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Identification and Characterization of Neuropsychological Phenotypes in Sport-Related Concussion

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IDENTIFICATION AND CHARACTERIZATION OF NEUROPSYCHOLOGICAL PHENOTYPES IN SPORTS-RELATED CONCUSSION

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ABSTRACT

OBJECTIVES: Sport-related concussion (SRC) is a mild form of neurotrauma, resulting in transient cognitive deficits and symptoms. Staggering heterogeneity in its clinical manifestation has been observed in practice. The purpose of the current study was to attempt to empirically elucidate neuropsychological subgroups of SRC.

METHODS: An archival consecutive clinical case series of 1366 (872 male, 494 female; M_{age}=15.6, SD_{age}=1.9) post-concussion athletes, referred for neuropsychological testing was utilized in this study. Athletes were administered the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT), including the Post-Concussion Symptom Scale (PCSS). A priori analyses included Latent Class Analysis (LCA), and post-hoc analyses included cluster analysis, ANOVA and MANOVA.

RESULTS: The LCA revealed no definite structure in the data, in either the overall sample or an acute sample (≤7 days post-concussion). There was vast disagreement between fit indices, with some indicating no cluster solution was appropriate. Cluster analysis yielded two cluster solutions, both of which primarily reflected levels of performance rather than distinct neuropsychological clusters. However, one cluster from each sample was comprised of poor cognitive scores and low symptom reporting.

CONCLUSIONS: No distinct neuropsychological profiles emerged from the data. Although there was one potentially interesting cluster from each of the solutions, the majority of solutions reflected levels of performance and reporting. Although it is possible that there are no subgroups of SRC, this question is far from resolved.

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CHAPTER 1:

INTRODUCTION AND BACKGROUND

Traumatic brain injury (TBI) is a leading global health concern in society today. Conservative estimates of its incidence report that approximately 10 million TBIs occur annually on a global scale (Hyder, Wunderlich, Puvanachandra, Gururaj, & Kobusingye, 2007). In the United States alone, there are 1.1 million annual emergency room visits, with estimates of total all-severity (including mild, mild-complicated, moderate, and severe) TBIs in the United States ranging from 1.4 million to 1.7 million total injuries, excluding military-related TBIs, TBIs treated in private physicians' offices, and those that never have contact with medical institutions (Langlois, Rutland-Brown, & Wald, 2006; Faul, Likang, Wald & Coronado, 2010). The rates in Canada are similarly high, with the incidence reported to be approximately 0.5% of the 2014 Canadian population, or a staggering 155,000 (Rao, McFaull, Thompson, & Jayaraman, 2017). These same authors report that the Canadian incidence of TBI in 2014 was more than double that in 2005, at 3.2% and 1.4% respectively. The reasons for this are unclear, but it is possible that an increased recognition of the importance of reporting and seeking medical assistance for milder injuries might be a contributing factor. Furthermore, Langlois, Rutland-Brown, and Thomas (2004) estimate that all-severity TBI results in approximately 50,000 annual deaths in the United States, and 4.5 million annual deaths worldwide (World Health Organization [WHO], 2004), accounting for approximately one third of injury related deaths in the United States (Roebuck-Spencer & Cernich, 2014). These are likely underestimations of the true incidence of TBI, because a large proportion of those who sustain a TBI never have contact with medical institutions. Estimates of proportions of those with TBIs who have contact with medical institutions range from 16% to 25% (Fife, 1987; McCrea, 2008). The aforementioned high

incidence rates combined with high rates of resulting disability and death underscore the importance of studying TBI of all severities. Mild TBI, or concussion, presents unique challenges given its ubiquity and complexity. Therefore, the purpose of the current study was to contribute to the knowledge about mild TBI by attempting to delineate subgroups of sport-related concussion, based on neurocognitive data.

Classification of Injury Severity

Traumatic brain injury occurs along a continuum of severity, along which it is typically classified into three categories: severe (STBI), moderate (MTBI), and mild (mTBI). There are various methods of classifying TBIs into these severity ratings, with the most frequently applied being the Glasgow Coma Scale (GCS; Teasdale & Jennett, 1974). The GCS assesses level of responsiveness in eye opening, verbalization, and motor responses. The scale ranges from 3 to 15, with lower scores indicating lower levels of responsiveness. STBI is delineated by scores less than or equal to eight, MTBI requires scores between nine and twelve, and mTBI is defined by scores greater than thirteen (Roebuck-Spencer & Cernich, 2014).

Another common severity classification system for TBI is the duration of loss of consciousness (LOC). The specific criteria for classification of a particular severity vary depending on the source, but one such classification system defines LOC longer than 24 hours as STBI, less than 24 hours but more than 30 minutes as MTBI, and less than 30 minutes as mTBI (Department of Defense and Department of Veterans Affairs, 2008). Similarly, the duration of post-traumatic amnesia (PTA), or the loss of memory for events that happen in the period following the injury, is often used as an additional metric for the classification of injury severity. Longer intervals of PTA are thought to indicate more severe TBI (Lezak et al., 2012), a notion that is supported by the finding that PTA duration is highly correlated with GCS scores (Sherer,

Struchen, Yablon, Wang, & Nick, 2008). However, while these classification systems are very useful and applicable to severe and moderate TBI, there is debate about their applicability to mTBI. For example, the GCS exhibits a ceiling effect, such that patients with mTBI often achieve scores of 15 (McCrea, 2008). Additionally, it is often the case that patients with mTBI did not experience LOC or PTA, limiting the usefulness of these metrics. Therefore, it appears that mTBI is a special case regarding the diagnosis and management of TBI. As such, a unique set of recommendations for the assessment of mTBI have been developed. These will be discussed below.

Mild Traumatic Brain Injury

Definitions of mTBI

Mild TBI has historically been a difficult condition to define with consensus. It is currently evaluated using a combination of neurocognitive tests and self-report symptomology (McCrory et al., 2013), with each injury manifesting as a unique combination of cognitive deficits and symptoms. This heterogeneity in presentation has resulted in multiple definitions of the injury. Another issue that commonly plagues attempts to adequately define mTBI is the controversy over the definition of mTBI versus concussion. Although many researchers and clinicians use the two terms interchangeably, there are some who advocate for the differentiation of the two. The three most recent consensus statements on concussion in sport (McCrory et al., 2009; McCrory et al., 2013, McCrory et al., 2017) have acknowledged this controversy. Although they did not report consensus on the matter, the Zurich statement acknowledges that concussion is a subset of TBI, and that concussion is "the historical term representing low velocity injuries that cause brain 'shaking' resulting in clinical symptoms and which are not necessarily related to a pathological injury" (McCrory et al., 2013, pg. 179). The most recent consensus statement also briefly addresses this controversy, stating that often the term mild

traumatic brain injury "is used interchangeably with concussion; however, this term is similarly vague and not based on validated criteria in this context." (McCrory et al., 2017, pg. 2) However, the pathophysiology of mTBI and concussion are identical, they manifest as similar cognitive deficits and symptomology, and except for complicated mTBI (discussed below) there are no structural aberrances visible to conventional structural neuroimaging methods. In my view, concussion is merely an instance of a mTBI that falls at the mild end of the continuum of severity within mTBI.

There are, however, contextual factors that do suggest the use of one term over the other. For example, concussion is often the preferred vernacular when referring to mTBI acquired in an athletic context. There are additionally inherent problems with the use of the term mTBI outside of the academic setting. There is conflicting evidence on this topic. For example, the term "mild" could lead laypeople to underestimate the severity of the injury (Reynolds et al., 2017). Conversely, the term "traumatic brain injury" might cause them equate mTBI with its more severe relatives (Dematteo et al., 2010). In general, concussion is a more accessible term that is often preferred for communicating the nature of the brain injury to clients and their caregivers. For these reasons, the terms concussion and mTBI will be used interchangeably in this paper.

As mentioned above, various groups have propounded several largely consistent definitions of mTBI and concussion. The most commonly cited definition comes from *The Mild Traumatic Brain Injury Committee of the Head Injury Interdisciplinary Special Interest Group of the American Congress of Rehabilitation Medicine* (ACRM). The ACRM (Kay et al., 1993) defines mTBI as:

a traumatically induced physiological disruption of brain function, as manifested by at least one of the following:
1. any period of loss of consciousness;
2. any loss of memory for events immediately before or after the accident;

3. any alteration in mental state at the time of the accident (e.g., feeling dazed, disoriented, or confused); and
4. focal neurological deficit(s) that may or may not be transient; but where the severity of the injury does not exceed the following:

- loss of consciousness of approximately 30 minutes or less;
- after 30 minutes, an initial Glasgow Coma Scale (GCS) of 13-15; and
- posttraumatic amnesia (PTA) not greater than 24 hours. (p. 86).

In the sports-related context, the 5th International Conference on Concussion in Sport held in Berlin (McCrory et al., 2017) outlined the following definition of concussion: a brain injury resulting in a complex set of pathophysiological processes in the brain, caused by a direct or indirect insult to the brain, with rapid onset of transient symptoms, reflecting functional rather than structural changes, and may include (but not necessarily) loss of consciousness. Symptoms typically resolve quickly, but occasionally last for prolonged periods of time. This most recent consensus statement stipulated that the clinical symptoms cannot be explained by drug or alcohol use or physical or psychological comorbidities. Clearly these two definitions are strikingly consistent, with the definition of sports-related concussion definition seemingly referring to a milder injury.

It is, however, important to differentiate mTBI from complicated mTBI. The latter is defined as a TBI meeting criteria (GCS, PTA, LOC) for a mild classification, but with evidence of brain lesion or bleeding (Griffen & Hanks, 2014). The cognitive and affective effects of this injury have been shown to be more severe than those of uncomplicated mTBI (Borgaro, Prigatano, Kwasnica, & Rexer, 2009; Iverson, 2006a). Indeed, it has even been shown to more closely resemble the effects of moderate TBI than mTBI (Kashluba, Hanks, Casey, & Millis, 2008). For this reason, this injury is not included in the current definition of mTBI, and will be differentiated throughout this paper.

Epidemiology of Mild Traumatic Brain Injury

Mild TBI is one of the most complex and controversial conditions in the field of Neuropsychology. Approximately 80% of the total number of TBIs the United States are classified as mild (McCrea, 2008). Estimates suggest that approximately 110 in 100,000 Canadians will experience concussion (Gordon, Dooley, & Wood, 2006), while the rates are higher in the United States with estimates ranging from 1.6 to 3.8 million (Bazarian et al., 2005; Langlois et al., 2006; McCrea, 2008). However, these rates are likely underestimates of the true incidence of the injury because many people who sustain a mTBI have no contact with medical institutions at any level. Although this is an issue with epidemiological research in all-severity TBI, it is particularly salient in mTBI given the mild nature of the injury and cultural pressures to "shake it off."

The demographic factors that predispose one to sustain TBI in general, appear to hold true in cases of mTBI. In an epidemiological study of mTBI in the United States, Bazarian and colleagues (2005) report that children less than 5 years old are at the highest risk of mTBI, with an incidence rate of 1115.2/100,000, followed by ages 5-14 and 15-24, with incidence rates of 733.3/100,000 and 688.7/100,000, respectively. The rates continue to drop over the course of the lifespan, until ages greater than 74 years, when the incidence rate spikes to an estimated 480.1/100,000. This distribution reflects a similar pattern to that seen in all-severity TBI, such that the youngest and oldest in the population are at the greatest risk of injury. Regarding ethnicity, Native Americans are most at risk, with an incidence of 1026.2/100,000, followed by African Americans and Caucasians with rates of 624.6/100,000 and 491.0/100,000, respectively. In terms of external cause of injury, falls and MVA were the most incident, with rates of 149.4/100,000 and 115.4/100,000, while sports-related mTBI has a lower incidence, with a rate of 32.3/100,000.

Given its high incidence rates, mTBI poses a large economic burden on society. While more severe TBI requires more intensive care, thus incurring significant medical costs, the high incidence of mTBI compared to those of moderate and severe TBI place its cost in competition with its more severe counterparts. The CDC (1999) provided estimates that the total cost of all-severity TBI in 1995 was somewhere in the range of 56 billion dollars in the United States, with mTBI accounting for 16.7 billion dollars of that cost; the costs in Canada are similarly high. Chen et al. (2012) showed that direct costs of TBI in Ontario alone are 120.7 million dollars. These figures are likely underestimates because current incidence rates are likely too low, and these figures do not include loss of productivity or indirect costs incurred by family members of patients with TBI. Little is known about the costs incurred from loss of productivity and delayed return to work, but they are suspected to be sizeable (McCrea, 2008). So although mTBI is, as the name suggests, a relatively mild injury, it still poses substantial economic burden on not only individuals who sustain the injury and their caregivers, but to society through direct and indirect medical costs, combined with lost productivity.

The Biomechanics of Concussion

A diagnosis of concussion requires the occurrence of an insult to the brain. There are, however, various potential mechanisms for this impact that could result in disparate clinical presentations. The first distinction to be made is injuries due to primary impact to the head versus inertial forces (Meaney & Smith, 2011). That is, concussion can result from an object colliding directly with the head, but this is not required. Concussion can also result when the primary force is to another part of the body, resulting in inertial (acceleration and deceleration) forces to the brain. For instance, in American football, if a player is tackled, the primary force is typically to the abdomen/chest regions, but the force to those areas results in rapid acceleration

of the head. This can result in the shaking of the brain and its collision with the inside of the skull, resulting in concussion. That is, the brain shakes within the skull, and makes contact with the skull, leading to temporary disruption of function. This will be discussed in more detail below.

The second distinction that must be made is the direction of the forces acting on the brain. That is, the head could be subject to linear, or oblique/rotational forces. Linear forces are those that hit the head "straight on," at the head's centre of gravity and perpendicular to the head. Oblique forces are those that occur at a non-orthogonal angle to the head and do not coincide with the head's centre of gravity. These directional forces result in differences in the nature of the energy transfer from the external impact to the brain. Linear forces result in semi-focal impact between the brain and the skull, while oblique forces cause the head and the brain to rotate, resulting in the pulling apart or shearing of the brain. That is, linear forces cause two types of impact between the brain and the skull. The first is called a coup injury, and refers to the initial point of impact between the brain and the skull. The second is called a contrecoup injury, and refers to the second impact of the brain with the opposite side of the skull to the initial impact. In other words, if the external object collides with the front of the head, the brain will first collide with the front of the skull (coup injury). The second step would be when the head rebounds, and the brain sustains an impact with the back of the skull (contrecoup injury). Although concussion is fundamentally a diffuse injury, the topographical locus of impact on the brain may lead to differential effects and trajectories of progression of the resulting injury.

Rotational forces, on the other hand, cause more shearing of axons in the brain. That is, when the brain is rotated quickly, it can compromise the integrity of the myelin sheaths of the axons, resulting in deficits and symptomology. This is discussed further below. So, while

concussion is generally regarded as a homogeneous injury, there are many variables to consider when contemplating the resulting presentation. Different forces acting on the brain in different locations and in different directions could result in different clinical presentations following concussion.

The Pathophysiology of Concussion

Concussion results in a transient disruption of brain function, in the absence of structural damage that is detectable by conventional imaging tools. Giza and Hovda (2014) outline the pathophysiological mechanisms of concussion, and a brief discussion will be presented here. Following a biomechanical force to the brain, there is a metabolic cascade of events, resulting in an energy crisis. The force on the brain results in mechanoporation of the neuronal membranes, resulting in an efflux of potassium ions and an influx of calcium and sodium ions. This results in a large increase in the release of glutamate. Attempting to return to its resting state, the neuron's ATP-dependent ionic pumps shift into overdrive, and thus require more energy. All of this occurs in the context of reduced cerebral blood flow (CBF), that occurs following insult to the brain. In other words, there is a mismatch between the supply and demand for energy in the brain.

These authors (Giza & Hovda, 2014) additionally provide a conceptual framework for the pathophysiological underpinnings of frequently reported post-concussion symptoms and deficits. For example, they suggest that perhaps the ionic flux observed after concussion underpins the experience of headache and other somatic symptoms such as nausea, dizziness, and so on. Furthermore, they suggest that the axonal dysfunction could cause the slowed cognition following concussion, and that altered or dysfunctional neurotransmission may underlie other cognitive impairments. Although much research is still needed in the development of theories

regarding the physiological underpinnings of post-concussion symptoms, this could suggest differential presentations following concussion dependent upon injury characteristics. For example, Meaney and Smith (2011) assert that rotational forces are more likely to result in axonal shearing, and thus injuries from rotational forces might be more likely to exhibit the pursuant slowed cognition. This is supported by the finding that advanced structural imaging techniques such as diffusion tensor imaging have detected mechanically-induced diffuse traumatic axonal injury (TAI) after concussion. Conversely, if the forces acting on the brain are linear or oblique, and thus result in more focal impact between the brain and the skull, this could present differently depending on the locus of impact. Taken together, these findings suggest the possible differentiation of neuropsychological profiles of concussion along the boundaries of mechanisms of injury.

