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CONCUSSIONS IN SPORT: INVESTIGATION OF ASSESSMENT MEASURES AND FUNCTIONAL DEFICITS

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ABSTRACT

One of the least understood, but most common injuries in sports is mild traumatic brain injury (MTBI), otherwise known as concussion. The severity of this injury is often dismissed and is euphemized as a bell-ringer or "ding". This lack of recognition leads to a gross under-reporting of MTBI in both the general population and in the sporting arena. Mild brain injuries present as a difficult diagnosis for practitioners to manage. The impairments that result subsequent to a concussion are due to a variety of neuropathological processes triggered by damage caused when the brain matter collides with the rough, ridged edges of the skull or due to the rapid acceleration/deceleration and/or rotation of the brain. A lack of objective pathognomic signs of concussion means that a physician's diagnosis often rests on an athlete's honest report of subjective symptoms (e.g., headache, irritability, fatigue) that are also common in the non-concussed population and known to vary day to day. As a result of the varying symptoms of concussions, currently employed tests used in concussion assessment and return to play decisions often give conflicting diagnoses and lack consistent results between testing methods. This has led to skepticism about the utility of these methods. At present, there are no evidence-based medical treatments for concussion that increase the speed or extent of recovery. Therefore, the best approach to concussion management emphasizes early recognition of symptoms, removal from sports and cognitively demanding activities, and prevention of additional concussive injuries. The underlying problem in concussion diagnosis is the application of current assessment methods; one-dimensional testing protocols have the potential to miss diagnosing a concussion if the

tests are not sensitive to an individual's symptoms or pathology. More advanced testing paradigms are needed that use a combination of testing modalities that are complementary to each other. The aim of this research was to examine the pathological mechanisms of concussion from a multimodal perspective. The pathological mechanisms refer to the disorders in behavior and responses to stimuli that result following concussion. The multimodal perspective combined three testing methods (neuropsychological, postural and electroencephalographic) to ensure a global assessment; neuropsychological, postural under virtual reality conditions and electroencephalographic (EEG) measures.

Four main conclusions are drawn from our results. First, neuropsychological symptoms resolve themselves more quickly than do postural or EEG changes. Second, there is a clear mismatch between subjects' injury classifications when neuropsychological, postural and EEG testing paradigms are compared. Third, the use of a testing paradigm that combines the most sensitive tests from each modality appears to provide a more effective system for diagnostic and return to play measurements than does any one method alone. Lastly, applying low resolution electromagnetic tomographic assessment (LORETA) emerges as an effective tool for localizing cortical areas that have been negatively affected by the concussive injury. The findings are discussed in relation to neural plasticity underlying functional changes and with respect to their clinical implications.

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"Every journey begins with a single step"

- author unknown

I have been fortunate in my life to have had unrelenting support from my family, which has given me the courage to take that first step so many times. It is that support at the beginning of each journey, and the unwavering support throughout, which has given me the strength to set high goals and continually accomplish them. For all they have done in helping me grow and accomplish my dreams, and for their continuing inspiration and support, I want to thank my parents, Michael and Lynda, and my brother and sister, Aaron and Katie. You all add constant joy to my life and I am so very proud of all your accomplishments.

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Chapter 1

Introduction

One of the least understood, but most common injuries in sports is mild traumatic brain injury (MTBI), otherwise known as concussion. The severity of this injury is often misunderstood or dismissed and is euphemized as a bell-ringer or "ding". This lack of recognition leads to a gross under-reporting of MTBI in both the general population and in the sporting arena. In spite of this probable under-reporting, it is estimated that two million traumatic brain injuries occur annually in the United States at a cost of $38 billion (Thatcher et al., 2001). In sport and recreational activities alone, there are approximately 300,000 concussions, carrying a $9 to $10-billion price tag for acute care and rehabilitation (Guskiewicz et al., 2003). In the National Hockey League there is an average of 100 concussions per year; that equates to approximately four concussions per team per season (Burnside, 2004). In Division 1-A college football there were 373 concussions on 87 teams in the 2001-2002 season, equating to almost 6 per 1000 athletic exposures (Booher, 2003). Although these numbers seem high, the true number of concussions in sports has been estimated to be even higher. Macciocchi et al. (1996) found the risk of a concussion in football to be 10%, while Gerberich et al. (1983) reported that 19% of high school athletes had experienced at least one concussion.

When athletes enter the sporting arena they assume the potential risk of incurring an injury, but frequently do not understand the potential detriments of those injuries. The pathology, symptomology and possible impairments to their quality of life are often numerous and yet understated, even by sports medicine professionals. In no instance is this more true than in the case of a mild traumatic brain injury. The consequences of a missed diagnosis are many and put people at risk for associated ailments such as second impact syndrome, cognitive deficits, slowed reaction time, motor impairments or even death (Barr, 2001; Guskiewicz et al., 2001; Hugenholtz et al., 1988; Macciocchi et al., 1996; Oliaro et al., 2001; Powell, 2001; Thatcher et al., 1989).

Mild Traumatic Brain Injury (MTBI) is a complicated injury requiring proper diagnosis and care. Numerous definitions of concussion have been proposed since it was first recognized. Over the past half century, concussion has predominantly been defined as a "short lasting", "temporary", or "transient" disturbance of neuronal function brought on by a sudden acceleration, deceleration and/or rotation of the head, usually without skull fracture (Shaw, 2002; Wilberger et al., 2006). However, this is a disputable definition in so far as the terms "short lasting", "temporary" and "transient" are not defined. More importantly, recent research has shown that the effects of a mild traumatic brain injury can persist for months or even years (Thatcher et al., 1989, 1998, 2001). In this regard, two classic definitions seem to be appropriate to describe a concussion. Sir Charles Symonds noted over 40 years ago that "concussion should not be confined to cases in which there is immediate loss of consciousness with rapid and complete recovery … the effects of the injury may or may not be reversible" (Shaw, 2002). This directly addresses the possible long term effects of a mild brain injury. Second, the neurosurgeon

Benjamin Bell wrote in 1787, two hundred and thirty years ago, that "every affection of the head attended with stupefaction, when it appears as the immediate consequence of external violence, and when no mark or injury is discovered, is in general supposed to proceed from commotion or concussion of the brain, by which is meant such a derangement of this organ as obstructs its natural and usual functions, without producing such obvious effects on it as to render it capable of having its real nature ascertained by dissection" (Shaw, 2002). This definition continues to be relevant in light of today's research in two main ways. First, it does not imply a short term deficit that resolves quickly. Second, it notes that the underlying pathology of the symptoms cannot be ascertained by dissection. This is a key factor in a definition of mild traumatic brain injury since it suggests the nature of the injury is physiological and not a result of anatomic pathology such as lesions, lacerations, edema or hemorrhage.

The ensuing symptom pattern that results from a concussion is referred to as the Post Concussion Syndrome. Broadly speaking, this refers to the constellation of injury-related symptoms which may be present in varying degrees including, but not limited to, impaired neurocognitive, neurological, and neurobehavioral functioning and physical symptoms such as impaired attention, concentration, memory and information processing, impaired vision, vomiting, tinnitus, photophobia, vertigo, disequilibrium, lassitude, irritability, depression, headache and sleep disturbance (Barr, 2001; Duff, 2004; Guskiewicz et al., 2001; Hugenholtz et al., 1988; Korn et al., 2005; Macciocchi et al., 1996; Oliaro et al., 2001; Powell, 2001; Thatcher et al., 1989; Wojtys et al., 1999). It has previously been reported that the multitude of symptoms that arise from MTBI usually resolve themselves within a one or two-week period (Echemendia et al., 2001;

Guskiewicz et al., 1997; Macciocchi et al., 1996; Macciocchi et al., 2001; Maddocks & Saling, 1996). This is a misleading statement and one that can have detrimental results. Though most athletes who experience a concussion are likely to recover, a subset of athletes may go on to experience chronic cognitive and neurobehavioral symptoms (Hessen, 2006). Thatcher (1989, 1997, 2001) has used electroencephalography (EEG) to detect residual sequelae in MTBI patients beyond one year post injury. Findings such as these show the persistence of the injury beyond its overt symptoms, and support the hypothesis that athletes who return to competition based only upon the apparent resolution of overt symptoms dramatically increase their risk of second impact syndrome, a syndrome with potentially fatal consequences (Amann, 2000; Barth, 2001; Guskiewicz et al., 2001; Kushner, 2001; Randolph, 2001). It thus appears that symptom resolution is not indicative of injury resolution (Thompson et al., 2005). Symptom resolution may occur due to the brain's ability to adapt to neurophysiological damage. The amazing plasticity of the brain may allow it to reallocate resources such that undamaged pathways and neurons are used to perform cognitive and motor tasks (Hallett, 2002). This functional reserve gives the appearance that the person has returned to pre-injury health while, in actuality, the injury is still present (Randolph, 2001).

Concussion injuries present as a difficult diagnosis for practitioners. The impairments resulting from concussion are due to a variety of neuropathological processes triggered by the rapid acceleration/deceleration and/or rotation of the brain (Giza, 2001; McAllister, 2001). Although individuals who suffer such an injury can be severely symptomatic post-injury, conventional radiological techniques (e.g., CT, MRI) generally fail to detect structural evidence of brain trauma (Thatcher, 1989). As reported

by Pellman et al. (2004), 91% of the concussion cases they studied in football did not have a concomitant loss of consciousness, thus making diagnosis more difficult. LeClerc (2001) also noted that 75-90% of concussions are believed to occur without loss of consciousness (LOC), with little to no post-traumatic amnesia (PTA), and only slight disorientation. The lack of objective pathognomic signs of concussion leaves a physician's diagnosis to rest on an athlete's honest report of subjective symptoms (e.g., headache, irritability, and fatigue) that are common in the non-concussed population and known to vary from day to day (Chan, 2001; Gouvier, 1988). More advanced testing is currently available using balance, EEG and neuropsychological tests. However, as a result of the varying symptomology of concussions these tests often give conflicting diagnoses and lack consistent results within each testing method. This has led to skepticism about the utility of these methods.

