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The role of premorbid factors and adverse childhood experiences in the persistence of symptoms post mild traumatic brain injury (persistent postconcussive symptoms)

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The Role of Premorbid Factors and Adverse Childhood Experiences in the Persistence of Symptoms Post Mild Traumatic Brain Injury (Persistent Postconcussive Symptoms)

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Abstract

Every year, more than 2.8 million individuals sustain a traumatic brain injury (TBI) in the U.S. At least 75% of these are designated as mild TBI (mTBI). While most are expected to spontaneously recover within days to weeks, a substantial minority continue to experience various somatic, cognitive, and affective symptoms for months/years postinjury. Several biopsychosocial factors (e.g., cognitive reserve, psychiatric illness) may influence the persistence of postconcussive symptoms (PPCS). Adverse childhood experiences (ACE) may be another psychosocial factor that influences PPCS, but few studies have assessed the relationship between ACEs and TBI. This study aimed to replicate previous findings and was the first to extend the literature to evaluate the relationship between ACEs and PPCS. Fifty-eight individuals (34 males; M = 16.82 years; SD = 2.28), who presented for a neuropsychological evaluation due to PPCS, were included in this archival study. Of the predictors examined (i.e., sex, maternal education, previous mTBI, psychiatric illness, attention-deficit/hyperactivity disorder and learning disorder diagnosis), only parent-reported anxiety and depressive symptoms were significantly correlated with PPCS; higher reported anxiety and depressive symptoms were related to higher reported PPCS. Hierarchical regression revealed that ACEs did not account for additional significant variance in PPCS outcomes. Current findings highlight the possibility of clinicians assessing for parent-reported psychiatric factors to identify adolescents and young adults who may be at higher risk for prolonged symptoms. Inconsistencies with previous literature also highlight the need for standardized definitions of mTBI and PPCS, as well as prospective studies to establish temporal relationships among ACEs, other predictors, and PPCS.

Keywords: mild traumatic brain injury, concussion, adverse childhood experiences, persistent postconcussive symptoms, postconcussive syndrome

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Introduction

It is estimated that each year, 2.8 million individuals experience a traumatic brain injury (TBI) within the United States (Taylor et al., 2017). At least 70% of these TBIs are designated as a mild TBI (mTBI; Kenzie et al., 2017). Although most individuals who have sustained mTBI typically recover within the following days to weeks postinjury, 10-20% of these cases may continue to experience various somatic, cognitive, and affective symptoms for months, sometimes years, postinjury (Hadanny & Efrati, 2018). While 10-20% may seem inconsequential, studies have indicated that from a public health perspective it can be quite costly. In one county in the midwestern U.S. alone, persons with mTBI had significantly higher mean medical costs after about 1-6 years post-injury ($3418 per person) compared to controls (Leibson et al., 2012). Research indicates that several factors can influence the persistence of postconcussive symptoms (PPCS), including premorbid influences such as psychiatric history and previous head injury (Ponsford et al., 2012). Despite exploration of a wide range of factors, the possibility that adverse childhood experiences (ACEs) may be an additional premorbid factor that contributes to the persistence of symptoms has not been explored.

ACEs have been implicated in adult physical and mental health, such that individuals who have endorsed exposure to ACEs are at increased risk of substance use, interpersonal violence, anxiety and depression (Hughes et al., 2017). ACEs are also a new frontier in TBI research; to date, only eight studies and one review have assessed simple associations between ACEs and TBI, revealing that individuals who endorse ACEs have higher rates of TBI (Ma et al., 2018). However, neither the directionality of this relationship nor the impact on long-term outcome have been illuminated. ACEs may be a contributing premorbid, psychosocial factor to increased risk of persistent symptoms following mTBI and should be considered in case

conceptualization. Originally a prospective, longitudinal study, this updated retrospective study seeks to replicate the literature on biopsychosocial predictors of persistent symptoms following uncomplicated mTBI in adolescents and young adults, such as cognitive reserve, sex, psychiatric factors, previous head injury, and history of learning disorder and/or attention-deficit/hyperactivity disorder. Additionally, this study will seek to evaluate the relative contribution of ACEs as a premorbid, psychosocial predictor of PPCS.

Background

Epidemiology

As previously mentioned, each year about 2.8 million people sustain TBI within the United States alone, 70-90% of which are mild cases (Faul & Coronado, 2015; Greenwald et al., 2012; Mansour & Lajiness-O'Neill, 2015; Stucky et al., 2014; Taylor et al., 2017). These incidence rates can be misleading, however, as it only includes those who have been hospitalized and only 20% of individuals ever seek medical care (Borg et al., 2004; Cassidy et al., 2004; Katz et al., 2015). Other institutions, such as the University of Pittsburgh Medical Center (UPMC), have estimated that between 1.7-3 million sports or recreation-related mTBI occur each year within the United States, with as many as half going undetected or unreported (UPMC, 2019). Rates differ among age, sex, and racial groups; males are twice as likely as females to sustain mTBI, with rates peaking between the ages of 15-24 years (Borg et al., 2004; Carroll et al., 2004b; Katz et al., 2015; Varriano et al., 2018). Research suggests that males are at higher risk due to increased risk-taking behaviors, contact sports and alcohol consumption (Frost et al., 2013). Rates are also higher among Blacks compared to Whites and are highest among Native Americans/Alaska Natives, although this may be confounded by other factors such as socioeconomic status or substance use (Bazarian et al., 2003). Within the general public, the most common causes of TBI vary by age group, with younger children sustaining TBI due to child abuse, adolescents and young adults from motor vehicle accidents, and older adults from falls (Stucky et al., 2014). Despite the evidently high prevalence and recent public spotlight on mTBI, effective means of diagnosing, determining prognosis, and providing treatment are lacking (Kenzie et al., 2017).

Traumatic Brain Injury

Traumatic brain injuries are classified as mild, moderate, or severe. Currently, there is no universally accepted classification system but the most commonly used criteria employ the Glasgow Coma Scale, loss of consciousness, and posttraumatic amnesia to assess for severity (see Table 1 below; Iverson et al., 2016). The GCS is a measure of arousal and awareness used in clinical and research settings; scores fall in the *severe* (3-8), *moderate* (9-12), or *mild* ranges (13-15; Carroll et al., 2004a; Katz et al., 2015; Mansour & Lajiness-O'Neill, 2015; Teasdale & Jennett, 1974). It can be more difficult to assess for loss of consciousness (LOC) and posttraumatic amnesia (PTA) as there are no established objective measures. Furthermore, LOC can be confused with PTA. According to a National Academy of Neuropsychology (NAN) education paper on diagnosing mTBI, Ruff and colleagues (2009) recommend obtaining collateral report of the event injury for LOC. If collateral report is unavailable, the clinician should ask the patient if others have reported that they were unconscious and examine medical records to rule out other medical factors (Ruff et al., 2009; Silverberg et al., 2016). Similarly, PTA should be assessed by taking great care to separate what the patient remembers and assumes from the event (Silverberg et al., 2016). Obtaining information in this way is somewhat flawed and subjective but still essential for establishing occurrence of mTBI.

Table 1

Common Traumatic Brain Injury Classification System

Classification	Duration of unconsciousness	Glasgow coma scale	Posttraumatic amnesia
Mild	< 30 minutes	13-15	< 24 hours
Moderate	30 minutes - 24 hours	9-12	1-7 days
Severe	> 24 hours	3-8	> 7 days

Note. Adapted from G. Iverson & R. Lange. (2011). Mild Traumatic Brain Injury. In Schoenberg, M.R. & Scott, J.G. (Eds.), *The Little Black Book of Neuropsychology: A Syndrome-Based Approach* (pp. 697-719). Springer.

Mild Traumatic Brain Injury

Currently, there is no consensus definition or criteria that spans across medical fields (Mayer et al., 2017). Kristman et al. (2014) reportedly found over 35 different definitions for their review of accepted studies alone. Four commonly utilized and cited definitions/criteria are displayed in Table 2. All definitions state that mTBI is "caused by a transfer of mechanical energy from an external force" (Silverberg et al., 2016, p. 44). While there is some overlap among the definitions, such as the Glasgow Coma Scale (GCS) score, loss of consciousness (LOC), and posttraumatic amnesia (PTA), each organization places emphasis on different symptoms to diagnose mTBI (Katz et al., 2015; Teasdale & Jennett, 1974).

Table 2

Most Widely Cited Definitions of Mild Traumatic Brain Injury from Various Professional Organizations

Entity	Year	Inclusion Criteria	Exclusion Criteria
American Congress of Rehabilitation Medicine	1993	GCS 13-15 and a minimum of 1 of the following: (1) any LOC; (2) any amnesia; (3) alteration in mental status (e.g., dazed, disoriented, or confused); or (4) focal neurological deficit(s) that may or may not be transient	(1) LOC >30 minutes; (2) GCS < 13 after 30 minutes; (3) PTA > 24 hours
Center for Disease Control	2003	Blunt trauma or acceleration/deceleration forces and a minimum of 1 of the following: (1) alteration in mental status (e.g., confused, disoriented, impaired consciousness); (2) any amnesia; (3) LOC < 30 minutes; or (4) signs of neurological or neuropsychological dysfunction	(1) LOC > 30 minutes; (2) PTA > 24 hours; (3) penetrating craniocerebral injury
World Health Organization	2004	GCS 13-15 after 30 minutes postinjury or later and 1 or more of the following: (1) confusion or disorientation; (2) LOC ≤ 30 minutes; (3) PTA < 24 hours; (4) transient neurologic abnormalities (focal signs or seizure); or (5) intracranial lesion not requiring surgery	(1) GCS < 13 after 30 minutes postinjury; (2) symptoms caused by other noncranial injuries; (3) caused by other problems (psychological or substance-related); or (4) caused by penetrating craniocerebral injury
Department of Veterans Affairs	2009	GCS 13-15 taking the best score in the first 24 hours and a minimum of 1 of the following; (1) LOC ≤ 30 minutes; (2) alteration in consciousness (e.g., dazed, disoriented, confused) < 24 hours; and (3) PTA < 24 hours	(1) abnormal structural imaging; (2) LOC > 30 minutes; (3) PTA > 24 hours; (4) GCS < 13; (5) alteration of consciousness > 24 hours

Note. GCS = Glasgow Coma Scale; LOC = loss of consciousness; PTA = posttraumatic amnesia. Adapted from "The spectrum of mild traumatic brain injury: A review," by A. R. Mayer, D. K. Quinn, and C. L. Master, 2017, *American Academy of Neurology, 89,* p. 625.

Complicated Versus Uncomplicated mTBI

A notable subtype of mTBI is complicated mTBI. It is estimated that about 5-10% of mTBI cases within the emergency department are classified as a complicated mTBI (Smits et al., 2008). The only differentiating feature between a complicated and uncomplicated mTBI is an abnormal computed tomography (CT) scan on the day of injury (Iverson & Lange, 2011; Maas et al., 2005). Abnormalities may include skull fractures, edema, hematoma, contusions (Iverson & Lange, 2011; Smits et al., 2008). Williams et al. (1990) have been credited with the creation of the mTBI complicated and uncomplicated subtypes when they noted that the course of recovery

of individuals with CT abnormalities were more like individuals who had sustained a moderate TBI. Other studies have also supported and extended the literature, revealing that individuals with complicated mTBI tend to have similar levels of short and long-term cognitive and functional outcome compared to individuals who have sustained a moderate TBI (Borgaro et al., 2003; Kashluba et al., 2008; Temkin et al., 2003; van der Naalt et al., 1999).

Pathophysiology and Neuroimaging of mTBI

mTBI occurs due to the rapid acceleration and deceleration of the brain within the skull (Andriessen et al., 2010). The frontal and temporal lobes are the most vulnerable sites due to different viscosities and densities of brain tissues (Hadanny & Efrati, 2016). The shearing of axons, or diffuse axonal injury (DAI), is commonly associated with mTBI and cognitive dysfunction (Hadanny & Efrati, 2016; Pearn et al., 2017). DAI triggers multiple neurometabolic processes that lead to disruption in the brain's ability to remove damaged tissue and pathogens, creating a "window of vulnerability" where the brain is susceptible to further damage (Asken et al., 2018). Although the aforementioned changes are not typically detected through standard neuroimaging techniques such as computed tomography (CT), other techniques have demonstrated abnormalities, such as diffusion tensor imaging (DTI), which measures movement of water molecules in brain tissue, and magnetoencephalography (MEG), which measures magnetic fields produced by the brain's electrical currents (Lewine et al., 2007; Pearn et al., 2017). DTI has revealed compromised white matter integrity in the internal capsule, corpus callosum, frontal lobe and limbic system post-mTBI, which has been associated with symptoms such as anxiety and slowed processing speed (Giza & Hovda, 2001; Narayana, 2017; van der Horn et al., 2016). MEG has also associated slow-wave activity with symptoms such as headaches (Lewine et al., 2007; Swan et al., 2015).

Symptoms of mTBI

Symptoms of mTBI are classified under three domains: (a) somatic; (b) cognitive; and (c) affective. Somatic symptoms tend to be reported during the acute phase of injury, defined as the period from point of injury through third day postinjury, while cognitive symptoms appear during the acute and subacute (i.e., four days through three months postinjury) phases (Lajiness-O'Neill et al., 2017; Prince & Bruhns, 2017; Stucky et al., 2014). Affective symptoms tend to remain, possibly into the chronic stages (i.e., three months postinjury and later; Lajiness-O'Neill et al., 2017). While phases of injury can differ in literature with regard to duration, the labels of "acute," "subacute," and "chronic," have remained consistent. Despite the idiosyncrasies of phases, studies commonly operationalize acute symptoms as those occurring within the first two weeks following injury (CDC, 2018; Katz et al., 2015; Polinder et al., 2018). Common somatic symptoms include headache and dizziness, caused by injuries to vestibular pathways stemmed from secondary diffuse injuries (Katz et al., 2015). Other reported somatic symptoms include sleep disruption (e.g., insomnia, hypersomnia), sensitivity to noise/light, nausea, visual disturbances and fatigue (Bergersen et al., 2017; Prince & Bruhns, 2017). Cognitive symptoms include problems with attention, slowed processing speed, and memory (Prince & Bruhns, 2017). Common affective symptoms post-mTBI include increased irritability, emotional lability, anxiety, and depression (Bergersen et al., 2017; Katz et al., 2015).

Neurocognitive Profile of mTBI

Lezak and colleagues (2012) recognized mTBI cognitive symptoms as a triad of attention deficits, impaired verbal retrieval, and forgetfulness. Attention deficits may encompass poor concentration, heightened distractibility, and difficulty completing multiple tasks at once. Verbal

retrieval and "memory" problems may also stem from attention difficulties rather than being separate constructs (Lezak et al., 2012).

Seminal reviews and meta-analyses have indicated that the cognitive effects of mTBI are nonsignificant after three months post injury (Belanger et al., 2005; Dikmen et al., 1986; Iverson & Lange, 2011; Rohling et al., 2011; Schretlen & Shapiro, 2003). An updated meta-analysis by Rohling and colleagues (2011) concluded that immediately after injury, effects were largest on verbal and visual memory domains compared to healthy control groups. However, these initial effects were small and dissipated quickly. Studies within the athlete population demonstrated similar results, although athletes who have sustained three or more mTBIs may have small, cumulative differences and require longer time for recovery (McCrea et al., 2003; Pellman et al., 2004).

Assessing for mTBI

As previously mentioned, clinicians and other trained professionals will measure severity of TBI by utilizing the GCS and assessing for LOC and PTA (Iverson & Lange, 2011). However, symptoms must also be assessed. There is currently no standardized measure for mTBI symptoms, but notable measures include the Post-Concussion Symptom Inventory (ImPACT-PCS), part of a computerized neurocognitive assessment called the Immediate Post-Concussion Assessment or ImPACT, as well as the Rivermead Postconcussion Symptoms Questionnaire (RPQ; King et al., 1995; Moore et al., 2017; Polinder et al., 2018; Thompson et al., 2015). Both measures are checklists that allow for continuous evaluation of symptoms over time.

Review of sports-related mTBI literature also reveals a lack of standardized measures for student athletes. While many may utilize the ImPACT-PCS, there is great variation in measures used. In a Concussion in Sport Group consensus statement, McCrory and colleagues (2018)

strongly recommend removing athletes from play and performing a brief sideline evaluation for suspected mTBI. Players are also recommended to complete a computerized neurocognitive assessment (CNA) during the acute stage. Most commonly used CNAs are the Sport Concussion Assessment Tool, Axon/Cogstate Sport (CogSport), and ImPACT (Collie et al., 2003; Echemendia et al., 2017; Lovell et al., 2006; Nelson et al., 2016b). A comprehensive evaluation with measures in all cognitive domains (e.g., premorbid functioning, attention/processing speed, learning/memory, visuospatial, language, executive functioning, sensorimotor, performance validity, and self-report of mood) would be ideal, but is not currently standard practice (Kolb & Whishaw, 2015; Prince & Bruhns, 2017; Stucky et al., 2014).

Persistent Postconcussive Symptoms

While full recovery is expected within three months postinjury, a minority of people will continue to report symptoms well into the chronic phase; this condition has been named *postconcussion syndrome* (PCS; Iverson & Lange, 2011; Polinder et al., 2018). Most research will report rates of 10-20%, but this may be misleading for reasons that will be discussed later in this section (Hadanny & Efrati, 2016; Iverson & Lange, 2011). PCS is a controversial diagnosis due to the nonspecificity of symptoms that are also reported in healthy subjects and other clinical populations (e.g., depression, trauma, chronic pain; McCrea, 2008; Rabinowitz et al., 2015). Researchers have more recently conceptualized PCS as a multidimensional construct, discussed later in further detail (Kenzie et al., 2017; Prince & Bruhns, 2017). Due to the controversial nature of PCS, some researchers have started to refer to PCS as *persistent postconcussive symptoms* (PPCS); this term will be adopted in this current review and study (Barlow, 2016; Grool et al., 2016; Polinder et al., 2018; Potter et al., 2016).

Currently, there is no consensus definition for PPCS. The three most commonly cited systems for diagnosing PPCS include the International Classification of Diseases (10th Ed.; ICD-10) and two editions, the fourth and fifth, of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; DSM-5; American Psychiatric Association, 2013; World Health Organization, 1992). See Table 3 for a comparison of criteria. Notably, the ICD-10 and DSM-IV definitions focus on presentation of symptoms and prerequisite history of brain trauma while the DSM-5 definition of *mild neurocognitive disorder due to TBI* emphasizes performance-based evidence and consideration of differential diagnoses (American Psychiatric Association, 2013). The DSM-IV definition requires at least three symptoms for at least three months post-mTBI; similarly, the ICD-10 definition requires at least three symptoms but duration of symptoms is unclear (Rose et al., 2015). The lack of guidance on the ICD-10 has led to idiosyncratic interpretations within clinicians and researchers, leading to sizeable variations in rates of PPCS ranging from 11% to 65% (Polinder et al., 2018; Rose et al., 2015). Despite the idiosyncrasies of the PPCS definition, several studies utilize a criterion of about 4 weeks post-injury for a PPCS diagnosis, referring to a "research criteria" (Friedland, 2015; Iverson & Lange, 2011; Meares et al., 2008). Additionally, the American Academy of Family Physicians have reported that it is during the 4-6 weeks post-injury mark that physicians or medical professionals start to consider referral to additional services (Mott et al., 2012). The current study will be utilizing the commonly utilized 4-week postinjury marker and ICD-10 criteria to measure PPCS, as it is more inclusive.

Table 3

Comparison of Three Definitions of Persistent Postconcussive Symptoms

	Diagnostic System		
	ICD-10	DSM-IV	DSM-5
Symptoms			
Headache	x	x	
Dizziness	x	x	
Fatigue	x	x	
Noise intolerance	x	x	
Irritability/lability/anxiety/depression	x	x	
Sleep problems	x	x	
Concentration problems	x[A]	x[B]	x[B]
Memory problems	x[A]	x[B]	x[B]
Alcohol intolerance	x		
Preoccupation with symptoms	x		
Personality change		x	
Apathy		x	
Perceptual-motor problems			x[B]
Social cognition			x[B]

Note. ICD-10 = International Classification of Diseases - 10; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; DSM-*5* = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.

Note: [A]Subjective report; [B]Objective test. Adapted from "A Multidimensional Approach to Post-concussion Symptoms in Mild Traumatic Brain Injury" by S. Polinder et al., 2018, *Frontiers in Neurology, 9*, p. 4.

PPCS Model

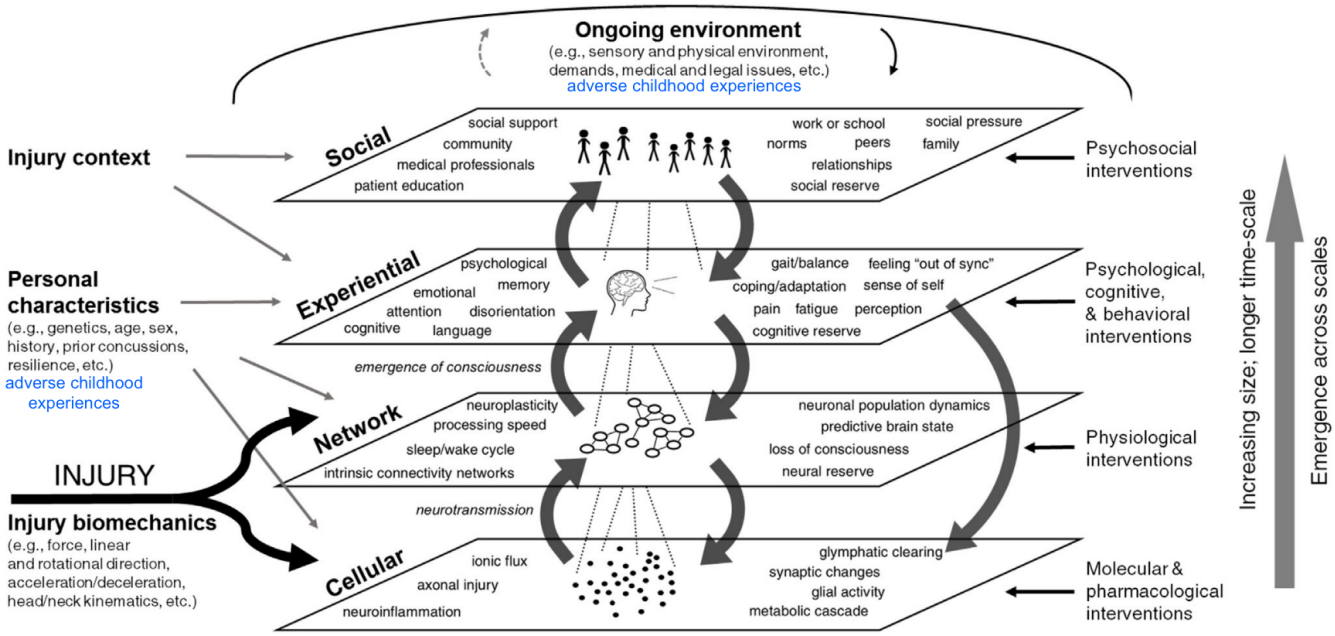
Newer models suggest that PPCS is the result of interaction among several biopsychosocial factors. Kenzie and colleagues' (2017) systems model, as presented in Figure 1, is composed of four scales (i.e., cellular, network, experiential, social). The current, prospective study proposes the addition of adverse childhood experiences to the model (as seen in blue in Figure 1). Different features of the injury and environment influence aspects of each scale at any point in time, with feedback loops existing within and between scales. For example, axonal injury within the cellular scale can affect processing speed in the network scale. Slowed

processing speed can then influence cognitive and attention factors of the experiential scale, creating a downstream effect on the social scale (e.g., problems at work/school and in relationships).

The current study proposes that adverse childhood experiences (ACEs) may be a vital yet unrecognized premorbid factor (e.g., personal history) that can influence recovery on multiple levels (e.g., cellular, network, experiential). As ACEs typically occur within the first 18 years of age, depending on the individual it can also be conceptualized as a factor within the ongoing environment, (i.e., ongoing adversity in a child with mTBI), that influences their recovery. The proposed influence of ACEs on recovery post-mTBI will be further discussed later. Ultimately, the model illustrates that "mTBI is a highly heterogeneous phenomenon, and numerous factors interact dynamically to influence an individual's recovery trajectory" (Kenzie et al., 2017, p. 1).

Figure 1

A Modified Model for Persisting Symptoms Following mTBI with Additional Proposed "Adverse Childhood Experiences" Factor



Note. Factors present at the time of injury are on the left. The four scales (e.g., social, experiential, network, cellular) represent ongoing environment that influences the injury characteristics and recovery. As depicted by the center black arrows, each scale may influence another. Interventions, located at the right of the figure, represent another set of factors that can influence recovery trajectory. Adapted from "Concussion as a Multi-Scale Complex System: An Interdisciplinary Synthesis of Current Knowledge," by E. S. Kenzie, E. L. Parks, E. D. Bigler, M. M. Lim, J. C. Chesnutt, and W. Wakeland, 2017, *Frontiers in Neurology*, *8*, p. 6 (https://doi.org/10.3389/fneur.2017.00513).