Assessment of Mild Traumatic Brain Injury

Current recommendations for the assessment of concussion include a combination of self-report symptomology, neurocognitive testing, and balance testing (Collins et al., 2016; Guskiewicz, 2001; McCrory et al., 2017). In emergency room settings, CT scans and other imaging methods are often employed (Rose et al., 2017), with a mere 3.1 % of CT scans and 1.5% of MRI scans revealing any abnormality. More recently, there has been a push to investigate potential biomarkers (Gatson & Diaz-Arrastia, 2014) and genetic factors (Terrell et al., 2008) related to concussion presentation, trajectory, and outcome. While these assessment and diagnostic methods generally perform well, there are significant shortcomings, including their ability to provide clinicians with information regarding prognosis, trajectory, treatment, and outcome. These limitations are partially due to the extreme heterogeneity in the presentation of concussions in nearly all domains. Concussions have historically been treated as one

homogeneous group, despite the staggering heterogeneity of clinical presentations. As a result of this mismatch between the observed variability and homogeneous management, improvement of prediction and management has been hindered. The assessment and presentation of concussions is discussed below to outline the extreme heterogeneity observed in this nebulous condition.

Post-Concussion Symptoms

Mild TBIs generally produce a heterogeneous constellation of post-concussion symptoms (see Table 1). Various scales have been developed to assess post-concussion symptom reporting, typically including similar symptoms. Factor analyses have revealed somewhat consistent factor structures between these scales, generally yielding three to four factors. For example, structural analysis of the Rivermead Post-Concussion Symptom Questionnaire (RPSQ) yielded a three-factor structure including: cognitive, somatic, and emotional symptom factors (Potter, Leigh, Wade, & Fleminger, 2006). A more recent factor analysis of the same measure also yielded a three-factor structure, albeit with divergent factors for: mood and cognition, general somatic, and visual somatic symptom factors (Hermann et al., 2009). It should be noted however, that the former study included mild and moderate injuries in their sample, while the latter included all severity of injuries. Furthermore, both studies were conducted in the post-acute to chronic stages of recovery, (1 year and 6 months, respectively; Piland, Motl, Guskiewicz, McCrea, & Ferrara, 2006). A similar three-factor structure has been demonstrated for the Head Impact Scale (HIS) and the Graded Symptom Checklist (GSC; Piland, Motl, Ferrara, & Peterson, 2003). Both factor structures were encompassed by a single second-order concussion factor.

The Post-Concussion Symptom Scale (PCSS) has somewhat consistently yielded a four-factor solution at baseline and acutely post-concussion, including factors for: cognitive, emotional, physical, and sleep symptoms (Merritt & Arnett, 2014; Pardini et al., 2004).

However, a more recent factor analysis of the Post-Concussion Symptom Scale at baseline and acute post-concussion revealed a divergent factor structure (Kontos et al., 2012). At baseline, results indicated a four-factor solution including factors for: cognitive-sensory, sleep-arousal, vestibular-physical, and affective symptoms. A factor analysis of the PCSS following concussion also indicated a four-factor solution, albeit with different factors for: Cognitive-Fatigue-Migraine, Affective, somatic, and sleep arousal symptoms (Kontos et al., 2012). The first factor accounted for most of the variance in the post-concussion sample, which the authors suggested could indicate a global concussion factor. However, methodological concerns in this study limit the conclusions that can be drawn from it. These limitations include the use of orthogonal, as opposed to oblique rotation, the criterion for number of factors to retain, and the retention of factors with only two variables (Preacher & MacCallum, 2003). Given these weaknesses, one cannot confidently assert that the "global concussion factor" in fact exists.

The most recent factor analysis of the PCSS utilized the 19-item version and found a three-factor structure in athletes post-concussion. This study revealed factors for cognitive, somatic, and emotional symptoms of concussion (Joyce, Labelle, Carl, Lai, & Zelko, 2015). This factor structure was supported by a confirmatory factor analysis. Clearly, more research is needed in this area to reconcile the divergent findings. Regardless of the exact factors delineated to describe these concussion symptoms, three realities are evident regarding these symptoms: (1) they are heterogeneous, (2) patients experience them at staggeringly different rates, intensities, and durations, and (3) they are not specific to concussion.

The most commonly endorsed symptoms immediately following concussion are headache (78.5 to 85%), dizziness (51.2 to 78%), drowsiness (66.2%) feeling mentally foggy (62.3 to 70%), having poor concentration (65.8 to 70%) fatigue (69.2%) and feeling mentally

slowed down (66.9 to 68%; Lovell et al., 2006; McCrea, 2008). Despite the agreement on their use in the diagnosis of concussion, these symptoms are non-specific to this injury. There is evidence that these symptoms are common in various other conditions including chronic pain (Smith-Seemiller, Fow, Kant, & Franzen, 2003) and depression (Garden & Sullivan, 2010; Iverson, 2006b). Indeed, these symptoms are observed in healthy populations (Asken, Snyder, Smith, Zaremski, & Bauer, 2016; Garden & Sullivan, 2010; Iverson & Lange, 2003; Wang, Chan, & Deng, 2006), and athletes at baseline (Abeare et al., in preparation; Piland, Ferrara, Macciochi, Broglio, & Gould, 2010). Interestingly, up to 16% of athletes meet criteria for post-concussion syndrome at baseline (Asken et al., 2017). Although superficially this seems to cast doubt on the validity of the PCS diagnosis, there are multiple possible explanations for this finding, including a sophisticated form of sandbagging (i.e. performing poorly on cognitive measures, reporting many symptoms, thus satisfying criteria for PCS). Although this is simply a hypothesis, it is supported by the high rates of invalid performance demonstrated in other studies discussed below. This provides further support for the assertion that multiple converging lines of evidence are necessary for a confident diagnosis of concussion. Furthermore, extant research demonstrates two clusters based on the temporal stability of post-concussion-like symptom reporting in healthy college students (Balasandaram, Athens, Schneiders, McCrory, & Sullivan, 2016). The two clusters consist of stable reporters (i.e. the same number and severity of symptoms reported daily over a period of a week) and unstable reporters (i.e. rates of post-concussion-like symptoms declined over the course of a week). The high rates of post-concussion symptoms in healthy populations and other disorders combined with the instability in reporting, underscore the importance of multiple converging lines of evidence in the diagnosis of concussion, and the improvement of the methods with which we diagnose and describe it.

Cognitive Consequences of mTBI

As demonstrated above, mTBI is an extremely variable condition, which manifests in deficits in various cognitive, affective, behavioural, and vestibular domains. Karr, Areshenkoff, and Garcia-Barrera (2014) conducted a systematic review of meta-analyses on the topic, with the results corroborating the striking variability reported elsewhere. Regarding global abilities and general memory, these authors report ranges of effect sizes (Cohen's d) of .24 to .81 and .35 to .78, respectively, with great variability in the size of the effect between the types of memory examined, and the largest effect size corresponding to learning verbal pairs. The effect size for verbal fluency (d=.77) was among the largest effects in any cognitive domain, as well.

Echemendia, Putukian, Mackin, Julian, and Shoss (2001) conducted a prospective study of the performance on neuropsychological tests of collegiate athletes who had sustained a concussion. After controlling for general intellectual ability, there were no differences at baseline on any of the measures between the control and concussed groups. However, two hours post-injury, the concussed group performed significantly worse on all measures of working memory, attention, verbal learning and memory, and delayed memory. Similarly, at 48 hours post-concussion, the concussed performed significantly worse than controls on measures of working memory, verbal learning and memory, divided attention, and speed of information processing. Interestingly, the injured athletes' performance deteriorated on a test of verbal learning and memory between two hours and two days post-injury. At one week post injury, the control group continued to outperform the concussed group, although the differences did not reach statistical significance. Notably, there were differences between the control group and the concussed group on post-concussion symptoms endorsed at two hours post-injury, but they seemingly resolved prior to the evaluation at 48 hours post-injury. The authors emphasize the importance of this

finding given the lingering cognitive deficits present for up to seven days post-injury. So in addition to self-reported symptoms, cognitive deficits are variable following concussion.

Affective Consequences of mTBI

The importance of considering affective consequences of mTBI has been gaining attention in recent years. Over three decades ago, Morgan (1980) outlined what is now considered the typical mood profile of a healthy, successful athlete, termed the "iceberg profile." This profile comprises low tension, depression, anger, fatigue, and confusion scores, combined with high vigor (Mainwaring et al., 2012). Following concussion, some research has suggested that there is a reversal of this profile in which athletes demonstrate the opposite characteristics, commonly referred to as the "concussion crevice" (Mainwairing et al., 2012). A study conducted by Brewer, Linder, and Phelps (1995) demonstrated a divergent mood profile of athletes with physical as opposed to concussive injury. The difference in profiles between concussed and musculoskeletal injured athletes suggests that concussion is a special case regarding mechanisms of emotional dysfunction, beyond as a secondary reaction to removal from play.

Previous research has demonstrated that concussed athletes demonstrate greater mood disturbance and higher levels of depression compared to non-injured controls (Mainwaring, & Hutchinson, Bisschop, Comper, & Richards, 2010), although those with ACL injuries report higher levels of depression symptoms for a longer duration than those with concussion. However, the concussed athletes reported overall mood disturbance, while those with ACL injuries did not. Other studies have revealed similar emotional deficits following mTBI (Dikmen, McLean, & Temkin, 1986; Levin et al., 1987). A study by Hutchinson, Mainwaring, Comper, Richards, & Bisschop (2009) demonstrated non-significant, but elevated, depressive symptom scores at two weeks post-injury.

Regarding recovery of emotional symptoms, it appears that they might follow a similar trajectory to cognitive deficits following concussion (Mainwaring et al., 2012). A similar study conducted by Hutchinson et al. (2016) demonstrated elevated tension, depression, anger, and confusion, and diminished vigor and self-esteem in the acute stage of recovery following concussion. The researchers followed up with the athletes at two subsequent time points: following symptom resolution, and following medical clearance for return to play. Following symptom resolution, mood scores were comparable to those of the control group. Previous research has suggested that these emotional disturbances can last up to 3 weeks (Mainwaring et al., 2004). After clearance for RTP, however, concussed athletes had lower depression and fatigue scores and better sleep quality, compared to the control group, suggesting some kind of rebound effect (Hutchinson et al., 2016). Taken together, these findings indicate that concussion typically results in some, typically transient, emotional dysfunction.

Balance Data in Concussion Assessment

It is now widely accepted that balance data should be included in the assessment of sport-related concussion (McCrory et al., 2017). The NCAA Concussion Study, conducted by McCrea et al. (2003) demonstrated substantial impairment in postural stability, measured by the Balance Error Scoring System (BESS), in a large sample of concussed collegiate athletes. These balance disturbances followed a similar trajectory of recovery to cognitive deficits and symptomology, recovering within 3 to 5 days. In fact, some studies have demonstrated that balance data may have incremental clinical utility to other forms of evaluation (cognitive and symptomology) in that it can detect abnormal balance, even following the resolution of cognitive deficits and self-reported symptoms (Howell, Osternig, & Chou, 2018). Various methods of measuring balance in the context of concussion assessment have emerged, ranging from rudimentary visual sideline

evaluations to relatively sophisticated balance-plate measurement of total sway of the centre of gravity. These have already been shown to be useful in the evaluation of concussion, and this is a burgeoning area of research in the concussion domain.

Impression Management in Sports-Related Concussion

Another factor to consider in the assessment of post-concussion symptoms is the degree to which athletes accurately report their symptoms. Because self-reported symptom inventories are inherently subjective, there is great potential for inaccuracy. There are various reasons this might be so, ranging from poor insight to deliberate deception. That is, individual differences in perceptions of bodily sensations and proprioception could lead to discrepant reports of symptoms despite no "actual" difference in the underlying pathophysiology. Because there is no way to objectively determine the extent to which these symptoms are experienced, there is room for error.

A second reason at the opposite end of the spectrum in terms of intent, is deliberate impression management, be it positive or negative. Athletes are generally very motivated to return to play, and thus often underreport symptoms to create the façade that they are recovered. This underreporting of symptoms motivated by eagerness to return to play is well-documented in the literature (Kroshus, Garnett, Hawrilenko, Baugh, & Calzo, 2015; Meier et al., 2015; Williamson & Goodman, 2006). Athletes who underreport symptoms, however, would presumably still demonstrate impairment in the cognitive and vestibular domains, representing a unique profile of scores on post-concussion testing. Similarly, there is a culture in sports to "shake it off." That is, athletes who experience this pressure might underreport symptoms to conform to the cultural pressures (Kroshus et al., 2015).

Some of these ideas additionally pertain to baseline testing, except the motivation is in the opposite direction. That is, at baseline, athletes will often under-perform on the cognitive measures (referred to as "sandbagging") to lower the bar for recovery in the event of a subsequent concussion. That is, they engage in negative impression management, and do not perform to their highest potential. This would result in a profile of scores reflecting high symptoms and lower cognitive performance at baseline.

There is a burgeoning literature on the assessment of performance and symptom validity in mTBI at baseline and post-injury. The ImPACT includes some embedded validity indicators (Lovell, 2011), but they generally do not perform well (Abeare, Messa, Zuccato, Merker, & Erdodi, 2018). There have been third-party attempts to develop logistic regression equations and other embedded indicators for the ImPACT, demonstrating high rates of invalid performance (Abeare et al., 2018). It has additionally been shown that common stand-alone validity indicators might be useful in the assessment of performance validity in athletes (Abeare et al., submitted), demonstrating that up to approximately 50% of athletes fail at least one performance validity test (PVT). Although this is below accepted forensic standards of failing two or more PVTs (Boone, 2013), it suggests a striking need for validity assessment in baseline and post-concussion assessment. It is possible that profiles reflecting the under- or over-reporting of symptoms or feigning of cognitive weaknesses could be shown through the delineation of subgroups of concussions based on symptoms and cognitive performance. Indeed, Morin and Axelrod (2017) delineated a four-cluster structure of a Veterans Affairs sample of veterans who underwent neuropsychological assessment, with performance and symptom validity status emerging as important variables in the delineation of these subgroups. A similar structure is expected to emerge in this study.

Sex and Gender Differences in the Effects of Concussion

It is widely recognized that increased research is needed into the differential experiences of females with concussion. The studies that have examined gender differences in the effects of concussion have found that females may be more likely to incur a concussion (Covassin, Swanik, & Sachs, 2003; Dick, 2009; Gessel, Fields, Collins, Dick, & Comstock, 2007), may experience worse outcomes compared to their male counterparts, and may take longer to return to play following a concussion (Stone, Lee, Garrison, Blueitt, & Creed, 2017). Females exhibit more substantial deficits in reaction time and visual memory, report more post-concussion symptoms, and are 1.7 times more likely than males to be cognitively impaired following concussion (Broshek et al., 2005; Covassin, Elbin, Harris, Parker, & Kontos, 2012; Covassin, Schatz, & Swanik, 2007; Lovell et al., 2006). Furthermore, extant research demonstrates differences at the individual symptom level such that men are more likely to endorse vomiting, sadness, confusion/disorientation, and amnesia. Conversely, females are more likely to report drowsiness and sensitivity to noise (Covassin et al., 2007; Frommer et al., 2011). Indeed, there are even differences observed at baseline between males and females such that males perform better on measures of visual memory, and females perform better on measures of verbal memory. Some research suggests that females might report more symptoms at baseline (Covassin et al., 2006; 2010; Lovell et al., 2006), while other studies find no difference (Garden & Sullivan, 2010). It is possible that these trends of females experiencing greater deficits following concussion are a artifact of the difference in athletic culture between male and female sports, namely that males are more under more pressure to "Shake it off" and are thus more likely to underreport symptoms following concussion. Furthermore, males may be more likely to sandbag their baseline tests, resulting in a diminished disparity between their baseline and post-concussion cognitive scores,

resulting in the illusion that they are less affected than females. This topic requires much further investigation. Interestingly, Asken et al. (2017) found that women are 1.7 times more likely to meet criteria for PCS at baseline compared to men, supporting the assertion mentioned above that men may simply underreport symptoms. Increased research is needed in this area to help to explain the mixed findings. Despite these mixed findings, some research suggests that females are more likely to continue to report post-concussion symptoms at three months post-injury (Bazarian, Blyth, Mookerjee, He, & McDermott, 2010).