Over the past decade advancements in technology and new understandings regarding the severity of a mild traumatic brain injury have increased awareness and research in the field and have improved the quality of care following this injury. A recent database search of PubMed using combinations of the terms EEG, balance, posture, neuropsychological, with mild brain injury returned almost 5000 articles. However, a search combing EEG + balance (or posture) + neuropsychological + concussion (or MTBI or mild brain injury) returned only 1 article. (Slobounov et al., 2006). This publication mentioned neuropsychological testing as the criteria by which athletes in the study were allowed to return to competition; it was not a testing parameter. This represents a severe lack of integration between fields in the area of concussion assessment and return to play measures. At this juncture there are no simple tests that

can determine the severity of a closed head injury or establish an appropriate timeline for return to play. As noted by Notebaert and Guskiewicz (2005), "the complexity of concussion injuries requires clinicians to use a variety of tools for information, but the current tendency is to base the return-to-play decision on the athlete's self-reporting of symptoms and ability to perform sport-specific tasks without a recurrence of concussion symptoms". Multiple authors have, in recent years, noted this shortcoming (Guskiewicz et al., 2001; Guskiewicz et al., 2004; Guskiewicz & Cantu, 2004; Oliaro et al., 2001). However, despite this clear deficiency in our ability to accurately assess an athlete's readiness for return to play, nothing has been done to address the need for improved diagnoses. Many concussions still go unrecognized or are improperly diagnosed in pediatric, adult, athletic and elderly populations.

At present, there are no evidence-based medical treatments for concussion that increase the speed or extent of recovery. Therefore, the best approach to concussion management emphasizes early recognition of symptoms and prevention of additional concussive injuries. Although the most widely used RTP guidelines provide physicians with general guidelines, they show an undue reliance on the initial diagnosis and use only a handful of tests that rely on subjective symptoms and on occasion utilize neuropsychological or functional assessments. When neuropsychological and balance tests are used the results are usually compared to population norms which may not adequately reflect the specific population being tested such as college athletes.

With the number of concussions in sport increasing and the long term negative effects of concussion being increasingly understood, it is the responsibility of new research to improve the reliability of concussion diagnosis and RTP testing protocols. A

valid contribution cannot be made to the advancement of concussion assessment by studying testing parameters in isolation. The underlying problem in concussion diagnosis is the application of current assessment methods. Concussion testing has no agreed upon *best test* for diagnosis, severity rating or return to play readiness. As a result, practitioners often decide upon a testing method based on their area of expertise. A neuropsychologist will test for a mild traumatic brain injury using a neuropsychological test battery, a neurologist will use an electroencephalogram (EEG) and a motor control specialist will most likely use postural assessments. This one-dimensional approach would be appropriate if all concussions resulted in deficits in all of these areas, but that is not the case. Each concussion is unique in its mechanism, symptomology and pathology (Cantu, 2006). For that reason, currently employed one-dimensional testing protocols have the potential to misdiagnose a concussion if the test was not sensitive to an individuals' symptomology or pathology. For example, an athlete who sustains a concussion may present with a balance deficit but not a cognitive deficit. In this instance a neuropsychologist may form a negative diagnosis whereas a motor control specialist may form a positive diagnosis. In other words, not all tests that claim to be validated as concussion assessment tests are truly valid since they do not test the full range of potential deficits that may occur following a concussion. We recognized the magnitude of this current limitation and set forth to alleviate this shortcoming.

Purpose

The purpose of this research was to investigate the pathological mechanisms of concussion from a multimodal perspective. The pathological mechanisms refer to the disorder in behavior and response of the subject to stimuli that has resulted from a concussion. The multimodal perspective combined three testing methods to ensure a global assessment. Specifically, this research introduced a more global context of concussion assessment to the field. This was accomplished by comparing group responses on functional testing and exploring the differences in cortical functioning following concussion.

We added to this field of research by studying concussion pathology and symptomology in combination (not in isolation) by employing the three most commonly used assessment methods; EEG recordings, neuropsychological testing and postural assessments. We tested differences between the sensitivity of these three testing methods and then combine the best tests from each assessment modality to increase concussion assessment sensitivity and reduce the number of false negatives in return to play measures.

Hypotheses

Based on previous research assessing timelines for the resolution of neurpsychological, postural and electroencephalographic abnormalities following concussion (Guskiewicz, 2001; Iverson et al., 2006; Thatcher et al., 1998) and the sensitivity of neuropsychological (Randolph, 2001), postural (Guskieveicz et al., 2004)

and electroencephalographic (Thatcher et al., 2001) testing following concussion, we hypothesize that:

1. There will be a mismatch in the classification of subjects into either a normal or injured group between current testing paradigms (neuropsychological, virtual reality posture assessment or electroencephalographic amplitude measures)

2. Combining tests from each of the three testing modalities will increase the sensitivity of return to play concussion assessment beyond any one modality used in isolation.

Sub-hypotheses:

Based upon previous research (Korn et al., 2005), there were two additional hypotheses:

a) EEG power differences between groups would be greater during difficult postural tasks as compared to the resting task.

b) Group differences in current sources (LORETA) between groups would coincide with surface EEG differences.

Our main aim in this study was to compare and contrast the three most accepted concussion assessment tests based on their ability to classify test subjects as either injured or normal. A mismatch between the classifications of athletes into either an injured or normal group would lead to confusion during initial diagnosis and return to play decision making. For example, if an athlete is cleared by neuropsychological testing but not by EEG there is an obvious inconsistency between testing methods. This causes conflict and confusion for athletes, coaches, parents and practitioners that are involved in the diagnostic and RTP process.

Our secondary aim was to improve concussion return to play testing by reducing the number of false negatives in return to play assessments. We combined the most sensitive tests from the three testing modalities to formulate a testing paradigm and discriminant function that was more comprehensive and sensitive than any one testing method used in isolation.

To improve our understanding of the brain regions most affected by concussion, we studied differences in the participant's neural resource allocation during different postural tasks following a concussion. Specifically we measured EEG differences in the frequency domain and localized modulation of the EEG as a function of MTBI. We studied changes in the amplitudes of these frequencies during both sitting and standing postures and determined the differing sources of EEG frequency power distributions using Low Resolution Electromagnetic Tomography (LORETA).

Operational Definitions

Electroencephalogram (EEG) - The neurophysiologic measurement of the electrical activity of the brain by recording from electrodes placed on the scalp. The recording reflects the temporal and spatial summated activity of both excitatory (EPSP) and inhibitory (IPSP) postsynaptic potentials on the pyramidal cells of the upper layers of the cortex (Kandel et al., 2000).

Low Resolution Electromagnetic Tomography (LORETA) - This procedure computes, from the recorded scalp electrical potential differences, the three-dimensional distribution of the electrically active neuronal generators in the brain as a current density value (A/m2) at each voxel (Pascual-Marqui et al., 2002).

Neuropsychological Testing (NS) - Tasks designed to measure a psychological function known to be linked to a particular brain structure or pathway. These tests offer an estimate of a person's peak level of cognitive performance. A person's raw score on a test is compared to a general population normative sample, from a comparable population (Wikipedia.com, 2006).

Virtual Reality Display - A technology which allows a user to interact with a computer-simulated 3D environment. In this instance, only animated visual displays are manipulated.

Mild Traumatic Brain Injury (Concussion) – It is disputable whether an agreed upon definition of concussion exists. Generally speaking, it is thought to include the following criteria: it is caused by a direct or indirect blow to the head or elsewhere on the body from an "impulsive" force transmitted to the head; it may cause an immediate and short-lived impairment of neurological function; it may cause neuropahologic changes, however, the acute clinical symptoms largely reflect a functional disturbance rather than a structural injury; it may cause a gradient of clinical syndromes and symptoms that may or may not include loss of consciousness; it most often has negative findings on neuroimaging (Guskiewicz, 2006).

Second Impact Syndrome (SIS) – Also called repetitive brain injury or cumulative syndrome. This occurs when an individual is subjected to a second head injury during the period of time in which they continue to have post-concussive symptoms (Cantu, 2006).

Diffuse Axonal Injury – A mechanically induced stretching or shearing of neural tissue that results in an increase in neuronal permeability, caused by acceleration and/or deceleration and/or angular rotation. This may result from trauma directly to the head or from trauma to the torso or axial skeleton with the force of the incident being transmitted indirectly to the brain matter (Thompson, 2006).

Mechanism - The fundamental processes involved in or responsible for an action, reaction, or other natural phenomenon (Merriam-Webster.com, 2006).

Pathology - The structural and functional deviations from the normal that constitute disease or characterize a particular disease. A condition of the body, or of some part or organ of the body, in which its functions are disturbed or deranged (Merriam-Webster.com, 2006).

Chapter 2

Review of the Literature

Current Assessment Methods

A review of the literature on mild traumatic brain injury demonstrates a large amount of interest in this topic and substantial progress in the field over the past decade. However, it also reveals that there is a gross lack of consistency and agreement in the research and clinical findings. There are many inconsistencies and conflicting opinions regarding the validity and reliability of initial assessments, return to play measures and the long term effects of concussion. In a recent study by Notebaert and Guskiewicz (2005) athletic trainers were given a survey and asked three general questions; what tools do you use to assess concussion; what tools do you use to determine safe return to play; what tools do you feel are the most sensitive for return to play decision making. This survey revealed that among athletic trainers there is very little agreement about the best combinations of available assessment tools to use. They reported that to assess concussion, 95% of trainers reported using the clinical examination, 85% used symptom checklists, 48% used the Standardized Assessment of Concussion, 18% used neuropsychological testing, and 16% used the Balance Error Scoring System. The most frequently used concussion grading scale and return-to-play guideline belonged to the

American Academy of Neurology. However, this "commonly" used measure was still only used by 30% of athletic trainers. When deciding whether to return an athlete to play, certified athletic trainers most often used the clinical examination (95%), return-to-play guidelines (88%), symptom checklists (80%), and player self-report (62%). The tests that trainers classified as the most sensitive for basing return to play decisions were the clinical examination (59%), symptom checklists (13%), and return-to-play guidelines (12%). Only 3% of certified athletic trainers surveyed complied with the recent position statement of the American Academy of Neurology, which advocated using a combination of symptom checklists, neuropsychological testing, and balance testing for managing sport-related concussion (Notebaert & Guskiewicz, 2005). This lack of compliance with the position statement may have many sources, one of the most probable being a lack of knowledge regarding the tests themselves.

