27$	$r = -0.12, n = 27$	$r = 0.05, n = 27$
WASI-II MR	$r = -0.01, n = 44$	$r = -0.10, n = 44$	$r = -0.24, n = 44$
WASI-II Vocab.	$r = 0.09, n = 45$	$r = 0.02, n = 45$	$r = -0.06, n = 45$
CVLT-II and -C Combined	$r = -0.09, n = 44$	$r = 0.02, n = 44$	$r = -0.16, n = 44$



**Figure 24.** Correlational analyses of how premorbid anxiety correlates with neurocognitive functioning on certain neurocognitive domains (i.e., processing speed, executive function) and neurocognitive tasks (i.e., Rey-O Copy, WASI-II MR, WASI-II Vocab., CVLT-II and -C Combined). Premorbid anxiety and the following neurocognitive tasks (i.e., WASI-II MR, WASI-II Vocab., CVLT-II and -C Combined) are plotted as T-Scores ( $M: 50$ ,  $SD: 10$ ), processing speed and executive function are plotted as scaled scores ( $M: 10$ ,  $SD: 3$ ), and Rey-O Copy is plotted as raw scores. **A.** This plot illustrates that there was no correlation between premorbid anxiety and processing speed or executive function. **B.** This plot illustrates that there was no correlation between premorbid anxiety and Rey-O Copy or WASI-II MR. **C.** This plot illustrates that there was no correlation between premorbid anxiety and WASI-II Vocab. or CVLT-II and -C Combined.



**Figure 25.** Correlational analyses of how premorbid depression correlates with neurocognitive functioning on certain neurocognitive domains (i.e., processing speed, executive function) and neurocognitive tasks (i.e., Rey-O Copy, WASI-II MR, WASI-II Vocab., CVLT-II and -C Combined). Premorbid depression and the following neurocognitive tasks (i.e., WASI-II MR, WASI-II Vocab., CVLT-II and -C Combined) are plotted as T-Scores ( $M: 50, SD: 10$ ), processing speed and executive function are plotted as scaled scores ( $M: 10, SD: 3$ ), and Rey-O Copy is plotted as raw scores. **A.** This plot illustrates that there was no correlation between premorbid depression and processing speed or executive function. **B.** This plot illustrates that there was no correlation between premorbid depression and Rey-O Copy or WASI-II MR. **C.** This plot illustrates that there was no correlation between premorbid depression and WASI-II Vocab. or CVLT-II and -C Combined.



**Figure 26.** Correlational analyses of how premorbid hyperactivity correlates with neurocognitive functioning on certain neurocognitive domains (i.e., processing speed, executive function) and neurocognitive tasks (i.e., Rey-O Copy, WASI-II MR, WASI-II Vocab., CVLT-II and -C Combined). Premorbid hyperactivity and the following neurocognitive tasks (i.e., WASI-II MR, WASI-II Vocab., CVLT-II and -C Combined) are plotted as T-Scores ( $M: 50, SD: 10$ ), processing speed and executive function are plotted as scaled scores ( $M: 10, SD: 3$ ), and Rey-O Copy is plotted as raw scores. **A.** This plot illustrates that there was no correlation between premorbid hyperactivity and processing speed or executive function. **B.** This plot illustrates that there was no correlation between premorbid hyperactivity and Rey-O Copy or WASI-II MR. **C.** This plot illustrates that there was no correlation between premorbid hyperactivity and WASI-II Vocab. or CVLT-II and -C Combined.

**Hypothesis 3b** stated that, in young people, there would be a negative correlation between psychosocial functioning following concussion and neurocognitive functioning following concussion. Specifically, high post-morbid anxiety, depression, and hyperactivity would be correlated with lower neurocognitive functioning following

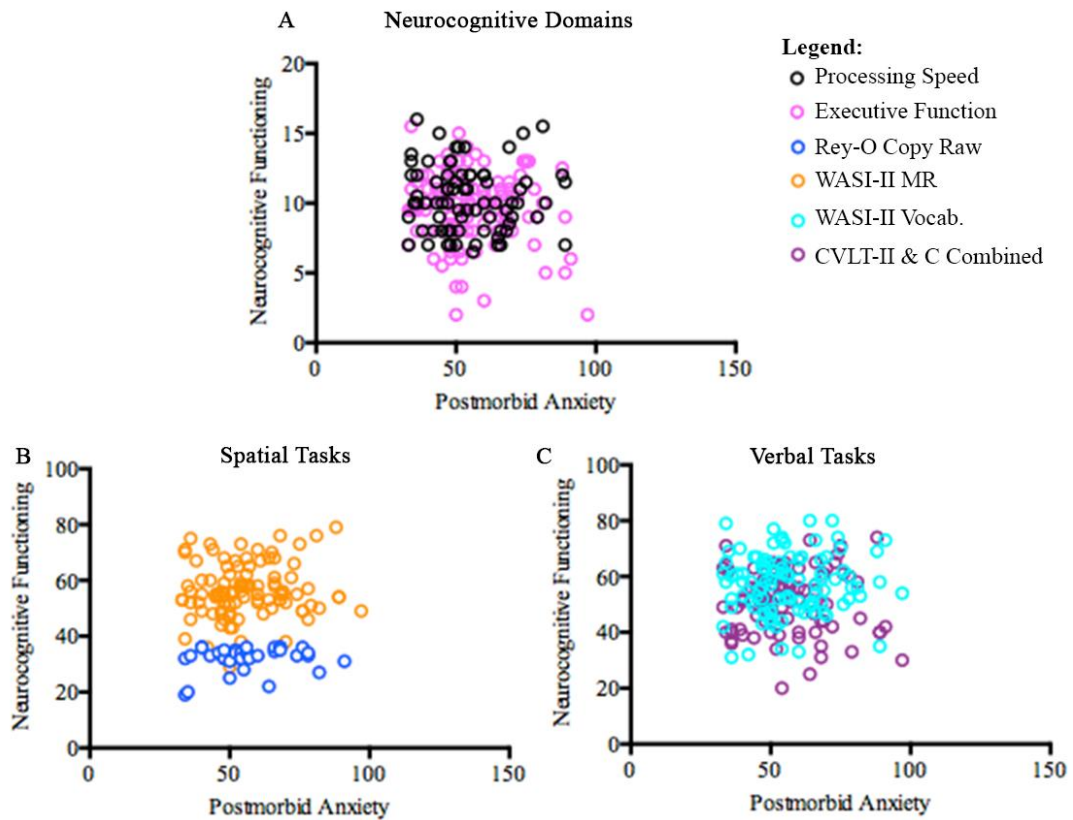
concussion and vice versa. A bivariate correlational analysis was conducted, including post-morbid anxiety, depression, and hyperactivity and performance in certain neurocognitive domains (i.e., processing speed and executive function) and neurocognitive tasks (i.e., Rey-O Copy, WASI-II MR, WASI-II Vocab., CVLT-II and -C Combined). These results are illustrated in Table 9 and Figures 27-29. Results indicated that there was a significant negative correlation between post-morbid depression and executive function ( $r=-0.20$ ,  $p<0.05$ ; Figure 28). However, per *a priori* analyses, these results yielded low power.