It has been proposed that at least part of the reason for these sex differences are differences in the levels of the hormones estrogen and progesterone between males and females (Brown, Elsass, Miller, Reed, & Reneker, 2015). Several studies have provided indirect evidence for this hypothesis. For example, Bazarian et al. (2010) showed that while women seem to report more post-concussion symptoms following concussion at all stages of life, this effect is particularly prominent during the childbearing years, when these hormones are in a state of relative flux. Furthermore, extant research shows that women currently consuming oral contraceptives, which regulate these hormones, tend to report fewer and less severe post-concussion symptoms (Mihalik, Ondrak, Guskiewicz, & McMurray, 2009). This study also demonstrated no difference across the menstrual cycle in eumenorrheic women. Although it is contrary to the previous study, some studies have shown symptom reports to vary across the menstrual cycle (Ross, Coleman, & Stojanovska, 2003). For example, Malleck and Abeare (in preparation) demonstrated that fluctuations in menstrual hormones in healthy female university students tend to affect the *nature* of their post-concussion symptoms, rather than the severity. No research to date has examined the experiences of members of the transgender or non-binary communities with concussion. Taken together, these findings suggest that perhaps males and

females might react differently to concussion, and thus exhibit different profiles of symptoms and deficits.

Recovery from mTBI

Recovery from mTBI is often divided into three consecutive stages: acute, sub-acute, and chronic (Barr, 2014). The acute phase is characterized by transient neurophysiological disruption, resulting in symptomology and neurocognitive dysfunction. This dysfunction typically resolves within 7-10 days. The sub-acute stage involves a period of continued brain recovery, typically observable only through advanced neuroimaging such as Diffusion Tensor Imaging (DTI) and functional magnetic resonance imaging (fMRI; Jantzen, Anderson, Steinberg, & Kelso, 2004). This stage can last several weeks, up to three months. The chronic stage is characterized by persistent symptoms beyond three months, and patients falling in this category reflect post-concussion syndrome (Lishman, 1988; Ryan & Warden 2003). This is discussed in a later section.

As discussed above, assessment of self-report symptomology is one component of the recommended protocol for the diagnosis of concussion. These symptoms are most prevalent and severe immediately following injury, and demonstrate improvement within two hours continuing in the following days (McCrea, 2008). In fact, 21% of patients seem to report full symptom recovery within 1 day, 64% between 1 and 7 days, 11% between 8 days and one month, with only about 3% experiencing symptoms beyond one month (McCrea, 2008). However, there is variability depending on several factors, including age. That is, younger people tend to have more prolonged and variable recovery times (Williams, Puetz, Giza, & Broglio, 2015).

Recovery of cognitive dysfunction following mTBI has been shown to follow a similar course to symptomology. That is, mTBI patients' cognitive functioning recovers rapidly and, it

would seem, completely (McCrea, 2008). Iverson, Brooks, Collins, & Lovell (2006) demonstrated impairment one day following concussion on verbal and visual memory. However, these two categories of memory appeared to recover at differing rates, with verbal memory remaining impaired at five, but not ten days post-injury, and visual memory exhibiting clinically significant change (i.e. no longer in the impaired range) by five days post-injury. Similarly, there was impairment at one day post-injury on processing speed and reaction time, with only reaction time remaining in the impaired range at five days. Consistently, mTBI-induced cognitive deficits have been shown to be very small at three months, and non-existent at one year (McCrea, 2008). Several meta-analyses have supported similar conclusions (Belanger, Curtiss, Demery, Lebowitz, & Vangerploeg, 2005; Frencham, Fox, & Maybery, 2005; Schretlen & Shapiro, 2003). Given that concussion falls at the mild end of the spectrum of mTBI, and that athletes tend to be healthier and may have other protective attributes, it should be no surprise that the recovery time appears to be much shorter. More specifically, athletes have been shown to recover cognitively within five to seven days (Iverson, 2006a; McClincy, Lovell Pardini, Collins, & Spore, 2006; Williams, Puetz, Giza, & Broglio, 2015), although their initial cognitive deficits have been shown to be comparable to those in other etiological categories of mTBI (Belanger & Vanderploeg, 2005). Similarly, balance scores tend to recover within three to five days (McCrea et al., 2003), although they may persist longer with more sensitive measures, given the evidence discussed above that balance deficits can be clinically useful in detecting lingering effects of the concussion, even following the resolution of cognitive deficits and symptoms (Howell, Osternig, & Chou, 2018).

Prediction of Recovery from Concussion

There is a burgeoning literature on the prediction of outcomes following concussion. Several studies have identified pre-and post-injury predictors of outcome following concussion. Merrit & Arnett (2014) demonstrated that physical and affective symptoms at baseline predicted athletes' classification into groups based on high and low levels of post-concussion symptoms, such that higher endorsement of affective symptoms increased the likelihood that athletes would be classified in the high post-concussion symptom group, and higher levels of physical symptoms at baseline reduced the likelihood of being in the high post-concussion symptom group. Collins and colleagues (2003) additionally showed that self-reported post-traumatic headache corresponded to poorer reaction time and memory scores.

Predictors of prolonged post-concussion recovery times include: low premorbid resilience and depressed mood (McCauley et al., 2013), being female, (Merritt & Arnett, 2014), poor sleep (Sullivan, Berndt, Edmed, Smith, & Allan, 2016), age (Field, Collins, Lovell, & Maroon, 2003), dizziness at time of injury (Lau, Kontos, Collins, Mucha, & Lovell, 2011), moderate to severe pain at time of injury, poor performance on emergency room tests of immediate and delayed recall, headache severity (Faux, Cheedy, Delaney, & Riopelle, 2011), premorbid physical and mental health status (McLean et al., 2009), and premorbid emotional function (Vargas, Rabinowitz, Meyer, & Arnett, 2015), among others. Despite the multitude of variables that have been identified to be predictive of concussion recovery time, the ability of clinicians to forecast those most at risk for protracted recovery is weak, at best. If more homogeneous subgroups can be delineated, the ability of the clinician to identify and target for intervention, those most at risk for poor outcome could be improved.

This approach has been investigated by Lau, Collins, and Lovell (2011a; 2011b; Lau, Lovell, Collins, & Pardini, 2009). These authors investigated the prognostic utility of total post-

concussion symptom score, as well as four symptoms clusters (migraine, cognitive, sleep, and neuropsychiatric) and four cognitive scores (verbal memory, visual memory, processing speed, and reaction time). These metrics were able to predict, with good sensitivity, specificity, and positive and negative predictive power, whether athletes would fall into one of two dichotomous groups: normal or prolonged recovery. These authors later developed cut-off scores for each of these clusters and demonstrated their predictive ability (Lau, Collins, & Lovell, 2011a; 2011b). These symptom and cognitive clusters demonstrated incremental utility above and beyond they typical ImPACT scoring system.

Post-Concussion Syndrome

It is generally agreed that the large preponderance of concussions, approximately 80-90%, will recover fully within 7 to 10 days (Collins et al., 2016; McCrory et al., 2017), with some variation between age groups and level of play (Field et al., 2003; Williams et al., 2015). Specifically, Williams et al. (2015) conducted a meta-analysis of concussion recovery times in high school and collegiate athletes and found that high school athletes tend to recover symptomatically within 16 days and cognitively within 7 days. Conversely, collegiate athletes tend to recover symptomatically within 5 days and cognitively within 7 days. So, it appears that younger athletes' recovery times are considerably longer and more variable. While most concussions recover within this timeframe, there is a small minority who experience prolonged, and occasionally indefinite, symptoms. This condition has been coined Post-Concussion Syndrome (PCS; Bigler, 2008; Lishman, 1988; Ryan, 2003), and its sufferers, "the miserable minority" (Wood, 2004).

Estimates of the prevalence of this condition range from 3% to 15% (McCrea, 2008; Alexander, 1995). The former is more likely to be closer to the true incidence because of

methodological concerns in studies with higher estimates. Both the International Classification of Diseases 10th edition (ICD-10; World Health Organization, 1992) and the Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM IV; American Psychiatric Association, 2000) have criteria that must be met for one to qualify for this diagnosis, but Post-Concussion Syndrome was not included in DSM-5 (APA, 2013). There has been a surge of research aimed at identifying those most at risk for protracted recovery, discussed above.

There are several theories in the literature pertaining to the etiological mechanisms of PCS, and a short discussion will be presented here. Lishman (1988) conducted the seminal work on PCS, postulating that neurobiological factors predominate the acute presentation of concussion, but there is a temporally-driven shift to primarily psychogenic propagation of the experience of symptoms in the sub-acute and chronic stages. Silverberg and Iverson (2011) conducted a systematic review of the literature to examine the predictions of Lishman's model. These authors report that there is a reciprocal causal relationship between acute emotional and post-concussion symptoms. They additionally confirm the link between emotional distress and PCS in the chronic stage of concussion recovery. The authors were unable to come to any conclusion regarding two of the predictions of Lishman's model: (1) that psychological distress should increase over time in those who do not recover, and (2) that the relationship between emotional distress and post-concussion symptoms should increase over time. The results of this study underscore the paucity of well-designed research in this area. Despite this, several theories in addition to Lishman's have been proposed regarding the etiological mechanisms of PCS.

Mittenberg, Digiulio, Perrin, and Bass (1992) proposed a theory implicating expectation as an etiological mechanism in PCS. These authors posit that patients in the chronic stage might continue to erroneously attribute symptoms to the head injury, when they are common in the

healthy population. Evidence for this hypothesis is provided by the finding that post-concussion symptoms are common in healthy populations (Asken, Snyder, Smith, Zaremski, & Bauer, 2016; Garden & Sullivan, 2010; Iverson & Lange, 2003; Wang, Chan, & Deng, 2006), and athletes at baseline (Abeare et al., in preparation; Piland, Ferrara, Macciochi, Broglio, & Gould, 2010). In the original paper, Mittenberg et al (1992) asked healthy lay people to report their current symptom levels, and then imagine that they have had a brain injury and report what they would expect to experience at 6 months post-injury. The symptom profile described mapped well onto the reports of PCS in the literature.

Another proposed etiological mechanism of PCS, called "the good old days hypothesis," was propounded by Gunstad and Suhr (2001). Their theory postulates that individuals tend to report fewer symptoms and better functioning in the past as opposed to the present. This theory is very similar to the expectation as etiology theory, except that the good old days hypothesis is more broad in that it postulates that following any negative event, not only head injury, individuals tend to attribute symptoms to that event. Other explanations include a general nocebo effect (McCrea, 2008), in which expectations of illness or being unwell causes symptoms to appear, and the stress-diathesis hypothesis (Wood, 2004), which integrates physiological, cognitive, and psychological variables in the explanation of PCS. The basis of this model is that there is a predisposition to PCS, and that stressors during the recovery process can bring out this predisposition. Despite these efforts, more research is needed regarding the etiology of PCS, and thus its prediction remains problematic. If more homogeneous subgroups can be delineated, this could lead to improved ability to identify those most at risk for PCS and target them for early intervention aimed at prevention.

Repeated mTBI

Concern over the long-term effects of repeated concussion has prompted a burgeoning literature regarding the effects of multiple mTBIs. Findings are mixed regarding the cumulative effects of multiple mTBIs. Karr et al. (2014) report that effect sizes for cognitive deficits following concussion are generally larger when participants with a history of mTBI are included in the analyses as opposed to when they are excluded, although the effect sizes are small. Indeed, there is some evidence for a dose-response gradient for worsened baseline neurocognitive performance beginning with a history of two concussions (Covassin, Elbin, Kontos, & Larson, 2010). That is, those with a history of three previous concussions would exhibit more significant cognitive deficits than those with two, and so forth, although some studies have found an effect of one previous concussion (Colvin et al., 2009).

Consistently, Iverson, Gaetz, Lovell, & Collins (2004) demonstrated that athletes with a history of multiple concussions are 7.7 times more likely to exhibit a substantial drop in memory performance following concussion than those with no history. Similarly, extant research demonstrates that athletes with a history of multiple concussions take longer to recover verbal memory and reaction time as well as migraine, cognitive, fatigue symptoms than those with no history of concussion (Covassin, Moran, & Wilhelm, 2013; Covassin, Stearne, & Elbin, 2008). Regarding on-field characteristics of concussion, Collins and colleagues (2002) showed that high school athletes with a history of three or more concussions are more likely to experience loss of consciousness, anterograde amnesia, and confusion following a subsequent concussion. In fact, they were 9.3 times more likely to exhibit three out of four indicators of more severe concussion.

Furthermore, previous research suggests that athletes with a history of concussion experience a higher number and more severe post-concussion symptoms at baseline (Gaetz, Goodman, & Weinberg, 2000; Piland et al., 2010), and display a delayed P300 (event-related

potential that is responsive to unexpected stimuli) compared to athletes with no history of concussion (Gaetz, Goodman, & Weinberg, 2000). Other studies have found no difference in neurocognitive performance or symptom reporting based on previous concussion history (Collie, McCrory, & Makdissi, 2006; Iverson, Brooks, Lovell, & Collins, 2006; Tsushima, Geling, Arnold, & Oshiro, 2016). Although evidence is incomplete (Carson, 2017), some studies have linked repeated concussion to early onset of dementia in the form of Chronic Traumatic Encephalopathy (CTE; Gardner & Yaffe, 2015). Some research has also demonstrated a higher risk of major depression (Guskiewicz, et al., 2007).

Along a similar vein, researchers have investigated the effect of sub-concussive hits on neurocognitive performance and symptom reporting. Although this literature is in its nascent stages, studies generally agree that if there is an effect, it is likely small (Belanger, Vanderploeg, & McAllister, 2016; Chrisman et al., 2016). Taken together, these findings suggest that athletes with a significant history of past concussions might present divergent neuropsychological and symptom profiles in the acute stages of the injury.

Subtypes of Concussion

Concussion is one of the most controversial topics in neuropsychology. One reason for this controversy is its extremely variable acute and chronic presentation. Despite this staggeringly heterogeneous presentation, it has historically been diagnosed and managed as a homogeneous condition. Several lines of evidence discussed above suggest possible differentiation of subgroups of concussion. First, different types of forces acting on the brain could result in different injury characteristics. Furthermore, there could be differences in injury characteristics based on direct vs. inertial forces on the brain. Moreover, it is possible that the loci of the impact could result in further differentiation. Further, emotional dysfunction may

underlie many of the symptoms such that people who are more anxious may be more aware of their symptoms or attribute pre-existing symptoms to the concussion. Similarly, because of the increased motivation to return to play, athletes might under-report symptoms post-concussion, resulting in a disjunction between cognitive deficits and symptoms.

For the reason discussed above, several researchers have made attempts to uncover more homogeneous subgroups within concussion. The earliest of these attempts of which I am aware was a thesis by Brian Mainland (2010). This researcher applied cluster analysis to a population of mTBI patients who had undergone a comprehensive neuropsychological evaluation. Two separate clusters were identified in each of the following cognitive domains: intelligence (based on WASI performance), memory (based on Logical Memory, CVLT-II, and Rey Complex Figure Test), Fluency (based on Controlled Oral Word Association Test and Ruff Figural Fluency Test), and cognitive flexibility and attention (based on Trail Making Test A and B, and Short Booklet Category test). This study also examined how demographic and comorbid psychiatric conditions affect group membership, finding that some of these variables contributed to membership.

A more recent investigation of this question came from Collins and colleagues (2014). In a conceptual paper, these authors outlined a comprehensive approach to the management of concussion including clinical "trajectories" of concussion, equipped with management and treatment recommendations for each. These authors assert (citing Kontos et al., 2012) that initially patients with concussion all conform to a global concussion symptom factor including cognitive deficits, fatigue, and migraine, but diverge after seven days into discrete trajectories. The authors outline six trajectories including: cognitive, vestibular, ocular-motor, post-traumatic migraine, cervical, and anxiety/mood. These trajectories will be discussed here. The cognitive

trajectory refers to patients with symptoms including fatigue, decreased energy levels, headache, and sleep disruption. The vestibular trajectory constitutes patients who experience "dizziness, fogginess, nausea, a feeling of being detached, anxiety, and overstimulation in more complex environments" (p. 241). The Ocular-motor trajectory reflects patients who experience "localized, frontally based headaches, fatigue, distractibility, difficulties with visually based classes, pressure behind the eyes, and difficulties with focus" (p. 241). The anxiety/mood trajectory includes patients who experience "anxiety, including ruminative thoughts, hypervigilance, feelings of being overwhelmed, sadness, and/or hopelessness" (p. 242). The post-traumatic migraine trajectory refers to patients who experience intermittent migraine following concussion. Lastly, the cervical trajectory reflects patients who do not fit into the other trajectories and report neck pain and headache. These clinical trajectories might assist the clinician in predicting outcomes and developing treatments that cater to the individual needs of each patient, consistent with the individualized nature of this injury.

Consistent with the previous study, Ellis, Leddy, and Willer (2015) proposed a framework for creating more homogeneous post-concussion disorders (PCD) to supplant the currently nebulous conceptualization of PCS. Three PCDs in total were delineated, including: physiologic, vestibulo-ocular, and cervicogenic. All three PCDs are characterized by persistent post-concussion symptoms, but differ on the causes of these protracted symptoms. The physiologic, vestibular-ocular, and cervicogenic PCDs attribute the prolonged recovery to impaired cerebral metabolism, impaired vestibulo-ocular system, and dysfunction of the spinal somatosensory system, respectively. These authors call for individualized treatment of PCDs based on group membership.