Neuropsychological Testing

Neuropsychological (NP) testing has become accepted as a means by which to detect and characterize neurocognitive impairment resulting from central nervous system traumas (Barr, 2001), such as concussion. Specific neuropsychological tests for assessing the level of severity of mild brain injuries have been developed and adapted from classic neuropsychological tests such as the 'Trails' tests and Symbol Digit Substitution Test. The Trails B test is used to assess processing speed and scanning ability while the Symbol Digit Substitution test assesses processing speed and working memory (Randolph et al., 2005). Differing reports of reliability have been calculated for these

tests. Echemendia et al. (1999), reported reliability scores of 0.70 and 0.54 for the Symbol Digit Substitution test and Trails B test respectively in a concussed population. In a review of reliability scores of neuropsychological testing following concussion, Barr (2003), determined scores of 0.73 and 0.65 for the Symbol digit and the Trails B tests, while Dikmen et al. (1999), reported reliability of 0.89 on both the Symbol Digit test and the Trails B test. Rating scales have also been developed to assess and track symptom severity following concussive injuries. The goal has been to further the understanding of the relation between brain and behavior and assess the resolution of the injury (Barr & McCrea, 2001). Essentially, NP testing has sought to make objective and quantifiable what has in the past been merely descriptive. At this time at least 17 sets of NP based guidelines exist to assist in concussion assessments, yet there is limited empirical evidence to support their use (Hinton-Bayre & Geffen, 2002), which points to the contradiction and lack of acceptance of any one neuropsychological testing method and to the need to re-examine neuropsychological testing as a stand alone assessment of concussion.

In recent years it has been noted that two of the main factors that can limit the sensitivity of NP testing are practice and learning effects (De Monte et al., 2005; Macciocch, 1990; Macciocchi et al., 1996; Rosenbaum et al., 2006; Tombaugh, 2006; Wilson et al., 2000). Practice effects are typically defined as some improvement in performance between concurrent test sessions based on familiarity with the procedures and/or previous exposure to the assessment. Learning effects relate to the retention of the improvement over a period of time (Valovich McLeod et al., 2004). Both practice and learning effects can be a confounding factor in the interpretation of test scores.

In their paper "*Cumulative effects of concussion in amateur athletes***"**, 2004, Iverson et al., concluded that their study provided "evidence to suggest that athletes with multiple concussions might have cumulative effects" (Iverson, et al., 2004). This study used the NP computer based testing program ImPACT to assess functioning. However, in a study conducted just two years later using the ImPACT program, Iverson et al. concluded that there was no measurable effect of one or two previous concussions on athlete's neuropsychological test performance or symptom reporting, and that if there was a cumulative effect of one or two previous concussions, it was very small and undetectable using their methodology (Iverson et al., 2006).

Due to a lack of difficulty or sensitivity in chosen neuropsychological tests it is entirely conceivable that an athlete may appear to be intact neuropsychologically, but may evidence mental impairment when performing under physically stressful athletic competitive conditions (Killam et al., 2005). In support of this, it was recently noted that "it is unclear that NP testing can detect impairment in players once concussion-related symptoms (e.g. headache) have resolved. Because no current guideline for the management of sport-related concussion allows a symptomatic player to return to sport, the incremental utility of NP testing remains questionable" (Randolph et al., 2005). The researchers go on to state that "despite the theoretic rationale for the use of NP testing in the management of sport-related concussion, no NP tests have met the necessary criteria to support a clinical application at this time" (Randolph et al., 2005). At this time it is generally agreed upon that, at a minimum, athletes should be removed from competition for as long as they are symptomatic. However, ascertaining when an athlete is fully asymptomatic may be problematic; symptoms are often minimized but not resolved.

Loss of Consciousness & Post-Traumatic Amnesia

A clear definition of loss of consciousness is not yet agreed upon in the literature. Consciousness is regarded as a subjective experience and can be thought of as synonymous with awareness and alertness (Cantu, 2006). The general commonality between current guidelines is the recommendation of prolonged periods out of play for severe grades of concussion. This is based on the presumption that the brain is vulnerable for a longer period following a severe concussion. The majority of guidelines use duration of loss of consciousness, and to a lesser degree post-traumatic amnesia, as the main measures of injury severity. There is disagreement on how to use early indicators to assign severity of concussion, particularly in cases of a brief loss of consciousness (LOC) or extended posttraumatic amnesia (PTA) (Hinton-Bayre & Geffen, 2002).

Recent studies have called into question the utility of these measures. In 1999, Lovell et al. failed to find any relationship between LOC and neuropsychological functioning in a large sample of patients with mild head trauma and called into question the importance of LOC in grading the severity of concussion. They also concluded that the study did not provide support for the use of guidelines that rely heavily on LOC in making return-to-play decisions. A 2003 study conducted by Collins et al. found that the presence of amnesia, not loss of consciousness, was predictive of symptom and neurocognitive deficits following concussion in athletes and advocated the refinement of sports concussion grading scales. These findings are in direct conflict with the conclusions drawn by Kelly (2001) who reported on the relative importance of LOC in

the evaluation of concussion by reviewing scientific and clinical evidence in the literature between 1966-2001. In his report, Kelly concluded that "the observation of LOC at the time of concussion must be viewed as reflecting a potentially worrisome traumatic brain injury. LOC is followed by more severe acute mental status abnormalities and carries a greater risk of intracranial pathology than concussion without LOC". On the other hand, Cantu (2006) clearly stated that "previous assumptions that a concussion was present only when individuals remained unconscious for a long amount of time are *just not right*".

Post traumatic amnesia refers to an assortment of memory deficits that results following concussion. Two types of post traumatic amnesia exist: retrograde and anterograde. Retrograde amnesia refers to an inability to remember events that preceded the injury. Anterograde amnesia is the inability to remember events that followed the injury. The duration of anterograde amnesia is believed to be correlated to the level of injury severity (Cantu, 2006). Neuropsychological testing assesses anterograde amnesia since it tests the subject's ability to form new memories. Anterograde amnesia is usually accompanied by difficulties with attention and is another reason that neuropsychological testing is able to pick up these dissociated cognitive deficits (Cantu, 2006).

Electroencephalography (EEG)

The first electroencephalographic recordings performed on humans are attributed to the German Physiologist Hans Berger in the early 20th century. His findings were described in a series of papers beginning in 1929 and it was Berger who thought up the

term electroencephalogram (Shaw, 2002). From 1938-1958 Bremer proposed the reasoning behind the genesis of EEG rhythmicities. This rested on four core ideas: *1*) the EEG rhythmicity is generated by the oscillatory activity of cortical neurons; *2*) the genesis of these oscillations depends on properties intrinsic to cortical neurons; *3*) EEG oscillations are generated by the synchronization of oscillatory activity in large assemblies of cortical neurons; and *4*) the mechanisms responsible for synchronization are due to intracortical excitatory connections. Further research validated these ideas and provided convincing evidence that the EEG reflects summated postsynaptic potentials. To explain the slow time course of EEG waves, Eccles, 1951, postulated that distal dendritic potentials, and their slow electrotonic propagation to soma, participate in the genesis of the EEG. This assumption was confirmed by intracellular recordings from cortical neurons, which demonstrated a close correspondence between the EEG and synaptic potentials (Destexhe & Sejnowski, 2003).

The EEG is a more direct measure of cerebral function than either intracranial pressure (ICP) or cerebral blood flow (CBF) (Ommaya and Gennarelli, 1976), and also, provides a measure of the subject's level of arousal. Electroencephalography (EEG) recordings measure the spontaneous rhythmic bioelectric potentials arising from the cortex (Shaw, 2002). They reflect the temporal and spatial summated activity of both excitatory (EPSP) and inhibitory (IPSP) postsynaptic potentials on the pyramidal cells of the upper layers of the cortex (Kandel et al., 2000). EEG records the current flow in extracellular space, and therefore detects the synchronized activity of a large number of cells. Pyramidal cells receive inputs in the more superficial layers (layers II and III) from cortico-cortical inputs and in the deeper layers (layers IV and V) from thalamo-cortical

inputs. This difference is reflected in the EEG. EPSPs in the superficial layers and IPSPs in the deeper layers will both result in an upward (negative) waveform in the EEG. Conversely, EPSPs received by pyramidal cells in the deeper layers and IPSPs in the more superficial layers will result in a downward (positive) deflection in the EEG (Kandel et al., 2000). Since the cortico-cortical neurons are greater in number and synapse in the more superficial layers, they contribute more to the surface EEG potential. EEG patterns are characterized by the frequency and amplitude of the electrical activity in the cortex. As the level of activation in the cortex increases, the EEG becomes increasingly desynchronized. EEG patterns are topographically localized in relation to nervous system organization and the interaction between specific and nonspecific sensory and cortical influences determines their frequency and cortical expression (Sterman, 1996). The frequency and amplitude of the oscillations vary widely across different behavioral states. Awake and attentive states are characterized by low-amplitude, high-frequency EEG activity. Large-amplitude alpha rhythms (8–12 Hz) appear mostly in the occipital cortex in aroused states with eyes closed and are reduced with eyes open (Destexhe & Sejnowski, 2003).