Neurocognitive Profile of PPCS

Generally, literature suggests that despite individual report of cognitive and memory issues, there is no objective difference in cognitive performance based on neuropsychological assessment between individuals with PPCS and healthy controls after three months. One seminal study reported significant differences only in their PPCS group with financial incentives (Binder et al., 1997). A few studies maintain that there are subtle differences, particularly in attention/processing speed, memory, and executive functioning (McInnes et al., 2017; Rabinowitz et al., 2015). However, mixed results may be due to lack of control for preinjury factors, as one study found differences in processing speed when comparing a PPCS group with psychiatric histories to one without (Bertisch et al., 2018). When reviewing the literature, researchers must also consider effects of biopsychosocial premorbid factors (e.g., cognitive reserve, psychiatric factors) as well as any other factors associated with PPCS as these factors may better explain significant differences found in the literature.

Assessing for PPCS

Assessing for PPCS is similar to assessing for mTBI in that there is no standardized assessment. While a comprehensive neuropsychological assessment is ideal as there are likely many factors contributing to an individual's presentation, it is not standard clinical practice. Many PPCS studies have tracked progress or recovery through ongoing assessment of post-mTBI symptom endorsement (e.g., using ImPACT-PCS), as well as secondary measures of comorbid diagnoses such as anxiety and depression (Ponsford et al., 2012; Polinder et al., 2018). One study by de Guise and colleagues (2016) even found that use of the Rivermead Postconcussion Symptom Questionnaire could help in predicting moderate to severe functional limitations three months post-mTBI. While continued assessment of symptom endorsement and

comorbidities are important, clinicians must again consider premorbid factors that may be contributing to the patient's symptom presentation.

Factors Associated with PPCS

Research has established that certain premorbid factors are associated with persistence of symptoms post-mTBI. Cognitive reserve, sex, pain, psychiatric factors, previous head injury, and social stressors have been factors empirically supported in PPCS literature.

Cognitive Reserve. Researchers have observed that there is no direct relationship between degree of brain damage and clinical manifestation of the damage and have proposed cognitive reserve (CR) as a theory to explain this phenomenon (Stern, 2002). CR is defined as: (a) the amount of damage that can be sustained before reaching threshold for clinical expression; and (b) differences in how a task is processed and use of compensatory strategies (Bigler & Stern, 2015; Stern, 2002). These conceptualizations of reserve are considered active and passive, respectively, and are likely both involved in providing reserve against damage (Mathias & Wheaton, 2014). Brain reserve capacity (BRC) is a construct of CR, such as brain size or synapse count capacity (Bigler & Stern, 2015). CR implies anatomic variability at the level of brain networks, while brain reserve implies differences in quantity of available neural substrate (Bigler & Stern, 2015). Although the construct cannot be directly measured, there are several proxies that can estimate reserve. The most commonly used proxies for cognitive reserve are socioeconomic status (i.e., income, occupational attainment; SES), educational attainment, IQ, and degree of literacy (Bigler & Stern, 2015). A commonly used measure of IQ is the Shipley-2, an updated version of the Shipley Institute of Living Scale that assesses for crystallized and fluid cognitive abilities (Shipley, 1940; Shipley et al., 2009). PPCS is associated with lower education in adults (Polinder et al., 2018; Silverberg et al., 2015). While higher SES has been associated with better cognitive

recovery, it may be indicative of access to resources in the recovery process (Rabinowitz et al., 2015). One study by Steward and colleagues (2018) analyzed the effect of CR on cognitive performance post-mTBI and influence on recovery rates. They found that higher premorbid IQ was associated with better cognitive performance at one-month post-mTBI, which supports CR as a neuroprotective factor (Steward et al., 2018). A study by Fay and colleagues (2011) somewhat supports this finding in which they found cognitive reserve was a moderator of outcomes in mTBI in children and adolescents. Children on the more severe end of mTBI and with lower cognitive reserve (IQ as proxy), were the most likely to have poorer outcomes (Fay et al., 2011).

Additionally, while educational attainment or tests of overlearned reading skills are used in adult populations, level of maternal education has been established as a proxy for cognitive reserve, particularly for children (Donders & Kim, 2019). In a study evaluating cognitive reserve and brain volumes in a pediatric acute lymphoblastic leukemia population, Kesler and colleagues (2010) found that parental education was a significant predictor of cerebral white matter volume. Another study by Babikian and colleagues (2013) found that maternal education was one of the predictors of 1-year outcome after pediatric mTBI. As described by Kesler et al. (2010), maternal education and a child's cognitive outcome is the result of several strongly connected relationships, including parent and child IQ, education level, and socioeconomic status, as well as the opportunity for more enriched environments: "High maternal education level represents a unique combination of increased genetic endowment and environmental enrichment" (p. 257).

Sex. Literature is mixed regarding the association between sex and PPCS (Brooke et al., 2014; Tator et al., 2016). Some attribute significant association to sex differences in head size or neck musculature or to sex differences in reporting style, with females having a tendency to be

more forthcoming with symptom endorsement (Rabinowitz et al., 2015). One review of sports literature found female sex was associated with higher report of early symptoms and longer return to play (Scopaz & Hatzenbuehler, 2013). However, these relationships may be superficially examined with no consideration for confounding factors, such as mechanism of injury. One study noted that a greater number of females sustained mTBI via motor vehicle accidents (MVA), whereas males tended to sustain mTBI via sports injuries (Ponsford et al., 2000). Several PPCS studies have mostly participants who have sustained mTBI via MVA, or a larger percentage of females, within their sample.

Pain. Pain has been conceptualized in PPCS literature as premorbid pain (e.g., migraines), or pain following mTBI (i.e., acute phase pain). Pain can also be conceptualized as pain interference or pain intensity (Askew et al., 2016). Acute phase pain appears to be associated with higher frequency of PPCS, particularly when a patient reports headache and dizziness (Ganti et al., 2014; Katz et al., 2015; Ponsford et al., 2012). This association extends into the sports-related mTBI literature, where players who reported migraine symptoms had a longer recovery time (Scopaz & Hatzenbuehler, 2013). However, one must be cognizant that chronic pain populations also tend to report PPCS symptoms (Iverson & Lange, 2011; Katz et al., 2015). Chronic pain in individuals post-mTBI has been significantly associated with depression, anxiety, and insomnia.

Pain intensity has also been associated with the mechanism of injury, where individuals who sustained brain injuries following explosions or falling from heights reported greater intensity and more unpleasantness (Mollayeva et al., 2017). A common measure of pain is the Visual Analogue Scale, a brief scale from 0 (*no pain*) to 10 (*extreme pain*) that has been utilized across populations for over 30 years (Huskisson, 1974; Ponsford et al., 2000). Additionally, the

National Institutes of Health (NIH) helped to fund and create the Patient-Reported Outcomes Measurement Information System (PROMIS®) profiles, which contain several aspects of health-related quality of life; the adult and pediatric profiles include items measuring pain interference and pain intensity (Bertisch et al., 2017; Cella et al., 2019).

Psychiatric Factors. Premorbid psychiatric illness is one of the most commonly cited predictors in PPCS literature. Pre-injury mental health status predicts PPCS in adult populations, with almost half of patients suffering from premorbid depression and anxiety (Bryant et al., 2010; Polinder et al., 2018; Ponsford et al., 2012; Reuben et al., 2014; Stein et al., 2017). Anxiety and depression, both premorbid and concurrent, predicted PPCS at one week and three months postinjury (Ponsford et al., 2012). Some studies have found that females who report premorbid psychiatric illness are also more likely to report persistent symptoms post-injury (Finnoff et al., 2011). While basic personality traits are not associated with PPCS, specific traits such as high anxiety sensitivity, alexithymia, avoidant coping styles, and low resilience are associated with PPCS (Scheenen et al., 2017; Sullivan et al., 2016; Wood et al., 2014). Causality is difficult to determine using current PPCS literature, as psychiatric status may be influenced by mTBI/PPCS, or premorbid psychiatric factors lead to increased symptom report. Sleep disturbances including fatigue are also commonly associated with mTBI and mood, with some individuals experiencing insomnia or excessive sleepiness; sleep disruptions have also been associated with concentration/memory difficulties and pain sensitivity (Henrie & Elovic, 2016; Hinds et al., 2016; Iaccarino & Zafonte, 2016; Mosti et al., 2016).

The Achenbach System of Empirically Based Assessment (ASEBA), consisting of the Child Behavior Checklist for Ages 6-18 (CBCL) and Youth Self-Report for Ages 11-18 (YSR) is a popular measure used in children and adolescents to measure externalizing behaviors, as well

as internalizing behaviors such as anxiety and depression (Achenbach & Rescorla, 2001). Adult versions of the CBCL and YSR, named the Adult Behavior Checklist (ABCL) and the Adult Self-Report (ASR), are also available for ages 18-59 (Achenbach & Rescorla, 2003).

Additionally, a history of learning disorder (LD) or attention-deficit/hyperactivity disorder (ADHD) has also been documented to increase risk of mTBI, as well as increase risk of PPCS. Nelson and colleagues (2016a) assessed the history of multiple sports-related mTBI in high school and college-level student athletes with ADHD and/or LD and compared to the history of student athletes who did not have these premorbid conditions. They found that students with ADHD were 2.93 times more likely to have had at least three prior mTBI, while those with LD were 2.08 times more likely to have had at least three prior mTBI; for student athletes that have both premorbid ADHD and LD, they were more than three times more likely to have had at least three prior mTBI (Nelson et al., 2016a). Premorbid learning difficulties have also been found to be a significant predictor of outcome over time, particularly at one-month post-mTBI (Bernard et al., 2016; Finnoff et al., 2011). A recent meta-analysis indicated that ADHD is an antecedent risk factor for mTBI and complicates the course of mTBI as they tend to report more severe symptoms such as fatigue and poor concentration (Biederman et al., 2015).

Previous Head Injury. Sports medicine literature has demonstrated that repetitive mTBI is associated with increased symptom prevalence, longer symptom resolution and minor long-term cognitive complaints (Pellman et al., 2004; Scopaz & Hatzenbuehler, 2013). Specifically, previous head injury was a factor at one-week postinjury, but not after 14 days (Scopaz & Hatzenbuehler, 2013). Previous head injury is mostly discussed in sports literature and has been associated with neurodegenerative conditions such as chronic traumatic encephalopathy, which has overlapping symptoms with PPCS (Polinder et al., 2018). While previous head injury has

shown to be a predictor, it is still unknown whether there is a threshold for number of concussions that is associated with increased risk of poor recovery (Tator et al., 2016). One study reported that of 221 individuals who had PPCS, 23.1% had reported no prior history of head injury; authors concluded that history of previous head injury was not a significant predictor of PPCS (Tator et al., 2016). As most research is completed in athlete populations, more research is needed within the non-athlete civilian populations to increase generalizability.

Social Support and Life Stressors. Adequate social support is associated with decreased symptoms of depression, posttraumatic stress, and fatigue in the TBI population (McCauley et al., 2010; McLean et al., 2014; Polinder et al., 2018; Stålnacke, 2007; Zeng et al., 2016). Social support has been measured through community integration, peer relationships, family dynamics, and perceived social support (Polinder et al., 2018; Zeng et al., 2016). As these aspects are considered to be part of health-related quality of life, peer relationships and ability to participate in social/community activities are included in the NIH PROMIS® adult and pediatric profiles (Bertisch et al., 2017; Cella et al., 2019). Social support may be a particularly relevant topic for individuals who have sustained mTBI due to its invisible nature compared to other orthopedic injuries. One study by Covassin and colleagues (2014) found that student athletes who sustained a sports-related mTBI were likely to report lesser perceived social support and satisfaction compared to athletes who sustained orthopedic injuries. Additionally, student athletes who sustain mTBI also reported greater trait anxiety; positive social support may help to reduce distress after mTBI and improve motivation in recovery (Covassin et al., 2014). Concurrent life stressors and recent stressors prior to mTBI can also lead to poor recovery (Ponsford et al., 2012). mTBI studies have included measures that assess for recent stressors or traumatic life events, such as Life Events Checklist (Dretsch et al., 2015; Kashluba et al., 2007). Notably,

stressors and environment may be particularly important for adolescents as well, with one study indicating that interpersonal stressors among family, friends, and school can have an impact on adjustment, measured as internalizing and externalizing symptoms (Lantagne et al., 2018).

Adverse childhood experiences

Adverse childhood experiences (ACEs), defined as stress/trauma that occurs within an individual's first 18 years, may be an additional psychosocial factor associated with PPCS (Felitti et al., 1998). ACEs typically fall into the following categories: (a) physical abuse, (b) emotional abuse, (c) sexual abuse, (d) physical neglect, (e) emotional neglect, (f) parental divorce, (g) living in a home with mental illness, (h) substance abuse within the household, (i) witnessing violence, and (j) having an incarcerated household member (Boullier & Blair, 2018; Bucci et al., 2016; Felitti et al., 1998). Around 62% of adults have experienced at least one ACE in the U.S., while 25% have endorsed at least three ACEs (Felitti et al., 1998; Merrick et al., 2018). Exposure to one ACE seems unsurprising due to higher divorce rates, but Merrick and colleagues (2018) revealed that the dominant ACE was actually emotional abuse (34.42%), followed by parental separation or divorce (27.63%). A seminal study by the Center for Disease Control and Kaiser revealed a dose-response relationship between the number of ACEs and negative health outcomes in adulthood, including both physical and psychiatric conditions (Felitti et al., 1998). From this seminal study, the Adverse Childhood Experiences Study Questionnaire was created and is still used in ACE studies today (Felitti et al., 1998; Oh et al., 2018). Identified health conditions include cancer, chronic pain, respiratory disease, illicit drug use, risky sexual behavior, suicide attempts, anxiety, depression, and violence perpetration/victimization (Hughes et al., 2017; Nelson et al., 2019). ACEs has a widespread effect on several aspects of a person's health, several which overlap with empirically supported

predictors of poor outcome following mTBI (e.g., premorbid pain, substance abuse, psychiatric illness, etc.). Given the significant correlation that ACEs have with these factors, ACEs themselves may contribute significantly to negative mTBI outcomes.

Inequalities in ACEs

Inequalities in ACE exposure have been documented in Blacks, Hispanics, multiracial individuals, and among people with disability or lower SES, paralleling health disparities among minority groups (Boullier & Blair, 2018; Cronholm et al., 2015; Maras, 2018; Mersky et al., 2017). Some researchers have proposed expanding the original ACEs to include parent absence, peer victimization, homelessness, financial problems, food insecurity, and violent crime victimization as these are issues frequently endorsed by individuals with lower SES (Mersky et al., 2017).

It is notable that sports, such as football, can have high rates of mTBI, with estimates as high as 50% per season; basketball also placed in the top ten sports with regard to rates of sports-related mTBI (Zuckerman et al., 2015; UPMC, 2019). Black athletes are disproportionately represented in these two sports. According to the National Collegiate Athletic Association (NCAA, 2018), about 39% of collegiate athletes playing football and 45% playing basketball are black males. Based on these inequalities in ACE exposure and possibly contribution of ACEs to poor mTBI outcomes, screening for ACEs in athletes may become an essential component of mTBI assessment in the future.

Effects of ACEs

ACEs contribute to early life stress that can affect subsequent brain development and influence cognition, emotional and behavioral functioning. Chronic levels of stress in childhood (and resulting cortisol) appear to inhibit growth of the hippocampus, prefrontal cortex and

amygdala (Guinosso et al., 2016; Hanson et al., 2014). These areas regulate the hypothalamic-pituitary-adrenal (HPA) axis and early life stress can alter the HPA axis, resulting in altered basal activity and thus, stress response, into adulthood (Essex et al., 2012; Guinosso et al., 2016; Juruena et al., 2020). These brain regions are associated with anxiety-related behavior, memory, emotional/reward processing, self-regulation, and executive functioning (Pechtel & Pizzagalli, 2011). ACE exposure is also associated with lower general cognitive ability; literature demonstrates that children with ACEs generally show the least improvement in executive functioning over time (Guinosso et al., 2016). Adults with ACEs have also demonstrated worse memory functioning compared to adults without ACE exposure (Pechtel & Pizzagalli, 2011). Alterations in the amygdala and the dopaminergic system (associated with reward processing) have been connected to higher selective attention to threat-related cues and higher reported symptoms of anhedonia; reward cues were rated as less positive amongst participants with ACEs (Pechtel & Pizzagalli, 2011). Greater cumulative stress is related to smaller amygdala and hippocampal volumes, and changes in these areas of the HPA axis are associated with downstream effects that can lead to behavioral problems, such as aggressive and oppositional behaviors (Hanson et al., 2014). Overall, ACEs can affect brain development in several regions such as the temporal and frontal lobes. Notably, the temporal and frontal lobes are also the most affected when sustaining an mTBI secondary to different viscosities and densities of brain tissues; the frontal lobe and inferior aspects of the temporal lobes are also vulnerable due to these tissues coming into contact with bony surfaces of the skull (Hadanny & Efrati, 2016; McKee & Daneshvar, 2015). Effects can be seen in retired NFL players with mild deficits in cognition (e.g., executive functioning), with hyperactivation and hypoactivity in dorsolateral and

frontopolar regions (Hampshire et al., 2013; Hart Jr. et al., 2013). Conceptually, insults to the brain from ACEs are very similar to insults to the brain from a mTBI.

Resilience

ACEs are not a guarantee of negative outcomes in adulthood; other factors can still serve to buffer the effects of toxic stress (Maras, 2018). Resilience, a newly emerging area within ACEs research, is defined as "positive adaptation within the context of significant adversity" (Minnesota Department of Health, 2019). Protective factors can include community and social connections, socioeconomic advantages, parent resilience, and cultivating a sense of purpose through faith or culture (Minnesota Department of Health, 2019, para. 1). While most literature focuses on nurturing resilience in childhood, research within the past decade has started to address adults with ACE exposure (Cameron et al., 2018; Korotana et al., 2016). Resilience is also an important component of post-mTBI literature, where some researchers have studied how personality and coping styles can affect persistence of symptoms following mTBI (Scheenen et al., 2017; Sullivan et al., 2016; Wood et al., 2014).

ACEs and Brain Injury

To date, eight studies and one review have evaluated the relationship between ACEs and TBI, as displayed in Table 4 (Brewer-Smyth et al., 2016; Colantonio et al., 2014; Cusimano et al., 2021; Deighton et al., 2016; Guinn et al., 2018; Ma et al., 2018; Post et al., 2013; Schneeberger et al., 2012; Song et al., 2018). All studies found that ACEs were associated with a higher rate of TBI (Cusimano et al., 2021; Ma et al., 2018). Statistically higher rates of physical abuse, sexual abuse, and substance abuse were reported in the TBI groups (Brewer-Smyth et al., 2016; Colantonio, 2016; Cusimano et al., 2021; Guinn et al., 2018). However, it is important to note that several of these studies have utilized vulnerable populations (i.e., homeless, foster care,

and prison populations) calling into question the overall generalizability of these findings (Brewer-Smyth et al., 2016; Colantonio et al., 2014; Cusimano et al., 2021; Song et al., 2018). Nascent research regarding ACEs and brain injury have only examined the correlations between these constructs–none have established a temporal relationship. Furthermore, none of these studies to date have evaluated outcomes following mTBI or rates of persistent symptoms following mTBI. Notably, one of these eight studies included adolescents within their participant group (Cusimano et al., 2021). Addressing possible effects of mTBI (particularly psychological), may assist in buffering risk for poor outcomes.

Table 4

Summary of Studies Assessing Association Between Adverse Childhood Experiences and Brain Injury

First Author; Year	Population	Study design	Sample size; % females	ACEs measures	TBI measures	Main findings
Brewer-Smyth; 2016	Female prison	C-S, C-C	135; 100%	Muenzenmaier's scale: PA, SA; self-reported family member incarceration	Clinician examined neurological histories	Abuse in adulthood was significant covariate in association between CA and neurological histories/abnormalities
Cusimano; 2021	Individuals with foster care history	C-S, C-C	74; 21%	ASQ	BISQ for lifetime TBI exposure and self-reported TBI status	Foster population had higher rate of TBI and ACE; those who reported TBI had significantly higher ACEs ($p < .001$)
Colantonio; 2014	Male and female prison	ancillary, C-S	235; 44%	Adverse life experiences ages 0-15 - PA, SA, neglet, WV, and FSA	CDC definition; time and age of TBI; LOC duration; hospital admission for TBI; lifetime number TBI	Females with TBI hx had significantly higher rates of abuse than females without TBI hx and males overall; males with TBI had significantly higher percentage of family alcohol abuse to non-TBI males

Table 4 *continued*

First Author; Year	Population	Study design	Sample size; % females	ACEs measures	TBI measures	Main findings
Deighton; 2016	High risk group for psychosis	C-S	1025; 44.6%	CTAS: PA, SA, EA; Family Interview for Genetic Studies: FMI	age first TBI; lifetime number TBI; rating of most severe TBI	"Clinical high risk [for psychosis] group with a history of mild TBI had significantly higher total trauma scores than those without a history of mild TBI (p = 0.04)"
Guinn; 2018	Non-institutionalised adults	ancillary retrospective, C-S	201; NR	BRFSS ACE module: EA, PA, SA, FMI, FSA, parental separation, FMC, PV	"Have you ever had a brain injury that limited you in any way for more than a week in any activities?"; cause of injury	SA, PA, FMI, and FMC exposure had significantly greater odds of TBI after adjusting for age, race/ethnicity, gender, income
Post; 2013	Individuals with bipolar disorder	C-S	968; NR	Modified ACEs Questionnaire: PA, SA, EA, family dysfunction (FMI; FSA)	Self-reported head injury with and without LOC	ACEs associated with 13.3% increase in TBI without LOC; PA and FSA associated with increase in TBI without LOC

Table 4 *continued*

First Author; Year	Population	Study design	Sample size; % females	ACEs measures	TBI measures	Main findings
Schneeberger; 2012	Individuals with history of severe mental illness	retrospecti ve, C-S	183; 39.34%	PASAQ: PA, SA; Modified ASQ; EA, PV, FMI, FSA, FMC	"Did you ever have a severe head injury or lose consciousness?"	Rate of head injuries increased in graded fashion as total ACE score increased
Song; 2017	Individuals experiencing homelessness	C-S survey	500; 40%	CTQ-SF: PA, SA, EA	"Have you ever had an injury to the head which knocked you out or at least left you dazed, confused, or disoriented?"	PA and EA were associated with TBI hx; SA, physical neglect, and emotional neglect were not

Note. C-S = cross-sectional; C-C = case-control; NR = not reported; CA = childhood abuse; PA = physical abuse; SA = sexual abuse; EA = emotional abuse; FMI = family mental illness; FSA = family substance abuse; FMC = family member incarceration; PV = partner violence; hx = history; CTAS = Childhood Trauma and Abuse Scale; CTQ-SF = Childhood Trauma Questionnaire - Short Form; PASAQ = Physical and Sexual Abuse Questionnaire; ASQ = ACEs Study Questionnaire. Adapted from "The Association Between Adverse Childhood Experiences and Adult Traumatic Brain Injury/Concussion: A Scoping Review," by Z Ma, M. T. Bayley, L. Perrier, P. Dhir, L. Depatie, ... S. E. P. Munce, 2018, *Disability and Rehabilitation*, *12*, p. 4.

Rationale for Current Study

Each year, over 2.8 million people sustain TBI across the United States, with almost all of these categorized as mild (Faul & Coronado, 2015; Greenwald et al., 2012; Mansour & Lajiness-O'Neill, 2015; Stucky et al., 2014; Taylor et al., 2017). Typically, individuals will recover in 4-6 weeks before physicians begin to refer to other specialists for treatment, but a small minority of individuals will experience PPCS and continue to report problems that can affect functioning and long-term outcome (Iverson & Lange, 2011; Polinder et al., 2018).

This small minority of individuals represent a disproportionate amount of the medical care costs associated with mTBI. Studies evaluating costs have found that pediatric mTBIs have accounted for nearly 81% of the $1.59 billion in pediatric TBI costs, accounting for 96.6% of 600,000 patients in a study (Graves et al., 2015). Another study evaluating adults with mTBI in Olstead County, Minnesota found that after 1-6 years post-injury, persons with mTBI had significantly higher costs compared to their matched controls ($3418; Leibson et al., 2012). These findings highlight the importance of screening for individuals at risk for persistent symptoms post-mTBI and demonstrate that not all mTBI can be considered a low-cost, quick-fix issue.