As shown by these studies, there is great potential for the delineation of more homogeneous subgroups of concussions. The implications of such work are vast. Firstly, regarding diagnosis, delineating more homogeneous subgroups would increase diagnostic accuracy and agreement. Regarding acute management of concussion, the various subgroups may require unique immediate treatment to optimize recovery. In this stage, the classification of patients into relatively homogeneous groups could provide clinicians with a method of identifying those most at risk for poor recovery and outcome and allow for early intervention to circumvent these issues. The delineation of subgroups could allow for the development of treatments tailored to these specific groups leading to quicker recovery and return to play, along with lower rates of prolonged recovery. These advantages in the early stages could ultimately improve trajectory of recovery, and outcome.

The purpose of the current study will be to attempt to empirically derive neuropsychological subgroups of concussion from neurocognitive data and self-report symptomology. Based on previous work, I propound two expectations for the outcomes of this study. First, I expect that subgroups will emerge from the data. Second, I expect that, similarly to the study by Morin and Axelrod (2017) discussed above, at least one cluster along the boundaries of impression management will emerge. Despite ample reasons to predict subtypes will emerge, specific hypotheses are not warranted given the paucity of previous work in this area and the exploratory nature of this study.

CHAPTER 2:

METHODS

Participants

This study utilized archival data collected during baseline and post-concussion assessments. Participants were a consecutive case series comprised of 1366 athletes (872 male, 494 female; M_{age}=15.6, SD_{age}=1.9). Athletes <10 or >24 years of age were excluded. This criterion excluded 22 participants, so the sample used in this study accounted for 98.4% of the total sample of post-concussion assessments. The former criterion is in place because the ImPACT is normed for children 10 years and older (Lovell, 2011), and thus would not represent a valid assessment of younger children. The latter criterion is in place given that those aged 25 and over represent a neurodevelopmentally distinct category. Mean education of the sample was 9.1 (*SD*=1.7), and the average number of previous concussions was 0.9 (*SD*=1.0). Participants are primarily English-speaking (99.6%), and dextral (87.2%).

The acute sample (time since injury ≤7 days) consisted of 330 post-concussion athletes (226 male, 104 female; M_{age}=15.6, SD_{age}=1.9). The same exclusion criteria listed above, in addition to the additional inclusion criterion of time since injury were applied to this sample. The mean education of this sample was 9.3 years (SD=1.8), and the average number of previous concussions is 1.0. Participants were primarily English-speaking (99.6%) and dextral (88.6%).

Procedure

Data consist of a consecutive series of baseline and post-concussion assessments between the years of 2007 and 2016 at Henry Ford Hospital in Detroit, Michigan. Baseline assessments were administered in a group setting with approximately 20 athletes per group. These sessions were supervised by either a registered neuropsychologist or an athletic trainer. Post-concussion assessments were conducted on an individual basis after athletes were suspected of having sustained a concussion. Post-concussion assessments were supervised by either a neuropsychologist, an athletic trainer, or a sports-medicine physician. In addition to the

ImPACT, balance testing and a neurological exam were administered at post-concussion. All guidelines pertaining to the ethical treatment of human participants in research were followed. This project was approved by the institutional research Board (IRB) at site of data collection, as well as the Research Ethics Board (REB) at the site of study.

Measure

The Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT; Lovell, 2011) is an online neurocognitive measure designed to assess concussion. The measure consists of the 22-item self-report PCSS, and five performance-based cognitive indexes for: Visual and Verbal Memory, Reaction Time, Visuo-Motor Speed, and Impulse Control. The PCSS demonstrates good internal consistency (α=.88 -.94) across age and gender and at baseline and post-concussion (Lovell et al., 2006). Test re-test reliabilities for the cognitive scales ranges from r=.45 (verbal memory composite) to r=.76 (Visuomotor Composite; Bruce, Echemendia, Meeuwisse, Comper, & Sisco, 2014). Maerlender et al. (2010) investigated the construct validity of the ImPACT by comparing it to a battery of standard neuropsychological tests. These authors showed that at least two scores from each of the ImPACT indexes except impulse control were related to standard neuropsychological tests in the same or similar domains (r=-.31 to .59). A factor analysis of the ImPACT in a non-concussed healthy sample supported a five-factor solution, but did not support the test's particular index structure (Allen & Gfeller, 2011). The same study found correlations between ImPACT scores and standard neuropsychological tests of r=-.39 to 0.49. Schatz, Pardini, Lovell, Collins, and Podell (2006) demonstrated significant differences between concussed and non-concussed athletes on all indexes included in the ImPACT. In this study, 82% of concussed athletes were correctly classified, compared to 89% of non-concussed athletes, with an overall classification accuracy of 85.5%.

Data Analysis

Latent Gold version 5.1 was used to conduct an exploratory latent class analysis (LCA) to identify latent groups underlying the data. This analysis is also known as Model-Based Clustering, Mixture Likelihood Approach to Clustering, mixture model clustering, probabilistic clustering, Bayesian Classification, Unsupervised Learning, and Latent Class Cluster Analysis (Hagenaars & McCutcheon, 2002). This technique is similar to conventional cluster analysis in its result, but the process is very different. That is, LCA assumes an underlying latent categorical variable, consisting of multiple probability distributions, that describe the clusters identified in the analysis. This technique clusters based on probability. In other words, it is a top-down approach, in which a model (see figure 1) is imposed on the data, and where parameter estimates are developed to maximally explain the covariation between the variables and cases. The degree that the model fits the data is then tested, to determine if it is an adequate explanation for the data. An advantage of this procedure is that it has more objective criteria for the number of classes and model fit (Akaike Information Criterion, Bayesian Information Criterion, Sample-Adjusted Bayesian Information Criterion, percent correctly classified, entropy R^2). While LCA does have advantages over conventional cluster analysis, there are strengths of conventional cluster analysis as well, such as its versatility, that a model does not need to be specified a priori, and that it is not technically a statistical technique, so it is not beholden to statistical assumptions in the same way as some techniques.

Various fit statistics are available in LCA, as mentioned above. First, Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), Sample-Adjusted Bayesian Information Criterion (SABIC), and Approximate Weight of Evidence (AWE) are all fit indices that take into account the amount of information lost in the data reduction process, as well as the parsimony of

the solution. AWE additionally considers classification accuracy. To interpret these indices, one should look for the point in the series of cluster solutions when the value reaches its lowest point and the value starts to increase again. Entropy R^2 (herein referred to as entropy) is another fit index in LCA. This is a measure that captures the overall classification accuracy of the models across all of the clusters. In this case, the higher the value (closer to 1.0), the better fit the model is for the data. Lastly, the proportion of total Bivariate Residuals (BVRs) above the cutoff point of 3.84 (chi square distribution; p=.01) was used as a fit index. In this case, if there are BVRs above the cutoff point, it indicates that the model is not adequately accounting for the association between those two variables, resulting in local dependence. So, models were considered to meet minimum requirements when the BVRs greater than the cutoff were at 0%.

Latent class analysis, controlling for time since injury, was applied to data from the ImPACT, five cognitive variables (visual and verbal memory, reaction time, visuomotor speed, impulse control) and four symptom clusters (cognitive, migraine, sleep, neuropsychiatric; see Table 1), obtained from concussed athletes to delineate subgroups. The symptom cluster scores were computed as sums of the ratings of their constituent items from the PCSS. The primary analysis was conducted on the overall sample of athletes who met inclusion criteria. Follow-up analyses included analysis of cognitive and symptom variables separately. These analyses were repeated in a sample of only athletes in the acute stage (≤7 days) of recovery.

Data Screening. Data were examined for missing values. There were missing values for education, years playing the sport, number of previous concussions, and time since injury. The number of values missing for each of these variables were 25, 287, 250, and 542, respectively. These missing values are an inevitability in retrospective clinical data due to participants simply not entering values. While it is not ideal to have this many missing values, the analyses were

computed because these are the best data available to the current study. Cases with missing data were included in the analysis, given LCA's ability to handle missing cases (Madgison, 2017).

Assumptions. Latent Class Analysis does not have explicit assumptions in the manner that many other statistical techniques do. For example, it is not required that the data conform to a normal distribution because the assumption of LCA is that there are multiple distributions underlying the manifest one, with each corresponding to a different latent class. The common assumptions, such as independence of observations, and multicollinearity do apply here, and are met. Each athlete's testing was conducted individually, so the observations are independent of one another, and examination of a bivariate correlation table reveals that there are no two variables so highly correlated so as to introduce an issue. One assumption that is specific to LCA is local independence. That is, following the analysis, the variables will be independent of one another within the classes because the model will account for the relations between them. This assumption can be relaxed by allowing direct paths between variables that would theoretically be expected to correlate even after the model is applied, and this method was used in the current analyses. The procedure is described below, since it was an iterative procedure, occurring after the first round of analyses revealed unacceptably high bivariate residuals among theoretically defensible associations. Lastly, no outliers were removed from the data because of the second expected outcome, that a performance validity cluster would emerge. Invalid performance/reporting is often detected by examining data for unfeasible patterns of performance/reporting. Thus, to remove outliers might have removed interesting cases that could fall into this cluster.

Specifications. Variables selected as indicators were the five cognitive variables (visual and verbal memory, reaction time, visuomotor speed, and impulse control) as well as the four

symptom clusters (migraine, cognitive, sleep, and neuropsychiatric symptoms; see Table 1). All of these were treated as continuous variables. Latent gold allows for the inclusion of active and inactive covariates. Active covariates are taken into account in the estimation of the model, while inactive covariates are simply used to characterize the resultant clusters, post hoc. The only variable included as an active covariate was time since injury, while inactive variables included age, gender, education, ADHD, Dyslexia, Autism, number of years playing the sport, number of previous concussions, and total symptoms. Time since injury was included as an active covariate because this is considered to be an important variable in concussion because of the very quick recovery from concussion. In terms of model specification, there is an option to include direct effects between indicators, if they are expected, based on theory, to still be associated even after the model is applied. This option was not used in the first iteration, but was used in later iterations based on the magnitude of bivariate residuals (BVRs; residual association between two variables after application of the model), and theoretical considerations (i.e. does it make sense that these two variables would still be associated?). Large-magnitude BVRs (>15.0) emerged for the associations between the migraine and cognitive symptom clusters, as well as between the visual and verbal memory cognitive scores, and the reaction time and visuomotor speed cognitive scores. Direct paths were included in the model between these variables for all further analyses. There were other lower magnitude (although still above the acceptable cutoff of 3.84; e.g. between VMS and migraine cluster, etc.) BVRs that were less theoretically defensible. Furthermore, given that these BVRs were closer to the acceptable level, the inclusion of more latent classes or clusters in the tested models would reduce these to within acceptable levels, in most cases. For these reasons, direct paths were not included between the remainder of the variables with BVRs above 3.84.

CHAPTER 3:

RESULTS

Overall Sample

The fit of an initial LCA model presented in figure 1 was tested with the data from all athletes in the sample (n=1366), including the five cognitive variables (verbal and visual memory, reaction time, visuomotor speed, and impulse control) and four symptom clusters (migraine, cognitive, sleep, and neuropsychiatric). Models including one through 10 clusters were tested, because a solution in excess of 10 clusters would have dubious utility. The initial models had several large magnitude BVRs between variables that would be theoretically related, even after the application of the model. For this reason, direct paths were specified between cognitive and migraine symptoms, visual and verbal memory, and visuomotor speed and reaction time, and then the models were re-run. Even with these specifications of the direct paths, none of the tested models included all BVRs in the acceptable range (see Table 4). BVRs are a metric of association between two variables that is unexplained by the tested model. Since the purpose of LCA is to explain the associations between variables using a latent variable, BVRs can be used as a fit metric. That several of the models included BVRs greater than 3.84 (chi-square distribution, df=1, p=.01) indicates that the models were not good fits for the data. Furthermore, with the exception of the approximate weight of evidence criterion (AWE), which bottomed out at eight classes, and Entropy, which indicated that any of the models could fit, all other indices indicated that there was no model that optimally fit the data. That is, the fit criteria continually improved as more clusters were added to the model (see Table 4).

It is possible that a different combination of variables would be more conducive to a well-fitting model. To this end, a model including only the five cognitive variables was then

tested, allowing direct pathways between the reaction time and visuomotor speed variables, as well as the visual and verbal memory variables, because these would theoretically be related (the rationale for direct paths is described above). This round of analyses revealed a somewhat different pattern of results. Each of the metrics indicated a different solution (see Table 5), with BIC indicating a five-cluster solution, AIC not indicating any solution, SABIC indicating a seven-cluster solution, and AWE indicating a two-cluster solution. The BVRs indicated that solutions including anywhere from six to 10 clusters were acceptable, and Entropy indicated that only the one cluster solution fit the data well. The same analysis was computed with the four symptom clusters. Except for the BVRs, which indicated that any of the solutions ranging from five to 10-cluters was acceptable, and Entropy, which indicated any of the models were minimally acceptable, none of the other indices indicated an acceptable solution (see Table 6). None of the analyses above yielded cluster solutions that indicated a good fit for the data.

Furthermore, for all analyses above, the clusters that emerged simply reflected "levels of performance," such that the within-cluster scores on each of the measures was at a consistent level, relative to the other clusters. Put another way, participants in each cluster performed at similar levels on all five cognitive variables and reported symptoms at levels that would be expected based on their cognitive scores. Moreover, as more clusters were included in the model, it simply reflected more fine-grained separation of the scores into narrower bands of performance. Theoretically, these clusters are not meaningful, which is further evidence that the models did not adequately explain the data.

Acute Sample

Given the null findings of the initial analysis, the analyses were repeated in a sample that included only cases who completed the ImPACT within seven days of their injury. As presented

earlier, the most severe cognitive deficits and symptoms would be present during this time, with most athletes recovering within seven to 10 days. When all nine variables (five cognitive variables and four symptom clusters) were included, all fit indices indicated different cluster solutions (see Table 7). BIC indicated an eight-cluster solution, AIC and SABIC continually improved with the addition of more clusters in the model, AWE indicated a three-cluster solution, BVRs indicated that any cluster solution from eight to 10 was acceptable, and Entropy indicated that any solution was acceptable (see Table 7). This disagreement, in addition to theoretical considerations discussed above, that the emerging clusters are not theoretically meaningful, suggested that there was no single best solution to these analyses either.

The same analyses were conducted with cognitive variables only (see Table 8). BIC indicated a three-cluster solution, AIC indicated an eight-cluster solution, SABIC indicated a six-cluster solution, AWE suggested two clusters, Entropy suggested only the one cluster solution, and BVRs indicated five through 10 clusters; in general, there was vast disagreement. Similarly, the analyses were repeated for the symptom clusters only (see Table 9). BIC, AIC, and SABIC did not indicate any optimal solution. AWE indicated a four-cluster solution, Entropy indicated that any of the ten cluster solutions were acceptable, and BVRs indicated three through 10 cluster solutions. Although there was some tenuous agreement between particular fit indices, overall, the continual improvement of some indices, disagreement between the ones that did indicate a solution, and the notion that BVRs and entropy indicate only minimally acceptable solutions signify great disagreement. This disagreement between indices again indicated that there was no tested model that optimally fit the data. Furthermore, these analyses parsed the data in a similar manner to the analyses above, such that they reflected "levels of performance," rather than distinct profiles with strengths and weaknesses in different domains. Again, this suggested that

the models do not well-explain the data and theoretically meaningful clusters did not emerge. Analyses including the five cognitive variables and 22 individual symptom scores from zero to six were also run in both the overall and acute samples, with the same result – the indices did not indicate any one optimal solution.

Post-Hoc Analyses

Given the null findings in the planned analyses, follow up analyses were conducted, namely cluster analysis, to assess whether the null findings were an artifact of the statistical techniques or genuine absence of neuropsychological profiles. Cluster analysis was selected because it is similar to LCA in its aim, but different in that it approaches the goal in a different way. That is, LCA imposes a model on the data and then tests the fit of the model, whereas cluster analysis simply groups cases based on proximity, in n-dimensional space, where n is the number of variables in the analysis. Because several renditions of the LCA yielded null findings, a change in strategy was a reasonable path forward.

Cluster Analysis

Cluster analysis is a procedure similar in result to LCA but very different in its process. That is, while LCA is a top-down process – it imposes a model and examines relationships among cases to test the model – cluster analysis is a bottom-up process in that it does not impose any a priori model on the data. In other words, cluster analysis examines relationships between cases on several variables specified a priori by the user, and attempts to maximize within group homogeneity and inter-group heterogeneity (Hair et al., 2009). Furthermore, cluster analysis is not a statistical technique, in contrast to its two relatives mentioned above.