**Table 9.** Aim 3 Correlation Analysis of Post-Morbid Psychosocial Functioning

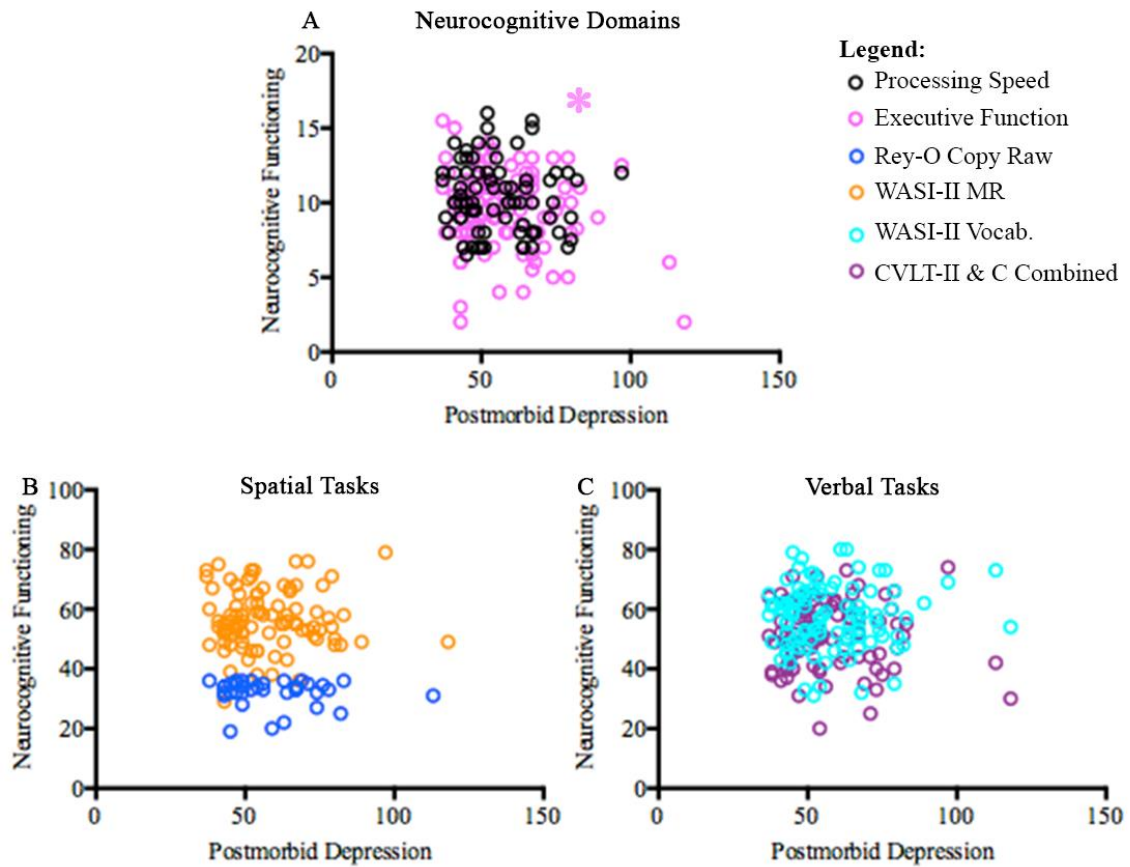
Variables	Post-Morbid Anxiety	Post-Morbid Depression	Post-Morbid Hyperactivity
Processing Speed	$r = -0.04$ , $n = 76$	$r = -0.08$ , $n = 75$	$r = -0.07$ , $n = 74$
Executive Function	$r = -0.15$ , $n = 103$	$r = -0.20^*$ , $n = 102$	$r = 0.03$ , $n = 101$
Rey-O Copy	$r = 0.22$ , $n = 36$	$r = -0.08$ , $n = 36$	$r = 0.12$ , $n = 36$
WASI-II MR	$r = 0.08$ , $n = 98$	$r = 0.02$ , $n = 97$	$r = 0.04$ , $n = 96$
WASI-II Vocab.	$r = 0.06$ , $n = 99$	$r = 0.04$ , $n = 98$	$r = 0.12$ , $n = 97$
CVLT-II and -C Combined	$r = -0.02$ , $n = 98$	$r = -0.03$ , $n = 97$	$r = 0.01$ , $n = 96$