Electroencephalography and Concussion

A review of the literature on EEG recordings to document the negative effects of concussion on cognitive functioning have been somewhat inconsistent with their results. Literature on the subject has claimed numerous findings. EEG studies have linked MTBI to reduced mean alpha frequency, reduced mean alpha power, decreased beta power,

increased coherence frontally and fronto-temporally, decreased power differences between anterior and posterior regions, and decreased gamma frequency activity (Hoffman et al., 1995; Montgomery et al., 1991; Tebano et al., 1988; Thatcher et al., 1989; Thatcher et al., 1998; Thatcher et al., 2001; Thompson et al., 2005; Watson et al., 1995). In the theta frequency range, some reports have shown decreases (Montgomery et al., 1991), while Thatcher (1989) found very little statistically significant distinction between groups in the theta and delta bands. The most indicative discriminating variables of MTBI were found to be in the alpha and beta frequencies (Thatcher et al., 1989; Thatcher et al., 2001). The physiologic alterations following concussion are numerous and greatly affect the ionic channels of neuronal membranes (e.g. Na^{+}, K^{+}, Ca^{++}). These changes cause a reduction in EEG amplitude due to the reduced average current flux. One hypothesis is that following MTBI the attenuation of EEG frequencies occurs because there are fewer functional ionic channels per unit volume (Thatcher et al., 2001). It should be noted that all of the above studies only recorded EEG in eyes-closed seated conditions.

The cumulative effect of these detriments is (1) localized dysfunction specific to areas of maximal injury, and (2) overall diminished information processing capability and cognitive functioning (Thatcher et al., 1989 &1998). Recent research (Gosselin, 2006; Korn, 2005; Shaw, 2002; Thatcher et al., 1989, 1998, 2001(a), 2001(b); Thompson et al., 2005;) has shown the validity and sensitivity of EEG in detecting structural damage post concussion and in evaluating the severity and extent of the injury. This has come about in light of the fact that MRI and CT scans are unable to detect this cortical damage (Barth et al., 2001; Guskiewicz, 2001; Kushner, 2001; Shaw, 2002; Thatcher et al., 1989, 1997,

2001(a)). Gosselin et al. (2006) reported that concussions seem to produce deficits in the early and late stages of auditory information processing, which possibly reflect impaired brain functioning in symptomatic and asymptomatic concussed athletes. The fact that asymptomatic athletes have an electrophysiological profile similar to that of symptomatic athletes challenges the validity of return-to-play guidelines for which the absence of symptoms is a major issue.

To aid in localizing the damage that results from MTBI a low resolution imaging technique can be employed. Low Resolution Electromagnetic Tomography (LORETA) (Pascual-Marqui, 2002) computes, from the surface recorded EEG, the three-dimensional distribution of the electrically active neuronal generators in the brain as a current density value (amplitude/m^2) at each voxel (Pascual-Marqui, 2002). Computations for source localization of EEG frequencies are limited to cortical gray matter and the hippocampus according to a digitized Probability Atlas (Brain Imaging Centre, Montreal Neurologic Institute). LORETA has been shown to be accurate in its generation of instantaneous scalp potential distribution maps to within 7mm (Korn, 2005). By integrating LORETA into concussion assessment the clinician is given a tool that can detect the location of gray matter damage post MTBI even in the absence of cortical lesions, a process that until now has not been possible. Korn et al. (2005) demonstrated that the generators for abnormal EEG rhythms following concussion were closely related the anatomic location of the blood-brain barrier (BBB) lesion. They determined that focal cortical dysfunction, BBB disruption and hypoperfusion were possible mechanisms for the pathogenesis of post concussion syndrome (PCS). These findings were also closely related to the anatomical locations as measured by SPECT giving increased validation for the use of

EEG and LORETA in evaluating brain injury. The LORETA technique is also considered to be a well established and inexpensive neuroimaging method in the evaluation of coup contra-coup patterns (Thatcher, 2006).

Despite the many positive findings associated with EEG's ability to detect cortical dysfunction following concussion, there are contradictory reports. It has been reported that there are no proven pathognomic signatures useful for identifying head injury as the cause of signs and symptoms especially late after the injury (Nuwer et al., 2005). Although this is to be expected due to the fact that not all injuries are the same in symptomology or pathology, it does point to the difficulty of using EEG post injury as a stand alone test for concussion. However, Duff (2005) claims that quantitative EEG has been shown to be highly sensitive (96%) in identifying post-concussion syndrome. This controversy was exemplified in a study by Pointinger et al. (2002). They concluded that EEG can be used for detecting pathologic unspecific alterations with a high accuracy, but that it is not useful in specifying the findings for an exact diagnosis. As was the case with neuropsychological testing, EEG testing has been shown to be useful in testing for mild brain injury, but it has not yet proven to be sensitive in all cases and an EEG *best test* has not yet been determined.

Postural Control Assessment

Over the past decade concussion research has begun to assess physical deficits following concussion. The most studied and clinically used physical test is the assessment of balance following injury. Balance is one of the most important features of

athletic performance, and as such the level of postural degradation resulting from MTBI should be measured when assessing the effects of any such injury. Balance can be defined as the process of maintaining the center of gravity (COG) within the body's base of support (Guskiewicz, 2001). The system responsible for the maintenance of balance is a complex one and involves the integration of many cortical and peripheral feedback mechanisms. The maintenance of balance is controlled through a hierarchy involving three separable levels (Vander et al., 1990). The highest level involves areas of the brain responsible for attention, concentration and memory, as well as the association cortex responsible for receiving and integrating inputs from other brain structures. The middle level involves the sensorimotor cortex, cerebellum, parts of the basal ganglia and some brainstem nuclei. Postural reflexes (afferent pathways from the eyes, vestibular apparatus, and proprioceptors) occur at this level, as do the efferent pathways (alpha motor neurons) controlling skeletal muscle, and the neurons of the integrating centers in the brainstem and spinal cord. The lowest level consists of the brainstem and spinal cord from which motor neurons exit (Guyton, 1986).

Areas of the brain that are known to be associated with the maintenance of equilibrium (visual, somatosensory, and vestibular systems) are also negatively affected by concussion (Guskiewicz et al., 1997; Guskiewicz, 2001; Guskiewicz et al., 2001; Haaland et al., 1994; Ingersoll & Armstrong, 1992; Oliaro et al., 2001). In bipedal stance, Geurts et al. (1999) found increases in the velocity of center of pressure and overall weight shifting speed indicating instability in both static and dynamic postures. In a study conducted on college athletes it was concluded by Slobounov et al. (2002) that there are transient functional changes in the brain that are associated with motor control

and coordination in MTBI subjects. Slobounov et al. also found a decrease in EEG power in concussed individuals during a task requiring the recognition of unstable postures and thus inferred that the ability of people who have sustained a MTBI to recognize the limits of their functional boundaries may be impaired. These findings may result from damage to the brain that not only reduces local excitation, but also reduces synchronization of the active generators of the higher frequency bands as measured by EEG (Thatcher et al., 1998).

Ratio scores were calculated in the Guskiewicz et al. (2001) experiment to reveal relative differences between the equilibrium scores of each of the sensory modalities involved in maintaining balance. Lower scores indicated an inability to compensate for disruptions in selected sensory modalities. The recovery of stability in the injured subjects coincided with reported ratio scores of the visual and vestibular systems suggesting that postural stability deficits in injured subjects could be linked to sensory integration problems that result from concussion (Guskiewicz et al., 2001). It is also suggested by Guskiewicz et al. (2001) that postural instability following a concussive incident could result from: (1) slowed sub-cortical activity and spatiotemporal disruption of postural responses (2) minor axonal disruption or (3) the abnormal metabolic cascade that may affect cortical neurons responsible for sending information to centers responsible for the maintenance of posture. Recovery to baseline levels of postural stability seems to run in the course of 1 – 3 days (Guskiewicz et al., 2001; Thompson et al., 2005).

Other studies confirm the findings and recovery curves suggested by Guskiewicz et al. (2001). In a previous study, (Guskiewicz et al., 1997) and follow-up study

(Guskiewicz, 2001), it was shown that injured subjects were significantly less stable than age matched normals on day 1 of testing and significantly less stable than their own pre-injury scores on day 3. Evidence of the recovery of postural stability in individuals suffering a mild injury was also shown in a study conducted by Ingersoll & Armstrong (1992) in which a difference between subject groups (all subjects injuries occurred greater than one year prior to testing) was not present for MTBI compared to normals but was present in the severely injured group.

Testing for balance impairments provides information concerning the functional abilities of the patient. The Romberg test has proven effective as a physical test of vestibular impairments (Ingersoll & Armstrong, 1992). Modifications to the Romberg test allow for the additional assessment of impairments in patients visual and proprioceptive systems. Such adaptations have been tested and validated by Guskiewicz (Guskiewicz, 2001; Guskiewicz et al., 2001), Ingersoll & Armstrong (1992) and Oliaro et al. (2001). The calculation of the functional area within which a person will move as a function of their base of support has been termed the index of stability (Slobounov et al., 1998). Testing the ability or willingness of subjects to move toward these limits of their base of support has been shown to be effective in distinguishing between concussed and non-injured individuals.

Controversy has erupted in the field, however, due to inconsistencies in the rate of recovery of posture following concussion. As more research is conducted, the previous findings of balance normalizing between 1-3 days are being challenged. The argument is that research claiming the short term, transient nature of measurable balance impairments is not sensitive enough (Slobounov et al., 2005(a), 2005(b); Thompson et al., 2005).