Although PPCS remains controversial and lack of a consensus definition remains an issue, several factors both premorbid and injury-related have been repeatedly shown to be related to PPCS. These biopsychosocial variables include cognitive reserve, sex, pain, psychiatric factors, previous head injury, litigation, and social support/life stressors (Kenzie et al., 2017; Polinder et al., 2018). More recently, researchers have started to assess the relationship between adverse childhood experiences and TBI, finding that those who endorse higher ACEs have higher rates of TBI (Ma et al., 2018). To our knowledge, only eight studies and one review have

assessed the relationship between adverse childhood experiences and TBI; however, it is notable that several of these studies utilize vulnerable (e.g., prisoners, individuals with severe psychopathology, foster care) populations and thus results may not be generalizable (Brewer-Smyth et al., 2016; Colantonio et al., 2014; Cusimano et al., 2021; Deighton et al., 2016; Guinn et al., 2018; Ma et al., 2018; Post et al., 2013; Schneeberger et al., 2012; Song et al., 2018). Furthermore, no study to date has assessed the relationship between ACEs and PPCS, despite several overlapping features of ACEs and mTBI with regard to effects on the brain, particularly within the children and adolescent population. Conceptualizing adverse childhood experiences as a premorbid, psychosocial factor may aid clinicians in more accurately assessing who is at higher risk for later developing PPCS and allowing for more specific interventions before injury symptoms become chronic. Taken together, assessing for ACEs, along with the currently known factors associated with PPCS, may assist clinicians in better understanding risk for persistent symptoms.

Aims of the Current Study

The initial longitudinal study (baseline and 4-weeks post injury) aimed to replicate the current literature regarding premorbid and injury-related factors (e.g., cognitive reserve, sex, pain, psychiatric factors, previous head injury, litigation) in the persistence of symptoms following mTBI, along with related cognitive, psychological, and functional outcomes using a group of participants with complicated and uncomplicated mTBI. Additionally, another primary aim of the initial prospective study was to evaluate the relative contribution of adverse childhood experiences (ACEs) compared to these established predictors in the persistence of symptoms after mTBI.

However, due to the COVID-19 pandemic and subsequent complications in human-subject research, the study design was adjusted to engender a retrospective, cross-sectional design; data was collected from the time in which a neuropsychological evaluation was completed, following the mTBI. The current retrospective study was part of a larger archival study and data was extracted from assessments that were conducted from December 2014 to September 2020. While the original intention was to pool prospective and retrospective data, prospective data collection was not feasible due to ongoing human subject research restrictions. The revised retrospective study still aimed to replicate the current literature regarding premorbid and injury-related factors in the persistence of symptoms following mTBI, as well as evaluate the relative contribution of ACEs compared to established predictors. Additional constructs, such as time since mTBI and age at mTBI were included in the revised study. In the following section, "proposed" refers to the aims and hypotheses of the originally proposed prospective study, while "revised" refers to the aims and hypotheses of the altered retrospective study. Please refer to Appendices A to F for originally proposed methods, measures, and other relevant study materials.

Specific Aim 1

- Examine and extend current literature on the relationship between cognitive reserve and persistence of symptoms following mTBI.
- **Proposed Hypothesis 1:** Individuals who perform lower on a measure of cognitive reserve will have a higher number of reported symptoms at one-month post injury.
- **Revised Hypothesis 1:** Individuals with a lower cognitive reserve, as measured by years of maternal education, will report a higher number of PPCS following injury.

- **Proposed Hypothesis 2:** The addition of ACEs will add variance not accounted for by cognitive reserve in predicting PPCS at one-month post injury.
- **Revised Hypothesis 2:** The addition of ACEs will add variance not accounted for by maternal education, a proxy for cognitive reserve, in predicting PPCS following injury.

Specific Aim 2

- Examine and extend current literature on the relationship between sex and persistence of symptoms following mTBI.
- **Proposed Hypothesis 3:** Females will report a higher number of symptoms, or more severe PPCS one-month post injury. Exploratory analyses will be conducted to characterize the relationship between sex and type of ACE.
- **Revised Hypothesis 3:** Females will report a higher number of PPCS following injury.
- **Proposed Hypothesis 4:** The addition of ACEs will add variance not accounted for by sex in predicting PPCS at one-month post injury.
- **Revised Hypothesis 4:** The addition of ACEs will add variance not accounted for by sex in predicting reported PPCS following injury.

Specific Aim 3

- Examine and extend current literature on the relationship between pain and persistence of symptoms following mTBI.
- **Proposed Hypothesis 5:** More severe mTBI-related pain will be positively associated with the number of (or higher severity of) endorsed symptoms at one-month post-injury.
- **Proposed Hypothesis 6:** The addition of ACEs will add variance not accounted for by pain in predicting PPCS at one-month post injury.

- Hypotheses 5 and 6 were not included in the updated retrospective study as there was insufficient retrospective data to assess for the relationship between injury-related pain and reported PPCS.

Specific Aim 4

- Examine and extend current literature on the relationship between psychiatric factors and persistence of symptoms following mTBI.
- **Proposed Hypothesis 7:** Individuals who report a higher number of, or more severe, symptoms related to premorbid psychiatric factors such as depression, anxiety, and substance use will report higher or more severe symptoms at one-month post injury.
- **Revised Hypothesis 7:** Individuals who report a higher number of, or more severe, symptoms related to depression and/or anxiety at time of the evaluation will report a higher number of PPCS following injury. Individuals who report a history of premorbid ADHD/LD diagnosis will report a higher number of PPCS following injury.
- **Proposed Hypothesis 8:** Individuals who report more symptoms, or more severe PPCS at one month will also report higher or more severe posttraumatic stress symptoms at one-month post injury.
- **Proposed Hypothesis 9:** Individuals who report premorbid substance use will continue to report substance use at one-month post injury. Substance use at one-month post injury will be positively correlated with mTBI-related symptom report.
- **Proposed Hypothesis 10:** Individuals who report premorbid psychiatric illness will report higher life stressors at one-month post injury. Higher life stressors at one-month post injury will be positively correlated with mTBI-related symptom report.

- Hypotheses 8, 9, and 10 were not included in the updated retrospective study as there was insufficient information among participants for substance use, PTSD, and life stressor variables.
- **Proposed Hypothesis 11:** The addition of ACEs will add variance not accounted for by premorbid psychiatric illnesses in predicting PPCS at one-month post injury.
- **Revised Hypothesis 11:** The addition of ACEs will add variance not accounted for by psychiatric illnesses in predicting reported PPCS following injury.

Specific Aim 5

- Examine and extend current literature on the relationship between previous head injury and persistence of symptoms following mTBI.
- **Proposed Hypothesis 12:** Individuals who report a higher number of prior head injuries will report a higher number, or more severe, symptoms at one-month post injury.
- **Revised Hypothesis 12:** Individuals who report a higher number of prior head injuries will report a higher number of PPCS following injury.
- **Proposed Hypothesis 13:** The addition of ACEs will add variance not accounted for by prior head injuries in predicting PPCS at one-month post injury.
- **Revised Hypothesis 13:** The addition of ACEs will add variance not accounted for by prior head injuries in predicting PPCS following injury.

Specific Aim 6

- Examine and extend current literature on the relationship between litigation and persistence of symptoms following mTBI.
- **Proposed Hypothesis 14:** Individuals who report that they are involved in litigation due to the currently evaluated mTBI will report a higher number of, or more severe,

symptoms at one-month post injury. Exploratory analyses will be conducted to evaluate the relationship between litigation, ACEs, and PPCS.

- **Proposed Hypothesis 15:** The addition of ACEs will add variance not accounted for by litigation in predicting PPCS at one-month post injury.
- Hypotheses 14 and 15 were not included in the updated retrospective study as there was insufficient information among participants regarding litigation status.

Methods

Participants

Participants with mTBI were recruited from the main Dartmouth-Hitchcock Medical Center campus (DHMC) and the C3 concussion clinic. Inclusion criteria for the mTBI group utilized the Center for Disease Control (2003) definition of mTBI, and included recent (< 2 week) history of blunt trauma or acceleration/deceleration forces and a minimum of one of the following: (a) alteration in mental status (e.g., confused, disoriented, impaired consciousness); (b) any amnesia; (c) LOC <30 minutes; or (d) signs of neurological or neuropsychological dysfunction. GCS was acquired when available and a criterion of a score of 13-15 on presentation was used. Other criteria included (a) age 10 years or over and (b) English speaking. Age range was 10-23 years to encompass adolescents, as defined by the World Health Organization, and the higher end of the age range with the highest prevalence rate of mTBI (Borg et al., 2004; Carroll et al., 2004; Katz et al., 2015; World Health Organization, 2021).

Participants were excluded if they (a) were intubated or required general anesthesia following the injury; (b) were under the influence of illicit substances at the time of injury; (c) had focal neurological signs that indicated injuries more severe than mTBI (e.g., hemorrhage, hemiparesis, cerebral contusions, subdural/epidural hematoma, seizures) or (d) had a history of intellectual disability, neurological illness, significant alcohol or drug abuse, or other psychiatric impairment currently affecting daily functioning. Individuals with a medical history of non-neurological illness (e.g., cardiac disease, hypertension, cancer, diabetes), psychiatric history (excluding psychosis), prior mTBI, and reported alcohol or cannabis use were included in the study if they did not report any significant preinjury cognitive difficulties.

Procedures of Revised Retrospective Study

Medical records from September 2014 to December 2020 were reviewed for outside documentation from time of concussion (if available), concussion history taken at the time of the interview, psychosocial history, and scores from a brief neuropsychological battery. Information for inclusion and exclusion criteria were also reviewed from medical records and neuropsychological report. Individuals who were diagnosed with post-concussion syndrome were included in the study. Seven potential participants were excluded from the current study; four were excluded due to sustaining a more severe TBI, two were excluded due to young age, and one was excluded due to a neurological illness. The study had approval from the Institutional Review Boards (IRB) at Dartmouth-Hitchcock Medical Center (please refer to Appendix G for IRB) and Eastern Michigan University, and all protected health information was de-identified in accordance with HIPAA's privacy policy after the initial gathering of records.

Measures of the Revised Retrospective Study

Postconcussive Symptoms

The primary dependent variable measured was reported postconcussive symptoms. Twenty-five of the participants utilized the Post-Concussion Symptom Inventory, Adolescent Version (PCSI-A). For individuals who did not complete a PCSI-A, symptoms reported in the background section of the report were collected. Data was collected either directly from the PCSI-A, or from symptoms reported in the neuropsychological assessment report that were directly related to the items on the PCSI-A.

The PCSI-A is a 22-item measure also addressing somatic, psychological, affective, and cognitive symptoms following mTBI, with answer choices again using a 7-point Guttman dimensional scale (Sady et al., 2014). The last item asks about how differently they have felt

since the injury, with scores ranging from “No Difference” to “Major Difference.” Internal consistency for the subscales ranged from $\alpha = 0.62–0.84$, with $\alpha = 0.90$ for the PCSI total symptom score; test-retest reliability over 3-14 days fell within the moderate to good range (total score ICC = 0.89, subscale ICC = 0.73-0.89; Sady et al., 2014). The measure also includes “Before the Injury/Pre-Injury” and “Current Symptoms/Yesterday and Today” sections to compare symptoms before and after the concussion.

In addition to the symptom items reflected in the PCSI-A, an “other cognitive issues” (e.g., reading issues) and “pain” items were included in the current retrospective study to include other symptoms reported by participants. However, as this reflected a very small minority of participants at completion of the data collection phase, this data could not be formally analyzed. Thus, persistent postconcussive symptoms in the current study reflects a frequency count of symptoms.

Acute Symptoms

Acute symptoms were obtained through information provided in background section of the neuropsychological report. Symptoms were considered to be those experienced within the first two weeks post-injury. Similarly to persistent postconcussive symptoms, acute symptoms in the current study reflects a frequency count.

Psychiatric Factors

Psychiatric factors were assessed using the Achenbach System of Empirically Based Assessment (ASEBA) Child Behavior Checklist for Ages 6-18 (CBCL), and Youth Self-Report for Ages 11-18 (YSR). These are widely used measures to assess for both emotional and behavioral problems in children and adolescents. Similarly, participants ages 18 and over completed the ASEBA Adult Behavior Checklist (ABCL), and Adult Self-Report (ASR;

Achenbach & Rescorla, 2003). The measures have three types of scales, including Competence & Adaptive, Empirically Based, and DSM-Oriented (Achenbach & Rescorla, 2001; Achenbach & Rescorla, 2003). The DSM-Oriented scales were utilized for the current retrospective study, which contain scales representing different patterns of co-occurring emotional and behavioral problems, and derived from expert consensus (Magyar & Pandolfi, 2017). Each DSM-oriented scale reflects a broad emotional or behavioral problem that corresponds to a broad DSM diagnostic category (Achenbach & Rescorla, 2001). For the current study, the T scores of the affective and anxiety problems subscales were collected.

Sex

The participant's sex was determined through information provided in the electronic medical records. Males were coded as "1" and females were coded as "2."

Date of mTBI

The participant's date of mTBI was obtained through information provided in the background section of the neuropsychological report. For reports that did not give a specific date, a date of the first was assigned (e.g., "she sustained a concussion in February 2016" was coded as "2/1/2016").

Time Since mTBI

The time since the participant's mTBI, measured in days, was calculated using the date of mTBI (described above) and the date of the evaluation, as listed in the neuropsychological evaluation report.

Previous Head Injuries

Number of previous injuries was obtained from information provided in the background section of the neuropsychological report, or from outside records, if available. Previous head

injuries were reported by the parent and/or participant. Previous head injuries were recorded as a frequency count.

History of Learning Disorder

History of learning disorder (LD) was obtained from information provided in the background section of the neuropsychological report, or from outside records, if available. A diagnosis of LD must have been confirmed through an IEP to be included in the study. A "1" was coded for individuals who were given a formal diagnosis of a learning disorder prior to their mTBI, while a "0" was coded for individuals who were not given a formal diagnosis.

History of Attention-deficit/Hyperactivity Disorder

History of attention-deficit/hyperactivity disorder (ADHD) was collected from information provided in the background section of the neuropsychological report, or from outside records, if available. A diagnosis of ADHD must have been confirmed through an IEP to be included in this study. A "1" was coded for individuals who were given a formal diagnosis of attention-deficit/hyperactivity disorder prior to their mTBI, while a "0" was coded for individuals who were not given a formal diagnosis. Data for history of LD and ADHD were collapsed into one group, due to the small number of individuals who were coded as "1"; there were no individuals who were diagnosed with both ADHD and LD.

Adverse Childhood Experiences

Adverse childhood experiences (ACEs) were obtained from the history questionnaire provided prior to the neuropsychological evaluation, as well as from the background section of the neuropsychological report or, if available, outside records. Within the history questionnaire completed by the parent, they are asked, "Has your child had any frightening or traumatic experiences?" and "Has your child ever experienced sexual or physical abuse?" For the current,

retrospective study, the number of total ACEs per participant was recorded as a frequency count. While a formal measure was not used to assess for ACEs, information reflecting the items from the ACEs Study Questionnaire was collected from medical records. This included parental divorce; death of a parent/guardian; incarceration of a parent/guardian; long-term separation from a parent/guardian; mental illness within the household; substance abuse within the household; witnessing violence within the household; and experience of physical, sexual, or emotional abuse/neglect (Felitti et al., 1998). The following items were also included in addition to the ACEs Study Questionnaire items: death of a significant other, bullying, and near-death experience (as reported by the participant). Near-death experiences were not associated with the mTBI within the current sample. These items are included in other stress inventory scales or extended ACE questionnaires and were included to better represent the participants collected in the retrospective study; several reported loss of a peer, close family friend, or second-degree relative (Holmes & Rahe, 1967).

Statistical Analysis

The updated study utilizes retrospective data collection with a cross-sectional study design.

Preliminary Analyses

Exploratory analysis was completed to ensure the main assumptions (e.g., normality, homogeneity of variance, independence, linearity) of the methods proposed were met. Distributions were examined (e.g., skewness, kurtosis) and bias analyzed by assessing for outliers or influential cases. Significant outliers were removed. If main assumptions were not met, nonparametric tests were utilized for completion of the main analyses.

Descriptive statistics for all predictor and outcome variables of interest within and across sex were computed prior to main analyses of hypotheses. Group differences in the dependent variables (please see Table 5 for list), were reported using parametric (t-tests) methods. There was no significant difference between the number of male and female individuals within the current study [$\chi^2(1, 58) = 1.72$, $p > .05$]. Variables were examined for potential covariates, where covariation were controlled for in the main analyses. A p-value of .05 was used for significance testing. Effect sizes were reported as warranted.

Table 5

Measures Organized by Construct

Postconcussive symptoms
Post-concussion symptom inventory - adolescent (PCSI-A)
Self-report
Acute symptoms
Self-report
Sex
Self-report
Psychiatric factors
ASEBA child behavior checklist for ages 6-18
Youth Self-report
ASEBA adult behavior checklist for ages 18-59
Adult Self-report
Previous head injuries
Self/parent-report
Date of concussion
Self/parent-report
History of learning disorder
Self/parent-report
History of attention-deficit/hyperactivity disorder
Self/parent-report
Adverse childhood experiences
Parent history questionnaire
Self/parent-report

Note. ASEBA = Achenbach System of Empirically Based Assessment.

Regression Analyses

A Pearson correlation matrix was computed on all continuous variables to assess relationships between predictor and outcome variables and to assess for multicollinearity. Regression diagnostics was completed to ensure the assumptions of regression were met. The variance of predictors and multicollinearity (e.g., tolerance, variance inflation factor, condition index) was examined, along with the assumptions of linearity and homoscedasticity (e.g., plots of Z residuals against Z predicted values; Bowerman & O'Connell, 1990; Field, 2018; Lajiness-O'Neill et al., 2015; Menard, 1995). Additionally, the following were examined: (a) independence of residuals (e.g., Durbin-Watson); (b) tests for normality of residuals (e.g., P-P plots, histograms); and (c) casewise diagnostics for undue influence (e.g., Cook's distance, Mahalanobis distance; Lajiness-O'Neill et al., 2015).

Hierarchical regression analyses were computed to address the proposed hypotheses for those variables that had significant unadjusted relationships according to their Pearson's *r* coefficient. PPCS was entered as the dependent, or outcome, variable in all analyses. Age at mTBI was entered as a covariate in Step 1 as a sex difference in age at injury was identified. The second variable of the significant relationship was entered in Step 2 (e.g., previous mTBI, psychiatric illness, maternal education, etc.), while ACEs was entered in Step 3.

Exploratory Analyses

Exploratory analyses were conducted using acute symptoms as an outcome (dependent) variable. Further exploratory analyses were also completed by computing Pearson's *r* correlations for male and female participants, separately. Again, hierarchical regression analyses were computed for significant relationships.

Sensitivity Analysis (Current Retrospective Study)

As the data for the current study was collected from a limited archival dataset, sample size was fixed. A sensitivity analysis was conducted using G*Power, where minimum detectable effect size is calculated based on sample size and power (Faul et al., 2007). With a sample size of 58 and 95% power, the current study could reliably detect a moderate effect size of 0.31 or higher, $N = 58$, $\lambda = 18.52$, $F = 2.78$, $df = 3, 52$.

Results

Descriptives

Descriptive statistics (frequencies, ranges, percentages, mean, and standard deviation) were computed for all demographic characteristics and study variables. A total of 58 participants were included in the study: 34 males and 24 females. Age at time of mTBI ranged from 10 and 23 years of age, with a mean age of 16.45 years. The time post-mTBI to assessment ranged from 10 to 1249 days, with a mean interval of 293.86 days. Please see Table 6 for participant characteristics. As a preliminary step for the regression, Pearson's *r* coefficients were computed to examine the relationships among all variables. Pearson's r coefficients were computed for the pooled sample (please refer to Table 7), and separately for male and female participants (please refer to Tables 8 and 9, respectively). Independent *t*-tests were computed to assess for sex differences in predictors and outcome variables. There were no significant differences between male and female participants, with the exception of age at mTBI, $t(56) = 2.10$, $p < .05$.

Regression Diagnostics

Regression diagnostics were computed to ensure that all model assumptions were met and to find any influential outliers. Assumptions were also evaluated, including (a) linearity, (b) homoscedasticity, (c) independence, and (d) normality. Linearity and homoscedasticity were assessed with the use of scatterplots (Z residuals versus Z predicted values). Multicollinearity was examined using the Tolerance, Variance Inflation Factor, and Conditional Index. Additionally, independence of residuals were evaluated using the Durbin-Watson test, while normality was visually measured with the use of P-P plots and histograms. Influential outliers were also assessed using Mahalanobis distance and Cook's distance, as well as variance of predictors.

An examination of the scatterplots displaying Z residuals versus Z predicted values demonstrated that assumptions of linearity and homoscedasticity were met. Test for normality of residuals were visually examined using P-P plots and histograms; they revealed generally normal distributions. There was multicollinearity among the psychiatric illness predictor variables, due to the variables being subscales of the same test (e.g., ASEBA CBCL, YSR, ABCL or ASR); however, multicollinearity was otherwise undetected among the other predictor variables. The variance of all predictors (i.e., previous number of mTBI, sex, maternal education, premorbid ADHD/LD diagnoses, psychiatric illness, ACEs, acute symptoms) were nonzero. The Variance Inflation Factor for predictors within all models was below the suggested cutoff of 10 (Bowerman & O'Connell, 1990). The Tolerance statistic was above 0.2 for predictors in all models, whereas below 0.2 is suggestive of an issue with multicollinearity (Menard, 1995). With regard to the Conditional Index statistic, the diagnostics indicated well-distributed variance of the predictors and Condition Number values lower than the threshold of 30 (Belsley et al., 1980). Independence of residuals using the Durbin-Watson test were also met, with values falling between 1 and 3. Influential outliers were examined using Mahalanobis distance and Cook's distance; with the exception of the ASEBA parent-reported anxiety problems variable, there were no significant outliers. The significant outlier for this predictor was deleted for subsequent regression analyses.

Table 6

Participant Characteristics

	Male			Female					Pooled		
Subject characteristics	M	SD	Range	M	SD	Range	*t*	*d*	M	SD	Range
Age (years)	16.8	2.28	10-22	15.9	2.36	12-23	1.47	0.39	16.45	2.33	10-23
mTBI variables											
Age at mTBI (years)	16.00	2.17	10-22	14.9	1.75	11-19	2.10*	0.56	15.53	2.07	10-22
Time since mTBI (days)	33.3	265	1249	239	197.8	21-63	1.45	0.39	293.86	242.10	10-1249
Premorbid variables											
Number of previous mTBI	2.09	1.82	0-7	1.46	1.5	0-5	1.40	0.37	1.83	1.71	0-7
Maternal education (years)	15.1	2.32	9-18	14.7	2.26	12-18	0.50	0.16	0.12	0.33	9-18
Premorbid ADHD or LD dx	0.18	0.33	0-1	0.13	0.34	0-1	-.09	-0.02	14.87	2.27	0-1
Psychiatric variables											
ASEBA PR affective problems	65.5	9.37	50-85	65.4	10.87	51-85	0.05	0.02	65.45	9.92	50-85
ASEBA PR anxiety problems	57.5	6.65	50-71	57.6	8.35	50-74	-0.04	-0.01	57.56	7.31	50-74
ASEBA SR affective problems	61.9	9.18	50-78	59.5	9.79	50-78	0.83	0.26	60.93	9.40	50-78
ASEBA SR anxiety problems	57.1	7.5	50-76	59.4	10.05	50-80	-0.86	-0.27	58.02	8.58	50-80
Adverse childhood experience variables											
Total number of ACEs	0.88	1.18	0-4	1.38	1.25	0-4	-1.54	-0.41	1.09	1.22	0-4

Table 6 *continued*

	Male			Female					Pooled		
Subject characteristics	M	SD	Range	M	SD	Range	*t*	*d*	M	SD	Range
Post-mTBI variables											
Total number of acute sx	3.59	2.32	0-11	4.04	2.01	0-8	-0.77	-0.21	3.78	2.19	0-11
Total number of postconcussive sx	5.97	4.13	0-18	6.92	5.39	0-21	-0.76	-0.20	6.36	4.67	0-21

Note. ASEBA = Achenbach System of Empirically Based Assessment, includes Child Behavior Checklist for Ages 6-18, Youth Self-Report, Adult Behavior Checklist for Ages 18-59, and Adult Self-Report measures. mTBI = mild traumatic brain injury; ACE = adverse childhod experiences; dx = diagnoses; PR = parent-reported; SR = self-reported; sx = symptoms. For ASEBA measures, M = 50; SD = 10.

* $p < .05$. *t* = t value of independent t- tests. *d* = Cohen's d.