\* =  $p<0.05$

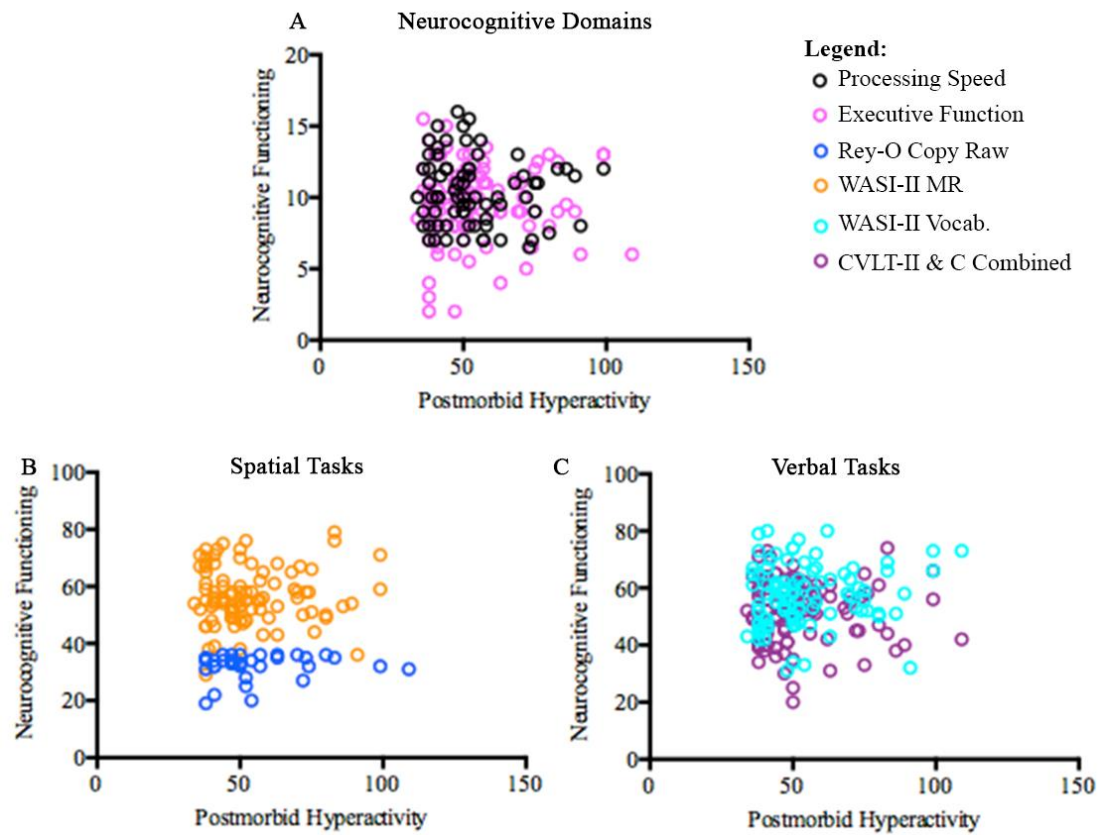




**Figure 27.** Correlational analyses of how post-morbid anxiety correlates with neurocognitive functioning on certain neurocognitive domains (i.e., processing speed, executive function) and neurocognitive tasks (i.e., Rey-O Copy, WASI-II MR, WASI-II Vocab., CVLT-II and -C Combined). Post-morbid anxiety and the following neurocognitive tasks (i.e., WASI-II MR, WASI-II Vocab., CVLT-II and -C Combined) are plotted as T-Scores ( $M: 50$ ,  $SD: 10$ ), processing speed and executive function are plotted as scaled scores ( $M: 10$ ,  $SD: 3$ ), and Rey-O Copy is plotted as raw scores. **A.** This plot illustrates that there was no correlation between post-morbid anxiety and processing speed or executive function. **B.** This plot illustrates that there was no correlation between post-morbid anxiety and Rey-O Copy or WASI-II MR. **C.** This plot illustrates that there was no correlation between post-morbid anxiety and WASI-II Vocab. or CVLT-II and -C Combined.



**Figure 28.** Correlational analyses of how post-morbid depression correlates with neurocognitive functioning on certain neurocognitive domains (i.e., processing speed, executive function) and neurocognitive tasks (i.e., Rey-O Copy, WASI-II MR, WASI-II Vocab., CVLT-II and -C Combined). Post-morbid depression and the following neurocognitive tasks (i.e., WASI-II MR, WASI-II Vocab., CVLT-II and -C Combined) are plotted as T-Scores ( $M: 50$ ,  $SD: 10$ ), processing speed and executive function are plotted as scaled scores ( $M: 10$ ,  $SD: 3$ ), and Rey-O Copy is plotted as raw scores. **A.** This plot illustrates that there was no correlation between post-morbid depression and processing speed. However, there was a significant negative correlation between post-morbid depression and executive function ( $r=-0.20$ ,  $p<0.05$ ). **B.** This plot illustrates that there was no correlation between post-morbid depression and Rey-O Copy or WASI-II MR. **C.** This plot illustrates that there was no correlation between post-morbid depression and WASI-II Vocab. or CVLT-II and -C Combined.



**Figure 29.** Correlational analyses of how post-morbid hyperactivity correlates with neurocognitive functioning on certain neurocognitive domains (i.e., processing speed, executive function) and neurocognitive tasks (i.e., Rey-O Copy, WASI-II MR, WASI-II Vocab., CVLT-II and -C Combined). Post-morbid hyperactivity and the following neurocognitive tasks (i.e., WASI-II MR, WASI-II Vocab., CVLT-II and -C Combined) are plotted as T-Scores ( $M: 50$ ,  $SD: 10$ ), processing speed and executive function are plotted as scaled scores ( $M: 10$ ,  $SD: 3$ ), and Rey-O Copy is plotted as raw scores. **A.** This plot illustrates that there was no correlation between post-morbid hyperactivity and processing speed or executive function. **B.** This plot illustrates that there was no correlation between post-morbid hyperactivity and Rey-O Copy or WASI-II MR. **C.** This plot illustrates that there was no correlation between post-morbid hyperactivity and WASI-II Vocab. or CVLT-II and -C Combined.