Comparing the timeframes for recovery of neurologic pathology to postural stability it seems as though the recovery times, as measured by the above studies, do not coincide. This may suggest that the normal pathways associated with control of balance and stability have not actually recovered. Two plausible explanations may account for this mismatch in recovery times. First, neural plasticity (Boroojerdi et al., 2001; Staudt et al., 2002) may allow for alternate pathways to perform the duties responsible for basic posture. Second, the currently used balance assessments do not adequately tax the systems involved in maintaining balance under the high demands of athletic competition. Alternatively, it may be a combination of the two above-mentioned shortcomings that may explain the mismatch between functional and physiological recovery.

A second shortcoming of balance testing was revealed by Valovich McLeod et al. (2004) who found that learning effects occur on normal subjects after multiple administrations of a well accepted postural assessment task for concussion, namely the Balance Error Scoring System (BESS). This learning effect was significant up to 60 days showing that the learning effects would still be present even in some of the longest periods that athletes are removed from play following a mild brain injury.

New research in this area of testing reveals that increasing the difficulty of the parameters of the postural assessments allows for the detection of residual functional deficits not detectable by traditional balance tests. In contrast to his previous work Guskiewicz, in collaboration with others, determined that "The effects of cerebral concussion on postural control appear to persist for longer than 3 to 4 days even among athletes with no signs of unsteadiness" (Cavanaugh & Guskiewicz, 2006). Research conducted by Slobounov, Sebastianelli and Newell (2006) revealed that long-lasting

destabilizing effects of visual field motion were revealed in spite of the fact that subjects were asymptomatic when standard balance tests were introduced. The findings demonstrate that advanced virtual reality (VR) technology may detect residual symptoms of concussion at least 30 days post-injury. In a follow up study, Slobounov et al. (2006) demonstrated that a destabilizing effect of visual field motion could be observed via a significant increase of the center of pressure data and reduced coherence values between an injured subject and a VR display. They concluded that this test allowed for the detection of residual sensory integration dysfunction in concussed individuals at least 30 days post-injury and may indicate a lower threshold for brain re-injury.

Similarly, Parker et al. (2006) found that gait stability was compromised in a concussed group for up to 4 weeks following injury. In this study concussed subjects were found to walk significantly slower during dual tasks on all testing days when compared with the uninjured controls. The injured subjects were also found to have greater sway and sway velocity than controls when attention was divided for up to 28 days post injury (Parker et al., 2006). The findings of this study suggest that concussion may have long-term observable and measurable effects on the control of gait stability.

The contradictions in recovery times based on differing assessment methods for the same abnormality (i.e. balance instability) following injury shows the need for further research in the area and the development of testing paradigms that are sensitive to lingering deficits. It is also indicative of the fact that not all concussions will result in balance impairments and that adjunctive testing should be performed to test other areas of dysfunction.

Plasticity and Recovery from Concussion

Over the 30 years the idea that the human cortex is hard-wired has come into question. The notion of plasticity and its role in recovery of function following brain injury has been of growing interest and is now considered a viable process through which recovery is possible. Much of the spontaneous recovery following injury probably occurs from resolution of edema and/or recovery of tissue function in tissues that were ischemic but not destroyed (Hallett, 2001). In the days to months that follow this initial change, the mechanism responsible for further recovery is likely plasticity. The property of plasticity results from the broad connectional organization of the cortex and the capacity for activity-driven synaptic strength changes (Sanes & Donoghue, 2000). Plasticity can occur via four processes. First, unmasking can occur whereby neural pathways that had been kept dormant by inhibition are made functional by the removal of the inhibitory signal (Jacobs & Donoghue, 1991). Second, a strengthening or weakening of existing synapses can occur through the process of long-term potentiation (LTP) or long-term depression (LTD) (Hess et al., 1996). Third, there can be a change in neuronal membrane excitability (Halter et al., 1995). Fourth, anatomical changes can occur such as the sprouting of new axon terminals or the formation of new synapses (Toni et al., 1999).

Studies of neural plasticity have demonstrated that functional changes coincide with cortical anatomical changes. Kolb (1999) looked at the changes in the motor cortex of rats with unilateral injuries. They demonstrated that following injury these rats showed behavioral improvement that stabilized about three weeks after injury. Upon examination

of the branching pattern of interneurons in layers II and III of the adjacent sensorimotor cortex on the lesion side and the same tissue on the intact side, analysis showed an increase in branching proximal to the injury but no change in the intact hemisphere thereby demonstrating the relationship between functional recovery and synaptic change. Plasticity has also been shown in learning studies. Pascual-Leone et al. (1995) looked at the cortical representation of the hand over a 5-day period as subjects learned a skilled task with their hand. As skill increased there was a concomitant increase in the size of the motor representation of the hand in the cortex.

These cortical changes are not limitless, however. Corkin (1989) reported that war veterans in the years following brain injury had a decline in cognitive abilities that had at first been recovered following the injury. He suggested that either the neural modifications that had initially allowed for the recovery of function were themselves susceptible to aging, or the processes were similar to the ones normally used for aging and that this adaptation was not able to occur in the normal aging process since the brain is only able to perform this modification once. The study by Kolb (1999) ten years later also supported this limit to plasticity. Following brain injury in older rats he did not observe the favorable behavioral outcome that he had first witnessed in younger rats with the same injury. Concomitant to this lack of behavioral recovery, he noted a failure for the older rats to show synaptic compensation. He supported the theory that functional changes coincide with synaptic changes by demonstrating that both occur in younger rats and neither occurred in older rats. He concluded that the results suggest that "(1) the brain may use similar mechanisms for ageing and recovery from brain injury; and (2) there is a limit to the plasticity of the cortex". If there is a limit to dendritic growth and

cortical plasticity following injury, returning athletes to play following a second injury in the same region as a first injury should be questioned since recovery of that area may not occur.

Pathophysiology

Introduction

Wilberger et al. (2006) stated that "there is a lack of complete understanding of the pathophysiology of cerebral concussion". Despite the relatively simple mechanism of injury involved with concussion—blunt trauma, acceleration/deceleration and/or axial rotation of the head—the potpourri of symptoms (Barr, 2001; Guskiewicz et al., 2001; Hugenholtz et al., 1988; Macciocchi et al., 1996; Oliaro et al., 2001; Powell, 2001; Thatcher et al., 1989; Wojtys et al., 1999;) that often result in the hours to weeks post injury hint at the true complexity of the injury. Any attempt to classify concussion as a traumatic event with predictable findings upon examination is erroneous. A review of current knowledge regarding concussions will hint at the heterogeneous nature of the injury and will aid in drawing conclusions regarding the common features of MTBI and help to amalgamate theories. This discussion will also provide evidence that is at odds with the all too common practice of clearing athletes to return to competition the day following, or even in the same game as a concussive incident.

Pathophysiology

The cascade of deficits associated with mild traumatic brain injury can occur in the absence of any measurable anatomic pathology, suggesting that these impairments are based on neuronal and chemical disruptions rather than on cell death alone. The pathophysiological standpoint of neuronal injury involves numerous neurometabolic changes that occur within the first five minutes following the initial trauma (primary neuronal injury) as well as the subsequent pathological and physiological changes that evolve over the next few minutes to months (secondary neuronal damage) (Wilberger, 1997). The cerebral physiological workings that are most affected include cerebral blood flow (CBF), glycolysis, and shifts in the ionic gradients involving potassium (K^+), calcium (Ca^{++}), sodium (Na^+), and glutamate. In addition, the structure of the blood-brain barrier is compromised.

Cerebral Blood Flow (CBF)

Numerous studies have measured cerebral blood flow (CBF) in the moments following MTBI. Included in these are studies by DeWitt et al. (1986), Meyer et al. (1970) and Nilsson & Nordstrom (1977), who all demonstrated immediate increases in CBF following brain injury. These transient increases (lasting approximately 1 minute) in CBF may serve to meet the increased energy demands needed to restore ionic membrane balances that have been altered by the biomechanical injury (Golding, 2002). This immediate and short-lived increase in CBF is followed by a subsequent decrease that can persist for weeks dependent upon the severity of the injury (Shaw, 2002). This

decrease in CBF may be as much as 50% and can cause an energy crisis during the period following injury when in fact an increase in blood flow is required to ensure a positive recovery (Giza & Hovda, 2001). Under normal circumstances, CBF is regulated by the metabolic demands of the tissues within the cerebrum. Following MTBI there is an uncoupling of this system in which glucose utilization increases (thus increasing the demand for the nutrients delivered in the blood stream) and CBF (which delivers the necessary nutrients) decreases. The reduction in CBF is associated with negative neurologic outcomes and has been implicated in rendering the brain vulnerable to second impact syndrome (Golding, 2002).

The most plausible cause of the decrease in CBF following injury is likely a disruption in the proper functioning of the endothelial cells. One of the best-known characteristics of the endothelium is its ability to release factors that can elicit either arterial dilation or constriction in the brain (Golding, 2002). The factors that elicit dilation are called endothelium-derived relaxing factors (EDRFs), while the factors that counteract these dilating factors are called endothelium-derived contracting factors (EDCFs). Following concussion there is an imbalance between the EDCFs and the EDRFs. There is a proportional increase in the amount of EDCFs and a dramatic decrease in the amount of EDRFs, the end result of which is that the effects of the EDCFs outweigh the effects of the EDRFs. The overall effect is a decrease in the regional cerebral blood flow (rCBF) that can result in ischemia (Martin et al., 1992).