Cluster analysis comes in several varieties, but they all have common features. One of these features is the measurement of similarity (although there are several variants of similarity

measures; e.g. correlation vs. distance), or the degree of agreement of each case to each other case on all the variables selected for the analysis (Hair et al., 2009). Once the similarities are calculated, there are two overarching categories of procedures to begin to form clusters: hierarchical and non-hierarchical. Hierarchical procedures proceed in a stepwise manner, with each case initially serving as its own cluster. The procedure then determines, using proximity, the two most similar cases and groups them, creating the first multi-case cluster. This procedure continues until all cases are classified into their nearest cluster. Non-hierarchical clustering techniques proceed by specifying random or pseudo-random "seeds" or starting centroids, and initially groups all cases into clusters based on the nearest centroid. It then iteratively reassigns cases to more appropriate clusters. These solutions are constrained by the a priori specification of parameters such as "maximum number of clusters."

Data Analysis

Analyses were run using Statistical Analysis Software (SAS) Proc Calis v.9.4. The sample was the same as that used for the a priori analyses (see "Participants" section above). Variables included in the analysis were the five interval-level cognitive scales from the ImPACT – verbal memory, visual memory, reaction time, visual motor speed, and impulse control – as well as all 22 items from the PCSS. In all analyses except the PCA, the same four symptom clusters – migraine, cognitive, sleep, and neuropsychiatric – were used in place of the 22 individual symptoms.

Principal Components Analysis (PCA). Prior to computation of the cluster analysis, a PCA was conducted on the five cognitive variables and 22-item PCSS for data reduction purposes. The analyses were computed based on correlation matrices, with prior communality estimates extracted from squared multiple correlations. Oblique oblimin rotation with a tau of 0.5

was selected given the relations between the items to be factored. The loading criterion was set at 0.32, per the suggestion of Tabachnick and Fidell (2013).

Cluster Analysis. A non-hierarchical k-means clustering approach was used. This method requires the user to specify a number of clusters. It then selects seeds, and assigns cases to clusters. An optimizing technique is employed that iteratively places cases into clusters and constantly monitors whether a particular case would better fit another cluster. This iterative process continues until a criterion is met that accounts for both minimizing intra-cluster distance and maximizing inter-cluster distance or the maximum number of iterations is reached. Euclidian distance was used as the measure of distance. This is calculated by determining the length of the hypotenuse of a right triangle between the two centroids in an n-dimensional (number of variables) problem space. Because non-hierarchical clustering techniques compute only one cluster solution (one cluster, two clusters, three clusters… six clusters) at a time, analyses for models including one through six clusters were computed. The option to update the cluster centroid with the addition of each case was selected in this analysis.

Cluster analytic methods are susceptible to scaling effects. That is, if variables are on different scales, the software does not weight variables differently to adjust for the scaling for the metric. For this reason, variables with scales that include higher numbers as opposed to those with lower numbers would have more of an effect on the analysis. Therefore, it is important to standardize the variables to remove the effects of scaling. SAS includes an option to do this as part of the analysis, by converting the scores to z-scores. This option was selected in the current analysis.

Cluster solution selection criteria. Several criteria are available for deciding on the number of clusters to be extracted from the data. The first criterion is the *pseudo F*, which is akin

to the similarly named *F statistic* in ANOVA. Basically, this statistic represents a ratio of *between* cluster distance to *within* cluster distance, so the higher the value the better. For example, if there is more variance between clusters (numerator) than between cases within clusters (denominator), then the value would be larger than if the opposite were true. In contrast to the *F statistic* in ANOVA, there is no associated significance test, so this is not an absolute measure of fit, it can only be assessed relative to other cluster solutions. Milligan and Cooper (1985) demonstrated this to be the strongest of the decision criteria for determining a correct cluster solution, although they acknowledge that its properties are likely to vary depending on the structure of the data.

A second decision criterion available in SAS v.9.4 is the *cubic clustering criterion* (CCC). This criterion is based on a ratio of the error in the clustering of random data to the error in the clustering of the target data. Intuitively, there should be more error in the random data cluster solution than in the actual cluster solution. Therefore, larger values indicate more appropriate cluster solutions.

Assumptions. Because cluster analysis is not a statistical technique, there are no statistical assumptions to meet. However, there are several factors that need to be considered before a cluster analysis is conducted. First, one must examine variables for multicollinearity because solutions produced by this technique can be greatly affected by highly overlapping variables (Hair et al., 2009). Bivariate correlations were examined – using Pearson's correlation coefficient – between all variables included in the cluster analysis for multicollinearity. While there were several correlations in the mid- to high- .50 range, there were no variables that were sufficiently overlapping to warrant their removal from the analysis.

The second assumption to be considered is sample size. Of course, this assumption is not referring to statistical power; it is more theoretical in referring to the notion that there might be very small clusters that would be missed if not for a large enough sample to increase the likelihood of their adequate representation in the sample. The sample size (>1300) is large enough to be confident that all clusters would be adequately represented. Another consideration is the presence of outliers and whether to remove them. Although there are likely both univariate and multivariate outliers in these data, given the expected outcome for the LCA that one cluster that might emerge would be along the lines of performance validity, it would not make theoretical sense to remove these cases that have the potential to form a distinct cluster.

Principal Components Analysis and Visualization of Data

As mentioned above, principal components analysis was conducted for data reduction and visualization purposes. Because cluster analysis is conducted in n-dimensional Euclidian space, with n being the number of variables included in the analysis, it is not possible to visualize the data in this dimensional space. A commonly employed method for projecting the data into a lower dimensional space is to compute a PCA on the data, with the purpose of producing component scores and plotting them in a two- or three-dimensional manner, depending upon the number of factors extracted. The assumptions of continuous variables, sampling adequacy, and suitability for data reduction (adequate relationships between variables to be factorable) were met. The assumption of linear relationships between variables was not met, but analyses were continued.

Results suggested a two-component solution (see Table 10), indicated by both the factor loading matrix of standardized regression coefficients and the structure matrix, consisting of correlations between the item scores and component scores. All items except the nausea

symptom had loadings >0.32 on one component, and there were no cross loadings. This solution also makes good sense on pragmatic and theoretical grounds. That is, given the purpose of the analysis, data reduction for visualization, two-dimensions make good sense, because it can easily be plotted and visualized on a typical two-dimensional plot. Secondly, the selection was made on theoretical grounds. Since the cognitive and symptom scores are dissociable metrics collected using different methods (i.e. performance-based vs. self-report), this solution is defensible, theoretically.

Scores were then computed for each of the two components. For the symptom component, the zero to six Likert-type responses to each symptom (excluding nausea, given its failure to load on the component) were summed and that total was used as the component score. A different procedure was employed for the cognitive indices for three reasons. First, because the directions of the scaling of each of the cognitive scores differed (i.e. for three of the five scales, higher numbers indicated good scores and for two of the five scores, lower scores indicated good scores). Second, each of the scores is on a different scale. Third, a simple sum of the scores would be meaningless for the two reasons mentioned previously, as well as the nature of the performance based measures. For these reasons, the Z-scores of the cognitive indexes were computed and averaged to create a composite cognitive score.

The two components were then plotted with the symptom component on the x-axis and the cognitive component on the y-axis (see figure 2). Visual examination of the plot revealed dense population at the Y-intercept, indicating a low modal score on the symptom component. There was some spread on the y-axis, but no visually discernable clusters were present. Given the loss of information as a result of the data reduction efforts (PCA), it is possible that there

were clusters present that were obfuscated by this lack of fine-grained analysis. Therefore, analyses were continued despite the lack of visual indication of clusters within the overall data.

Cluster Analysis: Overall Sample

Conventional cluster analysis was run to mirror the previously conducted LCA, with one exception, that cluster analysis is not able to control for time since injury. These analyses were run using the same variables as the LCA (nine cognitive variables, four symptom composite variables) The analysis was first run in the overall sample, including the five cognitive variables and four symptom clusters (see Table 11). Results revealed a similar pattern to that observed in the LCA. The pseudo F statistic and CCC continually worsened as more clusters were added to the data, so analyses were stopped at a six-cluster solution. An exception to the continual worsening of the fit is the four-cluster solution, in which there was a marginal jump in both aforementioned statistics. Upon closer inspection, one of the clusters included only one case, rendering it very unstable, so it was disregarded, and treated as an outlier. Two of the remaining three clusters conformed to the same pattern observed in the LCA (see figure 3). That is, they were again separated into levels of performance. However, the third cluster yielded a cognitively impaired group, with lower symptom reports than their less cognitively deficient counterparts. One of the clusters, cluster 4, reflected average to low average cognitive scores and very high symptom reports. The third cluster reflected athletes with intact cognition and low symptom reports. The gender breakdown of the three clusters were as follows: 66% male, 34% female (cluster 1); 61% male 39% female (cluster 3); and 53% male 47% female (cluster 4). Cluster two was excluded from analyses because it included only one case.

MANOVA. This pattern was confirmed by follow-up a Multivariate Analysis of Variance (MANOVA) using cluster membership as the independent variable and including as

dependent variables: the five cognitive variables, the four symptom clusters, the overall PCSS symptom score, age, and education (see Table 13). Because their inclusion would have substantially reduced the sample size for the MANOVA due to missing data, two Bonferonni-corrected (.05/2=.025) univariate ANOVAs were run to examine the differences between clusters on time since injury and number of previous concussions.

Data screening. The data were examined for univariate and multivariate outliers prior to the computation of the MANOVA. Univariate outliers were defined as z-scores greater than 3.29 (Chi-square distribution, p=.001). Univariate outliers were evident on number of years playing (22), number of previous concussions (13), verbal memory (2), visuomotor speed (3), reaction time (8), impulse control (15), total symptom score (13), migraine symptoms (19), cognitive symptoms (13), sleep symptoms (16), neuropsychiatric symptoms (24), and time since injury (15). Mahalanobis distance with a cut off of 36.123 (Chi-Square p=.001, df=14) revealed 38 multivariate outliers. Univariate outliers were not removed from the analysis because of the nature of the variables in question. To remove outliers in the case of clinical data such as these would be to reject valid, albeit extreme scores. Furthermore, in large sample sizes, some extreme values are expected based on the normal distribution (Tabachnick & Fidell, 2013). Multivariate outliers are more likely to represent participants who performed and reported in a way that is not representative of the typical clinical case. For this reason, the MANOVA was computed with and without multivariate outliers removed to determine whether their removal had a substantive effect on the analysis. The analysis did not change substantively when the multivariate outliers were removed, so they were included in the final analysis.

***Assumptions*.** Prior to computing the analysis, the assumptions of MANOVA were examined. The first assumption is multivariate normality. There are not tests available to test

multivariate normality, so it was approximated based on tests of univariate normality of each variable with each cluster. Kolmogorov-Smirnov tests revealed that this assumption was violated ($p<.05$) for all variables. The preponderance of skewness and kurtosis values were within acceptable limits. Central limits theorem begins with larger samples, so normality was treated as a met assumption. Homogeneity of variance was violated for all variables except for age, number of previous concussions, and time since injury. When sample sizes are large, MANOVA is robust to violations of both normality and homogeneity of variance (Tabachnick & Fidell, 2013), so the analyses were continued. The assumption of linearity was violated based on visual inspection of several bivariate scatterplots of variables included in the analyses. This assumption, however, is typically given less importance, because its violation results in a loss of power, possibly masking significant findings, rather than inflating significance (Tabachnick & Fidell, 2013). The final assumption of MANOVA is absence of multicollinearity. This assumption was met based on an inspection of a bivariate correlation matrix, which revealed no correlations of concerning magnitude.

Results. Multivariate Analysis of Variance revealed significant main effects for age, education, and all of the cognitive variables and symptom scores, including overall symptoms. The effects were non-significant for time since injury, and number of previous concussions (see Table 13). Due to the violation of the homogeneity of variance assumption, Games-Howell post-hoc tests was computed for contrasts for both the MANOVA and ANOVAs. The preponderance of contrasts yielded significant results between clusters (see Table 14). In cluster analysis, there is no "right" or "wrong" solution, it is the meaningfulness of the clusters that is important. In this case, one of the clusters is potentially meaningful, representing a group of athletes who are performing poorly and reporting few symptoms. This will be discussed further below.

Cluster Analysis: Acute Sample

The same analyses were computed in the acute sample (see Table 12), again with similar results. The pseudo F statistic and CCC continually worsened as more clusters were added to the solutions. Again, there was an exception to this rule at the five-cluster solution, at which point both the pseudo F and CCC improved. The clusters included 40, 50, and 237 cases. The gender breakdown of each of these clusters is as follows: 60% male, 40% female (cluster 1); 50% male, 50% female (cluster 2); and 75% male, 25% female (cluster 3).

MANOVA. These analyses were followed up with another MANOVA using cluster membership as the independent variable and including as dependent variables: the five cognitive variables, the four symptom clusters, the overall PCSS symptom score, age, and education (see Table 16). Clusters two and four were not included in analyses because they included only one and two cases, respectively.

***Data screening*.** The data were examined for univariate and multivariate outliers based on z-scores and Mahalanobis distance. The univariate outlier screening procedure revealed several univariate outliers in excess of the cutoff of 3.29. These outliers were observed on the following variables: number of previous concussions (5), visuomotor speed (1), reaction time (1), impulse control (4), total symptom score (1), migraine symptoms, (1), cognitive symptoms (5), sleep symptoms (7), and neuropsychiatric symptoms (6). There were 15 multivariate outliers based on a cutoff of 36.123 (Chi-Square p=.001, df=14). Given the nature of the variables, to exclude outliers would be tantamount to rejecting valid, albeit extreme scores. For this reason, no outliers were removed from the current analysis.

***Assumptions*.** Prior to computing the analysis, the assumptions of MANOVA were examined. The first assumption is multivariate normality. There are not tests available to test

multivariate normality, so it was approximated based on tests of univariate normality of each variable with each cluster. Kolmogorov-Smirnov tests revealed that this assumption was violated ($p<.05$) for all variables. The preponderance of skewness and kurtosis values were within acceptable limits. Central limits theorem states that as sample sizes get larger, the distribution begins to resemble a normal distribution, so normality was treated as a met assumption. Homogeneity of variance was violated for all variables except for age, number of previous concussions, and time since injury. When sample sizes are large, MANOVA is robust to violations of both normality and homogeneity of variance (Tabachnick & Fidell, 2013), so the analyses were continued. The assumption of linearity was violated based on visual inspection of several bivariate scatterplots of variables included in the analyses. This assumption, however, is typically given less importance, because its violation results in a loss of power, possibly masking significant findings, rather than inflating significance (Tabachnick & Fidell, 2013). The final assumption of MANOVA is absence of multicollinearity. This assumption was met based on an inspection of a bivariate correlation matrix, which revealed no correlations of concerning magnitude.

Results. Multivariate Analysis of Variance revealed significant main effects for age, education, and all of the cognitive variables and symptom scores, including overall symptoms. The effects were non-significant for time since injury, and number of previous concussions (see Table 16). Due to the violation of the homogeneity of variance assumption, Games-Howell post-hoc tests was computed for contrasts for the MANOVA. The preponderance of contrasts yielded significant results between clusters (see Table 17). In cluster analysis, there is no "right" or "wrong" solution, it is the meaningfulness of the clusters that is important. The clusters that emerged in this analysis were consistent with those observed in the overall sample; two clusters

emerged that reflected levels of performance and symptom reporting, while the third reflect a group that performed poorly on the cognitive tests, but did not report many symptoms. Again, the relatively consistent clusters reflected average to low average scores with high symptom reports, and low symptom reports with intact cognition, respectively.

CHAPTER 4:

DISCUSSION

The planned analyses (LCA) did not support either of the expected outcomes of this study. The first expected outcome, that clusters would emerge, was unsupported given the high level of disagreement between fit indices for all conducted analyses. These disagreements indicate that many, and in some cases all, of the fit indices selected differing solutions as optimal. Furthermore, in some cases, the indices never indicated an optimal solution. Further disconfirming evidence is the finding that none of the clusters that emerged were meaningful. That is, each cluster simply reflected a consistent "level of performance" across domains, rather than reflecting distinct neuropsychological profiles of strengths and weaknesses, or deficit and intact cognitive functions and symptomatic or asymptomatic reporting as a result of a concussion. The second expected outcome was dependent on the first, that if clusters emerged, one would represent a performance/symptom validity cluster, reflecting underreporting of symptoms to return to play more quickly. Because no optimal cluster solutions emerged, the second expected outcome could not be supported.

Similarly to the LCA, the conventional cluster analysis largely did not yield many meaningful results, although there is potential for some interpretation. In the case of both the overall and acute samples, the analysis revealed continually worsening pseudo F and CCC statistics with the addition of more clusters in the solutions, with some exceptions. Visual

inspection of all cluster solutions revealed clusters that reflected level of performance rather than distinct neuropsychological patterns of strengths and weaknesses. Exceptions to the continually worsening fit statistics were the four-cluster solution in the overall sample and the five-cluster solution in the acute sample. Because of spikes in both the pseudo F and CCC statistics, these solutions were followed up with a one-way Analyses of Variance, which revealed significant results for all the cognitive and symptom variables in both cases.