To increase power, the correlational analysis was re-conducted. However, this time, only selected factors were included in the analysis. Such factors included post-morbid anxiety, depression, and hyperactivity, executive function, WASI-II MR, WASI-II Vocab., and CVLT-II/C. The sample sizes are illustrated in Table 10. The same

significant finding was found, such that post-morbid depression was negatively correlated with executive function ( $r=-0.20$ ,  $p<0.05$ ).

**Table 10.** Aim 3 Revised Correlation Analysis of Post-Morbid Psychosocial Functioning

Variables	Post-Morbid Anxiety	Post-Morbid Depression	Post-Morbid Hyperactivity
Executive Function	$r = -0.15, n = 103$	$r = -0.20^*, n = 102$	$r = 0.03, n = 101$
WASI-II MR	$r = 0.08, n = 98$	$r = 0.02, n = 97$	$r = 0.04, n = 96$
WASI-II Vocab.	$r = 0.06, n = 99$	$r = 0.04, n = 98$	$r = 0.12, n = 97$
CVLT-II and -C Combined	$r = -0.02, n = 98$	$r = -0.03, n = 97$	$r = 0.01, n = 96$

\* =  $p<0.05$

## CHAPTER EIGHT

### DISCUSSION

Our overarching hypothesis stated that individuals with two or more concussions would exhibit more severe neurocognitive and psychosocial deficits than those with a single concussion. Furthermore, we hypothesized that concussion-induced deficits would be worse in females compared to males and in adolescents compared to younger children (based on age-related norms) and that males would perform better on spatial tasks, whereas females would perform better on verbal tasks. Finally, we hypothesized that higher pre- and post-morbid anxiety, depression, and hyperactivity would be correlated with worse neurocognitive functioning following concussion.

Our results demonstrate that, following concussion, those who experienced more depression were also likely to perform worse on tasks of executive function. Our results also show that there were no significant differences in neurocognitive or psychosocial functioning across concussion history, age, or gender amongst young people with at least 1 concussion. Specifically, group differences were either small or non-existent (statistically insignificant) or could not be interpreted due to violations of MANOVA assumptions or insufficient power. However, several trends were observed that will be discussed in more detail below.

Concussion history (single concussion vs. repeated concussion) appeared to have a small (non-significant) impact on psychosocial function (i.e., anxiety, depression, hyperactivity), but not on neurocognitive performance (i.e., processing speed, executive function). Specifically, contrary to Hypothesis 1a, concussion history did not impact neurocognitive performance (Figure 3). However, as Hypothesis 2a suggested,

individuals with two or more concussions endorsed a greater increase in anxiety and depression following their concussions than those with only 1 concussion (Figure 15a-b). Concussion history had no impact on hyperactivity following concussion (Figure 15c). Analyses of log transformed data sets yielded similar results.

Age (children [ $<12$  years old] vs. adolescents [ $\geq 12$  years old]) appeared to have a slight, but non-significant, impact on aspects of both neurocognitive and psychosocial functioning. Contrary to Hypothesis 1b, age did not impact processing speed performance (Figure 4a). Furthermore, contrary to Hypothesis 1b, children, rather than adolescents, performed worse on tasks of executive function, based on age-related norms (Figure 4b). This finding will be further explored later in this section. Contrary to Hypothesis 2b, children, rather than adolescents, endorsed a greater increase in hyperactivity following concussion, based on age-related norms (Figure 16c). Age had no significant impact on anxiety and depression in young people following concussion (Figure 16a-b). The data transformations suggested that children, rather than adolescents, also endorsed a greater increase in depression following concussion, based on age-related norms (ln transformation: Figure 19b; log transformation: Figure 22b). Overall, non-significant trends suggested that, contrary to hypothesis, children endorsed worse executive function and psychosocial functioning than adolescents following concussion, based on age-related norms.

Previous research suggests that adolescents are more susceptible to disruptions during their critical period of brain development (Wall et al., 2006); however, in the current study, children appeared to experience greater negative concussion-induced effects than adolescents. An explanation for this finding could be that adolescents' brains

are still further developed than that of children's brains, allowing them to perform better on these tasks, despite a concussion history.

Gender (male vs. female) had a slight, but non-significant, impact on aspects of both neurocognitive and psychosocial functioning. Contrary to Hypothesis 1c, females, rather than males, performed better on the spatial Rey-O Copy task (Figure 5b). As hypothesized in Hypothesis 1c, females also performed better than males on the verbal WASI-II Vocabulary task (Figure 5c). There were no gender differences in performance on the spatial WASI-II Matrix Reasoning or verbal CVLT-C and -II tasks. Furthermore, contrary to Hypothesis 2c, males, rather than females, endorsed a greater increase in depression and hyperactivity following concussion (Figure 17b-c). Gender had no significant impact on anxiety in young people following concussion (Figure 17a). Data transformations suggested similar results.

The current study did not demonstrate any significant interactions either; however, qualitative trends were observed. As Hypothesis 1d<sub>1</sub> suggested, there were no significant interactions between how age and concussion history affected neurocognitive functioning following concussion. Qualitative trends suggested that adolescents who underwent single concussion performed slightly better on tasks of processing speed than children who underwent single concussion, but the opposite was true amongst those who underwent repeated concussion (i.e., children performed slightly better than adolescents; Figure 9a). Adolescents always performed slightly better than children on tasks of executive function, irrelevant of concussion history (Figure 9b).

As Hypothesis 1d<sub>2</sub> suggested, there were no significant interactions between how gender and concussion history affected neurocognitive functioning after concussion.