Table 7

Pearson's r correlations between variables in all participants

Variable	1	2	3	4	5	6	7	8	9
1. Age (years)	--								
2. Age at mTBI (years)	.87***	--							
3. Time since mTBI (days)	.33*	-0.03	--						
4. Sex	-0.19	-0.27*	-0.19	--					
5. Number of previous mTBI	0.07	0.10	-0.01	-0.18	--				
6. Premorbid ADHD and LD dx	0.18	0.08	0.09	0.01	0.04	--			
7. Maternal education (years)	0.01	0.17	-0.16	-0.08	-0.13	-0.07	--		
8. ASEBA PR affective problems	0.17	0.10	0.16	-0.01	0.05	0.04	0.06	--	
9. ASEBA PR anxiety problems	0.07	0.06	0.18	0.01	0.07	0.24	0.07	.52***	--
10. ASEBA SR affective problems	-0.03	0.09	0.11	-0.13	0.11	0.07	-0.03	0.34*	0.43**
11. ASEBA SR anxiety problems	-0.18	-0.13	0.05	0.14	0.22	-0.04	-0.06	0.26	0.49**
12. Total ACEs	-0.03	-0.13	0.02	0.20	0.26*	0.24	-0.69***	0.19	0.25
13. Total acute sx	-0.05	-0.09	-0.15	0.10	-0.15	0.06	-0.34*	-0.10	0.13
14. Total postconcussive sx	0.00	-0.06	-0.03	0.10	-0.09	0.10	0.02	0.50**	0.52***

Table 7 *continued*

Variable	10	11	12	13	14
1. Age (years)					
2. Age at mTBI (years)					
3. Time since mTBI (days)					
4. Sex					
5. Number of previous mTBI					
6. Premorbid ADHD and LD dx					
7. Maternal education (years)					
8. ASEBA PR affective problems					
9. ASEBA PR anxiety problems					
10. ASEBA SR affective problems	--				
11. ASEBA SR anxiety problems	0.69***	--			
12. Total ACEs	-0.05	0.05	--		
13. Total acute sx	-0.18	-0.06	0.27*	--	
14. Total postconcussive sx	0.26	0.20	0.19	0.23	--

Note. M and SD represent mean and standard deviation, respectively. ASEBA = Achenbach System of Empirically Based Assessment, includes Child Behavior Checklist for Ages 6-18, Youth Self-Report, Adult Behavior Checklist, and Adult Self-Report. mTBI = mild traumatic brain injury; dx = diagnoses; PR = parent-reported; SR = self-reported; sx = symptoms.

* p <.05, ** p <.01, *** p <.001.

Table 8

Pearson's r correlations between study variables in male participants

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Age (years)	--												
2. Age at mTBI (years)	.919***	--											
3. Time since mTBI (days)	0.24	-0.12	--										
4. Number of previous mTBI	0.09	0.12	-0.03	--									
5. Premorbid ADHD and LD dx	-0.05	-0.04	-0.03	0.19	--								
6. Maternal education (years)	0.17	0.24	-0.22	-0.30	-0.18	--							
7. ASEBA PR affective problems	0.10	0.10	-0.09	0.09	-0.22	0.11	--						
8. ASEBA PR anxiety problems	0.20	0.20	0.19	0.15	0.10	-0.11	0.39	--					
9. ASEBA SR affective problems	0.07	0.04	0.21	0.28	0.00	-0.25	0.27	0.22	--				
10. ASEBA SR anxiety problems	0.01	-0.04	0.13	.543**	-0.12	-0.17	0.06	0.28	.652***	--			
11. Total ACEs	-0.19	-0.24	0.09	.446**	.353*	-.672**	0.22	.506**	-0.04	0.04	--		
12. Total acute sx	-0.23	-0.17	-0.21	-0.16	0.15	-0.41	-0.02	0.32	-0.17	-0.19	0.34	--	
13. Total postconcussive sx	-0.08	-0.04	-0.12	0.01	-0.11	0.04	.595**	.449*	0.15	0.03	0.31	0.20	--

Note. M and SD represent mean and standard deviation, respectively. ASEBA = Achenbach System of Empirically Based Assessment, includes Child Behavior Checklist for Ages 6-18, Youth Self-Report, Adult Behavior Checklist, and Adult Self-Report; PR = parent-reported; SR = self-reported; dx = diagnoses; sx = symptoms.

* $p < .05$, ** $p < .01$, *** $p < .001$.

Table 9

Pearson's r correlations between study variables in female participants

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Age (years)	--												
2. Age at mTBI (years)	.787***	--											
3. Time since mTBI (days)	.426*	-0.01	--										
4. previous mTBI	-0.05	-0.09	-0.09	--									
5. Premorbid ADHD and LD dx	.505*	0.32	0.33	-0.20	--								
6. Maternal education (years)	-0.23	0.04	-0.16	0.02	0.05	--							
7. ASEBA PR affective problems	0.24	0.12	.552*	-0.02	0.35	-0.03	--						
8. ASEBA PR anxiety problems	-0.05	-0.12	0.20	-0.03	0.41	0.27	.657**	--					
9. ASEBA SR affective problems	-0.20	0.04	-0.11	-0.23	0.16	-0.02	0.40	0.40	--				
10. ASEBA SR anxiety problems	-0.27	-0.15	-0.03	-0.11	0.06	-0.01	0.46	0.46	.810***	--			
11. Total ACEs	0.28	0.18	0.02	0.09	0.09	-.710**	0.17	0.17	-0.01	-0.01	--		
12. Total acute sx	0.29	0.15	0.02	-0.06	-0.07	-0.24	-0.23	-0.23	-0.11	-0.01	0.13	--	
13. Total postconcussive sx	0.13	-0.02	0.16	-0.19	0.32	0.01	0.41	0.41	0.40	0.33	0.04	0.26	--

Note. M and SD represent mean and standard deviation, respectively. ASEBA = Achenbach System of Empirically Based Assessment, includes Child Behavior Checklist for Ages 6-18, Youth Self-Report, Adult Behavior; PR = parent-reported; SR = self-reported; dx = diagnoses; sx = symptoms.

* p <.05, ** p <.01, *** p <.001.

Main Analyses

Specific Aim 1

Examine and extend current literature on the relationship between cognitive reserve and persistence of symptoms following mTBI.

Hypothesis 1: Inconsistent with the hypothesis, there was no significant relationship between years of maternal education, a proxy for cognitive reserve, and number of reported persistent post-concussive symptoms, $r(36) = .02$, $p = .91$.

Hypothesis 2: Regression analysis was not computed as Pearson's *r* coefficient did not indicate a significant unadjusted relationship between maternal education and PPCS.

Specific Aim 2

Examine and extend current literature on the relationship between sex and persistence of symptoms following mTBI.

Hypothesis 3: Inconsistent with the hypothesis, there was no significant relationship between sex and number of reported persistent postconcussive symptoms following injury, $r(56) = .10$, $p = .45$. Exploratory analyses are discussed at the end of this section.

Hypothesis 4: Regression analysis was not computed as Pearson's *r* coefficient did not indicate a significant unadjusted relationship between sex and PPCS.

Specific Aim 3

Examine and extend current literature on the relationship between pain and persistence of symptoms following mTBI. Specific Aim 3 and its associated hypotheses were unable to be examined in the updated retrospective study due to insufficient data.

Specific Aim 4

Examine and extend current literature on the relationship between psychiatric factors and persistence of symptoms following mTBI. Notably, some hypotheses (Hypotheses 5, 6, 8, 9, 10) were unable to be examined in the updated retrospective study due to insufficient data.

Hypothesis 7: Consistent with the hypothesis, there was a significant positive relationship between psychiatric illness and number of reported PPCS. Specifically, higher parent-report scores on affective problems, $r(42) = .50$, $p = .001$, and anxiety problems, $r(41) = .52$, $p < .001$, were associated with a higher number of reported PPCS. There were no significant relationships between self-reported affective problems, $r(40) = .26$, $p = .10$, or anxiety problems, $r(40) = .20$, $p = .21$, and number of reported PPCS. That is, a higher number of parent-reported depressive symptoms and a higher number of parent-reported symptoms of anxiety were noted in individuals who reported a higher number of PPCS. Multicollinearity was detected among the aforementioned psychiatric variables, as several of the variables are subscales of the same measure (ASEBA). However, they were included within the preliminary correlational analyses to subsequently evaluate whether some subscales could account for more variance than others when computing the regression analyses. Lastly, inconsistent with the hypothesis, there was no significant relationship between a premorbid ADHD/LD diagnosis and number of reported PPCS, $r(56) = .09$, $p = .47$.

Hypothesis 11: A three-step hierarchical multiple regression was conducted predicting reported PPCS following injury from age at mTBI, parent-reported affective problems, and ACEs. Age at mTBI was entered at stage one, parent-reported affective problems was entered at stage two, and ACEs was entered at stage three. See Table 10 for regression statistics. The regression revealed that at stage one, age at mTBI, $\beta = .11$, $t(42) = .71$, $p = .48$, did not

contribute significantly to the Step 1 Model, $F(1, 42) = .51$, $p = .48$, and accounted for 1.2% of the variation in reported PPCS. Introducing the parent-reported affective problems variable, β = .49, $t(41) = 3.62$, $p = .001$, explained an additional 23.9% of variation in reported PPCS and this change in R^2, $R^2 = 0.24$, $p = .001$, was significant, resulting in a significant the Step 2 Model, $F(2, 41) = 6.88$, $p = .003$. Although the Step 3 Model, $F(3, 40) = 4.51$, $p = .008$, was significant after the addition of ACEs, it explained only an additional 0.1% of the variation in PPCS, which was not a significant change in R^2, $R^2 = 0.001$, $p = .80$. ACEs was not a significant predictor, β = .04, $t(40) = .26$, $p = .80$, in the model. When all three variables were included in the Step 3 model, only parent-reported affective problems was a significant predictor of reported PPCS following injury and thus, the Step 2 Model was the best fit.

Table 10

Summary of hierarchical regression analysis for affective problems and ACEs predicting PPCS

Variables	*β*	*t*	*F*	R^2	ΔR^2
Step 1			0.51	0.01	0.01
Age at mTBI	0.11	0.71			
Step 2			6.88**	0.25	0.24**
Age at mTBI	0.06	0.43			
ASEBA parent-reported affective problems	0.49	3.62**			
Step 3			4.51**	0.25	0.001
Age at mTBI	0.05	0.39			
ASEBA parent-reported affective problems	0.49	3.48**			
ACEs	0.04	0.26			

Note. PPCS = persistent postconcussive symptoms; mTBI = mild traumatic brain injury; ACEs = adverse childhood experiences; ASEBA = Achenbach System of Empirically Based Assessment; β = standardized coefficient beta.

* $p < .05$, ** $p < .01$, *** $p < .001$.

A three-step hierarchical multiple regression was conducted predicting reported PPCS following injury from age at mTBI, parent-reported anxiety problems, and ACEs. Age at mTBI was entered at stage one, parent-reported anxiety problems was entered at stage two, and ACEs was entered at stage three. See Table 11 for regression statistics. The regression revealed that at stage one, age at mTBI, $\beta = .13$, $t(41) = .84$, $p = .41$, did not contribute significantly to the Step 1 Model, $F(1, 41) = .71$, $p = .41$, and accounted for 1.7% of the variation in reported PPCS. Introducing the parent-reported anxiety problems variable, $\beta = .52$, $t(40) = 3.87$, $p < .001$, explained an additional 26.8% of variation in reported PPCS and this change in R^2, $R^2 = 0.27$, $p < .001$, was significant in the Step 2 Model, $F(2, 40) = 7.97$, $p < .001$. Although the Step 3 Model, $F(3, 39) = 5.23$, $p = .004$, remained significant, the addition of ACEs, $\beta = .05$, $t(39) = .33$, $p = .74$, to the model explained only an additional .2% of the variation in PPCS, which was not a significant change in R^2, $R^2 = 0.002$, $p = .74$. When all three variables were included in the Step 3 Model, only parent-reported affective problems was a significant predictor of reported PPCS following injury and thus, the Step 2 Model was the best fit.

Table 11

Summary of hierarchical regression analysis for anxiety problems and ACEs predicting PPCS

Variables	*β*	*t*	*F*	R^2	ΔR^2
Step 1			0.71	0.02	0.02
Age at mTBI	0.13	0.84			
Step 2			7.97***	0.29	0.27***
Age at mTBI	0.1	0.75			
ASEBA parent-reported anxiety problems	0.52	0.387***			
Step 3			5.23**	0.29	0.002
Age at mTBI	0.1	0.7			
ASEBA parent-reported anxiety problems	0.51	3.64**			
ACEs	0.05	0.33			

Note. PPCS = persistent postconcussive symptoms; mTBI = mild traumatic brain injury; ACEs = adverse childhood experiences; ASEBA = Achenbach System of Empirically Based Assessment; β = standardized coefficient beta.

* p <.05, ** p <.01, *** p <.001.

Specific Aim 5

Examine and extend current literature on the relationship between previous head injury and persistence of symptoms following mTBI.

Hypothesis 12: Inconsistent with the hypothesis, there was no significant relationship between previous head injuries and PPCS, $r(56) = -.09$, $p = .49$.

Hypothesis 13: Regression analysis was not computed as Pearson's *r* coefficient did not indicate a significant unadjusted relationship between previous head injuries and PPCS.

Specific Aim 6

Examine and extend current literature on the relationship between litigation and persistence of symptoms following mTBI. Specific Aim 6 and its associated hypotheses were unable to be examined in the updated retrospective study due to insufficient data.

Exploratory Analyses

Descriptives of Other Study Variables

Aside from the aforementioned aims and hypotheses, other significant relationships were noted when computing the Pearson's *r* coefficients for the study variables. Within the pooled (male and female participant) sample, acute symptoms were significantly related to maternal education and total ACEs. More specifically, there was a significant negative correlation between years of maternal education and number of reported acute symptoms, $r(36) = -.34$, $p = .04$. That is, a higher number of reported acute symptoms were noted in individuals whose mothers had lower levels of educational attainment. Additionally, there was a significant positive relationship between the number of reported ACEs and acute symptoms ,$r(56) = .27$, $p = .04$. That is, a higher number of reported ACEs were noted in individuals who reported a higher number of acute symptoms.

Pearson's *r* coefficients were calculated among the study variables within the male participants and female participants, respectively. There were no significant relationships between total acute symptoms and other predictor variables within the male or the female participants of the study.

Regression Analyses

A three-step hierarchical multiple regression was conducted predicting reported acute symptoms following injury from age at mTBI, maternal education, and ACEs. Age at mTBI was entered at stage one, maternal education was entered at stage two, and ACEs were entered at stage three. See Table 12 for regression statistics. The regression revealed that at Step 1, age at mTBI, $\beta = -.14$, $t(36) = -.84$, $p = .41$, did not contribute significantly to the model, $F(1, 36) = .70$, $p = .41$, and accounted for 1.9% of the variation in reported acute symptoms. Introducing the

maternal education variable, β = -.33, $t(35) = -2.04$, $p = .05$, in the Step 2 Model explained an additional 10.4% of variation in reported acute symptoms and this change in R^2 was significant, $R^2 = 0.12$, $p = .05$, although the Step 2 Model was not significant, $F(2, 35) = 2.46$, $p = .10$. The addition of ACEs, β = .24, $t(34) = 1.07$, $p = .29$, to the model explained an additional 2.8% of the variation in PPCS, which was not a significant change in R^2, $R^2 = 0.15$, $p = .29$, although the Step 3 Model was not significant, $F(3, 34) = 2.03$, $p = .13$. When all three variables were included in the Step 3 regression model, there were no significant predictors for acute symptoms following injury.

Table 12

Summary of hierarchical regression analysis for maternal education and ACEs predicting acute symptoms

Variables	*β*	*t*	*F*	R^2	ΔR^2
Step 1			0.70	0.02	0.02
Age at mTBI	-0.14	-0.84			
Step 2			2.46	0.12	0.1
Age at mTBI	-0.08	-0.5			
Maternal education	-0.33	-0.204*			
Step 3			2.03	0.15	0.03
Age at mTBI	-0.11	-0.65			
Maternal education	-0.16	-0.71			
ACEs	0.24	1.07			

Note. PPCS = persistent postconcussive symptoms; mTBI = mild traumatic brain injury; ACEs = adverse childhood experiences; ASEBA = Achenbach System of Empirically Based Assessment; β = standardized coefficient beta.

* $p < .05$.

Discussion

Each year, at least 2.8 million people sustain mTBI within the U.S. (Faul & Coronado, 2015; Greenwald et al., 2012; Taylor et al., 2017). While most recover within the following 4-6 weeks, a minority of individuals will continue to experience and report symptoms that affect functioning and long-term outcomes (Iverson & Lange, 2011; Polinder et al., 2018). This minority of individuals represent a disproportionate amount of the medical costs associated with mTBI, with one study showing that each person accumulated almost $3500 more in medical costs compared to controls (Leibson et al., 2012). Despite the controversy surrounding PPCS, literature reveals several biopsychosocial factors that are connected to persistent symptoms, such as cognitive reserve, sex, psychiatric factors, and previous head injury (Kenzie et al., 2017; Polinder et al., 2012). Consequently, this demonstrates that not all mTBIs are a quick fix and highlights the importance of better understanding what places individuals at risk for persistent symptoms. Researchers have more recently started to evaluate the relationship between ACEs and TBI, given that ACEs are associated with changes in brain development and several mental and physical health conditions later in life (Hanson et al., 2014; Hughes et al., 2017; Pechtel & Pizzagalli, 2011). To date, eight studies and one review have assessed this relationship, and in vulnerable populations that may not allow for generalizability of results (Brewer-Smyth et al., 2016; Colantonio et al., 2014; Cusimano et al., 2021; Deighton et al., 2016; Guinn et al., 2018; Ma et al., 2018; Post et al., 2013; Schneeberger et al., 2012; Song et al., 2018). However, this is the first study that has assessed the relationship between ACEs, conceptualized as a premorbid psychosocial factor, and the aforementioned factors associated with PPCS to aid in better understanding risk for persistent symptoms in adolescents and young adults. The present study aimed to replicate and extend the current literature on factors such as sex, number of previous

mTBI, cognitive reserve, psychiatric factors and premorbid ADHD/LD diagnosis that affect the persistence of symptoms following mTBI, as well as the added influence of ACEs in PPCS.

Relevant Predictors of PPCS

Several predictors that have been reviewed and established in the PPCS literature were examined in the present study, including sex, number of previous mTBI, maternal education (cognitive reserve), psychiatric factors and premorbid ADHD/LD diagnosis. In the current retrospective study, sex was not related to reported PPCS. Literature is mixed with regard to this association, with some reporting that females tend to report a higher number of PPCS due to factors ranging from neck musculature or being more forthcoming in endorsement (Brooke et al., 2014; Rabinowitz et al., 2015; Scopaz & Hatzenbuehler, 2013; Tator et al., 2016). Some have posited, however, that the relationship between sex and reported PPCS may be superficial and that there are no sex differences when considering confounding factors (i.e., mechanism of injury, other sample characteristics); a study by Ponsford and colleagues (2000) noted that females tend to sustain mTBI via motor vehicle accidents, whereas males tended to sustain mTBI via sports injuries. The current finding suggests that, as other researchers have posited, there is no relationship between sex and reported PPCS.

However, within the sample, females experienced their mTBI at a younger age. Additionally, while number of ACEs was not significantly different between sexes, it approached a medium effect size, d = -.41. This suggests that with a larger sample size, a possible sex difference in ACEs may have been detected; prior research has found sex differences where females tend to report a higher number of ACEs, particularly sexual abuse (Alcalá et al., 2017; Sieben et al., 2019; Winstanley et al., 2020). Furthermore, those who reported sexual abuse were

more likely to fall into a high ACEs (i.e., four or more) category, and report emotional and physical abuse (Cavanaugh et al., 2015).

Number of previous mTBI was also not significantly related to reported PPCS; similar to sex, literature regarding previous mTBI as a predictor of later PPCS is mixed. Most studies evaluating this relationship have been within the context of sports medicine, with some studies finding that repetitive mTBI is associated with increased symptom prevalence, longer symptom resolution and minor long-term cognitive complaints (Pellman et al., 2004; Scopaz & Hatzenbuehler, 2013). Previous mTBI has also been more commonly evaluated within the context of acute symptoms and neurodegenerative conditions, such as chronic traumatic encephalopathy (Polinder et al., 2018; Scopaz & Hatzenbuehler, 2013). However, one meta-analysis found that previous head injury was not a significant predictor of PPCS and 23.1% of individuals within the study had no prior history of head injury, leading Tator and colleagues (2016) to suggest that confounding factors may be playing a role in the relationship between previous mTBI and PPCS. Our current finding that previous mTBI was not related to reported PPCS illustrates the need for further research in non-athlete populations and that the relationship may not be generalizable outside of athlete populations.

Notably, a higher number of previous mTBI was related to a higher number of ACEs. This finding was consistent with the nine studies that have evaluated the relationship between ACEs and TBI (Brewer-Smyth et al., 2016; Colantonio et al., 2014; Cusimano et al., 2021; Deighton et al., 2016; Guinn et al., 2018; Ma et al., 2018; Post et al., 2013; Schneeberger et al., 2012; Song et al., 2018). This is the first study that has evaluated the relationship between ACEs and specifically mTBI, rather than TBI across severities, suggesting that with replication, mTBI plays a role in driving the relationship. Although the population of the current study (i.e.,

adolescents and young adults) does not overlap with regard to characteristics of the recruited populations in the prior studies (i.e., homeless, foster care, and prison populations), adolescents may still be considered a vulnerable population as their access to resources is mediated by a parent/caregiver figure (Brewer-Smyth et al., 2016; Colantonio et al., 2014; Cusimano et al., 2021; Song et al., 2018). Future research with other populations (e.g., middle and older adult) may aid in generalizability of these findings.

Cognitive reserve has been well studied across different age populations with regard to mTBI and TBI outcomes in the pediatric and adolescent populations. Literature indicates that those with higher cognitive reserve have better outcomes at one-month post-mTBI (Steward et al., 2018). Another study by Fay and colleagues (2011) found cognitive reserve was a moderator of outcomes in mTBI in children and adolescents. Thus, I hypothesized that higher cognitive reserve would be associated with fewer reported PPCS following injury. Within the current retrospective study, maternal education was used as a proxy for cognitive reserve, which has been established as a proxy within pediatric populations (Donders & Kim, 2019). Maternal education was not related to reported PPCS, but higher years of maternal education was related to lower reported acute symptoms. Notably, cognitive reserve is a complex construct that cannot be directly measured (Bigler & Stern, 2015). Maternal education encapsulates a wide variety of strongly connected relationships, including parent and child IQ, socioeconomic status (e.g., access to and quality of healthcare) and enriched environmental opportunities (Kesler et al., 2010). It is possible that maternal education captures a separate facet of cognitive reserve compared to a direct measurement of a child's cognitive reserve (e.g., full-scale IQ, verbal skills, etc.). Furthermore, given that maternal education was significantly associated with acute

symptoms, but not PPCS, unique factors may be driving the report of these symptoms at different points in the recovery course.

Psychiatric factors are another well-studied predictor of PPCS. Studies have indicated that both premorbid and concurrent psychiatric illnesses affect persistence of symptoms following mTBI (Broshek et al., 2015; Bryant et al., 2010; Finoff et al., 2011; Polinder et al., 2018; Ponsford et al., 2012; Reuben et al., 2014; Stein et al., 2017). I hypothesized that anxiety and/or depression at the time of the evaluation would be associated with higher reported PPCS. Consistent with the hypothesis and replicating previous literature, higher parent-reported anxiety and depressive symptoms were related to higher number of reported PPCS. However, a temporal relationship cannot be reliably established using the current cross-sectional study design. Thus, it remains a possibility that the finding reflects psychiatric symptoms developed as a result of the most recent mTBI. For example, literature has indicated that mTBI versus more severe TBI is associated with posttraumatic stress symptoms due to longer durations of impaired consciousness (Bryant, 2011).

Interestingly, self-reported anxiety and depressive symptoms were not related to reported PPCS. Studies have indicated that children ages five and over can provide valid and reliable self-report (Conjin et al., 2019; Limbers et al., 2008; Varni et al., 2007). These findings may be explained by the specific sample characteristics of this study, with age of participants ranging from 10 to 22 years and a mean age of 16.45 years. Several of the participants presented to their neuropsychological assessment appointments with their parents; motivation for evaluation may have been primarily driven by a parent's concern for a child's symptoms, rather than by the child themselves. However, given that most children/adolescents seek medical care due to the

motivation of their caretaker, another possibility is that children/adolescents who sustained mTBI within the context of sports are minimizing symptoms due to a motivation to return to play.

A history of learning disorder (LD) or attention-deficit/hyperactivity disorder (ADHD) has also been documented to increase risk of mTBI and PPCS, and those who were diagnosed were two to three times more likely to have a history of multiple mTBI (Bernard et al., 2016; Biederman et al., 2015; Finnoff et al., 2011; Nelson et al., 2016a). For the present study, we hypothesized that individuals who were diagnosed with ADHD and/or LD prior to mTBI were more likely to report a higher number of symptoms following injury; those who were diagnosed with ADHD and/or LD did not report significantly higher PPCS. This was most likely due to having an underpowered sample. Additionally, individuals with premorbid ADHD and/or LD may be underreporting PPCS, particularly cognitive symptoms (i.e., attention and memory difficulties), if they attribute them to premorbid conditions rather than injury (APA, 2013).