The MANOVA for the overall sample four-cluster solution demonstrated significant differences between the clusters on all cognitive and symptom variables, as well as age and education (see Table 13). In order, the variables that maximally discriminated between clusters, based on effect sizes (partial eta-squared) were overall symptoms, cognitive symptoms, migraine symptoms, neuropsychiatric symptoms, and sleep symptoms. The cognitive variables also discriminated between clusters, but their effect sizes were smaller, ranging from 0.114 (impulse control) to 0.354 (verbal memory). Demographic and background variables yielded very small effect sizes ranging from .005 (time since injury) to .028 (age). The preponderance of contrasts between clusters were also significant (see Table 14). In the first two clusters, the aforementioned pattern of the clusters representing levels of performance, was noted. However, the third cluster appears to represent a group of athletes who consistently have the lowest scores in cognition out of the three groups, but are reporting fewer symptoms than the fourth cluster, which has better cognitive scores than the third cluster. While it is possible that this represents an impression management group, they are still reporting more symptoms than would be expected for a group of athletes who is deliberately underreporting. For example, their average overall symptom score is 12.65, which falls within the “unusual” range in the classification charts in the ImPACT manual for both males and females, and those who are in high school and university

(Lovell, 2011). An impression management group would likely report fewer symptoms than this, so as to be allowed to return to play more quickly. So, it is possible that this cluster represents a group of athletes who are experiencing deficits in cognition but are reporting few symptoms, perhaps simply as an artefact of a conservative response style.

In the acute sample five-cluster solution the latter two clusters empirically confirmed the pattern of cluster separation, that they reflect levels of performance/reporting, rather than meaningful clusters. The first cluster, was potentially interesting in its characteristics. None of these clusters differed significantly on number of previous concussions, or time since injury, but there were significant differences on age, education, and all of the cognitive and symptom variables (see Table 16). In order, the variables that were most discriminatory based on effect size (partial eta-squared) were overall symptoms, migraine symptoms, cognitive symptoms, neuropsychiatric symptoms, and sleep symptoms. The cognitive variables, although significant, were less discriminatory between clusters, with effect sizes ranging from 0.075 (impulse control) to 0.314 (reaction time). These results were broadly consistent with the gradient of discrimination between clusters for the overall sample cluster solution.

The third cluster of the acute sample five-cluster solution reflected the same pattern observed in the overall sample four-cluster solution. That is, consistently low cognitive scores, with low symptom reporting. Furthermore, the average cluster symptom score was again in the "unusual" range from the ImPACT manual (Lovell, 2011), again indicating that this likely does not reflect an impression management group, but rather a group of athletes with a conservative response style. So, it is possible that this cluster represents a group of athletes who are experiencing deficits in cognition but are reporting few symptoms, perhaps simply as an artefact of a conservative response style.

One of the three clusters for both samples emerged with low average to average cognitive scores and very high symptom reports. Although it is difficult to interpret these scores without examining athletes' baseline scores, this could represent a group of athletes with minimal or no detectable cognitive deficits following concussion, but a more liberal response style in reporting symptoms. Another possibility is that these athletes genuinely experience many symptoms in the absence of detectable cognitive deficits. Lastly, it is possible that the cognitive deficits resolved before the symptoms, resulting in the observed profile. This is certainly consistent with previous work demonstrating that cognition improves before symptoms (Williams et al., 2015). It is not likely that athletes are intentionally over-reporting symptoms, given that the incentive structure – to return to play as quickly as possible – is in the opposite direction. While the symptom reports seem out of proportion for the level of cognitive performance, it is important not to over-interpret the disproportionate symptom reports without examining change from baseline, because it is possible that there was still a significant decline from baseline that is not captured by the norms. In general, although the levels of symptom reporting are higher than expected given the level of cognitive deficits, two clusters for both samples are relatively consistent levels of deficits and reporting compared to the other clusters. That is, one cluster reflects intact cognition and low symptom reports, and one reflects slightly poorer cognition and high symptom reports, and as previously discussed – the exception to the consistency – one reflects poor cognition and low symptom reports.

Neither the LCA nor the conventional cluster analysis fully supported either of my expected outcomes, although there was some marginal, preliminary support for both. The first expected outcome was that clusters would emerge from the data. The LCA did not yield fit statistics that agreed on any solution, sometimes indicating no solution was acceptable at all. The

conventional cluster analysis yielded similar results. While two solutions were indicated by the fit indices, one in the overall sample and one in the acute sample, many of the clusters were not meaningful in that they simply separated the cases into levels of performance. This is considered to be a danger of cluster analysis, in that it will find clusters whether they are present or not (Hair, Black, Babin, & Anderson, 2009). However, one cluster from each of the cluster solutions that were indicated appeared to be meaningful. These will be discussed further below.

The second expected outcome, that an impression management cluster would emerge from the data, had some potential support. In both the overall and acute samples, cluster solutions emerged that consisted of a group of athletes who performed very poorly on the cognitive scores across domains, but who reported fewer symptoms than the athletes in other groups, whose cognitive scores were significantly better (see Tables 14 and 15). Based on the very poor cognitive scores in these clusters, one would expect them to report more symptoms than those athletes whose cognitive scores were that much better. However, as discussed above, their symptom reports were still higher than would be expected if this were truly an impression management group, who would be attempting to report as few symptoms as possible to go back to play more quickly. That their average score still fell within the "unusual" range, as outlined in the ImPACT manual (Lovell, 2011), leads to the conclusion that this group represents a cluster of athletes who are cognitively impaired, but have a conservative response style on self-report measures. Another possibility is that this represents a group with true cognitive impairment and few symptoms, irrespective of response style, although the first is more likely. Another interpretation could be that the athletes in this cluster are minimizing their symptoms, but are still mildly elevated, nonetheless.

Overall, both the LCA and the conventional cluster analysis yielded clusters that resembled levels of performance or amount of cognitive deficit and symptom reports, rather than distinct neuropsychological profiles. While one cluster from each of the conventional cluster solutions had potentially interesting characteristics, still these did not entirely support the expected outcomes of the current study. The expected clusters would have reflected strengths and weaknesses in different cognitive domains and higher symptom reports in particular domains of symptoms, rather than consistent intra-cluster levels across domains, for example, a cluster with only emotional symptoms, or only sleep symptoms, etc. Collins et al. (2014) propounded such an interesting model, so it will be discussed here in relation to the current results.

It should be made clear that the current study was not directly testing Collins et al's (2014) model. Theirs is simply a conceptual model of potential clusters generated from the literature. The present analyses were an exploration of data with no definite model imposed on it, but instead testing several different models that could account optimally for the data. That being said, their model is theoretically interesting, so it will be discussed here in relation to the present results. Collins et al. (2014) postulated the following clusters in concussion: cognitive, vestibular, ocular-motor, post-traumatic migraine, cervical, and anxiety/mood. Three of these clusters align with three of the symptomatic variables that were included in these analyses: cognitive, migraine, and neuropsychiatric symptoms. Furthermore, the current study included five cognitive variables, which, if athletes scored poorly on the cognitive variables, and were thus cognitively impaired by the concussion, would contribute to the cognitive cluster postulated by Collins and colleagues. These authors additionally postulated a vestibular cluster. While some items on the PCSS (balance problems, dizziness) could contribute to a vestibular scale, they were included in the migraine symptom group from Lau et al. (2011), potentially losing some

information in the analysis. In any case, a more appropriate metric of vestibular impairment would have been performance-based balance testing data, instead of self-report. Unfortunately, these data were not available and future studies should examine this question using the type of vestibular data described above. Ocular-motor and cervical data were also not available for this study. So, it is possible that these analyses would have conformed more closely to Collins and colleagues' hypotheses if different types of data had been available for this study. There was some support for the first expected outcome, in that there were cluster solutions that were indicated in the conventional cluster analysis, but the majority of the clusters that emerged were not meaningful. However, in each of the two cluster solutions that emerged, one of the clusters was potentially meaningful.

Because this study was the first to attempt to address this particular question, it is difficult to determine the cause of the unexpected results in this case. There are several possibilities, some of which were discussed above, but will be further explored here. First, it is possible that if the present study had examined athletes at different points in their concussion recovery period, such as immediately post-concussion (e.g. ≤3 days), subacute (≥8 days), or even in the chronic phase (>30 days post injury), clusters might have emerged. There are many possibilities for temporally parsing the time post-injury. So, one possibility is that the current study examined the wrong time period. Second, it is possible that if other, more appropriate or more comprehensive variables were included in the study, that clusters would emerge. For example, if performance-based balance data, more comprehensive neuropsychological assessment data, or data on pre-morbid risk factors were available, clusters might have emerged. Third, perhaps if the data were coded in a different way, it is possible that this would have changed the outcome. For example, if the data were parsed into ordinal-level groups and the analysis was conducted that way, the

findings might have differed. Another possibility would be to take into account baseline performance on the ImPACT and examine their scores relative to their baseline scores. That is, to parse the scores for each of the variables into groups based on change from baseline, to get a more individualized metric of their performance. Fourth, it is possible that there are different clusters in males and females or different age groups, or that different clusters would emerge if the data were parsed by some other variable. For example, the literature shows that younger individuals take longer to recover from concussion. This, combined with the heterogeneity in neurodevelopmental trajectories could introduce noise into the data that could obscure the identification of subgroups. To preserve the necessary sample sizes, the sample was not divided based on age in the current study, so it is possible that this is one of the reasons that subgroups were not identified. The final possibility to be discussed here is that that these findings might be a statistical artefact. LCA and conventional cluster analysis both initiate their procedures by placing pseudo-random seeds, which serve as the beginnings of the eventual clusters. While LCA attempts to correct for this by running each analysis with several different sets of seeds, it is still possible that the initial seeds for these analyses were inappropriate, resulting in the null findings described here.

All of the questions propounded above should be investigated in future research in this field. However, it is possible that, in reality, there are no subgroups in sport-related concussion. In other words, it is possible that each concussion is unique, as an interaction of numerous idiosyncratic variables. This is certainly consistent with clinical experience, where it is continually observed that each concussion seems to present differently. Another possibility is that there is simply a dose-response relationship between the "severity" of the concussion and the cognitive deficits and symptomology experienced in the aftermath. Despite these possibilities,

this question is far from answered. This is the first investigation of this potentially important area, and future research should continue to examine it using different methods and variables.

Limitations

This study had several limitations. First, the data used were retrospective, clinical data, and thus there were several variables that were not available that would have been preferable to have had the study been designed prospectively. For example, medical and psychiatric history, balance, and comprehensive neuropsychological data. The retrospective design was out of necessity, in that an adequate sample could not have been collected in the time frame of this project for the type of analyses that were conducted. A second limitation of this study was that there was a very large age range in these data. This was necessary because large sample sizes are required for this type of analysis, but ideally these data would have been separated by age into more homogeneous groups. In addition to the questions suggested above, future research should attempt to address the limitations of the current study. A third possible limitation is the scaling of the variables in the conventional cluster analysis. It is possible that, because z-scores force each variable to take on a mean of zero and a standard deviation of one, it is possible that this is another contributing factor to the surprising results. Had a different scaling technique been used, it is possible that the results may have differed. Future research should investigate this question.

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Table 1

The Post-Concussion Symptom Scale

Symptom	Symptom Composite
Headache	Migraine
Nausea	Migraine
Vomiting	Migraine
Balance Problems	Migraine
Dizziness	Migraine
Fatigue	Cognitive
Trouble Falling Asleep	Sleep
Excessive Sleep	Sleep
Loss of Sleep	Sleep
Drowsiness	Cognitive
Light Sensitivity	Migraine
Noise Sensitivity	Migraine
Irritability	Neuropsychiatric
Sadness	Neuropsychiatric
Nervousness	Neuropsychiatric
Feeling More Emotional	Neuropsychiatric
Numbness	Migraine
Feeling Slowed Down	Cognitive
Feeling Mentally Foggy	Cognitive
Difficulty Concentrating	Cognitive
Difficulty Remembering	Cognitive
Visual Problems	Migraine

Table 2

Descriptive Statistics for the variables in the overall sample

Variable	Mean(SD)
Verbal Memory	82.37(12.68)
Visual Memory	71.43(14.04)
Visuomotor Speed	36.13(7.47)
Reaction Time	0.63(0.11)
Impulse Control	7.043(5.98)
Migraine Symptoms	4.24(6.02)
Cognitive Symptoms	3.27(4.71)
Sleep Symptoms	1.35(2.18)
Neuropsychiatric Symptoms	1.28(2.95)
Total Symptoms	10.56(14.59)
Time Since Injury	12.84(11.70)

Table 3

Descriptive Statistics for the variables in the acute sample

Variable	Mean(SD)
Verbal Memory	83.05(12.37)
Visual Memory	72.07(13.76)
Visuomotor Speed	36.22(7.21)
Reaction Time	0.62(0.12)
Impulse Control	6.95(6.33)
Migraine Symptoms	4.77(6.32)
Cognitive Symptoms	1.44(2.36)
Sleep Symptoms	4.58(1.69)
Neuropsychiatric Symptoms	1.36(3.07)
Total Symptoms	11.45(15.12)
Time Since Injury	4.58(1.69)

Table 4. Fit indices for Overall Sample (n=1366) Cognitive Variables and Symptom Clusters

	1 class	2 class	3 class	4 class	5 class	6 class	7 class	8 class	9 class	10 class
BIC	65,164.06	55,635.57	51,922.69	50,322.65	49,724.57	48,399.73	47,931.66	47,341.87	47,097.65	46,839.83
AIC	65,054.45	55,405.90	51,572.98	49,852.88	49,134.75	47,689.86	47,931.66	46,391.90	46,027.63	45,649.75
SABIC	65,097.35	55,679.57	51,709.86	50,036.75	49,365.61	47,967.71	47,426.59	46,763.73	46,446.45	46,115.57
AWE	65,378.67	56,141.33	52,768.79	51,442.93	51,180.44	50,217.75	49,918.23	**49,545.66**	**49,549.54**	49,582.67
Entropy	**1.00**	**0.97**	**0.95**	**0.94**	**0.93**	**0.90**	**0.93**	**0.93**	**0.93**	**0.93**
BVR>CO	78%	47%	27%	22%	14%	14%	14%	14%	8%	6%

Note. BIC=Bayesian Information Criterion; AIC=Aikeke Information Criterion; SABIC=Sample Adjusted Bayesian Information Criterion; AWE=Approximate Weight of Evidence; BVR>CO= the number of bivariate residuals above the cutoff of 3.84. Models indicated by each of the indices are in bold.

Table 5. Fit indices for Overall Sample (n=1366) Cognitive Variables only

	1 class	2 class	3 class	4 class	5 class	6 class	7 class	8 class	9 class	10 class
BIC	36,905.21	35,527.18	35,238.46	35,162.55	**35,152.50**	35,182.85	35,180.50	35,236.34	35,271.17	35,339.98
AIC	36,842.57	35,391.47	35,029.67	34,880.69	34,797.57	34,754.84	34,679.42	34,662.18	34,623.93	34,619.67
SABIC	36,867.09	35,444.59	35,111.40	34,991.02	34,936.49	34,922.37	**34,875.55**	34,886.91	34,877.27	34,901.61
AWE	37,027.84	**36,256.84**	36,466.92	37,115.75	37,388.88	37,706.88	37,919.41	38,300.77	38,750.95	38,865.72
Entropy	**1.00**	0.70	0.68	0.61	0.61	0.60	0.64	0.64	0.62	0.64
BVR>CO	80%	60%	20%	20%	10%	**0%**	**0%**	**0%**	**0%**	**0%**

Note. BIC=Bayesian Information Criterion; AIC=Aikeke Information Criterion; SABIC=Sample Adjusted Bayesian Information Criterion; AWE=Approximate Weight of Evidence; BVR>CO= the number of bivariate residuals above the cutoff (CO) of 3.84. Models indicated by each of the indices are in bold.

Table 6. Fit indices for Overall Sample (n=1366) Symptom Clusters only

	1 class	2 class	3 class	4 class	5 class	6 class	7 class	8 class	9 class	10 class
BIC	28,258.85	19,032.68	15,638.89	13,973.56	13,411.63	12,014.71	11,426.01	11,340.85	10,761.57	10,378.49
AIC	28,211.88	18,928.29	15,477.08	13,754.33	13,134.99	11,680.65	11,034.53	10,891.96	10,255.27	9,814.77
SABIC	28,230.26	18,969.15	15,540.41	13,840.14	13,243.27	11,811.41	11,187.76	11,067.66	10,453.44	10,035.42
AWE	28,350.82	19,285.69	16,135.05	14,599.47	14,252.85	13,071.93	12,502.80	12,770.09	12,124.49	11,850.83
Entropy	**1.00**	**0.97**	**0.96**	**0.95**	**0.92**	**0.91**	**0.94**	**0.89**	**0.93**	**0.93**
BVR>CO	83%	83%	33%	17%	**0%**	**0%**	**0%**	**0%**	**0%**	**0%**

Note. BIC=Bayesian Information Criterion; AIC=Aikeke Information Criterion; SABIC=Sample Adjusted Bayesian Information Criterion; AWE=Approximate Weight of Evidence; BVR>CO= the number of bivariate residuals above the cutoff (CO) of 3.84. Models indicated by each of the indices are in bold.