Qualitative trends suggested that, amongst those who endured a single concussion, males performed slightly better than females on tasks of processing speed, but the opposite was true amongst those who endured repeated concussion (i.e., females performed slightly better than males; Figure 10a). Furthermore, in terms of performance on executive function tasks, females who endured a single concussion performed slightly better than males who endured a single concussion, but no gender differences were found amongst those who underwent repeated concussion (Figure 10b).

As Hypothesis 1d<sub>3</sub> suggested, amongst young people with a history of concussion, female children performed slightly better on tasks of executive function than male children (Figure 11b), although not significant. However, contrary to the hypothesis, male children performed slightly better on tasks of processing speed than female children (Figure 11a). Additionally, contrary to the hypothesis, amongst adolescents, females performed slightly better than males on tasks of processing speed (Figure 11a) and executive function (Figure 11b).

As Hypothesis 1d<sub>4</sub> suggested, there were no significant interactions between how concussion history, age, and gender affected neurocognitive functioning after concussion (Figure 12).

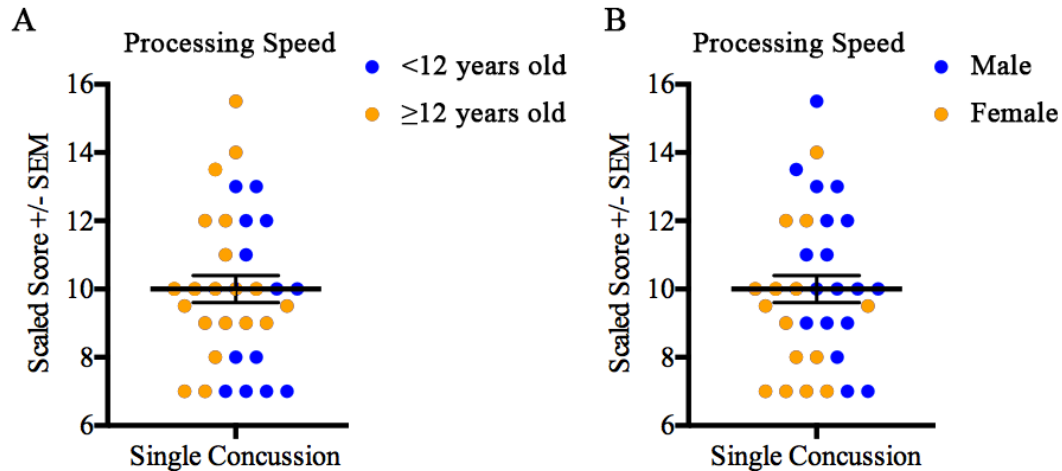
Data from Aims 1 and 2 were analyzed together to see whether a relationship existed between the neurocognitive and psychosocial functions of young people with a history of concussion. As hypothesized in part of Hypothesis 3b, there existed a significant negative correlation between post-morbid depression and executive function in young people with a history of concussion (Figure 28a). Contrary to Hypothesis 3a, there were no significant correlations between premorbid psychosocial functioning (i.e.,



anxiety, depression, hyperactivity) and neurocognitive functioning following concussion (Figures 24-26).

Some interesting trends were observed in the data distribution. For instance, multimodal distributions and cluster trends were observed in Figures 3a (i.e., processing speed performance amongst those who endured a single concussion) and 4a (i.e., processing speed performance amongst children and adolescents). These figures were explored under a closer lens to determine whether any factors could explain these data distribution patterns.

The age and gender distributions amongst individuals who endured a single concussion in Figure 3a were explored and illustrated in Figure 30 (i.e., age distribution illustrated in Figure 30a, gender distribution illustrated in Figure 30b). There appeared to be a bimodal distribution in this data subset. Specifically, one mode existed at a scaled score of 10 and the other at a scaled score of 7 ( $n_{children} = 13$ ,  $n_{adolescents} = 20$  [Figure 30a];  $n_{males} = 18$ ,  $n_{females} = 15$  [Figure 30b]).



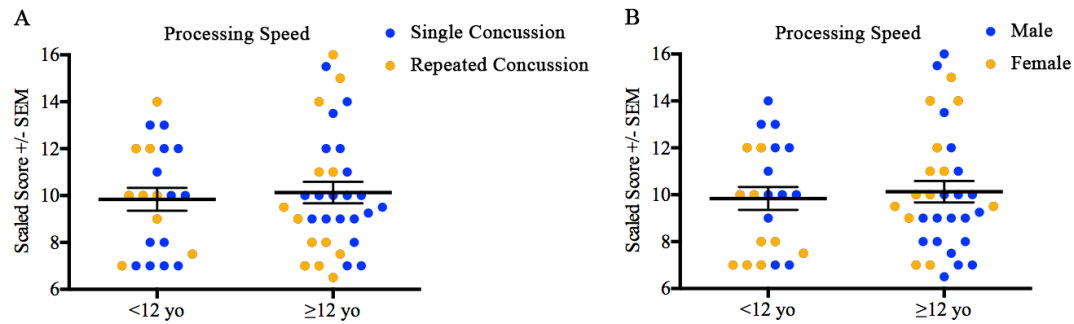
**Figure 30.** Age and gender distributions amongst individuals who endured a single concussion illustrated in Figure 3a. **A.** This plot illustrates the age distribution amongst individuals who endured a single concussion in Figure 3a. The majority of individuals who performed at a scaled score of 10 (i.e., first modal peak) were adolescents. **B.** This plot illustrates the gender distribution amongst individuals who endured a single concussion in Figure 3a. The majority of individuals who performed at a scaled score of 7 (i.e., second modal peak) were females.