This is the first study to have assessed the relationship between number of reported ACEs and PPCS. Findings suggest that number of reported ACEs was not related to reported PPCS. However, in our exploratory analyses, a higher number of ACEs was related to a higher number of reported acute symptoms. While there is no literature specifically evaluating these relationships with PPCS and acute symptoms, respectively, research suggests that individuals with a history of trauma are more likely to report somatic symptoms (Gupta, 2012; Kealy et al., 2018; Kugler et al., 2012; Loeb et al., 2018). ACEs also provide early life stress that can affect brain development in regions such as the temporal and frontal lobes–regions that are most likely to be disturbed when sustaining mTBI (Giza & Hovda, 2001; Guinosso et al., 2016; Hanson et al., 2014; Pechtel & Pizzagalli, 2011). This early life stress can affect development and have a downstream effect on cognitive, affective, and behavioral functioning. ACE literature suggests

that exposure to ACEs is associated with mood disorders (i.e., anxiety and depression) and externalizing behavior problems in adolescents and adults (Elmore & Crouch, 2020; Kealy et al., 2018; Lee at al., 2020; McLaughlin, 2017; van Nierop et al., 2014). Cognitive issues have also been noted, such as poorer attention, generally worse memory functioning, and poorer development of executive functioning over time (Bücker et al., 2012; Pechtel & Pizzagalli, 2011; Guinosso et al., 2016). These cognitive, affective, and behavioral issues overlap with symptoms following mTBI, such as attention/memory problems, irritability, feeling "on edge," and feeling down (Katz et al., 2015; Lajiness-O'Neill et al., 2017; Prince & Bruhns, 2017). Although further research is imperative to better understand these relationships, it is possible that individuals with ACEs are reporting more somatic symptoms during the acute stage, and attributing other symptoms (affective, cognitive) to factors other than mTBI as there is an increase in time post-injury.

Influence of ACEs as a Predictor of PPCS

The second aim of this investigation was to enhance our understanding of the relationship between commonly researched predictors of PPCS and the influence of ACEs. As discussed in the previous section, findings from the current study indicated that parent-reported anxiety and depressive symptoms were related to reported PPCS. However, ACEs did not add significant variance in PPCS outcomes when examining its contribution with parent-reported anxiety and depressive symptoms to PPCS outcome. Although there is a lack of literature specifically evaluating these relationships, literature indicates that individuals with a trauma history tend to endorse somatic symptoms, and that ACEs can have downstream effects on cognitive, emotional, and behavioral functioning (Bücker et al., 2012; Guinosso et al., 2016; Gupta, 2012; Hanson et al., 2014; Kugler et al., 2012; Lee et al., 2020; Loeb et al., 2018; McLaughlin, 2017; Pechtel &

Pizzagalli, 2011; van Nierop et al., 2014). The current findings underscore the need for further research in assessing the relationships and mechanisms of ACEs versus anxiety/depression as predictors of PPCS.

Exploratory analyses also indicated that maternal education and ACEs were related to reported acute symptoms. As previously discussed, lower maternal education (cognitive reserve) was related to higher reported acute symptoms, and higher reported ACEs were also related to higher reported acute symptoms. However, neither maternal education nor ACEs predicted reported PPCS. While many studies have evaluated the relationship between cognitive reserve and persistent symptoms, there is no literature that has explored the relationship between cognitive reserve, or ACEs, and acute symptoms. With replication, maternal education and ACEs may be related to acute symptoms if it reflects the individual having sustained a more severe mTBI. Overall, current findings underscore the need to further explore these two constructs (i.e., cognitive reserve and ACEs) and their relationship to acute symptoms, as addressing acute symptoms may aid in preventing later PPCS.

Conversely, while much of ACEs research is focused on trauma, there is emerging literature regarding ACEs and resilience, or factors that potentially provide a buffer to toxic stress. Individuals within the current sample may have several protective factors such as parent engagement and community-level factors (i.e., safe neighborhood, safe school, and religious engagements), and thus, ACEs may not be an adequate construct (Soleimanpour et al., 2017). While operationalization of ACEs in the current study was considered a limitation, it is also possible that ACEs were underreported in the sample because families did not consider some ACE events to be traumatic.

Overall, several of the current findings were not consistent with the mTBI/PPCS literature. Parent-reported anxiety and depressive problems were associated with reported PPCS, but a temporal relationship cannot be established, and it is possible that the most recent mTBI played a role in the assessed anxiety and depressive problems. ACEs did not add significant variance to the relationship between parent-reported psychiatric factors and PPCS, but further examination of ACEs suggests that, like mTBI and PPCS, it is a fairly complex construct that can be difficult to capture. ACEs are merely a reflection of adversity but do not accurately reflect the experiences of trauma or resilience within an individual's life.

Implications

When considering the current findings within the context of clinical applicability, physicians and other healthcare providers alike may benefit from having a parent-report completed (i.e., ASEBA CBCL) in the acute stages post-mTBI to assess for a child's psychiatric factors, which may assist in predicting risk for later PPCS. Perhaps additional education or addressing underlying psychiatric factors as preventative care, in conjunction with standard clinical care, may be beneficial.

ACEs were also related to acute symptoms, where higher reported ACEs were related to higher reported acute symptoms. An individual who reports a higher number of symptoms shortly following their mTBI may give clinicians a clue to further assess for ACEs and potentially identify someone who may benefit from further specialized care and treatment.

ACEs may also be another consideration in individuals who are already experiencing PPCS or even for those who report them during the acute stages following mTBI. While the current findings do not support the notion that ACEs influence PPCS, previous literature suggests that individuals who have experienced trauma experience several types of symptoms

that overlap with PPCS (Bücker et al., 2012; Guinosso et al., 2016; Gupta, 2012; Hanson et al., 2014; Katz et al., 2015; Kugler et al., 2012; Lajiness-O'Neill et al., 2017; Lee et al., 2020; Loeb et al., 2018; Pechtel & Pizzagalli, 2011; Prince & Bruhns, 2017; McLaughlin, 2017; van Nierop et al., 2014). If an individual endorses ACEs during their PPCS follow-up appointments, it may be beneficial for trauma-related treatment to be incorporated into their care. Newer interventions have arisen in the ACEs literature, such as the "ACE overcomer's program," which is a 12-week-long, group therapy that includes homework assignments (Cameron et al., 2018). During a phase II trial, Cameron and colleagues (2018) found that individuals who completed the program had significant improvement in emotion regulation, psychological resilience, mental well-being, physical symptoms/illness, and aspects of quality of life; this inspires further areas of potential research and treatment for those who experience ACEs and PPCS. Developing and nurturing these skills are beneficial, regardless of ACE's role in acute symptoms or PPCS.

Limitations

While several limitations can arise within a retrospective study design, a main limitation in the current study was the method of operationalizing ACEs. ACEs were collected from information provided throughout the neuropsychological evaluation reports, as well as from one question in the parent history questionnaire; these were later tabulated into a frequency count. There was no explicit ACE questionnaire that was provided to patients and thus, several experiences may have been overlooked, resulting in an overall underreporting of ACEs in our sample. This may partly explain why ACEs was not a significant predictor in several of the analyses.

Additionally, the small number of participants is another limitation of the current study, contributing to an overall lack of power in the statistical analyses. An apriori power analysis

indicated a group of at least 65 were needed to detect a moderate effect; Field (2018) also reported that one should always have a sample size of about 55, and a sample size of 100 should suffice with up to six predictors. Lastly, an overarching limitation in mTBI and PPCS research is the heterogeneity of definitions, likely further contributing to inconsistencies in literature. There is currently no consensus definition or criteria that spans across medical fields (Mayer et al., 2017). One study found over 35 definitions for mTBI in their review of accepted studies alone; while there are four commonly utilized and cited definitions/criteria, each organization places emphasis on different symptoms to diagnose mTBI (see Table 2 for details; Katz et al., 2015; Kristman et al., 2014; Silverberg et al., 2016).

In addition to the lack of a consensus definition/criteria for mTBI, there is also the inherent heterogeneity of the condition. Some definitions and research include the GCS score, LOC, and PTA; what is the difference between two individuals who both have a GCS of 15, normal imaging, LOC, but different durations of PTA? What is the difference between an individual who barely meets criteria for mTBI, versus an individual who is at the ceiling of the definition? Mechanism of injury can also vary, ranging from whiplash, sports, motor vehicle accidents, falls, or physical assault (Azouvi et al., 2017; Roozenbeek et al., 2009).

The definition of PPCS faces similar issues; to date, there is no consensus definition or criteria for the group of symptoms and the three most widely cited definitions emphasize different aspects of clinical presentation (see Table 3 for details; APA, 2013; WHO, 1992). Several utilize the definition provided by the ICD-10, but a lack of guidance regarding duration of symptoms has led to idiosyncratic interpretations among clinicians and researchers (Rose et al., 2015). Some studies will consider symptoms as persistent or chronic at four weeks post-injury, while others utilize a three-month post-injury criteria (Bergersen et al., 2017). On one

expert consensus statement on sports-related mTBI, symptoms lasting more than 10 days were considered persistent (McCrory et al., 2018; Rose et al., 2015). Creating a consensus definition would allow for less variation among studies and thus, opportunities for data synthesis.

Future Directions

The current study used retrospective data collection and a cross-sectional design to replicate and extend the current literature on factors such as sex, number of previous mTBI, cognitive reserve, psychiatric factors and premorbid ADHD/LD diagnosis, that affect the persistence of symptoms following mTBI, as well as the added influence of ACEs in PPCS. To date, only nine studies have evaluated the relationship between ACEs and TBI; this was the first study to evaluate the relationship between ACEs, mTBI and PPCS. However, all studies used a cross-sectional design and only correlational relationships could be established. Future investigations may utilize prospective data collection and a longitudinal design, such as the originally proposed study design, in order to establish a temporal relationship between ACEs and subsequent mTBI. Additionally, there is generally a lack of literature evaluating the relationship between ACEs and mTBI; much of the current sample captures participants who may still be experiencing ongoing ACEs due to their age (under 18). Future research should also seek to separate and to understand the effects that ACEs may have on mTBI, and subsequent PPCS, based on an individual's age.

With regard to ACEs research, several studies evaluated ACEs as one construct, combining several disparate social experiences such as exposure to violence, household dysfunction, and abuse. While the majority of the literature still evaluates ACEs in the form of a frequency count, some studies have started to group ACEs into types of experiences (e.g., abuse, household dysfunction, community violence, etc.), acknowledging their differential impact and

that not all ACEs have the same effect (Hughes et al., 2017; Trotta et al, 2015). Future research could benefit from separating ACEs to better understand the differential impact that each play in the persistence of symptoms post-mTBI. Separating the construct in this way may also allow for elucidating particularly synergistic combinations of ACEs in PPCS.

Trauma research has also indicated that individuals who have experienced trauma report higher somatic complaints (Loeb et al., 2018). Similar to separating ACEs into different constructs, it may prove valuable to separate PPCS into separate constructs as well. While several studies have sought to separate symptoms into categories such as somatic, affective, and cognitive, this has not been done specifically within the context of ACEs and PPCS research.

An additional factor that should be considered, briefly mentioned earlier in the discussion, is that adversity and trauma are not synonymous–that is, not all ACEs are traumatic. Depending on an individual's resources and coping skills, several buffering factors may play a role in increasing resilience. With the acquisition of a larger sample size, an aforementioned limitation, more complex statistical analyses such as moderation analyses could be computed. Rather than evaluating whether ACEs adds significant variance to established predictors of PPCS, ACEs may provide an interaction effect that is dependent upon an interplay of risk and protective factors.

Conclusion

Literature indicates that PPCS is a highly heterogeneous, complex condition that is the result of interaction among several biopsychosocial factors. Adverse childhood experiences may be an additional psychosocial factor that plays into the risk and persistence of symptoms following mTBI. The current study indicated a significant relationship between parent-reported psychiatric factors (i.e., anxiety and depression) and PPCS, while ACEs did not contribute

significant variance. Additionally, exploratory analyses demonstrated a significant positive relationship between ACEs and acute symptoms, ACEs and previous mTBI, and a significant negative relationship between maternal education and acute symptoms. A central issue with mTBI/PPCS literature, leading to mixed results, is the lack of standardized definitions and the inherent heterogeneity of mTBI. Additionally, the current findings indicate that ACEs may also be a potentially complex construct that needs to be further deconstructed into different experiences (i.e., abuse, neglect, and household dysfunction); the interplay of trauma and resilience should also be considered. Meanwhile, clinicians may benefit in assessing current psychiatric factors and ACEs when treating an individual who has sustained mTBI to identify potential risk of persistent symptoms. Incorporating relevant interventions (i.e., trauma-focused intervention) into the individual's treatment plan may also provide a buffer in persisting symptoms.

References

Achenbach, T. M., & Rescorla, L. A. (2001). *Manual for the ASEBA school-age forms & profiles*. University of Vermont, Research Center for Children, Youth, & Families.

Achenbach, T. M., & Rescorla, L. A. (2003). *Manual for the ASEBA adult forms & profiles.* University of Vermont, Research Center for Children, Youth, & Families.

Alcala, H.E., Tomiyama, A.J., & von Ehrenstein, O.S. (2017). Gender differences in the association between adverse childhood experiences and cancer. *Womens Health Issues, 27*(6), 625-631. 10.1016/j.whi.2017.06.002

Alla, S., Sullivan, S. J., Hale, L., & McCrory, P. (2009). Self-report scales/checklists for the measurement of concussion symptoms: A systematic review. *British Journal of Sports Medicine*, *43*(Suppl I), i3–i12. https://doi.org/10.1136/bjsm.2009.058339

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders: DSM-5* (5th ed.). American Psychiatric Publishing.

Andriessen, T. M. J. C., Jacobs, B., & Vos, P. E. (2010). Clinical characteristics and pathophysiological mechanisms of focal and diffuse traumatic brain injury. *Journal of Cellular and Molecular Medicine*, *14*(10), 2381–2392. https://doi.org/10.1111/j.1582-4934.2010.01164.x

Asken, B. M., Dekosky, S. T., Clugston, J. R., Jaffee, M. S., & Bauer, R. M. (2018). Diffusion tensor imaging (DTI) findings in adult civilian, military, and sport-related mild traumatic brain injury (mTBI): A systematic critical review. *Brain Imaging and Behavior*, *12*, 585–612. https://doi.org/10.1007/s11682-017-9708-9

Askew, R. L., Cook, K. F., Revicki, D. A., Cella, D., & Amtmann, D. (2016). Clinical validity of PROMIS pain interference and pain behavior in diverse clinical populations. *Journal of*

Clinical Epidemiology, 73, 103-111.

Azouvi, P., Arnould, A., Dromer, E., & Vallat-Azouvi, C. (2017). Neuropsychology of traumatic brain injury: An expert overview. *Revue Neruologique*, *173*, 461–472.

Babikian, T., McArthur, D., & Asarnow, R. F., (2013). Predictors of 1-month and 1-year neurocognitive functioning from the UCLA longitudinal mild, uncomplicated, pediatric traumatic brain injury study. *Journal of the International Neuropsychological Society*, *19*(2), 145-154.

Barlow, K. M. (2016). Postconcussion syndrome: A review. *Journal of Child Neurology*, *31*(1), 57–67. https://doi.org/10.1177/0883073814543305

Bazarian, J., Pope, C., McClung, J., Cheng, Y. T., & Flesher, W. (2003). Ethnic and racial disparities in emergency department care for mild traumatic brain injury. *Academic Emergency Medicine*, *10*(11), 1209–1217. https://doi.org/10.1197/S1069-6563(03)00491-3

Belanger, H. G., Curtiss, G., Demery, J. A., Lebowitz, B. K., & Vanderploeg, R. D. (2005). Factors moderating neuropsychological outcomes following mild traumatic brain injury: A meta-analysis. *Journal of the International Neuropsychological Society*, *11*, 215–277. https://doi.org/10.1017/S1355617705050277

Belsley, D. A., Kuh, E., & Welsch, R. E. (1980). *Regression diagnostics: Identifying influential data and sources of collinearity*. John Wiley and Sons.

Bergersen, K., Halvorsen, Ø., Tryti, A., Taylor, I., & Olsen, A. (2017). A systematic literature review of psychotherapeutic treatment of prolonged symptoms after mild traumatic brain injury. *Brain Injury*, *31*(3), 279–289. https://doi.org/10.1080/02699052.2016.1255779

Bernard, C. O., Ponsford, J. A., McKinlay, A., McKenzie, D., & Krieser, D. (2016). Predictors of post-concussive symptoms in young children: Injury versus non-injury related factors.

Journal of the International Neuropsychological Society, *22*(8), 793-803.

Bertisch, H., Rivara, F. P., Kisala, P.A., Wang, J., Yeates, K.O., Durbin, D., Zonfrillo, M. R., Bell, M. J., Temkin, N., & Tulsky, D.S. (2017). Psychometric evaluation of the pediatric and parent-proxy patient-reported outcomes measurement information system and the neurology and traumatic brain injury quality of life measurement item banks in pediatric traumatic brain injury. *Quality of Life Research, 26*(7), 1887-1889.

Bertisch, H., Satris, G., Temkin, N., Barber, J., & Manley, G. T. (2018). Rehabilitation trajectories and outcomes in individuals with mild traumatic brain injury and psychiatric histories. *Journal of Head Trauma Rehabilitation*, *34*(1), 1. https://doi.org/10.1097/HTR.0000000000000399

Biederman, J., Feinberg, L., Chan, J., Adeyemo, B. O., Woodworth, K. Y., Panis, W., McGrath, N., Bhatnagar, S., Spencer, T. J., Uchiga, M., Kenworthy, T., Grossman, R., Zafonte, R., & Faraone, S. V. (2015). Mild traumatic brain injury and attention-deficit hyperactivity disorder in young student athletes. *Journal of Nervouse and Mental Disease, 203*(11), 813-819.

Bigler, E. D., & Stern, Y. (2015). Traumatic brain injury and reserve. In J. Grafman & A. M. Salazar (Eds.), *Handbook of clinicalnNeurology* (pp. 691–710). Elsevier B.V. Retrieved from https://illiad.emich.edu/illiad/illiad.dll?Action=10&Form=75&Value=321600

Binder, L. M., Rohling, M. L., & Larrabee, G. J. (1997). A review of mild head trauma. part I: Meta-analytic review of neuropsychological studies. *Journal of Clinical and Experimental Neuropsychology*, *19*(3), 421–431. https://doi.org/10.1080/01688639708403870

Boonstra, A. M., Schiphorst Preuper, H. R., Reneman, M. F., Posthumus, J. B., & Stewart, R. E. (2008). Reliability and validity of the visual analogue scale for disability in patients with

chronic musculoskeletal pain. *International Journal of Rehabilitation Research, 31*(2), 165-169.

Borg, J., Holm, L., Peloso, P., Cassidy, J. D., Carroll, L., von Holst, H., Paniak, C., Yates, D., & WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. (2004). Non-surgical intervention and cost for mild traumatic brain injury: Results of the WHO collaborating centre task force on mild traumatic brain injury. *Journal of Rehabilitation Medicine*, *36*(43 Suppl), 76–83.

Borgaro, S. R., Prigatano, G. P., Kwasnica, C., & Rexer, J. L. (2003). Cognitive and affective sequelae in complicated and uncomplicated mild traumatic brain injury. *Brain Injury, 17*(3), 189-198.

Boullier, M., & Blair, M. (2018). Adverse childhood experiences. *Paediatrics and Child Health*, *28*, 132–137. https://doi.org/10.1016/j.paed.2017.12.008

Bowerman, B. L., & O'Connell, R. T. (1990). *Linear statistical models: An applied approach* (2nd ed.). Duxbury.

Brewer-Smyth, K., Pohlig, R. T., & Bucurescu, G. (2016). Female children with incarcerated adult family members at risk for lifelong neurological decline. *Health Care for Women International*, *37*(7), 802–813. https://doi.org/10.1080/07399332.2016.1140768

Brooke, K. D., Horswill, M. S., & Geffen, G. M. (2014). Athlete's age, sex, and years of education moderate the acute neuropsychological impact of sports-related concussion: A meta-analysis. *Journal of the International Neuropsychological Society, 20*(1), 81-87.

Broshek, D. K., De Marci, A. P., & Freeman, J. R. (2015). A review of post-concussion syndrome and psychological factors associated with concussion. *Brain Injury*, *29*(2), 228-237.

Bryant, R. (2011). Post-traumatic stress disorder vs traumatic brain injury. *Dialogues in Clinical Neuroscience, 13*(3), 251-262.

Bryant, R. A., O'Donnell, M. L., Creamer, M., McFarlane, A. C., Clark, C. R., & Silove, D. (2010). The psychiatric sequelae of traumatic injury. *American Journal of Psychiatry*, *167*(3), 312–320. https://doi.org/10.1176/appi.ajp.2009.09050617

Bucci, M., Marques, S. S., Oh, D., & Harris, N. B. (2016). Toxic stress in children and adolescents. *Advances in pediatrics, 63*(1), 403-428. https://doi.org/10.1016/j.yapd.2016.04.002

Bücker, J., Kapczinski, F., Post, R., Cereser, K. M., Szobot, C., Yatham, L. N., Kapczinski, N. S., & Kauer-Sant'Anna, M. (2012). Cognitive impairment in school-aged children with early trauma. *Comprehensive Psychiatry*, *53*(6), 758-764.

Cameron, L. D., Carroll, P., & Hamilton, W. K. (2018). Evaluation of an intervention promoting emotion regulation skills for adults with persisting distress due to adverse childhood experiences. *Child Abuse & Neglect*, *79*, 423–433. https://doi.org/10.1016/j.chiabu.2018.03.002

Carroll, L., Cassidy, J. D., Holm, L., Kraus, J., Coronado, V, & WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. (2004a). Methodological issues and research recommendations for mild traumatic brain injury: The WHO Collaborating Centre Task Force on mild traumatic brain injury. *Journal of Rehabilitation Medicine*, *36*(0), 113–125. https://doi.org/10.1080/16501960410023877

Carroll, L. J., Cassidy, J. D., Peloso, P. M., Borg, J., Von Holst, H., Holm, L., Paniak, C., Pepin, M., & WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. (2004b). Prognosis for mild traumatic brain injury: Results of the WHO Collaborating Centre Task

Force on mild traumatic brain injury. *Journal of Rehabilitation Medicine*, (43 Suppl), 84–105. https://doi.org/10.1080/16501960410023859

Carroll, L. J., David Cassidy, J., Cancelliere, C., Côté, P., Hincapié, C. A., Kristman, V. L., Holm, L. W., Borg, J., Nygren-de Boussard, C., & Hartvigsen, J. (2014). Systematic review of the prognosis after mild traumatic brain injury in adults: Cognitive, psychiatric, and mortality outcomes: Results of the international collaboration on mild traumatic brain injury prognosis. *Archives of Physical Medicine and Rehabilitation*, *95*(3), 152–173. https://doi.org/10.1016/j.apmr.2013.08.300

Cassidy, J. D., Carroll, L. J., Peloso, P. M., Borg, J., Von Holst, H., Holm, L., Kraus, J., Coronado, V. G., & WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. (2004). Incidence, risk factors and prevention of mild traumatic brain injury: Results of the WHO Collaborating Centre Task Force on mild traumatic brain injury. *Journal of Rehabilitation Medicine*, *36*(43 Suppl), 28–60. https://doi.org/10.1080/16501960410023732

Cavanaugh, C. E., Petras, H., & Martins, S. S. (2015). Gender-specific profiles of adverse childhood experiences, past year mental and substance use disorders, and their associations among a national sample of adults in the United States. *Social Psychiatry and Psychiatric Epidemiology*, *50*(8), 1257-1266.

Cella, D., Choi, S. W., Condon, D. M., Schalet, B., Hays, R. D., Rothrock, N. E., Yount, S., Cook, K. F., Gershon, R. C., Amtmann, D., DeWalt, D. A., Pilkonis, P. A., Stone, A. A., Weinfurt, K., & Reeve, B. B. (2019). PROMIS® adult health profiles: efficient short-form measures of seven health domains. *Value in Health, 22*(5), 537-544.

Centers for Disease Control and Prevention. (2018). *Behavioral risk factor surveillance system.* https://www.cdc.gov/brfss/index.html

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Erlbaum.

Colantonio, A. (2016). Sex, gender, and traumatic brain injury: A commentary. *Archives of Physical Medicine and Rehabilitation* https://doi.org/10.1016/j.apmr.2015.12.002

Colantonio, A., Kim, H., Allen, S., Asbridge, M., Petgrave, J., & Brochu, S. (2014). Traumatic brain injury and early life experiences among men and women in a prison population. *Journal of Correctional Health Care*, *20*(4), 271–279. https://doi.org/10.1177/1078345814541529

Collie, A., Maruff, P., Makdissi, M., McCrory, P., McStephen, M., & Darby, D. (2003). CogSport: Reliability and correlation with conventional cognitive tests used in postconcussion medical evaluations. *Clinical Journal of Sports Medicine*, *13*(1), 28–32.

Conjin, J. M., Smits, N., & Hartman, E. E. (2019). Determining at what age children provide sound self-reports: An illustration of the validity-index approach. *Journal of Indexing & Metrics*, *27*(7), 1604-1618.