Table 7. Fit indices for Acute Sample (n=330) Cognitive Variables and Symptom Clusters

	1 class	2 class	3 class	4 class	5 class	6 class	7 class	8 class	9 class	10 class
BIC	15,972.67	13,964.87	13,335.48	13,207.28	12,970.19	12,941.24	13,002.14	**12,916.58**	12,931.13	12,962.67
AIC	15,892.89	13,797.71	13,335.48	13,207.28	12,540.89	12,424.57	12,398.08	12,225.14	12,152.32	12,096.48
SABIC	15,906.06	13,825.30	13,122.95	12,865.37	12,611.75	12,509.85	12,497.79	12,339.27	12,280.87	12,239.45
AWE	16,157.45	14,366.30	**13,958.22**	14,051.51	14,019.33	14,209.99	14,473.23	14,594.54	14,815.11	15,028.45
Entropy	1.00	**0.97**	**0.95**	**0.94**	**0.95**	**0.93**	**0.93**	**0.94**	**0.94**	**0.95**
BVR>CO	56%	17%	6%	6%	6%	6%	3%	**0%**	**0%**	**0%**

Note. BIC=Bayesian Information Criterion; AIC=Aikeke Information Criterion; SABIC=Sample Adjusted Bayesian Information Criterion; AWE=Approximate Weight of Evidence; BVR>CO= the number of bivariate residuals above the cutoff of 3.84. Models indicated by each of the indices are in bold.

Table 8. Fit indices for Acute Sample (n=330) Cognitive Variables Only

	1 class	2 class	3 class	4 class	5 class	6 class	7 class	8 class	9 class	10 class
BIC	9,018.42	8,719.03	**8,660.39**	8,681.22	8,723.56	8,761.86	8,816.96	8,848.43	8,923.50	8,959.60
AIC	8,972.83	8,620.25	8,508.43	8,476.07	8,465.22	8,450.33	8,452.25	**8,430.53**	8,452.41	8,435.33
SABIC	8,980.36	8,836.55	8,533.51	8,509.93	8,507.86	**8,501.75**	8,512.45	8,499.51	8,530.17	8,521.87
AWE	9,124.01	**9,065.72**	9,195.09	9,360.27	9,615.20	9,047.49	9,978.69	10,146.85	10,341.68	10,482.25
Entropy	1.00	0.70	0.70	0.70	0.68	0.73	0.72	0.74	0.76	0.78
BVR>CO	50%	20%	10%	10%	**0%**	**0%**	**0%**	**0%**	**0%**	**0%**

Note. BIC=Bayesian Information Criterion; AIC=Aikeke Information Criterion; SABIC=Sample Adjusted Bayesian Information Criterion; AWE=Approximate Weight of Evidence; BVR>CO= the number of bivariate residuals above the cutoff of 3.84. Models indicated by each of the indices are in bold.

Table 9. Fit indices for Acute Sample (n=330) Symptom Clusters Only

	1 class	2 class	3 class	4 class	5 class	6 class	7 class	8 class	9 class	10 class
BIC	6,954.25	4,993.31	4,402.34	4,171.88	4,077.13	3,941.23	3,974.37	3,787.27	3,793.02	3,736.12
AIC	6,920.06	4,917.33	4,284.56	4,012.32	3,875.78	3,698.09	3,689.43	3,460.55	3,424.51	3,325.83
SABIC	6,925.70	4,929.87	4,304.00	4,038.66	3,909.01	3,738.22	3,736.47	3,514.48	3,485.33	3,393.55
AWE	7,033.44	5,181.25	4,708.84	**4,583.67**	4,606.95	4,604.55	4,742.06	4,624.81	4,715.75	4,756.49
Entropy	**1.00**	**0.97**	**0.95**	**0.95**	**0.93**	**0.91**	**0.90**	**0.92**	**0.94**	**0.96**
BVR>CO	83%	33%	**0%**	**0%**	**0%**	**0%**	**0%**	**0%**	**0%**	**0%**

Note. BIC=Bayesian Information Criterion; AIC=Aikeke Information Criterion; SABIC=Sample Adjusted Bayesian Information Criterion; AWE=Approximate Weight of Evidence; BVR>CO= the number of bivariate residuals above the cutoff of 3.84. Models indicated by each of the indices are in bold.

Table 10. Standardized Regression Coefficients for PCA of ImPACT Data

Symptom	Symptom Component	Cognitive Component
Verbal Memory	0.10002	**0.71132**
Visual Memory	0.07474	**0.67028**
Visuomotor Speed	0.11102	**0.72652**
Reaction Time	-0.06044	**-0.64875**
Impulse Control	0.00485	**-0.38804**
Headache	**0.54256**	-0.29635
Nausea	0.20646	-0.10793
Vomiting	**0.46649**	-0.1466
Balance Problems	**0.54414**	-0.29185
Dizziness	**0.59297**	-0.2561
fatigue	**0.51795**	-0.08512
Trouble Falling Asleep	**0.56544**	-0.07788
Excessive Sleep	**0.36161**	-0.16978
Loss of sleep	**0.42081**	-0.01875
Drowsiness	**0.52753**	-0.28385
Light Sensitivity	**0.64807**	-0.15648
Noise Sensitivity	**0.53208**	-0.22558
Irritability	**0.66207**	-0.06034
Sadness	**0.5737**	0.03601
Nervousness	**0.66889**	0.11474
More Emotional	**0.70998**	0.15631
Numbness	**0.37924**	-0.0713
Feeling Slow	**0.6406**	-0.16015
Foggy	**0.71405**	-0.12682
Difficulty Concentrating	**0.68459**	-0.21658
Difficulty Remembering	**0.53408**	-0.15837
Visual_Problems	**0.57900**	-0.14206

Note. Items loading (>0.32) on each component are indicated in bold.

Table 11
Cluster solutions for the overall sample with five cognitive variables and four symptom scores

Solution	Cluster	Freq.	RMS SD	Max Dist.	Near. Clus.	Dist. Btw.	Pseudo F	Overall R^2	CCC
6	1	171	0.9452	5.7797	2	3.4360	235.06	0.289	72.601
	2	899	0.6069	3.9795	5	2.8217			
	3	49	1.1745	7.2107	1	4.0078			
	4	1	.	0	3	11.6136			
	5	230	0.8369	5.4904	2	2.8217			
	6	16	1.2375	5.2563	3	5.029			
5	1	1	.	0	5	11.5500	262.31	0.250	78.058
	2	910	0.6153	3.9593	4	2.7914			
	3	162	1.0295	6.2543	4	3.7315			
	4	243	0.8415	5.5168	2	2.7914			
	5	50	1.3142	7.5240	3	3.9190			
4	**1**	**996**	**0.6516**	**4.6983**	**3**	**3.2372**	**285.95**	**0.204**	**78.650**
	2	**1**	**.**	**0**	**4**	**12.5976**			
	3	**208**	**0.9516**	**6.9260**	**1**	**3.2372**			
	4	**161**	**1.1927**	**8.5699**	**3**	**3.9217**			
3	1	1131	0.7222	6.7845	2	4.1638	279.53	0.150	64.282
	2	234	1.2746	8.6920	1	4.1638			
	3	1	.	0	2	12.5771			
2	1	140	1.3518	11.5140	2	4.9697	461.02	0.085	101.062
	2	1226	0.7909	6.9794	1	4.969			

Table 12
Cluster solutions for the acute sample with five cognitive variables and four symptom scores

Solution	Cluster	Freq.	RMS SD	Max Dist.	Near. Clus.	Dist. Btw.	Pseudo F	Overall R^2	CCC
6	1	1	.	0	4	5.4251	54.96	0.30	29.87
	2	238	0.6446	3.7599	3	3.4312			
	3	37	0.9052	4.5949	2	3.4312			
	4	51	0.9903	5.8579	3	3.4987			
	5	1	.	0	4	12.4138			
	6	2	1	2.1214	4	7.6221			
5	**1**	**40**	**0.9092**	**4.6574**	**5**	**6.7212**	**66.83**	**0.26**	**37.53**
	2	**1**	**.**	**0**	**3**	**5.0107**			
	3	**50**	**0.9997**	**5.8434**	**1**	**3.1269**			
	4	**2**	**1**	**2.1214**	**3**	**6.0443**			
	5	**237**	**0.6454**	**3.7613**	**1**	**3.1269**			
4	1	79	1.0786	5.9945	2	5.2890	63.99	0.21	31.05
	2	247	0.6758	4.5328	1	3.5512			
	3	3	1.4061	6.3149	1	5.9856			
	4	1	.	0	3	3.5512			
3	1	10	1.4187	6.2353	3	3.1567	40.67	0.16	8.32
	2	1	.	0	1	3.1567			
	3	319	0.8784	6.8098	1	6.5785			
2	1	329	0.968	11.3592	2	13.987	23.13	0.09	-5.79
	2	1	.	0	1	13.987			

Table 13
Omnibus MANOVA results for overall sample four-cluster solution with conventional cluster analysis

Variable	*df*	*F*	*p*	Partial eta^2
Verbal Memory	2	367.013	0.000	.354
Visual Memory	2	287.377	0.000	.301
Visuomotor Speed	2	272.330	0.000	.289
Reaction Time	2	290.340	0.000	.303
Impulse Control	2	86.274	0.000	.114
Migraine Symptoms	2	782.079	0.000	.539
Cognitive Symptoms	2	837.048	0.000	.556
Sleep Symptoms	2	524.046	0.000	.439
Neuropsychiatric Symptoms	2	605.046	0.000	.475
Overall Symptoms	2	1289.659	0.000	.659
Age	2	18.932	0.033	.028
Education	2	11.750	0.048	.017
Number of Concussions[a]	2	.377	.686	.001
Time Since Injury[a]	2	.968	.380	.002

Note. Cluster 2 was excluded because it included only one case.
[a]Run in a separate univariate ANOVA because missing data would have substantially reduced sample size for MANOVA.

Table 14
MANOVA contrasts for overall sample four cluster solution from conventional cluster analysis

Variable	First cluster	Second Cluster	*p*
Verbal Memory	1	3	.000
		4	.000
	3	4	.000
Visual Memory	1	3	.000
		4	.000
	3	4	.000
Visuomotor Speed	1	3	.000
		4	.000
	3	4	.000
Reaction Time	1	3	.000
		4	.000
	3	4	.005
Impulse Control	1	3	.000
		4	.003
	3	4	.228
Migraine Symptoms	1	3	.000
		4	.000
	3	4	.000
Cognitive Symptoms	1	3	.000
		4	.000
	3	4	.000
Sleep Symptoms	1	3	.005
		4	.000
	3	4	.000
Neuropsychiatric Symptoms	1	3	.022
		4	.000
	3	4	.000
Total Symptoms	1	3	.000
		4	.000
	3	4	.000
Age	1	3	.022
		4	.627
	3	4	.378
Education	1	3	.055
		4	.601
	3	4	.515
Time Since Injury[a]	1	3	.488
		4	.744
	3	4	.982
Num. Concussions[a]	1	3	.693
		4	.912
	3	4	.967

Note. Cluster 2 was excluded because it included only one case.
[a]Run in a separate univariate ANOVA because missing data would have substantially reduced sample size for MANOVA; Bonferroni corrected, p=.025.

Table 15
Cluster Means for the overall sample four-cluster solution from the conventional cluster analysis

Variable	Cluster 1 Mean(SD) n=996	Clinical Interpretation	Cluster 3 Mean(SD) n=208	Clinical Interpretation	Cluster 4 Mean(SD) n=161	Clinical Interpretation
Verbal Memory	86.70(8.98)	Average	66.41(12.26)	Borderline to impaired	76.67(13.38)	Average
Visual Memory	75.91(11.31)	Average	55.61(11.41)	Borderline	64.49(14.44)	Low Average
Visuomotor Speed	38.41(6.29)	Average	27.64(5.78)	Low Average to impaired	32.96(7.06)	Average
Reaction Time	0.59(0.07)	Average	0.76(0.15)	Borderline	0.67(0.11)	Low Average
Impulse Control	5.88(4.27)		11.04(7.86)		8.67(7.27)	
Migraine Symptoms	2.05(2.89)		5.81(5.33)		15.67(7.22)	
Cognitive Symptoms	1.60(2.56)		4.00(4.07)		12.53(4.61)	
Sleep Symptoms	0.70(1.31)		1.38(1.78)		5.24(2.77)	
Neuropsychiatric Symptoms	0.46(1.15)		0.92(1.43)		6.74(5.22)	
Overall Symptoms	5.02(6.41)	Normal	12.65(10.87)	Unusual	41.78(14.13)	Very High
Age	15.71(1.87)		14.79(1.83)		15.52(1.75)	
Education	9.23(1.76)		8.59(1.63)		9.24(1.66)	
Number of Concussions	1.07(0.25)		1.07(0.25)		1.07(0.26)	
Time Since Injury	12.51(11.03)		13.91(12.67)		13.59(12.67)	

Note. Reaction time is in seconds. Empty cells = no clinical percentile scores available in ImPACT manual. Because clusters include males *and* females and a range of ages, clinical interpretations are approximate based on norms for both high school girls and boys aged 13 to 15 from ImPACT technical manual (Lovell, 2011).

Table 16
Omnibus ANOVA results for acute sample five-cluster solution with conventional cluster analysis

Variable	*df*	*F*	*p*	Partial Eta^2
Verbal Memory	2	68.299	0.000	.271
Visual Memory	2	54.882	0.000	.168
Visuomotor Speed	2	54.640	0.000	.233
Reaction Time	2	70.612	0.000	.290
Impulse Control	2	12.509	0.001	.050
Migraine Symptoms	2	201.453	0.000	.567
Cognitive Symptoms	2	196.945	0.000	.561
Sleep Symptoms	2	142.215	0.000	.480
Neuropsychiatric Symptoms	2	107.929	0.000	.412
Overall Symptoms	2	368.469	0.000	.705
Age	2	5.207	0.006	.033
Education	2	5.998	0.003	.037
Number of Concussions	2	0.741	0.478	.005
Time Since Injury	2	0.385	0.681	.002

Note: Clusters two and four were not included in analyses because they contained only one and two cases, respectively.

Table 17
ANOVA contrasts for acute sample five-cluster solution from conventional cluster analysis

Variable	First cluster	Second Cluster	*p*
Verbal Memory	1	3	.000
		5	.000
	3	5	.000
Visual Memory	1	3	.000
		5	.008
	3	5	.000
Visuomotor Speed	1	3	.000
		5	.000
	3	5	.010
Reaction Time	1	3	.000
		5	.000
	3	5	.000
Impulse Control	1	3	.000
		5	.000
	3	5	.000
Migraine Symptoms	1	3	.000
		5	.000
	3	5	.000
Cognitive Symptoms	1	3	.000
		5	.000
	3	5	.001
Sleep Symptoms	1	3	.000
		5	.044
	3	5	.000
Neuropsychiatric Symptoms	1	3	.000
		5	.043
	3	5	.000
Total Symptoms	1	3	.000
		5	.000
	3	5	.000
Age	1	3	.041
		5	.013
	3	5	.983
Education	1	3	.016
		5	.003
	3	5	.983
Time Since Injury	1	3	.792
		5	.991
	3	5	.696

Table 18
Cluster Means for the acute five-cluster solution from the conventional cluster analysis

Variable	Cluster 1 Mean(SD) n=40	Clinical Interpretation	Cluster 3 Mean(SD) n=50	Clinical Interpretation	Cluster 5 Mean(SD) n=237	Clinical Interpretation
Verbal Memory	67.2(11.59)	Borderline	78.42(13.04)	Low Average to Average	87.05(8.87)	Average
Visual Memory	55.15(9.45)	Borderline	67.52(13.47)	Average	76.22(11.38)	Average
Visuomotor Speed	27.09(5.33)	Borderline to impaired	35.08(6.37)	Average	38.12(6.30)	Average
Reaction Time	0.78(0.18)	Borderline	0.64(0.08)	Average	0.58(0.07)	Average
Impulse Control	10.30(6.61)		7.5(5.54)		5.992(4.56)	
Migraine Symptoms	5.90(5.10)		14.20(5.50)		2.23(2.99)	
Cognitive Symptoms	4.35(4.40)		11.60(3.95)		1.53(2.43)	
Sleep Symptoms	1.30(1.73)		4.96(2.71)		0.62(1.28)	
Neuropsychiatric Symptoms	1.03(1.35)		5.22(4.47)		0.40(1.15)	
Overall Symptoms	13.03(10.86)	Unusual	36.68(9.05)	Very High	4.95(6.11)	Normal
Age	14.63(2.00)		15.62(1.59)		15.65(1.88)	
Education	8.53(1.66)		9.46(1.39)		9.43(1.83)	
Number of Concussions	1.08(1.32)		0.82(1.11)		0.91(0.92)	
Time Since Injury	4.58(1.93)		4.38(1.74)		4.60(1.64)	

Note. Reaction time is in seconds. Empty cells = no clinical percentile scores available in ImPACT manual. Because clusters include males *and* females and a range of ages, clinical interpretations are approximate based on norms for both high school girls and boys aged 13 to 15 from ImPACT technical manual (Lovell, 2011).