As illustrated in Figure 30a, the majority of individuals who performed at a scaled score of 10 happened to be adolescents rather than children. Although this is likely to be the case, given that there were a slightly greater number of adolescents than children in the data subset, it is interesting to see how those adolescents performed compared to children. As illustrated in Figure 30b, the majority of individuals who performed at a scaled score of 7 happened to be females rather than males. The age distribution amongst individuals who performed at a scaled score of 7 (Figure 30a) and the gender distribution amongst individuals who performed at a scaled 10 (Figure 30b) were generally even.

Concussion history and gender distributions amongst the data subset represented in Figure 4a were explored and illustrated in Figure 31 (i.e., concussion history distribution in Figure 31a, gender distribution in Figure 31b). There appeared to be a multimodal distribution amongst children's performance on tasks of processing speed

(Figure 31). Specifically, these modes existed at scaled scores of 12, 10, and 7.

Concussion history and gender distributions appeared to be relatively even amongst children who performed at a scaled score of 12 and 10 (Figure 31).



**Figure 31.** Concussion history and gender distributions of data illustrated in Figure 4a. **A.** This plot illustrates the concussion history distribution within Figure 4a. Amongst children who performed at a scale score of 7 on tasks of processing speed, majority of them endured a single concussion rather than a repeated concussion. A cluster of adolescents who endured repeated concussion performed towards the lower end of the data subset on tasks of processing speed. **B.** This plot illustrates the gender distribution within Figure 4a. Amongst children who performed at a scale score of 7 on tasks of processing speed, majority of them were females rather than males.

However, amongst children who performed at a scaled score of 7, majority of them happened to have undergone a single concussion rather than a repeated concussion (Figure 31a) and majority of them were females rather than males (Figure 31b).

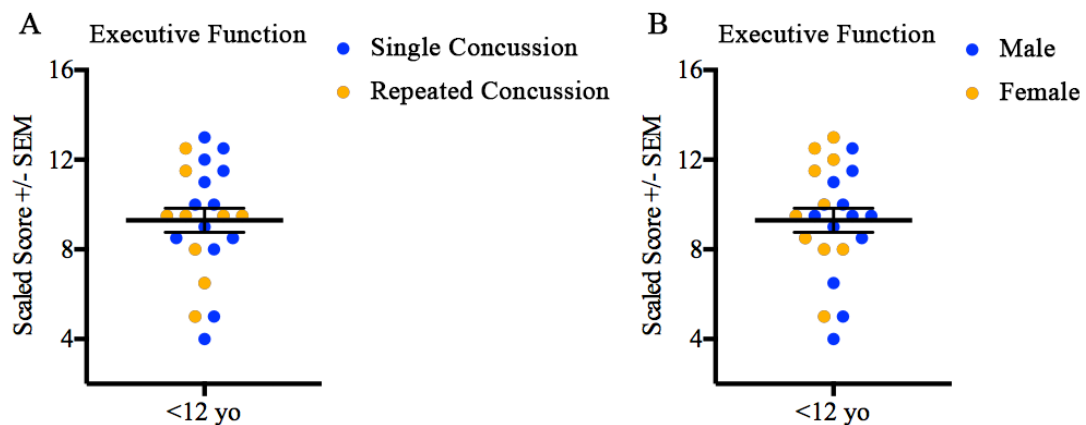
Interestingly, the opposite trend was observed amongst adolescents' performance on tasks of processing speed. Specifically, it appears as though majority of adolescents who performed towards the lower end on tasks of processing speed had endured repeated concussion rather than single concussion (Figure 31a) and were males rather than females (Figure 31b).

Overall, these results suggest that the bimodal distribution observed in Figure 3a could partly be explained by age and gender differences (Figure 30). Specifically, the majority of individuals who performed at a scaled score of 10 on tasks of processing speed (i.e., first modal peak) were adolescents, and the majority of individuals who performed at a scaled score of 7 on tasks of processing speed (i.e., second modal peak) were females. Additionally, the multimodal distribution observed in Figure 4a could partly be explained by concussion history and gender (Figure 31). Specifically, majority of children who performed at a scaled score of 7 on tasks of processing speed had undergone single concussion rather than repeated concussion (Figure 31a) and majority of them were females rather than males (Figure 31b). Additionally, performance of adolescents who endured repeated concussion tended to conglomerate towards the lower end of the data subset (Figure 31a).

Upon analyses, some findings suggested slight differences in means rather than significant differences. Specifically, in Figure 4b, it appears as though children scored slightly worse on tasks of executive function than adolescents, although that difference was not significant. This finding was discrepant from what was stated in Hypothesis 1b. Looking closely at Figure 4b, there appear to be three data points amongst children's performance that fell slightly lower than the rest of the data points. If these three data points shared one common factor that differentiated them from the rest of the data subset, then it could provide more insight into children's performance on tasks of executive functioning as a factor of concussion history and gender.

Figure 32 illustrates the concussion history and gender distributions of children's performance on tasks of executive functioning from Figure 4b. Findings suggested that

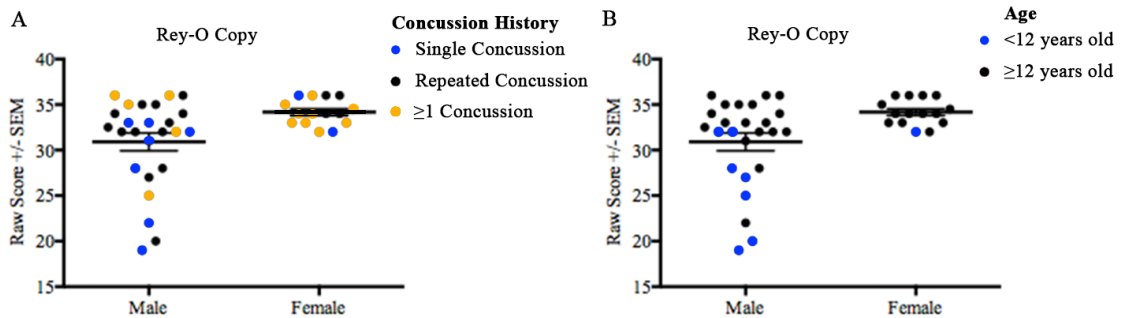
there were no common factors amongst the three data points mentioned above. Specifically, the individuals who these data points represented included a male who underwent single concussion, a male who underwent repeated concussion, and a female who underwent single concussion. Although no common factors were found across concussion history and gender factors, this finding suggested that these three data points are just as integrated into the entire data subset as any other data point. Circling back to Hypothesis 1b, it appears as though children performed slightly lower than adolescents on tasks of executive function due to individual differences rather than to group differences.