Covassin, T., Crutcher, B., Bleecker, A., Heiden, E. O. Dailey, A., & Yang, J. (2014). Postinjury anxiety and social support among collegiate athletes: A comparison between orthopaedic injuries and concussions. *Journal of Athletic Training, 49*(4), 462-468.

Cronholm, P. F., Forke, C. M., Wade, R., Bair-Merritt, M. H., Davis, M., Harkins-Schwarz, M., Pachter, L. M., & Fein, J. A. (2015). Adverse childhood experiences: Expanding the concept of adversity. *American Journal of Preventive Medicine*, *49*(3), 354–361. https://doi.org/10.1016/j.amepre.2015.02.001

Cusimano, M. D., Zhang, S., Mei, X. Y., Kennedy, D., Saha, A., Carpino, M., & Wolfe, D. (2021). Traumatic brain injury, abuse, and poor sustained attention in youth and young adults who previously experienced foster care. *Neurotrauma Reports*, *2*(1), 94-102.

De Guise, E., Belanger, S., Tinawi, S., Anderson, K., LeBlanc, J., Lamoureux, J., Audrit, H., & Feyz, M. (2016). Usefulness of the rivermead postconcussion symptoms questionnaire and the trail-making test for outcome prediction in patients with mild traumatic brain injury. *Applied Neuropsychology: Adult, 23*(3), 213-222.

Deighton, S., Buchy, L., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., McGlashan, T. H., Perkins, D. O., Seidman, L. J., Tsuang, M. T., Walker, E. F., Woods, S. W., Bearden, C. E., Mathalon, D., & Addington, J. (2016). Traumatic brain injury in individuals at clinical high risk for psychosis. *Schizophrenia Research*, *174*(174), 77–81. https://doi.org/10.1016/j.schres.2016.04.041

Derogatis, L. R. (2001). *Brief Symptom Inventory (BSI) 18 Administration, scoring, and procedures manual*. NCS Pearson.

Dikmen, S., McLean, A., & Temkin, N. (1986). Neuropsychological and psychosocial consequences of minor head injury. *Journal of Neurology, Neurosurgery, and Psychiatry*, *49*, 1227–1232. https://www-ncbi-nlm-nih-gov.proxy.lib.umich.edu/pmc/articles/PMC1029069/pdf/jnnpsyc00103-0015.pdf

Donders, J., & Kim, E., (2019). Effect of cognitive reserve on children with traumatic brain injury. *Journal of the International Neuropsychological Society*, *25*(4), 355-361. https://doi.org/10.1017/S1355617719000109

Dretsch, M. N., Williams, K., Emmerich, T., Crynen, G., Ait-Ghezala, G., Chaytow, H., Mathura, V., Crawford, F., C., & Iverson, G., L. (2015). Brain-derived neurotropic factor polymorphisms, traumatic stress, mild traumatic brain injury, and combat exposure contribute to postdeployment traumatic stress. *Brain and Behavior, 6*(1), 1-12.

Dube, S. R., Williamson, D. F., Thompson, T., Felitti, V. J., & Anda, R. F. (2004). Assessing the

reliability of retrospective reports of adverse childhood experiences among adult HMO members attending a primary care clinic. *Child Abuse & Neglect*, *28*, 729–737. https://doi.org/10.1016/j.chiabu.2003.08.009

Echemendia, R. J., Meeuwisse, W., Mccrory, P., Davis, G. A., Putukian, M., Leddy, J., Makdissi, M., Sullivan, S. J., Broglio, S. P., Raftery, M., Schneider, K., Kissick, J., McCrea, M., Dvorak, J., Sills, A. K., Aubry, M., Engebretsen, L., Loosemore, M., Fuller, G., Kutcher, J., … Herring, S. (2017). The Sport Concussion Assessment Tool 5th edition (SCAT5). *British Journal of Sports Medicine*, *51*(11), 848-850. https://doi.org/10.1136/bjsports-2017-097506

Elmore, A. L., & Crouch, E. (2020). The association of adverse childhood experiences with anxiety and depression for children and youth, 8 to 17 years of age. *Academic Pediatrics*, *20*(5), 600-608.

Essex, M. J., Shirtcliff, E. A., Burk, L. R., Ruttle, P. L., Klein, M. H., Slattery, M. J., Kalin, N.H., & Armstrong, J. M. (2012). Influence of early life stress on later hypothalamic-pituitary-adrenal axis functioning and its covariation with mental health symptoms: A study of the allostatic process from childhood into adolescence. *Devleopmental Psychopathology, 23*(4), 1039-1058.

Faul, M., & Coronado, V. (2015). Epidemiology of traumatic brain injury. In J. Grafman & A. M. Salazar (Eds.), *Handbook of clinical neurology* (Vol. 127, pp. 3–13). Elsevier B.V. https://doi.org/10.1016/B978-0-444-52892-6.00001-5

Faul, F., Erdfelder, E., Lang, A., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behaviora, and biomedical sciences. *Behavioral Research Methods, 39*(2), 175-191.

Fay, T. B., Yeates, K. O., Taylor, H. G., Bangert, B., Dietrich, A., Nuss, K. E., Rusin, J., & Wright, M. (2011). Cognitive reserve as a moderator of postconcussive symptoms in children with complicated and uncomplicated mild traumatic brain injury. *Journal of the International Neuropsychological Society, 16*(1), 94-105.

Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V., Koss, M. P., Marks, J. S. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. *American Journal of Preventive Medicine*, *14*(4), 245–258. https://doi.org/10.1016/S0749-3797(98)00017-8

Field, A. (2018). *Discovering statistics using IBM SPSS statistics* (5th ed.). London: SAGE Publications Ltd.

Finnoff, J. T., Jelsing, E. J., & Smith, J. (2011). Biomarkers, genetics, and risk factors for concussion. *PM&R, 3(*10 Suppl 2), S452-S459.

Forrest, C. B., Devine, J., Bevans, K. B., Becker, B. D., Carle, A. C., Teneralli, R. E., Moon, J., Tucker, C. A., & Ravens-Sieberer, U. (2017). Development and psychometric evaluation of the PROMIS pediatric life satisfaction item banks, child-report, and parent-proxy editions. *Quality of Life Research, 27*(1), 217-234.

Friedland, D. (2015, April). Postconcussion syndrome/disorder or mild traumatic brain injury: diagnostic issues and treatment. https://www.acnr.co.uk/2015/04/postconcussion-syndromedisorder-or-mild-traumatic-brain-injury-diagnostic-issues-and-treatment/

Frost, R. B., Farrer, T. J., Primosch, M., & Hedges, D. W. (2013). Prevalence of traumatic brain injury in the general adult population: A meta-analysis. *Neuroepidemiology*, *40*, 154–159. https://doi.org/10.1159/000343275

Gallagher, E. J., Bijur, P. E., Latimer, C., & Silver, W. Reliability and validity of a visual analog

scale for acute abdominal pain in the ED. *American Journal of Emergency Medicine, 20*(4), 287-290.

Ganti, L., Khalid, H., Patel, S., Daneshvar, Y., Bodhit, A. N., & Peters, K. R. (2014). Who gets post-concussion syndrome? An emergency department-based prospective analysis. *International Journal of Emergency Medicine*, *7*(31), 1–7. https://doi.org/10.1186/s12245-014-0031-6

Gillihan, S. J., Aderka, I. M., Conklin, P. H., Capaldi, S., & Foa, E. B. (2013). The Child PTSD Symptom Scale: Psychometric properties in female adolescent sexual assault survivors. *Journal of Psychological Assessment, 25*(1), 23-21.

Giza, C. C., & Hovda, D. A. (2001). The Neurometabolic cascade of concussion. *Journal of Athletic Training*, *36*(3), 228–235. http://www.ncbi.nlm.nih.gov/pubmed/12937489%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC155411

Graves, J. M., Rivara, F., P., & Vavilala, M. S. (2015). Health care costs 1 year after pediatric traumatic brain injury. *American Journal of Public Health, 105*(10), 35-41.

Greenwald, B. D., Ambrose, A. F., & Armstrong, G. P. (2012). Editorial: Mild brain injury. *Rehabilitation Research and Practice*, *2012*. https://doi.org/10.1155/2012/469475

Grool, A. M., Aglipay, M., Momoli, F., Meehan, W. P., Freedman, S. B., Yeates, K. O., Gravel, J., Gagnon, I., Boutis, K., Meeuwisse, W., Barrowman, N., Ledoux, A., Osmond, M. H., Zemek, R., & Pediatric Emergency Research Canada (PERC) Concussion Team. (2016). Association between early participation in physical activity following acute concussion and persistent postconcussive symptoms in children and adolescents. *Journal of the American Medical Association, 316*(23), 2504-2514

Gupta, M. A. (2012). Review of somatic symptoms in post-traumatic stress disorder. *International Review of Psychiatry*, *25*(1), 86-99. https://doi.org/10.3109/09540261.2012.736367

Guinn, A. S., Ports, K. A., Ford, D. C., Breiding, M., & Merrick, M. T. (2018). Associations between adverse childhood experiences and acquired brain injury, including traumatic brain injuries, among adults: 2014 BRFSS North Carolina. *Injury Prevention*, *0*, 1–7. https://doi.org/10.1360/zd-2013-43-6-1064

Guinosso, S. A., Johnson, S. B., & Riley, A. W. (2016). Multiple adverse experiences and child cognitive development. *Pediatric Research*, *79*(1–2), 220–226. https://doi.org/10.1038/pr.2015.195

Hadanny, A., & Efrati, S. (2016). Treatment of persistent post-concussion syndrome due to mild traumatic brain injury: current status and future directions. *Expert Review of Neurotherapeutics*, *16*(8), 875–887. https://doi.org/10.1080/14737175.2016.1205487

Hampshire A., MacDonald, A., & Owen, A.M. (2013). Hypoconnectivity and hyperfrontality in retired American football players. *Scientific Reports, 3*, doi: 10.1038/srep02972.

Hanson, J. L., Nacewicz, B. M., Sutterer, M. J., Cayo, A. A., Schaefer, S. M., Rudolph, K. D., Shirtcliff, E. A., Pollak, S. D., & Davidson, R. J. (2014). Behavior problems after early life stress: Contributions of the hippocampus and amygdala. *Biological Psychiatry*, *77*(4), 314–323. https://doi.org/10.1016/j.biopsych.2014.04.020

Hart Jr., J., Kraut, M. A., Womack, K. B., Strain, J., Didehbani, N., Bartz, E., Conover, H., Mansinghani, S., Hanzhang, L., & Cullum, C. M. (2013). Neuroimaging of cognitive dysfunction and depression in aging retired National Football League players: A cross-sectional study. *JAMA Neurology, 70*(3), 326-335.

Hays, R. D., Spritzer, K. L., Schalet, B. D., & Cella, D. (2018). PROMIS®-29 v2.0 profile physical and mental health summary scores. *Quality of Life Research, 27*(7), 1885-1891.

Henrie, M., & Elovic, E. P. (2016). Selected somatic disorders associated with mild traumatic brain injury: Fatigue, dizziness and balance impairment, and whiplash injury. In F. S. Zollman (Ed.), *Manual of traumatic brain injury: Assessment and management* (2nd ed., pp. 100–108). Demos Medical Publishing.

Holmes, T. H., & Rahe, R. H. (1967). The social readjustment rating scale. Journal of *Psychosomatic Research*, *11*(2), 213-218. https://doi.org/10.1016/0022-3999(67)90010-4

Hughes, K., Bellis, M. A., Hardcastle, K. A., Sethi, D., Butchart, A., Mikton, C., Jones, L., & Dunne, M. P. (2017). The effect of multiple adverse childhood experiences on health: A systematic review and meta-analysis. *The Lancet: Public Health, 2*(8), e356-e366. https://doi.org/10.1016/S2468-2667(17)30118-4

Huskisson, E. C. (1974). Measurement of pain. *The Lancet, 2*(7889), 1127-1131.

Iaccarino, M. A., & Zafonte, R. (2016). Sport-related concussion II: Managing the injured athlete and return-to-play decision making. In F. S. Zollman (Ed.), *Manual of traumatic brain injury: Assessment and management* (2nd ed., pp. 65–70). Demos Medical Publishing.

Iverson, G. L., & Lange, R. T. (2011). Mild traumatic brain injury. In M. R. Schoenberg & J. G. Scott (Eds.), *The little black book of neuropsychology: A syndrome-based approach* (pp. 697–719). Springer Science+Business Media, LLC.

Iverson, G. L., Silverberg, N. D., & Lange, R. T. (2016). The natural history of mild traumatic brain injury. In F. S. Zollman (Ed.), *Manual of traumatic brain injury: Assessment and management* (2nd ed., pp. 59–64). Demos Medical Publishing.

Juruena, M. F., Eror, F., Cleare, A. J., & Young, A. H. (2020). The role of early life stress in

HPA axis and anxiety. *Advances in Experimental Medicine and Biology,* 1191, 141-153.

Kashluba, S., Hanks, R. A., Casey, J. E., & Millis, S. R. (2008). Neuropsychologic and functional outcome after complicated mild traumatic brain injury. *Archives of Physical Medicine and Rehabilitaiton, 89*(5), 904-911.

Kashluba, S., Paniak, C., & Casey, J. E. (2007). Persistent symptoms associated with factors identified by the WHO Task Force on mild traumatic brain injury. *The Clinical Neuropsychologist, 22*(2), https://doi.org/10.1080/13854040701263655.

Katz, D. I., Cohen, S. I., & Alexander, M. P. (2015). Mild traumatic brain injury. In J. Grafman & A. M. Salazar (Eds.), *Handbook of clinical neurology* (3rd ed., pp. 131–156). Elsevier B.V. https://doi.org/10.1016/B978-0-444-52892-6.00009-X

Kaya, F., Delen, E., & Bulut, O. (2012). Test review: Shipley-2 manual. *Journal of Psychoeducational Assessment, 30*(6), 593-597.

Kealy, D., Rice, S. M., Ogrodniczuk, J. S., & Spidel, A. (2018). Childhood trauma and somatic symptoms among psychiatric outpatients: Investigating the role of shame and guilt. *Psychiatry Research*, *268*, 169-174. https://doi.org/10.1016/j.psychres.2018.06.072

Kenzie, E. S., Parks, E. L., Bigler, E. D., Lim, M. M., Chesnutt, J. C., & Wakeland, W. (2017). Concussion as a multi-scale complex system: An interdisciplinary synthesis of current knowledge. *Frontiers in Neurology*, *8*, 1–17. https://doi.org/10.3389/fneur.2017.00513

Kesler, S. R., Tanaka, H., & Koovakkattu, D. (2010). Cognitive reserve and brain volumes in pediatric acute lymphoblasic leukemia. *Brain Imaging and Behavior, 4*(3-4), 256-269.

King, N. S., Crawford, S., Wenden, F. J., Moss, N. E., & Wade, D. T. (1995). The rivermead post concussion symptoms questionnaire: A measure of symptoms commonly experienced after head injury and its reliability. *Journal of Neurology, 242*, 587-592.

Kolb, B., & Whishaw, I. Q. (2015). *Fundamentals of Human Neuropsychology* (7th ed.). Worth Publishers.

Korotana, L. M., Dobson, K. S., Pusch, D., & Josephson, T. (2016). A review of primary care interventions to improve health outcomes in adult survivors of adverse childhood experiences. *Clinical Psychology Review*, *46*, 59–90. https://doi.org/10.1016/j.cpr.2016.04.007

Kristman, V. L., Borg, J., Godbolt, A. K., Rachid Salmi, L., Cancelliere, C., Carroll, L. J., Holm, L. W., Nygren-de Boussard, C., Hartvigsen, J., Abara, U., Donovan, J., & Cassidy, J. D. (2014). Methodological issues and research recommendations for prognosis after mild traumatic brain injury: Results of the international collaboration on mild traumatic brain injury prognosis archives of physical medicine and rehabilitation. *Archives of Physical Medicine and Rehabilitation*, *95*(3), 265–277. https://doi.org/10.1016/j.apmr.2013.04.026

Kugler, B. B., Bloom, M. Kaercher, L. B., Truax, T. V., & Storch, E. A. (2012). Somatic symptoms in traumatized children and adolescents. *Child Psychiatry & Human Development*, *43*, 661-673.

Lajiness-O'Neill, R. R., Erdodi, L., & Lichtenstein, J. (2017). Traumatic brain injury. In J. M. Kaufmann & D. P. Hallahan (Eds.), *Handbook of special education* (2nd ed.). Routledge.

Lajiness-O'Neill, R., Hoodin, F., Kentor, R., Heinrich, K., Colbert, A., & Connelly, J. A. (2015). Alterations in memory and impact on academic outcomes in children following allogeneic hematopoietic cell transplantation. *Archives of Clinical Neuropsychology, 30*(7), 657-669.

Lancaster, M. A., McCrea, M. A., & Nelson, L. D. (2016). Psychometric properties and normative data for the Brief Symptom Inventory-18 (BSI-18) in high school and collegiate athletes. *The Clincial Neuropsychologist 30*(2), 338-350.

Lantagne, A., Peterson, R. L., Kirkwood, M. W., Taylor, H. G., Stancin, T., Yeates, K. O., & Wade, S. L. (2018). Interpersonal stressors and resources as predictors of adolescent adjustment following traumatic brain injury. *Journal of Pediatric Psychology, 43*(7), 703-712.

Lee, H. Y., Kim, I., Nam, S., & Jeong, J. (2020). Adverse childhood experiences and the associations with depression and anxiety in adolescents. C*hildren and Youth Services Review*, *111*, https://doi.org/10.1016/j.childyouth.2020.104850

Leibson, C. L., Brown, A. W., Long, K. H., Ransom, J. E., Mandrekar, J., Osler, T. M., & Malec, J. F. (2012). Medical care costs associated with traumatic brain injury over the full spectrum of disease: A controlled population-based study. *Journal of Neurotrauma, 29*, 2038-2049.

Lewine, J. D., Davis, J. T., Bigler, E. D., Thoma, R., Hill, D., Funke, M., Sloan, J. H., Hall, S., & Orrison, W. W. (2007). Objective documentation of traumatic brain injury subsequent to mild head trauma: Multimodal brain imaging with MEG, SPECT, and MRI. *Journal of Head Trauma Rehabilitation*, *22*(3), 141–155. https://doi.org/10.1097/01.HTR.0000271115.29954.27

Lezak, M. D., Howieson, D. B., Bigler, E. D., & Tranel, D. (2012). *Neurospychological assessment* (5th ed.). Oxford University Press.

Limbers, C. A., Newman, D. A., & Varni, J. W. (2008). Factorial invariance of child self-report across age subgroups: A confirmatory factor analysis of ages 5 to 16 years utilizing the PedsQL 4.0 Generic Core Scales. *Value in Health, 11*, 659-668.

Loeb, T. B., Joseph, N. T., Wyatt, G. E., Zhang, M., Chin, D., Thames, A., & Aswad, Y. (2018). Predictors of somatic symptom severity: The role of cumulative history of trauma and adversity in a diverse community sample. *Psychological Trauma: Theory, Research,*

Practice, and Policy, *10*(5), 491-498. https://doi.org/10.1037/tra0000334

Lovell, M. R., & Collins, M. W. (1998). Neuropsychological assessment of the college football player. *Journal of Head Truama and Rehabilitation, 13*(2), 9-26.

Lovell, M. R., Iverson, G. L., Collins, M. W., Podell, K., Johnston, K. M., Pardini, D., Pardini, J., Norwig, J., & Maroon, J. C. (2006). Measurement of symptoms following sports-related concussion: Reliability and normative data for the post-concussion scale. *Applied Neuropsychology*, *13*(3), 166-174. https://doi.org/10.1207/s15324826an1303_4

Ma, Z., Bayley, M. T., Perrier, L., Dhir, P., Dépatie, L., Comper, P., Ruttan, L., Lay, C., & Munce, S. E. (2018). The association between adverse childhood experiences and traumatic brain injury/concussion in adulthood: A scoping review. *Disability and Rehabilitation*, *12*, 1–7. https://doi.org/10.1136/bmjopen-2017-018425

Maas, A. I. R., Hukkelhoven, C. W. P. M., Marshall, L. F., & Steyerberg, E. W. (2005). Prediction of outcome in traumatic brain injury with computed tomographic characteristics: A comparison between the computed tomographic classification and combinations of computed tomographic predictors. *Neurosurgery*, *57*(6), 1173-1182.

Magyar, C. I., & Pandolfi, V. (2017). Utility of the CBCL DSM-oriented scales in assessing emotional disorders in youth with autism. *Research in Autism Spectrum Disorders*, *37*, 11-20.

Mansour, A., & Lajiness-O'Neill, R. (2015). Call for an integrative and multi-disciplinary approach to traumatic brain injury (TBI). *Psychology*, *6*, 323–374. https://doi.org/10.4236/psych.2015.64033

Maras, D. (2018). *Adverse childhood experiences: Traumas that set the framework for life*. http://blog.time2track.com/adverse-childhood-experiences-traumas-that-set-the-framework-

for-life/

Mathias, J. L., & Wheaton, P. (2015). Contribution of brain or biological reserve and cognitive or neural reserve to outcome after TBI: A meta-analysis (prior to 2015). *Neuroscience and Biobehavioral Reviews*, *55*, 573–593. https://doi.org/10.1016/j.neubiorev.2015.06.001

Mayer, A. R., Quinn, D. K., & Master, C. L. (2017). The spectrum of mild traumatic brain injury: A review. *Neurology*, *89*(6), 623–632.

McCauley, S. R., Boake, C., Levin, H. S., Contant, C. F., & Song, J. X. (2010). Postconcussional disorder following mild to moderate traumatic brain injury: Anxiety, depression, and social support as risk factors and comorbidities. *Journal of Clinical and Experimental Neuropsychology, 23*(6), 792-808. https://doi.org/10.1076/jcen.23.6.792.1016

McCrea, M. (2008). *Mild traumatic brain injury and postconcussion syndrome: The new evidence base for diagnosis and treatment*. (1st ed.). Oxford University Press.

McCrea, M., Guskiewicz, K. M., Marshall, S. W., Barr, W., Randolph, C., Cantu, R. C., Onate, J. A., Yang, J., & Kelly, J. P. (2003). Acute effects and recovery time following concussion in collegiate football players the NCAA concussion study. *Journal of the American Medical Association*, *290*, 2556–2563.

McCrory, P., Meeuwisse, W., Dvorak, J., Aubry, M., Bailes, J., Broglio, S., Cantu, R. C., Cassidy, D., Echemendia, R. J., Castellani, R. J., Davis, G. A., Ellenbogen, R., Emery, C., Engebretsen, L., Feddermann-Demont, N., Giza, C. C., Guskiewicz, K. M., Herring, S., Iverson, G. L., Johnston, K. M., … Vos, P. E. (2018). Consensus statement on concussion in sport: the 5th international conference on concussion in sport held in Berlin, October 2016. *British Journal of Sports Medicine*, *51*, 838–847. https://doi.org/10.1136/bjsports-2017-097699

McInnes, K., Friesen, C. L., Mackenzie, D. E., Westwood, D. A., & Boe, S. G. (2017). Mild traumatic brain injury (mTBI) and chronic cognitive impairment: A scoping review. *PLoS ONE*, *12*(4), 1–19. https://doi.org/10.1371/journal.pone.0174847

McKee, A. C., & Daneshvar, D. H. (2015). The neuropathology of traumatic brain injury. In J. Grafman & A. M. Salazar (Eds.), *Handbook of clinical neurology* (3rd ed., pp. 45–66). Elsevier B.V. https://doi.org/10.1016/B978-0-444-52892-6.00009-X

McLaughlin, K. (2017, April). The long shadow of adverse childhood experiences. *Psychological Science Agenda.* http://www.apa.org/science/about/psa/2017/04/adverse-childhood

McLean, A. M., Jarus, T., Hubley, A. M., & Jongbloed, L. (2014). Associations between social participation and subjective quality of life for adults with moderate to severe traumatic brain injury. *Disability and Rehabilitation*, *36*(17), 1409–1418. https://doi.org/10.3109/09638288.2013.834986

McLeod, T. C. V, & Leach, C. (2012). Psychometric properties of self-report concussion scales and checklists evidence-based practice. *Journal of Athletic Training*, *2012*(2), 221–223. https://www.nata.org/jat

Meachen, S. J., Hanks, R. A., Millis, S. R., & Rapport, L. J. (2008). The reliability and validity of the brief symptom inventory – 18 in persons with traumatic brain injury. *Archives of Physical Medicine and Rehabilitation, 89*, 958-965.

Meares, S., Shores, E. A., Taylor, A. H., Batchelor, J. S., Bryant, R. A., Baguley, I. J., Chapman, J., Gurka, J., Dawson, K., Capon, L., & Marosszeky, J. E. (2008). Mild traumatic brain injury does not predict acute postconcussion syndrome. *Journal of Neurology, Neurosurgery, and Psychiatry, 79*, 300-306.