Glycolysis

In an attempt to restore homeostasis, the dramatic increases in extracellular K+ and intracellular Ca^{2+} triggers the activation of energy-requiring membrane pumps (Shaw, 2002). This energy must come in the form of adenosine triphosphate (ATP). With the exhaustion of stored ATP, glycolysis provides the most efficient method for the production of further needed ATP. The byproduct of glycolysis is lactate. Therefore, coupled with the hyperglycolysis that occurs there is a dramatic increase in lactic acid. Intracellular Ca^{2+} may also be removed from mitochondria resulting in decreased oxidative metabolism. This places further demands on glycolysis as the means for ATP production and decreases the ability to remove accumulating lactic acid from the system. This increase in lactic acid production, concurrent with the decrease in lactic acid metabolism, results in an accumulation of lactic acid. Further damage results from this accumulation since elevated lactate levels can result in neuronal dysfunction by inducing acidosis, membrane damage, altered blood-brain permeability, and cerebral edema. The hyperglycolysis that accompanies brain injury peaks at about 6 minutes post injury and gradually decreases (Giza & Hovda, 2001). This decrease is not a simple and immediate return to baseline. Following the initial period of hyperglycolysis is a prolonged period of hypoglycolysis. This decrease in cerebral glucose metabolism is global and may last 2-4 weeks and is not correlated with overt clinical symptoms (Giza & Hovda, 2001). The mismatch between glucose delivery and brain glycolysis is exacerbated by the decrease in cerebral blood flow (CBF) that accompanies MTBI.

Potassium (K^+) Efflux

The initial response to MTBI is an immediate efflux of potassium (K^+) from cortical neurons due to the disruption of neuronal membranes, opening of K^+ channels and axonal stretching (Giza & Hovda, 2001). This increase in extracellular K^+ levels is exacerbated by the nonspecific depolarization that occurs. This in turn leads to the indiscriminate release of the excitatory amino acid (EAA) glutamate and the opening of the receptor channels, kainate, N-methyl-D-aspartate (NMDA), and D-amino-3-hydroxy-5-methyl-4-isoxazole-proprionic acid (AMPA). The activation of glutamate receptors causes a further efflux of K^+ due to the influx of Ca^{++} (Golding, 2002).

Insults to the brain that are large enough to cause concussion overcome the normal extracellular K^+ uptake by glial cells. The resulting increase in extracellular K^+, increases neuronal depolarization and leads to a further release of EAAs, opening of EAA receptor channels and further K^+ efflux. This cycle continues with the rapid efflux of K^+ ceasing within about five minutes post injury. This massive excitation is followed by a *spreading depression* (Giza & Hovda, 2001). In an attempt to restore the ionic gradient to normal levels the sodium-potassium pump works overtime, thus increasing energy consumption and putting increased demands on energy production. In the presence of decreased CBF, the result of this hypermetabolism is the creation of an energy crisis due to a mismatch between energy supply and demand.

Calcium (Ca^{2+}) Influx

In conjunction with the efflux of K^+ from cortical neurons there is an influx of calcium (Ca^{2+}). Currently there are three proposed theories as to the cause of this Ca^{++} influx. First, it may be a result of the activated N-methyl-D-aspartate (NMDA) receptors. A pore through which extracellular Ca^{2+} can enter the cell is formed with the activation of NMDA receptors (Giza & Hovda, 2001). Second, Gennarelli et al. (1996) proposed a mechanism in which the "development of transient defects in the cell membrane are due to its mechanical deformation" (Gennarelli et al., 1996). They termed this "mechanoporation". Mechanically induced pores (which are either transient or stable) would allow Ca^{++} to flow into the cell due to the large extracellular gradient. Combined with Ca^{++} release triggered from extracellular stores, cytosolic free Ca^{++} would be cytotoxic if Ca^{++} levels remained elevated. Wolf et al. (2001) posit a third theory. They suggested that following a mechanically induced stretch to the axonal membrane there was an abnormal influx of Na^+. This in turn leads to a reversal of the Na^+ - Ca^{++} exchange and activation of voltage gated Ca^{++} channels, which causes a net influx of Ca^{++} (Wolf et al., 2001).

The negative effects of this Ca^{++} influx are numerous. "Intracellular Ca^{2+} may trigger cell death by a variety of mechanisms, including over activation of phospholipases, calpains, protein kinases, nitric oxide synthase, and endonucleases. These alterations may then lead to free radical overproduction, cytoskeletal reorganization, and activation of apoptotic genetic signals." (Giza & Hovda, 2001). As was the case with the K^+ efflux, the energy depletion that occurs due to a mismatch

between glycolytic demands and glucose delivery causes a loss of the ionic gradients needed to maintain membrane potential. A depolarization of neurons and glia occurs and voltage dependent Ca^{++} channels become activated, thus releasing excitatory amino acids (EAAs) such as glutamate into the extracellular space (Golding, 2002). The cycle continues as the activation of glutamate channels causes a further neuronal influx of Ca^{++}. Unlike the fleeting efflux of K^{+}, the increase in Ca^{2+} has been measured for up to 4 days post injury. This persistent increase in Ca^{++} levels continues the impairment of oxidative metabolism in cerebral structures by impairing the function of mitochondria. The impairment of mitochondria can lead to reduced ATP production, which places further demands on glycolysis. Cytochrome oxidase histochemistry (a measure of oxidative metabolism) shows reductions for up to 10 days post injury (Giza & Hovda, 2001). These persistent increases in axonal Ca^{2+} are also responsible for microtubule breakdown. The intra-axonal cytoskeletal abnormalities lead to organelle accumulation at the injury site. Focal axonal swellings develop constrictions that lead to secondary axonal disconnection that has been reported to persist over days and even weeks in MTBI patients (Giza & Hovda, 2001).

Blood-Brain Barrier (BBB)

The blood-brain barrier (BBB) is comprised of three cellular structures: the endothelial cell, the pericyte, and the astrocyte. The primary purpose of this structure is to filter substances within the blood as they try and pass to the brain parenchyma (Golding, 2002). The BBB allows for diffusion of essential nutrients and small, essential

molecules such as oxygen and carbon dioxide, while excluding large molecules from entering the interstitial space of the central nervous system (CNS). A hallmark of concussion pathophysiology is a prolonged opening of the BBB and extravasation of many blood components the BBB normally filters out. Included in these substances are red blood cells (RBCs), plasma proteins and water (Golding, 2002). Opening of the BBB is brought about individually or by the combined effects of three main factors: shear stresses, the release of foreign substances, or an elevation in arterial pressure that forces apart tight junctions at the arterioles and large arteries. Not only does this opening of the BBB result in the influx of many unwanted substances into the brain parenchyma, but it also impairs the flow of nutrients, which are vital to proper CNS functioning. An example of this is the decrease in glucose delivery across the endothelium following concussion despite the need for increased glucose delivery due to increases in brain glycolysis.

Diffuse Axonal Injury (DAI)

The first allusion to DAI dates to the 19th century. It was a mystery to neurologists how such a severe paralysis of neuronal function could occur in the absence of obvious anatomical damage (Shaw, 2002). In 1835, J. Gama proposed that "fibers as delicate as those of which the organ of mind is composed are liable to break as a result of violence to the head" (Shaw, 2002). DAI occurs from mechanically induced stretching, shearing or tearing of nerve fibers. Theses forces are produced by acceleration or deceleration with angular rotation and may result from trauma directly to the head or

trauma to the torso or axial skeleton with the force of the incident being transmitted indirectly to the brain matter (Amann, 2000). This is the primary pathologic feature of brain injury in all severity levels of concussion (Kushner, 2001). Holburn (1943) and Strich (1961) described the primary microscopic feature observed in neural tissue as diffuse degeneration of white matter without obvious damage to the cortex (Gaetz, 2003). It was concluded that nerve fibers were torn or stretched at the time of injury based on cadaver studies in which large numbers of nerve fibers with retraction balls (the appearance of severed axons with axoplasm extruded from the proximal and distal segments) were observed (Gaetz, 2003). Recent findings by Smith et al. (1999) have hinted at the ability of neuronal axons to withstand large stretch forces and a remarkable threshold for primary axotomy. They showed that no primary axotomy occurred in human neuronal cultures at tensile strains causing deformation of up to 65% of the neurons original length. In addition, Smith et al. (1999) showed that post injury axons showed a gradual recovery to their original shape, although there were multiple swellings along the length of many axons. A major consequence of this pathology is an increase in neuronal permeability, especially to Ca^{2+}, and possible loss of consciousness and post-traumatic amnesia (retrograde and/or anterograde) (Giza & Hovda, 2001). The numerous negative effects of increased neuronal permeability have been noted above.

It is well known that the brainstem reticular cells play a vital role in consciousness, and it has been put forth that it is damage to this structure that leads to decreased arousal or lack of consciousness following MTBI (Shaw, 2002). It may be the case, however, that it is not damage to the reticular cells themselves that causes this depression of arousal. Rather, it may be that mild DAI cause's damage to cortical

structures, which under normal functioning provide stimulation to the brainstem. In the face of damage to these cortical structures that provide excitatory inputs to the brainstem, reticular cells are suppressed due to lack of input (Gaetz, 2003).

One major difficulty facing concussion assessment today is that shear strain injury (DAI) is frequently not detectable in MTBI using gross neuroimaging techniques (Barth et al., 2001). As noted, DAI is the most prominent cause of concussive injury. Therefore, it is necessary to study these effects using a diagnostic tool that is able to detect the effects of DAI, namely EEG.

Second Impact Syndrome

The seriousness of a first injury does not determine the full extent to which a MTBI will affect an athlete. Following a first insult, the likelihood of a person receiving a second concussion is greatly increased. A first injury can lead to a pathology referred to in the literature as second-impact syndrome, the effects of which can be fatal (Amann, 2000; Harmon, 1999; Marchie & Cusimano, 2003). This syndrome occurs in players who return to competition before the symptoms of a first concussion have completely resolved and receive a second MTBI during this symptomatic period. Since each physiologic parameter that contributes to the second impact syndrome has its own healing time period, and each head injury is different in its pathology, a vulnerability period is difficult to ascertain. However, based on derangements in cerebral glucose metabolism and persisting axonal damage, Giza and Hovda (2001) determined that persons suffering

from MTBI may remain vulnerable to a second impact injury for periods of up to a few months depending on the severity of the first insult.