**Figure 32.** Concussion history and gender distributions amongst children’s performance on tasks of executive function illustrated in Figure 4b. **A.** This plot illustrates the concussion history distribution amongst children’s performance in Figure 4b. Concussion history appears to be evenly distributed amongst the three data points that fall slightly lower than the other points. **B.** This plot illustrates that the gender distribution amongst children’s performance in Figure 4b is evenly distributed. Males’ and females’ performance appears to be evenly distributed amongst the three data points that fall slightly lower than the other points.

An interesting trend was also observed in Figure 5b, such that males’ and females’ performance on the Rey-O Copy task differed in how they were distributed

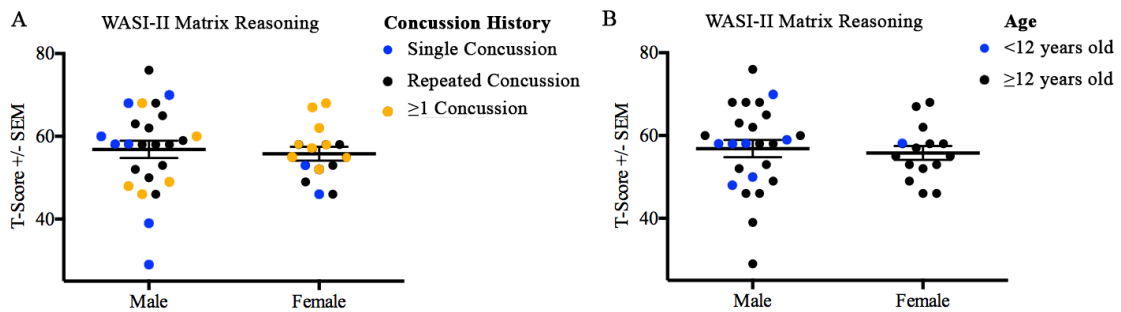
around the mean. Specifically, males' performance on the Rey-O Copy task appeared to be more dispersed around the mean, whereas females' performance was more concentrated around the mean. To determine whether any discriminating factors could explain this distribution trend, concussion history and age distributions of data represented in Figure 5b were illustrated in Figure 33.



**Figure 33.** Concussion history and age distributions amongst individuals' performance on Rey-O Copy task illustrated in Figure 5b. **A.** This plot illustrates the concussion history distribution amongst data represented in Figure 5b. Performance as a factor of concussion history appears to be evenly distributed amongst the data subset. **B.** This plot illustrates the gender distribution amongst data represented in Figure 5b. Majority of males who performed lowest on this task happened to be younger males (<12 years old).

Figure 33a illustrates that the concussion history distribution amongst data presented in Figure 5b appears to be evenly distributed amongst males' and females' performance on the Rey-O Copy task. However, an interesting pattern is observed amongst the age distribution of this data subset (Figure 33b). Specifically, it appears as though majority of the males who performed below the mean on the Rey-O Copy task were children rather than adolescents. In other words, it appears as though the main discriminating factor that makes males' performance on the Rey-O Copy task lower than that of females' is the poor performance of young males (<12 years old).

Given that the Rey-O Copy task is a spatial task, the findings described above makes us wonder whether the age distribution observed in Figure 33b would be observed in males' performance amongst all spatial tasks. As a result, the concussion history and age distributions of data presented amongst individuals' performance on the WASI-II MR task (spatial task) from Figure 5a were explored and illustrated in Figure 34.



**Figure 34.** Concussion history and age distributions amongst individuals' performance on WASI-II MR task illustrated in Figure 5a. **A.** This plot illustrates the concussion history distribution amongst data represented in Figure 5a. Performance as a factor of concussion history appears to be evenly distributed amongst the data subset. **B.** This plot illustrates the gender distribution amongst data represented in Figure 5a. Similarly to Figure 34a, performance as a factor of age appears to be evenly distributed amongst the data subset.

Figure 34a illustrates that the concussion history distribution appears to be evenly distributed amongst males' and females' performance on the WASI-II MR task.

Additionally, despite the age distribution observed in individuals' performance on the Rey-O Copy spatial task (Figure 33b), the age distribution observed in individuals' performance on the WASI-II MR spatial task was generally even (Figure 34b). This finding suggests that the age distribution observed in Figure 33b was specific to the Rey-O Copy task and could not be generalized to all spatial tasks.

Figure 13 illustrates the premorbid and post-morbid T-scores for psychosocial functioning (i.e., anxiety, depression, hyperactivity). As depicted in this figure, the majority of subjects experienced an increase in anxiety, depression, and hyperactivity from premorbid to post-morbid status. However, it is important to consider that other factors may be driving this increase besides concussion alone. Such factors may include the natural psychosocial, hormonal, and emotional changes that individuals go through as they develop into adolescents. In addition, as children grow into adolescents, they become physically larger and grow stronger muscles and bones, providing more resistance to the negative effects of concussion. These factors must be considered as children and adolescents experience concussions.