Menard, S. (1995). *Applied logistic regression analysis.* In *Sage university paper series: Quantitative application in the social sciences*. (2nd ed., pp. 07-106). Sage Publications, Ltd.

Merrick, M. T., Ford, D., Ports, K. A., & Guinn, A. S. (2018). Prevalence of adverse childhood experiences from the 2011-2014 behavioral risk factor surveillance system in 23 states. *JAMA Pediatrics, 172*(11), 1038-1044.

Merritt, V. C., Bradson, M. L., Meyer, J. E. & Arnett, P. A. (2018). Evaluating the test-retest reliability of symptom indices associated with the ImPACT post-concussion symptom scale (PCSS). *Journal of Clinical and Experimental Neuropsychology, 40*, 377-388.

Mersky, J. P., Janczewski, C. E., & Topitzes, J. (2017). Rethinking the measurement of adversity: Moving toward second-generation research on adverse childhood experiences. *Child Maltreatment*, *22*(1), 58–68. https://doi.org/10.1177/1077559516679513

Minnesota Department of Health. (2019). *Resilience to ACEs*. https://www.health.state.mn.us/communities/ace/resilience.html

Mollayeva, T., Cassidy, J. D., Shapiro, C. M., Mollayeva, S., Colantonio, A. (2017). Concussion/mild traumatic brain injury-related chronic pain in males and females: A diagnostic modelling study. *Medicine (Baltimore), 96*(7), e5917. https://www.doi.org/10.1097/MD.0000000000005917

Moore, P., Mawdsley, L., Jackson, C., & Atherton, M. J. (2017). Psychological interventions for persisting postconcussion symptoms following traumatic brain injury. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.CD012755

Mosti, C., Spiers, M. V., & Kloss, J. D. (2016). A practical guide to evaluating sleep disturbance in concussion patients. *Neurologoy Clinical Practice, 6*(2), 129-137.

Mott, T. F., Mcconnon, M. L., & Rieger, B. P. (2012). *Subacute to Chronic Mild Traumatic*

Brain Injury (Vol. 86). www.aafp.org/afpAmericanfamilyphysician1045

Narayana, P. A. (2017). White matter changes in patients with mild traumatic brain injury: MRI perspective. *Concussion*, *2*(2), CNC35. https://doi.org/10.2217/cnc-2016-0028

National Center for Injury Prevention and Control. (2003). *Report to congress on mild traumatic brain injury in the United States: Steps to prevent a serious public health problem*. https://www.cdc.gov/traumaticbraininjury/pdf/mtbireport-a.pdf

National Collegiate Athletic Association (2018*). NCAA demographics database*. http://www.ncaa.org/about/resources/research/ncaa-demographics-database.

Nelson, L. D., Guskiewicz, K. M., Marshall, S. W., Hammeke, T, Barr, W., Randolph, C., & McCrea, M. A. (2016a). Multiple self-reported concussions are more prevalent in athletes with ADHD and learning disability. *Clinical Journal of Sports Medicine, 26*(2), 120-127. https://doi.org/10.1097/ JSM.0000000000000207

Nelson, L. D., LaRoche, A. A., Pfaller, A. Y., Lerner, E. B., Hammeke, T. A., Randolph, C., Barr, W. B., Guskiewicz, K., & McCrea, M. A. (2016b). Prospective, head-to-head study of three computerized neurocognitive assessment tools (CNTs): Reliability and validity for the assessment of sport-related concussion. *Journal of the International Neuropsychol Society, 22*(1), 24-37. https://doi.org/10.1017/S1355617715001101

Nelson, S., Smith, K., Sethna, N., & Logan, D. (2019). Youth with chronic pain and a history of adverse childhood experiences in the context of multidisciplinary pain rehabilitation. *Clinical Journal of Pain, 35*(5), 420-427.

Oh, D. L., Jerman, P., Purewal Boparai, S. K., Koita, K., Briner, S., Bucci, M., & Harris, N. B. (2018). Review of Tools for Measuring Exposure to Adversity in Children and Adolescents. *Journal of Pediatric Health Care, 32*(6), 564-583.

https://doi.org/10.1016/j.pedhc.2018.04.021

Pearn, M. L., Niesman, I. R., Egawa, J., Sawada, A., Almenar-Queralt, A., Shah, S. B., Duckworth, J. L., & Head, B. P. (2017). Pathophysiology associated with traumatic brain injury: Current treatments and potential novel therapeutics. *Cellular and Molecular Neurobiology*, *37*(4), 571–585. https://doi.org/10.1007/s10571-016-0400-1

Pechtel, P., & Pizzagalli, D. A. (2011). Effects of early life stress on cognitive and affective function: An integrated review of human literature. *Psychopharmacology*, *214*(1), 55–70. https://doi.org/10.1007/s00213-010-2009-2

Pellman, E., Lovell, M. R., Viano, D., Casson, I., & Tucker, A. (2004). Concussion in professional football: Neuropsycholgoical testing - part 6. *Neurosurgery*, *55*, 1290–1305. https://doi.org/10.1227/01.neu.0000149244.97560.91

Polinder, S., Cnossen, M. C., Real, R. G. L., Covic, A., Gorbunova, A., Voormolen, D. C., Master, C. L., Haagsma, J. A., Diaz-Arrastia, R., & von Steinbuechel, N. (2018). A multidimensional approach to post-concussion symptoms in mild traumatic brain injury. *Frontiers in Neurology*, *9*, 1113. https://doi.org/10.3389/fneur.2018.01113

Ponsford, J., Cameron, P., Fitzgerald, M., Grant, M., Mikocka-Walus, A., & Schönberger, M. (2012). Predictors of postconcussive symptoms 3 months after mild traumatic brain injury. *Neuropsychology*, *26*(3), 304–313. https://doi.org/10.1037/a0027888

Ponsford, J., Willmott, C., Rothwell, A., Cameron, P., Kelly, A. M., Nelms, R., Curran, C., & Ng, K. (2000). Factors influencing outcome following mild traumatic brain injury in adults. *Journal of the International Neuropsychological Society*, *6*(5), 568-579. https://doi.org/10.1017/s1355617700655066

Post, R. M., Altshuler, L. L., Leverich, G. S., Frye, M. A., Suppes, T., McElroy, S. L., Keck Jr,

P. E., Nolen, W. A., Kumpka, R. W., Grunze, H., & Rowe, M. (2013). Role of childhood adversity in the development of medical co-morbidities associated with bipolar disorder. *Journal of Affective Disorders*, *147*, 288–294. https://doi.org/10.1016/j.jad.2012.11.020

Potter, S. D., Brown, R. G., & Fleminger, S. (2016). Randomised, waiting list controlled trial of cognitive-behavioural therapy for persistent postconcussional symptoms after predominantly mild-moderate traumatic brain injury. *Journal of Neurology, Neurosurgery, and Psychiatry, 87*, 1075-1083. https://doi.org/10.1136/jnnp-2015-312838

Prince, C., & Bruhns, M. E. (2017). Evaluation and treatment of mild traumatic brain injury: The role of neuropsychology. *Brain Sciences*, *7*, 1–14. https://doi.org/10.3390/brainsci7080105

Rabinowitz, A. R., Li, X., McCauley, S. R., Wilde, E. A., Barnes, A., Hanten, G., Mendez, D., McCarthy, J. J., & Levin, H. S. (2015). Prevalence and predictors of poor recovery from mild traumatic brain injury. *Journal of Neurotrauma*, *32*, 1488–1496. https://doi.org/10.1089/neu.2014.3555

Reinert, D. F., & Allen, J. P. (2002). The Alcohol Use Disorders Identification Test (AUDIT): a review of recent research. *Alcoholism, Clinical and Experimental Research, 26*(2), 272-279.

Reuben, A., Moffitt, T. E., Caspi, A., Belsky, D. W., Harrington, H., Schroeder, F., Hogan, S., Ramrakha, S., Poulton, R., & Danese, A. (2016). Lest we forget: Comparing retrospective and prospective assessments of adverse childhood experiences in the prediction of adult health. *Journal of Child Psychology and Psychiatry*, *57*(10), 1103–1112. https://doi.org/10.1111/jcpp.12621

Reuben, A., Sampson, P., Harris, A. R., Williams, H., & Yates, P. (2014). Postconcussion syndrome (PCS) in the emergency department: predicting and pre-empting persistent symptoms following a mild traumatic brain injury. *Emergency Medicine Journal*, *31*(1), 72–

77. https://doi.org/10.1136/emermed-2012-201667

Rohling, M. L., Binger, L. M., Demakis, G. J., Larrabee, G. J., Ploetz, D. M., & Langhinrichsen-Rohling, J. (2011). A meta-analysis of neuropsychological outcome after mild traumatic brain injury: re-analyses and reconsiderations of Binder et al. (1997), Frencham et al. (2005), and Pertab et al. (2009). *The Clinical Neuropsychologist, 25*(4), 608-623.

Roozenbeek, B., Maas, A. I., Lingsma, H. F., Butcher, I., Lu, J., Marmarou, A., McHugh, G. S., Weir, J., Murray, G. D., Steyerberg, E. W., & IMPACT Study Group. (2009). Baseline characteristics and statistical power in randomized controlled trials: Selection, prognostic targeting, or covariate adjustment. *Critical Care Medicine*, *37(*10), 2683-2690. https://doi.org/10.1097/CCM.0b013e3181ab85ec

Rose, S. C., Fischer, A. N., & Heyer, G. L. (2015). How long is too long? The lack of consensus regarding the post-concussion syndrome diagnosis. *Brain Injury*, *29*(7–8), 798–803. https://doi.org/10.3109/02699052.2015.1004756

Ruff, R. M., Iverson, G. L., Barth, J. T., Bush, S. S., Broshek, D. K., & NAN Policy and Planning Committee. (2009). Recommendations for diagnosing a mild traumatic brain injury: A national academy of neuropsychology education paper. *Archives of Clinical Neuropsychology*, *24*(1), 3–10. https://doi.org/10.1093/arclin/acp006

Sady, M. D., Vaughan, C. G., & Gioia, G. A. (2014). Psychometric characteristics of the postconcussion symptom inventory in children and adolescents. *Archives of Clinical Neuropsychology*, *29*(4), 348-363. https://doi.org/10.1093/arclin/acu014

Saunders, J. B., Aasland, O. G., Amundsen, A., & Grant, M. (1993). Alcohol consumption and related problems among primary health care patients: WHO collaboartive project on early detection of persons with harmful alcohol consumption—I. *Addiction, 88*(3), 349-362.

https://doi.org/10.1111/j.1360-0443.1993.tb00822.x

Scheenen, M. E., Spikman, J. M., de Koning, M. E., van der Horn, H. J., Roks, G., Hageman, G., & van der Naalt, J. (2017). Patients "at risk" of suffering from persistent complaints after mild traumatic brain injury: The role of coping, mood disorders, and post-traumatic stress. *Journal of Neurotrauma*, *34*(1), 31–37. https://doi.org/10.1089/neu.2015.4381

Schneeberger, A. R., Muenzenmaier, K. H., Battaglia, J., Castille, D., & Link, B. G. (2012). Childhood abuse, head injuries, and use of medical emergency services in people with severe mental illness. *Journal of Aggression, Maltreatment & Trauma*, *21*(5), 570–582. https://doi.org/10.1080/10926771.2012.678468

Schretlen, D. J., & Shapiro, A. M. (2003). A quantitative review of the effects of traumatic brain injury on cognitive functioning. *International Review of Psychiatry*, *15*(4), 341–349. https://doi.org/10.1080/09540260310001606728

Scopaz, K. A., & Hatzenbuehler, J. R. (2013). Risk modifiers for concussion and prolonged recovery. *Sports Health*, *5*(6), 537–541. https://doi.org/10.1177/1941738112473059

Shipley, W. C. (1940). A self-administering scale for measuring intellectual impairment and deterioration. *The Journal of Psychology: Interdisciplinary and Applied, 9*, 371-377. https://doi.org/10.1080/00223980.1940.9917704

Shipley, W., Gruber, C., Martin, T., & Klein, M. (2009). *Shipley Institute of Living Scale-2*. Western Psychological Services.

Sieben, A., Lust, K., Crose, A., Renner, L., & Nguyen, R.H.N. (2019). Race and sex differences in adverse childhood experiences among Asian/Pacific Islander college students. *Journal of American College Health*. Advance online publication. https://doi.org/10.1080/07448481.2019.1677671

Silverberg, N. D., Gardner, A. J., Brubacher, J. R., Panenka, W. J., Li, J. J., & Iverson, G. L. (2015). Systematic review of multivariable prognostic models for mild traumatic brain injury. *Journal of Neurotrauma*, *32*(8), 517–526. https://doi.org/10.1089/neu.2014.3600

Silverberg, N. D., Lange, R. T., & Iverson, G. L. (2016). Concussion and mild traumatic brain injury: Definitions, distinctions, and diagnostic criteria. In F. S. Zollman (Ed.), *Manual of traumatic brain injury: Assessment and management* (2nd ed., pp. 43–49). Demos Medical Publishing.

Smits, M., Hunink, M. G., van Rijssel, D. A., Dekker, H. M., Vos, P. E., Kool, D. R., Nederkoom, P. J., Hofman, P. A., Twijnstra, A., Tanghe, H. L., & Dippel, D. W. (2008). Outcome after complicated minor head injury. *American Journal of Neuroradiology, 29*(3), 506-513. https://doi.org/10.3174/ajnr.A0852

Song, M. J., Nikoo, M., Choi, F., Schütz, C. G., Jang, K., & Krausz, R. M. (2018). Childhood trauma and lifetime traumatic brain injury among individuals who are homeless. *Journal of Head Trauma Rehabilitation*, *33*(3), 185–190. https://doi.org/10.1097/HTR.0000000000000310

Stålnacke, B.-M. (2007). Community integration, social support and life satisfaction in relation to symptoms 3 years after mild traumatic brain injury. *Brain Injury*, *21*(9), 933–942. https://doi.org/10.1080/02699050701553189

Stein, E., Howard, W., Rowhani-Rahbar, A., Rivara, F. P., Zatzick, D., & McCarty, C. A. (2017). Longitudinal trajectories of post-concussive and depressive symptoms in adolescents with prolonged recovery from concussion. *Brain Injury*, *31*(13–14), 1736–1744. https://doi.org/10.1080/02699052.2017.1380843

Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve

concept. *Journal of the International Neuropsychological Society*, *8*, 448–460.

Steward, K. A., Kennedy, R., Novack, T. A., Crowe, M., Marson, D. C., & Triebel, K. L. (2018). The role of cognitive reserve in recovery from traumatic brain injury. *Journal of Head Trauma Rehabilitation*, *33*(1), E18–E27. https://doi.org/10.1097/HTR.0000000000000325

Stucky, K. J., Kirkwood, M. W., & Donders, J. (2014). Traumatic brain injury. In K. J. Stucky, M. W. Kirkwood, & J. Donders (Eds.), *Neuropsychology study guide & board review* (pp. 432–447). Oxford University Press.

Sullivan, K. A., Kempe, C. B., Edmed, S. L., & Bonanno, G. A. (2016). Resilience and other possible outcomes after mild traumatic brain injury: A systematic review. *Neuropsychology Review*, *26*(2), 173–185. https://doi.org/10.1007/s11065-016-9317-1

Swan, A. R., Nichols, S., Drake, A., Angeles, A., Diwakar, M., Song, T., Lee, R. R., & Huang, M. X. (2015). Magnetoencephalography slow-wave detection in patients with mild traumatic brain injury and ongoing symptoms correlated with long-term neuropsychological outcome. *Journal of Neurotrauma*, *32*(19), 1510–1521. https://doi.org/10.1089/neu.2014.3654

Tator, C. H., Davis, H. S., Dufort, P. A., Tartaglia, M. C., Davis, K D., Ebraheem, A.,& Hiploylee, C. (2016). Postconcussion syndrome: demographics and predictors in 221 patients. *Journal of Neurosurgery, 125*(5), 1206-1216. https://doi.org/10.3171/2015.6.JNS15664

Taylor, C. A., Bell, J. M., Breiding, M. J., & Xu, L. (2017). Traumatic brain injury-related emergency department visits, hospitalizations, and deaths – United States, 2007 and 2013. *MMWR Surveillance Summaries, 66*(9), 1-16. doi: 10.15585/mmwr.ss6609a1

Teasdale, G., & Jennett, B. (1974). Assessment of coma and impaired consciousness. A practical

scale. *Lancet (London, England)*, *2*(7872), 81–84. http://www.ncbi.nlm.nih.gov/pubmed/4136544

Temkin, N. R., Machamer, J. E., & Dikmen, S. S., (2003). Correlates of functional status 3-5 years after traumatic brain injury with CT abnormalities. *Journal of Neurotrauma, 20*(3), 229-241. https://doi.org/10.1089/089771503321535281 5

Thompson, H. J., Vavilala, M. S., & Rivara, F. P. (2015). Common data elements and federal interagency traumatic brain injury research informatics system for TBI research. *Annual Review of Nursing Research*, *33*(1), 1–11. https://doi.org/10.1891/0739-6686.33.1

Trotta, A., Murray, R. M., & Fisher, H. L. (2015). The impact of childhood adversity on the persistence of psychotic symptoms: A systematic review and meta-analysis. *Psychological Medicine, 45*(12), 2481-2498. https://doi.org/10.1017/S0033291715000574

University of Pittsburgh Medical Center. (2019). Concussion facts and statistics. https://www.upmc.com/services/sports-medicine/services/concussion/facts-statistics

van der Horn, H. J., Liemburg, E. J., Aleman, A., Spikman, J. M., & van der Naalt, J. (2016). Brain networks subserving emotion regulation and adaptation after mild traumatic brain injury. *Journal of Neurotrauma*, *33*(1), 1–9. https://doi.org/10.1089/neu.2015.3905

van der Naalt, J., van Zomeren, A. H., Sluiter, W. J., & Minderhoud, J. M. (1999). One year outcome in mild to moderate head injury: The predictive value of acute injury characteristics related to complaints and return to work. *Journal of Neurology, Neurosurgery, and Psychiatry, 66*(2), 207-213. https://doi.org/10.1136/jnnp.66.2.207

Van Nierop, M., Viechtbauer, W., Gunther, N., van Zelst, C., de Graaf, R., Ten Have, M., van Dorsselaer, S., Bak, M., & van Winkel, R. (2014). Childhood trauma is associated with a specific admixture of affective, anxiety, and psychosis symptoms cutting across traditional

diagnostic boundaries. *Psychological Medicine*, *45*(6), 1277-1288. https://doi.org/10.1017/S0033291714002372

Varni, J. W., Limbers, C. A., & Burwinkle, T. M. (2007). Literature review: Health-related quality of life measurement in pediatric oncology: Hearing the voices of the children. *Journal of Pediatric Psychology, 32*, 1151-1163. https://doi.org/10.1093/jpepsy/jsm008

Varriano, B., Tomlinson, G., Tarazi, A., Wennberg, R., Tator, C., & Tartaglia, M. C. (2018). Age, gender and mechanism of injury interactions in post-concussion syndrome. *The Canadian Journal of Neurological Sciences*, *45*, 636–642. https://doi.org/10.1017/cjn.2018.322

Wilde, E. A., Whiteneck, G. G., Bogner, J., Bushnik, T., Cifu, D. X., Dikmen, S., French, L., Giacino, J. T., Hart, T., Malec, J. F., Millis, S. R., Novack, T. A., Sherer, M., Tulsky, D. S., Vanderploeg, R. D., & von Steinbuechel, N. (2010). Recommendations for the use of common outcome measures in traumatic brain injury research. *Archives of Physical Medicine and Rehabilitation*, *91*(11), 1650–1660. https://doi.org/10.1016/j.apmr.2010.06.033

Williams, D. H., Levin, H. S., & Eisenberg, H. M. (1990). Mild head injury classification. *Neurosurgery, 27*(3), 422-428. https://doi.org/10.1097/00006123-199009000-00014

Winstanley, E.L., Mahoney III, J.J., Lander, L.R., Berry, J.H., Marshalek, P., Zheng, W., & Haut, M.W. (2020). Something to despair: Gender differences in adverse childhood experiences among rural patients. *Journal of Substance Abuse Treatment*, 116, 108056. https://doi.org/10.1016/j.jsat.2020.108056

Wood, R. L., O'Hagan, G., Williams, C., McCabe, M., & Chadwick, N. (2014). Anxiety sensitivity and alexithymia as mediators of postconcussion syndrome following mild

traumatic brain injury. *The Journal of Head Trauma Rehabilitation*, *29*(1), E9–E17. https://doi.org/10.1097/HTR.0b013e31827eabba

World Health Organization. (1992). *The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines*. Geneva: World Health Organization.

Zeng, E. Q., Zeng, B. Q., Tian, J. L., Du, B., Tian, X. B., & Chen, H. (2016). Perceived social support and its impact on mental fatigue in patients with mild traumatic brain injury. *Balkan Medical Journal*, *33*(2), 152-157. https://doi.org/10.5152/balkanmedj.2016.15701

Zuckerman, S. L., Kerr, Z. Y., Yengo-Kahn, A., Wasserman, E., Covassin, T., & Solomon, G. S., (2015). Epidemiology of sports-related concussion in NCAA athletes from 2009-2010 to 2013-2014: Incidence, recurrence, and mechanisms. *American Journal of Sports Medicine, 43*(11), 2654-2662. https://doi.org/10.1177/0363546515599634

Appendix A

Eligibility Screener

"Thank you for your interest in this study. Before I send you any surveys, I would like to ask you a few questions to determine whether you are eligible to participate in the study."
A concussion or mild traumatic brain injury is defined as a blunt trauma or through acceleration/deceleration forces.

1. How old are you?

2. Is English your primary language?

3. Have you had a concussion/mild traumatic brain injury within the last two weeks? If so, how did you sustain the concussion?

4. Who diagnosed you with a concussion? (athletic trainer, emergency department, other)

5. Did you have a period of confusion/disorientation/impaired consciousness? How long?

6. What was the first thing you remember after your concussion?

7. Did you require medical care? If so, were you intubated or receive general anesthesia? Did you receive a CT scan?

8. Did you have seizures, balance issues, weakness/paralysis on one side of body, dilated pupils?

9. Were you under the influence of alcohol or other substances at the time of the injury?

10. Do you have a history of neurological illness (such as seizures)?

11. Do you have a history of psychiatric illness that is affecting your daily functioning or has required inpatient hospitalization? A history of substance use that has affected daily functioning or required treatment?

12. Do you have a history of nonneurological illness (such as cardiac disease, hypertension, cancer, diabetes)?

13. Have you ever required special education classes or an IEP plan in school?

Appendix B

Demographic Questionnaire

1. How old are you? _____
2. Do you identify as male/female/transgender/nonbinary?

   _____
3. What race do you identify as? _____
4. Currently, what grade are you in? If not currently in school, how far did you get in school? _____
5. Please indicate your ACT/SAT scores and GPA.

   ACT score: _____

   SAT score: _____

   Current GPA: _____
6. Have you ever been diagnosed with a learning disorder?

   _____
7. Have you ever been diagnosed with attention-deficit/hyperactivity disorder (ADHD)?

   _____
8. If you currently work, what is your occupation?

   _____
9. How many previous head injuries have you had?

   _____

Appendix C

Eastern Michigan University Survey Consent Form

RESEARCH @ EMU

Consent Form

Project Title: The role of premorbid factors and adverse childhood experiences in the persistence of symptoms post mild traumatic brain injury (persistent postconcussive symptoms)
Principal Investigator: Tiffany Andersen, Graduate Student
Faculty Advisor: Dr. Renee Lajiness-O'Neill, Professor of Psychology

Purpose: The purpose of this research study is to replicate current literature about the predictors of the persistence of symptoms following mild traumatic brain injury (mTBI), commonly referred to as a concussion, as well as extend the literature and assess the relative contributions of adverse childhood experiences to persistent symptoms. You are being asked to participate in this study because you have either had a mTBI or another injury in the past two weeks.

Study Procedures: Participation in this study involves completing an online survey at two time points: (1) at baseline, within two weeks of the mTBI; and (2) at follow-up, within four weeks of the concussion/mTBI. It will take between 35-45 minutes to complete each survey.

Types of Data Collected: We will ask questions related to your sociodemographics (e.g., age, gender, education, race, etc), thinking, behavior, head injury history, and emotions.

Risks: The primary risk of participation in this study is a potential loss of confidentiality. REDCap is a HIPAA compliant online survey system used for research. Some of the survey questions are personal in nature and may make you feel uncomfortable. You do not have to answer any questions that make you uncomfortable or that you do not want to answer.

Benefits: You will not directly benefit from participating in this research. Benefits to society include understanding predictive factors that influence the persistence of symptoms following a mTBI.

Confidentiality: We will keep your information confidential by using a study ID code in the data set instead of your name. The code will be linked to your name using a separate key. Your information will be stored in a password-protected computer file. We will store your information for at least five years after the project ends, but we may store your information indefinitely so that we can use your information for future studies.