The syndromes onset results from a loss of autoregulation of the cerebral vasculature, leading to vascular engorgement and herniation of the brain (Harmon, 1999; Marchie & Cusimano, 2003). In the initial stages following injury (within 30 minutes) cerebral hypermetabolism occurs. Irreversible neuronal damage (i.e. cell death) is a distinct possibility if either an increase in energy is required or a decrease in CBF occurs due to a second concussive incident (Giza & Hovda, 2001). At further stages in the recovery period of MTBI, second impact syndrome is still a major risk. One, or a combination of factors, may contribute to the brains inability to respond appropriately to a second injury. First, CBF may not respond appropriately to a stimulus-induced increase in cerebral glucose metabolism. Second, the continued intracellular Ca^{++} increase continues to impair mitochondrial metabolism at a time when the cell most needs continued ATP production to restore normal membrane potential. Third, impaired neurotransmission occurs as a result of altered NMDA receptor composition. A second injury can lead to further decrements in excitatory neurotransmission and greater cognitive dysfunction. As well, a change in inhibitory neurotransmission leaves neurons more susceptible to depolarization and EAA release causing further increases in energy demand (Giza & Hovda, 2001). In athletics, cognitive awareness is particularly important due to the speed at which many decisions must be made. Any impairment of this ability can put an athlete at risk for further injury. The reduction in inhibitory transmissions can result in excess “noise” in the in the cortex when attention and focus are required during sport (Hebb, 1976).

Each of the above discussed parameters leading to second impact syndrome has its own time frame and is dependent upon injury severity. This makes it difficult to determine a time duration within which a second impact injury is most likely. Reports have suggested that since 1992 there are an average of 1-2 reported cases of second impact syndrome per year in football alone (Harmon, 1999).

Summary

What is evident from the above review is that within the literature there is not a clear consensus on what, if any, common features are present in mild traumatic brain injury. This has resulted in sub-standard evaluation and return-to-play measures and ultimately puts the health of athletes in jeopardy. The fact that so many contradictions exist within and between the three most commonly accepted mild traumatic brain injury assessment methods indicates that past research has not properly addressed the issue. Since no one testing method will detect injury in all subjects, and since all injuries are unique in symptomology and pathology, there is an obvious need for testing protocols that addresses the many variations within concussive injuries. This provides the necessary justification for the line of research undertaken in this study that compares and combines multiple concussion assessment methods.

Under the high task demands of a game situation, athletes are placed under mental and physical stressors that practitioners are often unable to simulate under concussion testing conditions. Because of this, athletes who test negatively using a uni-modal assessment protocol may be allowed to return to play prematurely. It is therefore

suggested that with the use of a multi-modal assessment model that incorporates tests that support each other, it is possible to detect lingering neurophysiological damage that could put injured athletes at risk during the high physical and cognitive demands of competition.

Chapter 3

Methods

Subjects

Sixty-one participants were recruited for this experiment. Subjects were university athletes from either the Pennsylvania State University or the University of Toronto. Both male and female subjects were involved in the study. Subjects were assigned to either a healthy group (n = 31) or an injured group (n = 30) based on their concussion history at the time of testing. The normal subjects' ages ranged between 17.78 years and 27.83 years with a mean of 19.54 years. The injured subjects' ages ranged between 17.88 years and 27.43 years with a mean of 21.02 years.

Injured subjects were classified as those that had incurred a MTBI within the previous three months, as assessed by a team physician or athletic trainer. The assessment criteria used by the trainers and physicians was: loss of consciousness, loss of memory (retro/anterograde amnesia), SCAT Symptom scale (if all symptoms reported disappear (scale 0) in 10-15 minutes after the trauma then possible return to play if no other positive tests), history of head trauma, abnormal cranial nerves I-XII, abnormal dermatome/myotome tests, abnormal orientation/coordination, behavioral/emotional change. The definition of concussion given to the athlete by the research group at the

beginning of the NP, EEG and VR testing session was a change in cortical functioning caused by acceleration/deceleration or rotational forces applied to the brain. The average number of days between injury date and testing for the injured subjects was 13.93 days with a range of between 2 to 73 days. The normal group consisted of age matched individuals that had not incurred a MTBI within the previous 6 months. At the time of testing normals did not have any neurological symptoms of concussion based on conventional neurological testing for mild brain injury. These tests were the same tests used by the athletic trainers and physicians for assessment of cranial nerves I-XII and dermatome/myotome tests. Prior to any testing procedures all subjects were required to read and sign an informed consent form approved by the Institutional Review Board of the Pennsylvania State University. The information for normal subjects is summarized in Table 3.1 and for injured subjects in Table 3.2.

Table **3.1**

Table **3.1**: Control Subjects Demographics: NP represents 'Normal Penn State" subjects, NT represents 'Normal U of T subjects'

Subject #	Sex	Previous # of Mild Traumatic Brain Injuries	Age (years)
NP1	f	0	21.73
NP2	f	0	18.98
NP3	f	0	19.07
NP4	f	0	18.73
NP5	f	0	19.33
NP6	f	0	18.34
NP7	f	0	19.57
NP8	f	0	18.70
NP9	f	0	21.10
NP10	f	0	18.85
NP11	f	1	18.48
NP12	f	3	20.15
NP13	m	0	19.46
NP14	f	0	18.91
NP15	f	1	19.01
NP16	f	1	18.01
NT17	m	0	27.83
NT18	f	1	19.60
NT19	f	0	17.78
NT20	f	0	18.92
NT21	m	0	18.27
NT22	f	0	17.99
NT23	m	0	18.86
NT24	m	0	18.51
NT25	f	0	18.20
NT26	f	1	21.59
NT27	f	0	23.75
NT28	m	0	22.48
NT29	m	0	19.32
NT30	m	2	18.81
NT31	m	0	18.44

Table **3.2**

Table **3.2**: Injured Subjects Demographics: IP represents 'Injured Penn State" subjects, IT represents 'Injured U of T subjects'

Subject #	Sex	Previous # of Mild Traumatic Brain Injuries	Age (years)	Injury to recording (days)
IP1	m	0	20.01	13.00
IP2	m	1	20.06	33.00
IP3	m	0	19.93	16.00
IP4	m	0	17.88	19.00
IP5	f	2	38.54	6.00
IP6	f	0	20.36	5.00
IP7	m	2	18.27	22.00
IP8	m	2	18.23	8.00
IP9	f	1	18.64	27
IP10	m	0	21.72	73.00
IP11	m	0	20.20	23.00
IP12	m	0	19.48	1.00
IP13	m	0	19.61	2.00
IP14	m	1	20.83	2.00
IP15	f	0	19.85	14.00
IP16	m	0	18.80	5.00
IP17	m	0	20.72	4
IT18	f	2	23.18	5.00
IT19	f	0	24.30	3.00
IT20	f	1	19.81	4.00
IT21	f	1	19.85	17.00
IT22	m	2	20.79	19.00
IT23	m	3	27.43	5.00
IT24	f	0	21.68	2.00
IT25	m	1	18.63	9.00
IT26	m	1	18.69	30.00
IT27	m	2	18.36	5.00
IT28	f	1	20.97	23.00
IT29	f	0	19.47	9.00
IT30	f	0	21.74	5.00

Experimental Procedures

General

Subjects entered the testing room and were seated comfortably in a chair to read and sign the informed consent form. Each subject was verbally instructed as to the testing order and procedures and was encouraged to ask any questions they had regarding the testing or the study in general. Subjects were asked to provide relevant demographic medical information (date of birth, sex, relevant medical history, concussion history). At this juncture tests were administered in the following order; Neuropsychological (NP) testing, EEG testing, virtual reality (VR) with postural component testing. The tests within each subsection (NP, EEG and VR) were randomized between subjects.

Neuropsychological Testing

The neuropsychological tests were administered as standard paper and pencil tests for which the subject was seated at a table and administered the test battery by the tester. The subject was instructed to complete the tests as quickly and accurately as possible. The testing battery consisted of three tests: The Trails B test to assess processing speed and scanning ability, Symbol Digit Substitution test assesses processing speed and working memory (Randolph et al., 2005) and the Symptom Rating Scale to assess symptom severity specific to concussion. The neuropsychological testing component lasted approximately 10 min.

EEG Testing

Subjects were seated in a comfortable chair for EEG preparation. The subject's scalp and earlobes were cleaned thoroughly using a cotton swab saturated with rubbing alcohol. A 19-lead Quickcap (Electro-Cap International, Inc) was then placed on the subject's head. Reference electrodes were gelled and attached to the subject's earlobes. Using a blunt-ended syringe, Electro-gel (Electro-Cap International, Inc) was put in the 19-electrodes and one ground electrode of the cap and the scalp sites were lightly abraded to improve the conduction of the electrical signal from the scalp to the electrodes. Impedence was measured at all sites and was kept below 5Kohms.

EEG recordings were taken under three experimental conditions: eyes closed (EC) seated, EC bipedal with feet together stance on a firm surface, EC bipedal stance with feet together on a foam surface. The foam surface was used in order to increase the difficulty of the standing task. Seated trials consisted of 3 minutes of continuous data collection. Subjects were instructed to sit as still as possible to avoid muscle artifact in the EEG record. Standing trials were performed with shoes off using a bipedal stance with feet together and hands resting comfortably on their hips. Trials on the firm surface were conducted on a hard, even level floor. Subjects were instructed to remain as still as possible. Trials on the foam surface were conducted using the same posture as the trials on the firm surface. Subjects were required to stand on a medium-density foam surface (thickness 45cm^2 x 13 cm, density 60 kg/m^3) and were again instructed to remain as still as possible. Standing trials were 2 min in duration for each condition. All seated and standing trials were randomized between subjects.