Figure 1.
Graphical representation of the model tested using LCA

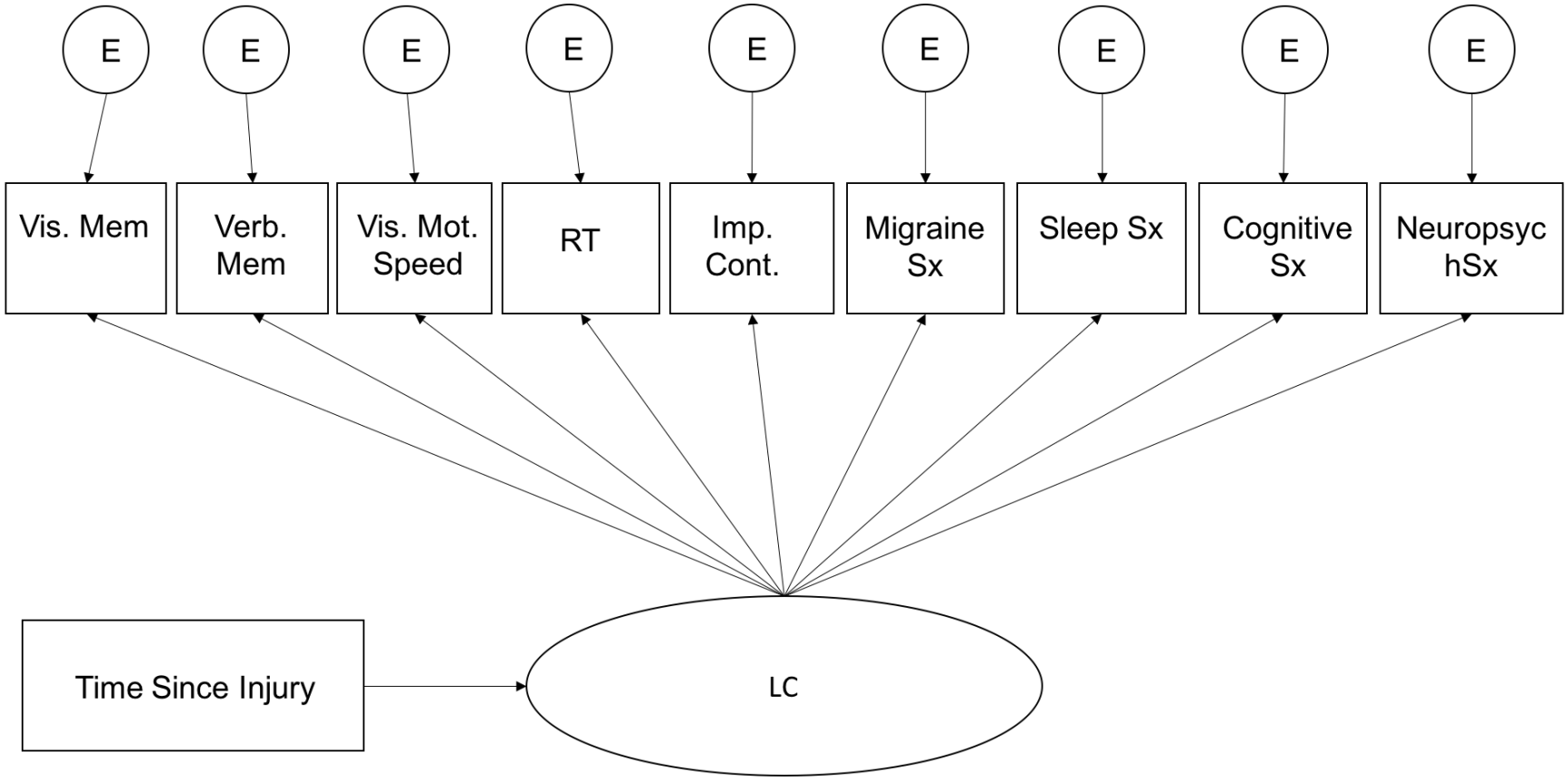
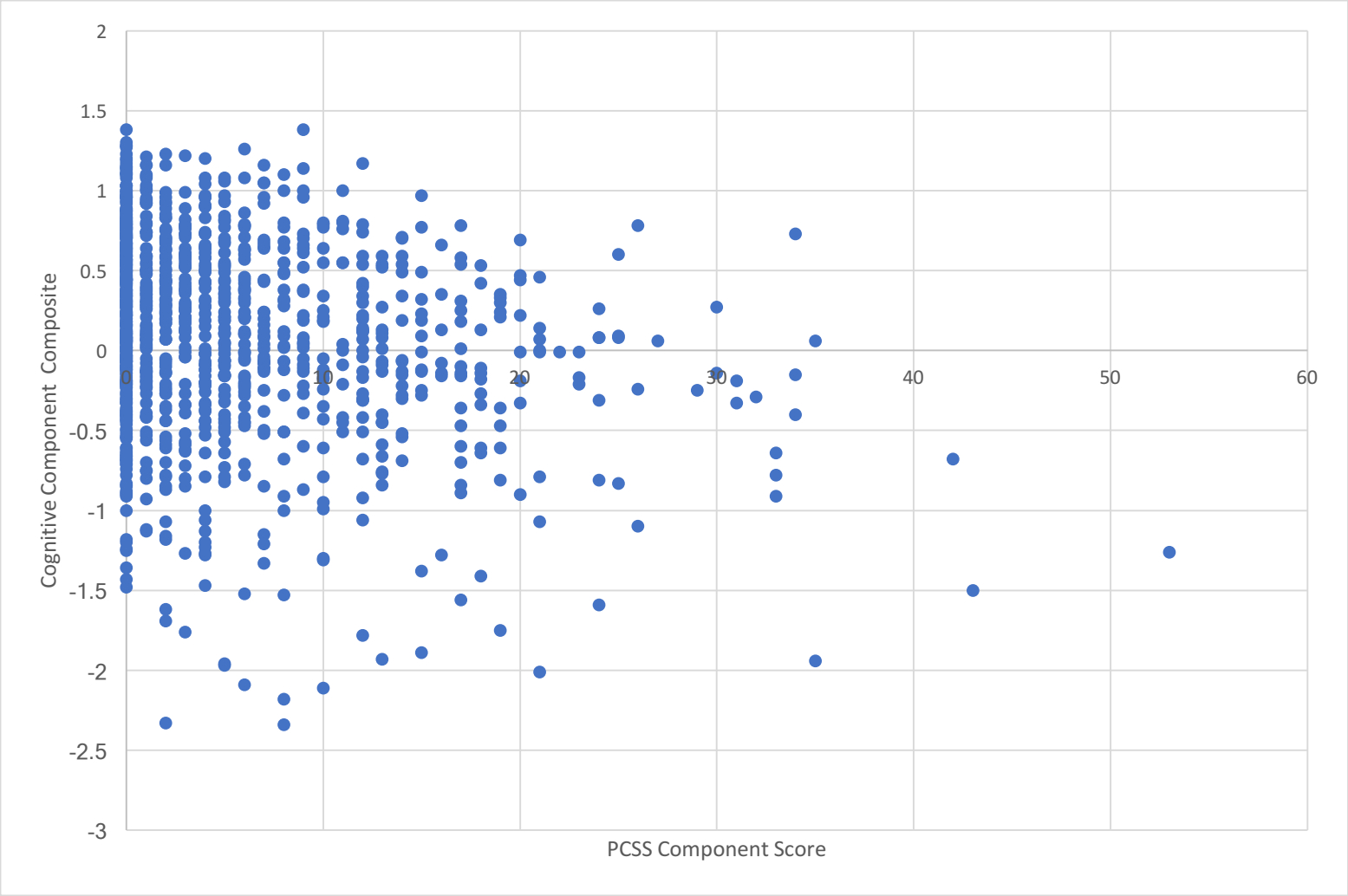


Figure 2
Bivariate scatter plot of two-component data for cognitive and symptom variables.



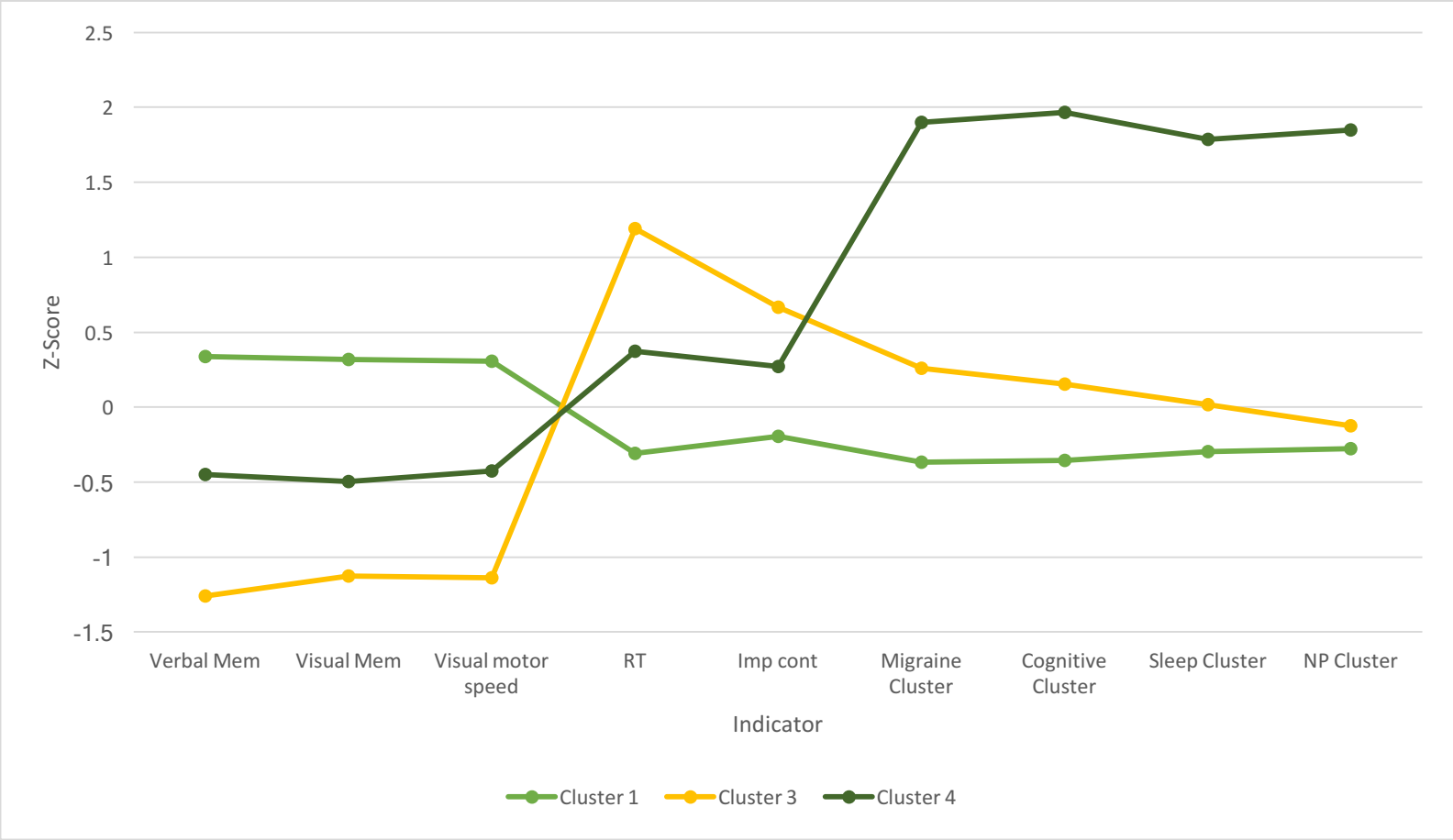


Figure 3. Four-cluster solution for five cognitive and four symptom cluster variables in the overall sample. Note Migraine Cluster=headaches, visual problems, dizziness, noise sensitivity, light sensitivity, nausea, vomiting, balance problems, numbness/tingling; cognitive cluster=fatigue, fogginess, drowsiness, difficulty concentrating, difficulty remembering, cognitive slowing; sleep cluster= difficulty falling asleep, sleeping more than usual, sleeping less than usual; NP (neuropsychiatric) cluster=more emotional, sadness, nervousness, irritability. Note: Cluster two removed because it contained only one case.

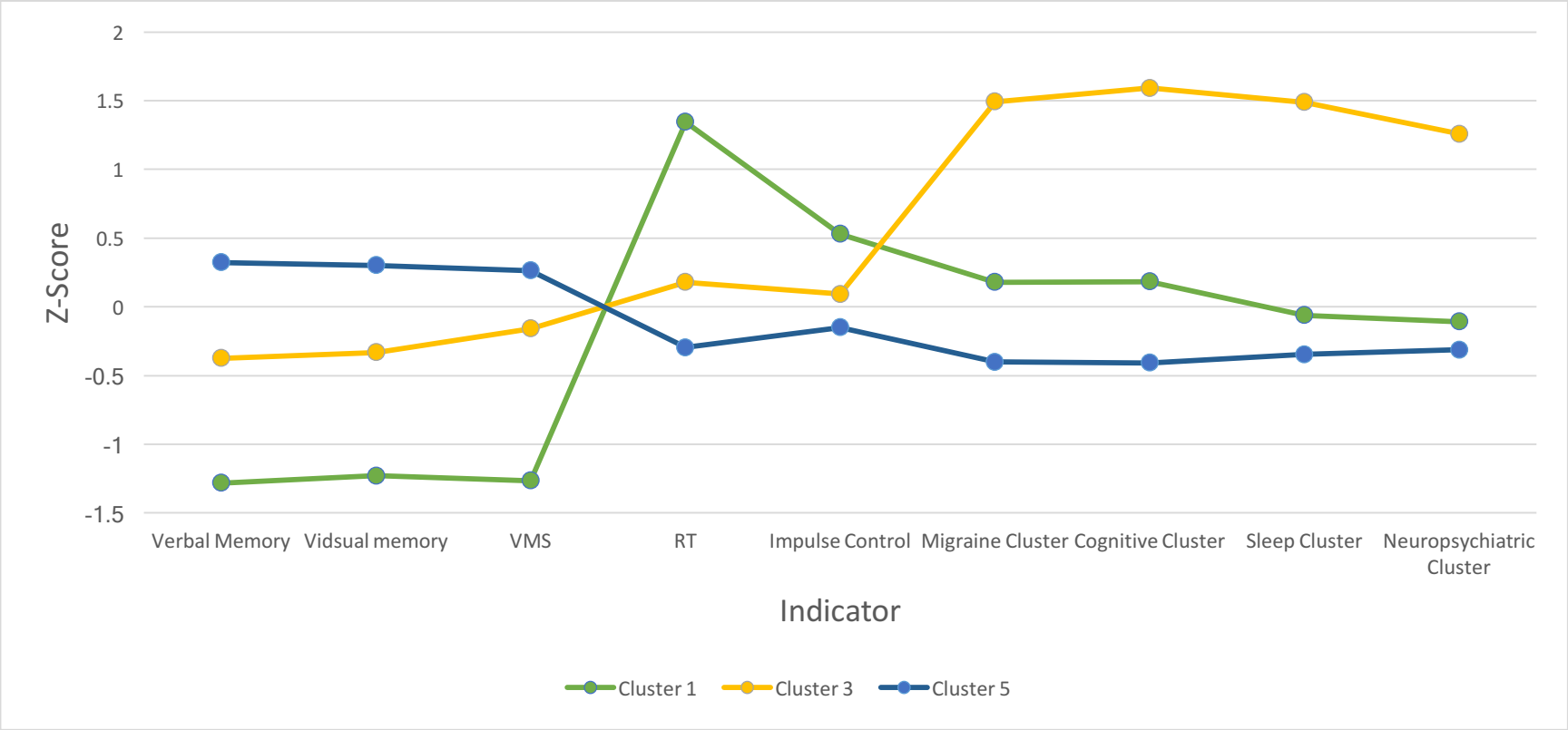


Figure 4. Three-cluster solution for five cognitive and four symptom cluster variables in the acute sample. Note Migraine Cluster=headaches, visual problems, dizziness, noise sensitivity, light sensitivity, nausea, vomiting, balance problems, numbness/tingling; cognitive cluster=fatigue, fogginess, drowsiness, difficulty concentrating, difficulty remembering, cognitive slowing; sleep cluster= difficulty falling asleep, sleeping more than usual, sleeping less than usual; NP (neuropsychiatric) cluster=more emotional, sadness, nervousness, irritability. Note: clusters two and four were removed because they contained only one and two cases, respectively.

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