The principal investigator and the research team will have access to the information you provide for research purposes only. We may share your information with other

researchers outside of Eastern Michigan University. If we share your information, we will remove any and all identifiable information so that you cannot reasonably be identified. De-identified information will be transferred by email or encrypted servers.

The results of this research may be published or used for teaching. Identifiable information will not be used for these purposes and data will only be displayed in aggregate, as a group, rather than individual data.

Compensation: A gift card will be emailed to you for participating in this research study. We will collect your name and email address at the end of the survey so that we can send you an electronic gift card that you can print and use.

Contact Information: If you have any questions about the research, you can contact the Principal Investigator, Tiffany Andersen at tander33@emich.edu. You can also contact Tiffany's adviser, Dr. Renee Lajiness-O'Neill, at rlajines@emich.edu or by phone (EMU Psychology Department 734-487-1155).

For questions about your rights as a research subject, you can contact the Eastern Michigan University Office of Research Compliance at human.subjects@emich.edu or by phone at 734-487-3090.

Voluntary participation

Participation in this research study is your choice. You may refuse to participate at any time, even after signing this form, with no penalty or loss of benefits to which you are otherwise entitled. You may choose to leave the study at any time with no loss of benefits to which you are otherwise entitled. If you leave the study, the information you provided will be kept confidential. You can withdraw your consent by emailing the Principal Investigator listed above. You may request, in writing, that your identifiable information be destroyed. However, we cannot destroy any information that has already been published.

Statement of Consent

I have read this form. I have had an opportunity to ask questions and am satisfied with the answers I received. I click "continue" below to indicate my consent to participate in this research study.

Appendix D

Eastern Michigan University Assent Form

RESEARCH @ EMU

Assent Form

Introduction

You are being asked to participate in a research study. Research studies are conducted by scientists or other researchers to answer questions and learn new things. The researcher conducting this study is Tiffany Andersen. Tiffany Andersen is a graduate student and her supervisor is Dr. Renee Lajiness-O'Neill. In this form, Tiffany will be referred to as the investigator. The purpose of this study is to better understand what factors influence how long symptoms last after a concussion. You are being asked to participate in this study because you have either had a concussion or another injury in the past two weeks. Please read this form carefully and ask any questions you have before deciding to participate in this study.

Study Procedures

If you agree to participate in this study, we will ask you to complete two surveys. Each survey will take about 35-45 minutes to complete. The first survey will be completed within two weeks of your injury, and the second survey will be completed within four weeks of your injury.

Risks

- There is a risk that people outside of the research study might find out some of your information. The investigator will do her best to protect your information, but cannot guarantee complete confidentiality.
- You might feel uncomfortable answering some of the questions in the interview/survey. You do not have to answer any questions that make you feel uncomfortable. If any questions make you feel uncomfortable, you can also talk to the investigator about this, take a break, or stop the survey.
- If you are feeling upset after the completion of the surveys, you may contact the investigator and she can help you find mental health services in your area.

Benefits

You will not benefit from participating in this study, but others may benefit from your participation in this study by having a better understanding of what factors influence persistence of symptoms following mTBI. This may help in creating more screeners or questionnaires to identify individuals who are at higher risk.

Confidentiality

- The investigator will do everything she can to protect your information. However, the investigator cannot guarantee complete confidentiality. Research data may be reviewed by the Institutional Review Board, governmental agencies, and in rare cases, can be subpoenaed by the Court.

- Due to its nature, security cannot be guaranteed with an online survey, although precautions have been taken with the REDCap online program, which is HIPAA compliant.
- Case identification numbers, rather than names, will be placed on all research materials and master lists linking participants names and numbers will be maintained separately. Only research personnel will have access to these lists. All data, including hard copies and electronic files, will be accessible only to study personnel.
- The investigator is a mandated reporter in the state of Michigan if child abuse or neglect is suspected, or if a participant reports suicidal ideation or plan, or intent to harm others.

Payments

You will be compensated each time you complete a survey. At the end of the survey, you will be asked to type in your name and email address. An electronic gift card will be sent to the email address provided.

Voluntary Participation

- The decision to participate is up to you. You can refuse to participate in this study now or at any time. You can choose to participate and then, at any time during the study, choose to stop participating.
- Your parents will also be asked to give permission for you to participate. Even if your parents let you participate, you can still refuse to participate.
- If you choose to participate and change your mind, you can ask the investigator to destroy all of your information collected. Please be aware that any published information cannot be destroyed.

Contact Information

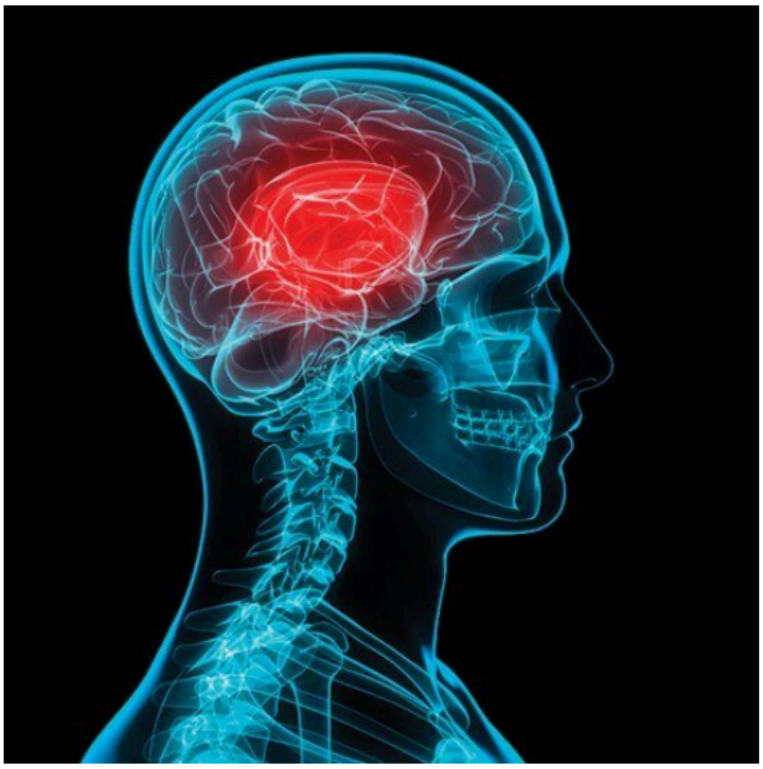
- If you have questions about this study at any time, you can contact the investigator, Tiffany Andersen at tander33@emich.edu. You can also contact Tiffany's advisor, Dr. Renee Lajiness-O'Neill, at rlajines@emich.edu with any questions.
- If you have questions about your rights as a research participant, you can contact the Eastern Michigan University Human Subjects Review Committee (UHSRC) at 734-487-3090 or human.subjects@emich.edu. The UHSRC reviews and monitors research studies to make sure that participants' rights are respected.

Assent Statement

- By continuing, you indicate that you have read this form, that all of your questions have been answered to your satisfaction, and that you agree to participate in this research study.

Appendix E

Eastern Michigan University Recruitment Flyer



Research Participants Needed

For a study investigating changes in mood and thinking for adolescents and adults who have had a recent concussion or other injury

Complete two online surveys and receive a $30 gift card upon completion

Contact Tiffany Andersen at tander33@emich.edu

Research Participation
tander33@emich.edu

Research Participation
tander33@emich.edu
Research Participation
tander33@emich.edu
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Research Participation
tander33@emich.edu

Appendix F

Proposed Dissertation Measures and Methods

Measures

Permission was obtained by all relevant publishing companies (e.g., WPS Publishing, ImPACT, Inc., Pearson Assessments) to convert all measures to an online format to administer via the REDCap online system.

Demographic questionnaire. *After the participant is found eligible for the study, the participant will be consented. After the consenting process, sociodemographic data (e.g., age, sex, race, educational attainment, occupational status) will be collected. This data will be collected and included in the set of baseline measures.*

Postconcussive symptoms. The primary dependent variable, post concussive symptoms (PPCS), will be measured using the ImPACT Post-Concussion Symptom Inventory (ImPACT-PCS) and Rivermead Postconcussion Symptoms Questionnaire (King et al., 1995). The ImPACT-PCS consists of 22 items addressing common somatic, psychological, and affective symptoms following mTBI (Lovell & Collins, 1998). Answer choices are based on a 7-point Likert type scale based on 0 = none to 6 = severe. A total score is created, with a higher score signifying a higher number or severity of symptoms. The ImPACT Post-Concussion Symptom Inventory has been tested on several collegiate populations with good internal consistency (α = .88-.94; McLeod & Leech, 2012; Alla, Sullivan et al., 2009). Test-retest reliability was .44-.80 (Merritt et al., 2018).

Cognitive reserve. The Shipley-2 is an updated version of the Shipley Institute of Living Scale that assesses for crystallized and fluid cognitive abilities (Shipley, 1940; Shipley et al., 2009). The age range for Shipley-2 had been extended to include individuals aged 7-89 years.

The Shipley-2 consists of the three scales: (a) Vocabulary; (b) Abstraction; and (c) Block Patterns (Shipley et al., 2009). For the current study, only the Vocabulary scale will be utilized during the baseline evaluation. The Vocabulary scale is self-administered and consists of 40 items; the participant is given a word and must choose the most appropriate word closest in meaning among four-word choices (Kaya et al., 2012). The Vocabulary scale demonstrated good internal consistency ranging from .81-.89 with a median of .84. Test-reliability was analyzed in adolescents and adults within 1-2 week intervals; the test-retest correlation coefficients ranged from .74-.94 among the three scales, indicating stability over time (Shipley et al., 2009). With regard to construct validity, the authors found strong consistency with other established tests such as the Wechsler Adult Intelligence Test, Third Edition and Wide Range Achievement Test, Third Edition. The Vocabulary subscale is also highly correlated with the Vocabulary subscale from the Wechsler Adult Intelligence Test, Fourth Edition (Kaya et al., 2012).

Academic achievement. During the baseline, both adolescent and adult participants will be asked on the Demographic questionnaire to disclose their SAT score, ACT score, and grade point average (GPA) as an indicator of academic achievement. Participants who are no longer in school, or are also working, will be asked to indicate their employment or occupational status.

Sex. The Demographic questionnaire will contain a single question regarding sex: "Do you identify as male/female/transgender/nonbinary?"

Pain. Participants will be asked to indicate how they sustained a mTBI (e.g., sports-related concussion, motor vehicle accident, etc.) on the eligibility screener. Pain will be assessed using the Visual Analogue Scale (VAS), a commonly utilized measure across clinical populations where participants are asked to rate their pain on a scale from 0-10 with 0 indicating "*no pain*" and 10 indicating "*worst pain*" (Huskisson, 1974; Ponsford et al., 2000). Test-retest

reliability for one minute VAS scores were high (0.99), while convergent validity with the Short-Form Health Survey items ranged from 0.16-0.51 and with the Roland-Morris Disability Questionnaire items ranged from 0.38-0.43 (Boonstra et al., 2008; Gallagher et al., 2002). Pain interference and intensity will also be measured using the adult and pediatric PROMIS® profiles, as described below (please see Table 15 for all components of PROMIS® profiles).

PROMIS® measures. The NIH funded the creation of the Patient Reported Outcomes Measurement Information System (PROMIS®) for the purpose of creating an extensively validated item pool that can be readily integrated into clinical research and practice (Forrest et al., 2017). Items have been developed using literature review, investigator consensus process, item response theory analysis and expert review of results from multiple data sets (Cella et al., 2019). Many profiles and measures have been created to assess for quality of life and entail physical functioning, anxiety, depression, fatigue, peer relationships, ability to participate in social activities, fatigue, sleep disturbance, pain interference, and pain intensity (please see Table 7; Cella et al., 2019). Depending on the participant's age, the PROMIS®-43 or pediatric PROMIS®-37 profile will be utilized. With regard to pain, items have been validated and shown to be sensitive to changes in pain (Askew et al., 2016). Internal consistency was high for two samples (0.94 and 0.95; Hays et al., 2018).

Psychiatric factors. Both adolescent and adult participants will be asked to complete the Brief Symptom Inventory – 18 Item (BSI-18) at the baseline and follow-up questionnaires (Derogatis, 2001). The BSI-18 is an 18-item measure that measures distress on three subscales: (a) depression; (b) anxiety; and (c) somatization. Item responses are also added up for a global severity index that reflects general psychological distress of the participant (Derogatis, 2001). The BSI-18 has been validated within the community and medical populations, as well as with

individuals with TBI of varying severity (Derogatis, 2001; Lancaster et al., 2016; Meachen et al., 2008).

As previously mentioned, depending on the participant's age the PROMIS®-43 profile or the pediatric PROMIS®-37 profile will be utilized. The adult profile has six items covering anxiety, six items covering depression, and 12 items covering fatigue and sleep disturbance (see Table 15; Cella et al., 2019). The pediatric profile contains similar items, but only covers fatigue with six items. The PROMIS mental health components were highly correlated with the Short Form-36 mental component summary score (0.82; Hays et al., 2018). Internal consistency for anxiety (0.90 and 0.86),depressive symptoms (0.93 and 0.86), and fatigue (0.91 and 0.91) were high for two samples (Hays et al., 2018).The PROMIS® measures have been recommended for use in TBI research (Wilde et al., 2010).

Additionally, the Alcohol Use Disorders Identification Test, self-report version (AUDIT) will be utilized to measure drinking behaviors, alcohol consumption, and possible alcohol-related problems (Saunders et al.,1993). The AUDIT was created by the World Health Organization (WHO) and is a 10-item screener using responses on a five-point Likert type scale (Saunders et al., 1993). While psychometric properties are unavailable specifically to the TBI population, the screener has been utilized in several primary care patient samples, the median reported internal consistency was within .80, with test-retest reliability at .81 for 6 weeks (Reinert & Allen, 2002; Saunders et al., 1993). A cut-off score of 8 indicates possible alcohol abuse (Saunders et al., 1993).

Participants will also be asked to indicate whether they have been previously diagnosed with a learning disorder or attention-deficit/hyperactivity disorder on the Demographic Questionnaire.

Life stressors/social support. Participants will be asked to complete the Life Events Checklist (LEC) which is a brief screening measure of 17 items that assesses for potentially traumatic events (e.g., accidents, disasters, sexual/physical assault, combat-related exposure; Gray et al., 2004). The psychometric properties of the LEC have been evaluated using college undergraduate students and combat veterans; with the college student sample, the LEC demonstrated adequate temporal stability and good convergence with an established measure of trauma, the Traumatic Life Events Questionnaire (Gray et al., 2004).

Social support and participation in social activities will be addressed using a handful of questions (6 items) within the PROMIS® measures for both adolescent and adult participants. While information on psychometric properties is still somewhat limited due to the recent development of the items, internal consistency in recent samples were high for ability to participate in social activities (0.93 and 0.90; Hays et al., 2018).

Previous head injuries. Participants will be asked on the Demographic Questionnaire a single question regarding previous head injuries: "How many previous head injuries have you had?" A dropdown list will be provided for participants to indicate a range.

Adverse childhood experiences. Participants will complete the Adverse Childhood Experiences Study Questionnaire (ACESQ) during baseline. The ACESQ assesses for emotional/physical/sexual abuse, parental substance abuse within the household, parental mental illness, caregiver violence, and incarceration in the household (Felitti et al., 1998). The ACESQ has 10 items and are given as a dichotomous Yes/No format. Test-retest reliability within a 15-22 month interval was .64, with items ranging from good to substantial (.41-.76; Dube et al., 2004: Reuben et al., 2016). Information with regard to the validity of the ACESQ is unavailable.

Table 13

Measures completed by participants at each timepoint for originally proposed study

Measures	Baseline		Follow-up	
	Adult	Adolescent	Adult	Adolescent
Demographics Questionnaire	✓	✓		
ImPACT Post-concussion Symptom Inventory	✓	✓	✓	✓
Adverse Childhood Experiences Study Questionnaire	✓	✓		
Shipley-2 Vocabulary Scale	✓	✓		
Pediatric PROMIS®-37 Item Profile		✓		✓
Adult PROMIS®-43 Item Profile	✓		✓	
Alcohol Use Disorders Identification Test	✓	✓	✓	✓
Academic Achievement/Occupational Status			✓	✓
Updated Life Events Status			✓	✓
Estimated Completion Time (minutes)	**35-45 minutes**			

Note. Adults range from ages 18 and above. Adolescents range from ages 12 to 17.

Table 14

Measures organized by construct for originally proposed study

Postconcussive Symptoms
ImPACT Post-concussion Symptom Inventory
Cognitive Reserve
Shipley-2 Vocabulary scale
Demographic Questionnaire (SAT/ACT, GPA, occupation)
Sex
Demographic questionnaire
Pain
Adult and pediatric PROMIS® Profiles
Psychiatric Factors
Adult and pediatric PROMIS® Profiles
Alcohol Use Disorders Identification test
Life Events Question
Previous Head Injuries
Demographic Questionnaire
Adverse Childhood Experiences
Adverse Childhood Experiences Study Questionnaire

Table 15

Components of pediatric and adult PROMIS® measures

Construct (number of items)	Adult	Pediatric
Physical functioning (6)	✓	✓
Anxiety (6)	✓	✓
Depression (6)	✓	✓
Fatigue (6)	✓	✓
Sleep disturbance (6)	✓	
Peer relationships (6)		✓
Ability to participate in social activities (6)	✓	
Pain interference (6)	✓	✓
Pain intensity (6)	✓	✓

Note. Adult measures will be administered to participants ages 18 and older.

Pediatric version will be administered to participants ages 12-17 years.

Participants

Fifty-five participants with mTBI were to be initially recruited from Henry Ford Health Systems (HFHS), Eastern Michigan University (EMU) and Concordia College (CC). Inclusion criteria for the mTBI group utilized the Center for Disease Control (2003) definition of mTBI, and included recent (< 2 week) history of blunt trauma or acceleration/deceleration forces and a minimum of one of the following: (1) alteration in mental status (e.g., confused, disoriented, impaired consciousness); (2) any amnesia; (3) LOC <30 minutes; or (4) signs of neurological or neuropsychological dysfunction. GCS was acquired when available and a criterion of a score of 13-15 on presentation was used. Other criteria included: (1) age 12 years or over; and (2) English speaking.

Participants were excluded if they (1) were intubated or required general anesthesia following the injury; (2) were under the influence of illicit substances at the time of injury; (3) had focal neurological signs that indicated injuries more severe than mTBI (e.g., hemorrhage,

hemiparesis, cerebral contusions, subdural/epidural hematoma), seizures; or (4) have a history of intellectual disability, neurological illness, significant alcohol or drug abuse or other psychiatric impairment currently affecting daily functioning. Individuals with a medical history of nonneurological illness (e.g., cardiac disease, hypertension, cancer, diabetes), psychiatric history (excluding psychosis), prior mTBI, and reported alcohol or cannabis use were included in the study if they did not report any significant preinjury cognitive difficulties.

A trauma control (TC) group was to be comprised of patients presenting with minor injuries not involving the head and no LOC or PTA following their injury. This group was to be utilized to compare the effects of ACE exposure at baseline to PPCS endorsement within a nonclinical population. Other inclusion and exclusion criteria was the same as the mTBI group. Assent was to be obtained from participants under the age of 18, as well as consent from their legal guardians.

All Institutional Review Board (IRB) approvals were obtained from all participating institutions, following APA ethical guidelines.

Recruitment and procedures

Potential participants for the prospective study were initially planned to be recruited from three locations in southeastern Michigan: Henry Ford Health Systems (HFHS), Eastern Michigan University (EMU) and Concordia College (CC). The Henry Ford Concussion Clinic, both Novi and Detroit locations, will be utilized for potential participants.

At HFHS, potential participants will be seen after his/her scheduled appointment and if he/she expresses interest in participating, a research assistant will screen for eligibility using an eligibility screener. If the participant is eligible, the research assistant will complete the assenting and/or consenting process. The RA will discuss the REDCap online system during the

consenting process. The research assistant will have participants complete the baseline questionnaires using the REDCap online survey site. Each participant will be emailed a gift card following the completions of the baseline questionnaires. The participant will be contacted via email or phone (via Tracfone) at two weeks prior, one week prior, and three days prior to the second data collection point time (two to four weeks post-baseline). The participant will be emailed a REDCap link to complete follow-up questionnaire (please see "follow-up appointment" in Table 13 under *Measures*). A gift card will be emailed after completion of the follow-up questionnaires.

EMU will be a second site for recruitment. A flyer will be utilized for recruitment of control participants. Additionally, a research assistant from the study will visit various undergraduate Psychology classes and inform them of the study, providing students with contact information. When potential participants contact the research assistant, an eligibility screener will be conducted over the phone and if the individual is eligible to participate in the study, the participant will be consented and subsequently enrolled in REDCap and sent a REDCap online survey link to complete within two weeks of screening. For potential participants within the mTBI/PPCS group, the RA will meet with the athletic director or athletic trainer on a weekly basis to determine which students may have sustained a concussion. These student athletes will be contacted by phone (via Tracfone) and email regarding the study. If the student athlete conveys interest, the RA will complete the eligibility screener. Should the student be eligible to participate in the study, he/she will be consented and subsequently enrolled in REDCap and sent a REDCap online survey link. Survey baseline questionnaires must be completed within two weeks of injury. Each participant will be emailed a gift card following the completions of the baseline questionnaire. For both groups, the RA will contact the participant via email or phone

(via Tracfone) at two weeks prior, one week prior, and three days prior to the second data collection point time (two to four weeks post-baseline). The participant will be sent a REDCap link to complete the follow up questionnaires (please see "follow-up appointment" in Table 5 under *Measures*). A gift card will be emailed after completion of the follow-up questionnaire. Concordia College will be a third location for recruitment, following the same protocol as the EMU site. However, only student athletes for the mTBI/PPCS group will be recruited from the site.

Eligibility and consent/assent

Prior to participation in the study, individuals will be screened for eligibility. If eligible, they will first be consented. Individuals who are seen in person, such as at the HFHS Concussion Clinic Detroit and Novi locations, will be consented in person at the time of the appointment. For potential participants under 18, the assenting process will be conducted in person, as well as the consenting process with their legal guardians. For potential participants that will be contacted via phone from EMU and CC, oral consent will be obtained during the eligibility screener and a formal consent will be obtained online through REDCap, prior to the initiation of the survey. For both scenarios, participants will receive contact information for the principal investigator and faculty sponsor (e.g., Tiffany Andersen and Dr. Renee Lajiness-O'Neill), should there be any questions or concerns.

The eligibility screener will assess whether a subject has had a recent (<2 week) history of trauma to the head or other physical injury. Age and English-speaking abilities will also be assessed. They will be asked whether they were intubated or required general anesthesia following injury, and if they were under the influence of illicit substances at the time of injury. Signs of focal neurological signs that indicate more severe injuries will be assessed. History of

intellectual disability, neurological illness, significant alcohol or drug abuse or other psychiatric impairment currently affecting daily functioning will be assessed.

Power analyses (proposed prospective study)

An a priori analysis indicated greater than 80% power to detect moderate effect sizes in a group of 65 [effect size (f^2) = 0.15, λ = 12.75, F = 2.49, df = 4, 77]. All analyses were two-tailed, with α level set at 0.05. Field (2018) reported that one should always have a sample size of about 55, and, if one is expecting a medium effect, then a sample size of 100 should suffice with up to six predictors. According to Cohen (1988), a sample size of 86 would be sufficient for the anticipated seven predictors using the same parameters [R^2 = 0.15, λ = 15.1, u = 7, power = .8, α = 0.05.

Appendix G

Original Dartmouth-Hitchcock Medical Center IRB Approval

OFFICE OF RESEARCH OPERATIONS
Dartmouth-Hitchcock

EXEMPT DETERMINATION

June 25, 2020

Jonathan Lichtenstein
1 Medical Center Drive
Lebanon, NH 03756-1000
Jonathan.D.Lichtenstein@Dartmouth.edu

Dear Jonathan Lichtenstein:

On 6/25/2020, the D-HH IRB reviewed the following submission:

Type of Review:	Initial Study
Title:	Obstetric Complications and Neurodevelopmental Outcomes
Investigator:	Jonathan Lichtenstein
IRB ID:	STUDY02000377
Exempt Category(ies)	4 (iii)
Determinations:	Waiver of HIPAA Authorization granted
Documents Reviewed:	• Data Review Protocol • Departmental Scientific Review_Form OCs

The IRB determined that this protocol meets the criteria for exemption from IRB review.

In conducting this protocol you are required to follow the requirements listed in the INVESTIGATOR MANUAL (HRP-103).

Ongoing IRB review and approval by this organization is not required. This determination applies only to the activities described in the IRB submission and does not apply should any changes be made. If changes are made and there are questions about whether these activities impact the exempt determination, please submit a new request to the IRB for a determination.

If you have any questions about this review, please contact the Dartmouth-Hitchcock Health Institutional Review Board at 603-650-1846 or IRB@hitchcock.org.

Sincerely,

Kristen Katopol
HRPP Director