## CHAPTER NINE

### LIMITATIONS AND FUTURE RESEARCH

The current study determined the neurocognitive and psychosocial effects of repeated concussions in children and adolescents and assessed the interactions with age and gender. However, this study was not without limitations. One main limitation from the current study was the low sample size amongst certain factors. We collected data for a total of 118 subjects; however, not every subject had data for every measure that was incorporated into the current study. Specifically, out of a total of 118 subjects, all of them had data for the age and gender variables, but only 76 of them recorded their concussion history, 83 completed measures assessing processing speed, 114 completed measures assessing executive function, 41 completed the Rey-O Copy task, 108 completed the WASI-II MR task, 109 completed the WASI-II Voc. Task, 107 completed the CVLT-II/C tasks, 47 completed premorbid reports of psychosocial functioning, and 103 completed post-morbid reports of psychosocial functioning. When the MANOVA for Aim 1 was conducted, one condition consisted of only three subjects (Table 2; child females who endured repeated concussion). The MANOVA for Aim 2 could not be carried out to interpret interaction effects, as multiple conditions consisted of only zero or one subject (Table 4; child females who endured single concussion,  $n = 0$ ; adolescent females who endured single concussion,  $n = 1$ ; child females who endured repeated concussion  $n = 1$ ). As a result, only main effects were interpreted for Aim 2 (Table 5).

Another limitation was the demographic variability of the subjects included in the study. Results must be interpreted with caution, given that some subjects came from varying demographic backgrounds. Specifically, a minority of the subjects endorsed

variable personal and family medical and psychological history, which may have influenced their susceptibility to adverse effects following repeated concussion.

This study did not explore the effect of time elapsed between concussions or the number of concussions sustained. The effect of time between concussions on the neurocognitive and psychosocial outcomes following repeated concussion may be worth studying for future research since a certain amount of recovery may take place during that time interval. As such, that possible period of recovery may have influenced the severity of the neurocognitive and psychosocial impairment following the repeated concussion. The current study also did not assess the number of concussions sustained. This may also have played a role in the severity of outcomes following repeated concussions, which may be of interest for future studies. The current study's approach to this limitation was to dichotomize the concussion history variable to include single concussion and repeated concussion (sustained more than one concussion).

It is important to note that the results from the current study do not reflect the neurocognitive and psychosocial performance of the typically recovering individual from concussion. These individuals sought out a neuropsychological evaluation due to persisting symptoms following their concussion. As a result, they were not typically recovering individuals. It is important to remember that these results could not be translated to the typical child's neurocognitive and psychosocial functioning following concussion.

In addition, this study was a retrospective study, such that, the data had been collected before the design of the study had been determined. As a result, the same measures were not administered to each subject. This made it difficult to select

neurocognitive measures and domains to explore, as some had fairly low sample sizes. For future studies, it would be important to include a larger data set to more accurately assess the effects measured in the current study.

A typical pressing concern when interpreting the effects of concussion is intention and motivation. In other words, it is important to be cognizant of subjects' effects of effort and malingering. In athletes, it is typically seen that they want to return back to the game as soon as possible, resulting in them to underreport many of their concussion-induced symptoms. Underreporting does not occur as often in children and adolescents. Children and adolescents tend to over-report their concussion-induced symptoms for a variety of reasons to either avoid or put off un-preferred responsibilities (i.e., returning back to school, taking the Scholastic Aptitude Test [SAT]; Kirkwood, Peterson, Connery, Baker, & Grubenhoff, 2014). Reasons for wanting to avoid returning back to school may include wanting to avoid anxiety, stressful peer interactions, or poor academic functioning. This may provide an explanation for why many of the subjects performed average or above average for many of the measures, despite their concussion history. Perhaps an exclusion criterion for malingering could have filtered those individuals out of the analyses.

Due to the concerns of effort and malingering, it is important for future studies to include measures that assess such factors as an exclusion criterion. In other words, it would be beneficial to exclude individuals from the study who scored below or above a certain performance level on such measures to filter out individuals who engage in either under- or over-reporting of their concussion-induced effects. Such measures include the TOMM and MSVT, which were described in detail in the Introduction. The current study

planned to incorporate these measures as exclusion criteria, but given that not each subject was administered these measures, the measures did not have a large enough sample size to be incorporated as an exclusion criteria into the current study.

As described in the Introduction, the current retrospective study collected plenty of data that assessed motor skills (i.e., balance, speed, dexterity, coordination). Given the complexity of this data, these measures could be utilized into their own study to assess the effects of concussion on motor skills.

Despite these limitations, the current study provided strong construct and internal validity to be able to translate the findings to the general population endorsing atypical recovery from concussion. This suggests strong external validity. Given that the current study had an appropriate control and experimental group, it had strong conclusion validity. Further research is necessary to clarify findings addressing specific details of the concussion, strengthening the current study's external validity.

## **CHAPTER TEN**

### **CONCLUSION**

There is need for longitudinal investigations focused on the neurocognitive and psychosocial impact of concussion on the developing brain. All of the research studies that explore these affects play a role in contributing to that knowledge set. The current study showed that, following concussion, those who experienced more depression were also likely to perform worse on tasks of executive function. Other trends suggested that repeated concussion yielded a greater increase in anxiety and depression than single concussion. In addition, children performed worse on tasks of executive function and endorsed a greater increase in hyperactivity following concussion than adolescents. Females performed better on the spatial Rey-O Copy and verbal WASI-II Vocabulary tasks than males, following concussion; however, males endorsed a greater increase in depression and hyperactivity following concussion.

The findings from the current study may help provide more information about how concussion affects the developing brain. This study has set a baseline for how the neurocognitive and psychosocial concussion-induced effects following single concussion compare to those following repeated concussion and how that is affected by a factor of age and gender. The findings of the current study may also help improve the remedial treatments for the developing brain that encounters concussion. Lastly, it may lead to modifications in the level of participation in physical activities and suggest what areas of further exploration are required regarding the neurocognitive and psychosocial effects of children and adolescents following repeated concussions.

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