Following the EEG recording trials the subject was again seated in a chair and the electro-cap was removed. The subjects scalp was again cleaned using a cotton swab saturated with rubbing alcohol to remove the conductive paste from the ears and scalp. The EEG recording session lasted approximately 45 min including preparation, recording, instructions and clean-up.

Virtual Reality with Postural Testing

At the onset of the virtual reality and postural testing the subject was asked to put on the Flock of Birds (Ascension Technology Corporation, Burlington, VT) vest such that the middle sensors on the back of the vest were along the spine of the subject. The vest buckles were fastened comfortably, but tight enough to not allow movement of the sensors in relation to the subject's body. Three-dimensional viewing glasses with a Flock of Birds sensor attached were also worn by the subject. The subject was then instructed to stand on the force plate, without shoes, with their feet shoulder width apart. A tracing of their feet was made for placement and reproducibility purposes. Once the subject was comfortably standing in the testing position the lights of the testing room were turned off and the door to the testing room was closed. The subject was then shown the room paradigm on the 3D virtual reality screen (Figure 3-1). Four 60 s trials were performed. There were two sets of instructions given to the subjects. The instruction to the subject for the first trial was to "stand as still as possible". The first trial in the group is a controlled trial where there is no movement in the room paradigm. The remaining three trials were randomized and consisted of the following movements of the virtual reality

room: 1) whole room anterior-posterior oscillations within 18 cm displacement at 0.2 Hz, 2) whole room anterior-posterior oscillations within 18 cm displacement at 0.3 Hz, 3) whole room lateral "side-to-side roll" around the Z-axis with the center of rotation at the center of the wall screen, displacement was 10 degrees at an oscillating frequency of 0.2 Hz. The instruction to the subject in the trials with the moving display was to "move in phase with the room. You are to sway, moving only at the ankles, in the same direction as the moving portion of the room and the same distance as the moving portion of the room". The moving walls trials were randomized.

The data were saved following each trial. Once the data were saved the subject was told that the next trial would begin momentarily. The room movement was then started by the tester.

Following the completion of the 12 trials the lights were turned on in the room and the subject was asked to carefully step off the platform. The Flock of Birds vest was removed as were the 3D glasses. This ended the testing session.

Figure **3-1**

Figure **3-1**: Virtual Reality condition with subject wearing Flock of Birds vest.

Data Acquisition

EEG Data Acquisition

The continuous EEG was recorded using Ag/AgCl electrodes mounted in a 19-channel spandex Electro-cap (Electro-cap International Inc., Eaton, OH). The electrical activity from the scalp was recorded at 19-sites: FP1, FP2, FZ, F3, F4, F7, F8, CZ, C3, C4, T3, T4, T7, T8, PZ, P3, P4, O1, O2 according to the International 10-20 system (Jasper, 1958). The ground electrode was located 10% anterior to FZ, linked earlobes served as references and electrode impedances were below 5 Kohms. EEG signals were recorded using a programmable DC coupled broadband SynAmps amplifier (NeuroScan, Inc., El Paso, TX.) at the Pennsylvania State University. At the University of Toronto the EEG was recorded using a Mitsar amplifier and the WinEEG software program (Mitsar Inc., St. Petersburg, Russia). In both cases the EEG signals were bandpass filtered in the DC to 70 Hz frequency range. A notch filter was set at 60 Hz to remove artifact resulting from electrical signals at this range, which are common in North American circuitry. The EEG data were sampled at 250 Hz, using a separate 16-bit analog-to-digital converter for each channel. For the SynAmps amplifier, data were collected using NeuroScan's Scan 4.2 software package and written to and stored on a Dell Precision 530 computer running an Intel XEON processor. For data collected using the Mitsar system, data were collected using the WinEEG software program and stored to a Hewlett Packard hp Pavilion ze5400 notebook running an Intel Pentium III processor.

Virtual Reality with Postural Testing Data Acquisition

A 3D stereo visual field display was generated in the VR laboratory in front of where the subject stands for the tests. A 6x8 foot one wall screen with back projection material, an Electrohome Marquis 8500 projector with full color stereo workstation field (2034x768) at 200 Hz, a dual Xenon processor PC with a Visia Quadro 4900XGl graphics card and Crystal Eyes generated the image. The subject was required to wear a pair of StereoGraphics Inc. glasses in order to view the display. The VR system was synchronized with the Flock of Birds Motion analysis system.

The Flock of Birds (Ascension Technology Corporation, Burlington, VT) apparatus recorded whole body kinematics data obtained from the Flock of Birds magnetic motion tracking sensors. The sensors recorded a time series of data related to positional coordinates, orientation angles and displacement along X, Y and Z axes.

In our study the sensors were attached to a vest and to the glasses that the subject wore, in order to provide data on the head and torso movements of the subject during the virtual reality display and motion tasks. Data were transferred and stored to a host computer (IBM Windows ’98, Intel Pentium processor, 64 MB RAM).

Data Analysis

Neuropsychological Data Analysis

The scores from the neuropsychological tests were scored using the standard scoring procedures for each test. The Trails-B test score was recorded as the number of seconds to complete the test. If the subject made an error during the task, the subject was asked to return to the place prior to where they made the error and continue in the correct sequence. The Symbol Digit Substitution test was scored as the total number of correct responses made in a 90 second period. The Symptom Rating Scale was scored as the total of symptom severity scores, ranging from 0 (no change) through 6 (most severe) from each of the 21 sub-categories.

EEG Data Analysis

An off-line analysis was performed using Neuroguide's 2.3.5 software (Applied Neuroscience Inc., St. Petersburg, Fl.). Each EEG trial was also visually inspected to eliminate any artifact that was undetected by the software's artifact rejection process. Epochs which contained movement artifacts or excessive muscle activity at any electrode site were eliminated from further analyses.

A minimum of one minute of artifact-free EEG was used in the analysis of each of the three EC tasks (seated, firm surface, foam surface). Using Neuroguide's software program, bandpass filtering between 0.5 Hz and 30 Hz with zero phase-shift was applied to each of the artifact-free records. A Fast Fourier Transform (FFT) in the frequency

domain was performed on the artifacted EEG records for each of the 19 recording sites. Frequency bandwidths were divided according to the following divisions: theta (4-7.5 Hz), alpha (8-12 Hz), beta1 (12-15 Hz), beta2 (15-17.5 Hz) and beta3 (18-25Hz). From the computed FFTs, overall power (uV Sq) averages were computed for each bandwidth using Neuroguide's analysis program. Text documents were formed containing the power averages for individual 1 Hz frequencies between 1 Hz and 30 Hz as well as for the averages for each grouped bandwidth at all 19 electrode locations for each subject for each of the three posture conditions. From the 19 sites and bandwidth averages, three other conditions were calculated for each site for each of the theta, alpha, beta1 and beta2 bandwidths, these were; EC seated - EC standing, EC seated - EC foam, EC standing - EC foam.

The bandwidth averaged files were imported into the SPSS 14.0 program for statistical analysis. Due to the large number of variables inherent in 19-channel EEG analysis the number of variables was reduced by comparing injured and normal groups based on means and their 90% confidence interval. Variables that did not overlap at the 90% confidence interval were kept for inclusion into the EEG discriminant function. This data reduction reduced the subject to variable ratio to an acceptable number (61 subjects to 18 EEG variables).

Based on this data reduction process 18 EEG variables were kept for input into the discriminant function. The seated variables were: T5 alpha, P3 alpha, P4 alpha, P4 10Hz, Pz 10Hz, T5 beta2, T5 beta3. The standing variables were: P3 alpha, Pz 10Hz, T5 beta3. The variables from the standing on foam condition were: P3 alpha, P4 alpha, P4 10Hz, Pz 10Hz, P4 beta2, O2 10 Hz, T5 alpha, T5 beta2

Virtual Reality Data Analysis

A specially developed MATLAB (The Mathworks, Natick, MA, USA) program was used to estimate whole body kinematics data obtained from the Flock of Birds motion tracking sensors. Specifically, the time series of the torso motion along X and Y axes and coherence values between quantities of moving room and postural responses as reflected in whole body kinematics were assessed using a specially developed m-code in MATLAB 6.5. It should be noted that coherence is a measure of the linear dependency (or coupling) of two signals at a specific frequency. The auto-spectra for each signal were calculated by using Welsh's averaged periodogram method. Coherence was calculated based on the cross-spectra f_{xy} and auto- spectra f_{xx}, f_{yy} with the spectra estimated from segments of data and the coherence R_{xy} estimated from the combined spectra:

$$R_{xy}(\lambda)|2=|f_{xy}(\lambda)|^2/(f_{xx}(\lambda)f_{yy}(\lambda))$$

Statistical Analysis

Comparison of Testing Modalities

Following the EEG data reduction there were two data analyses performed. The first compared the three testing modalities, namely neuropsychological testing, virtual reality posture assessment and EEG testing. Discriminant analysis was used for this purpose. Discriminant analysis attempts to find linear combinations of those variables that best separate groups of cases, in this study, injured versus normal cases. This

analysis also allowed us to determine which athletes were differentially classified by the three tests.

The tests within each modality were placed into their own discriminant function such that three separate discriminant functions were created and compared. The discriminant functions were each reduced by removing tests that were not significant contributors to the model as assessed by tests performed during the formation of the discriminant, namely; significance of the function, which tells how well the model performs compared to a base model and classification tables, which show the practical results of the discriminant model.

The formation of a combined discriminant function involved forcing a combination of the tests from the three modalities into a universal discriminant function. All tests from the neuropsychological and VR modalities were included as were the 18 EEG tests that remained from the EDA. A stepwise process was used to remove variables that did not contribute significantly to the discriminant function. Variables were removed based on three subtests; correlation to other variables; tests of equality of group means using one-way ANOVA's (Analysis of Variance) and independent t-tests. This reduction improved the subject-variable ratio and reduced the function to the group of factors that produced the most accurate discriminant function.

All discriminant functions were then tested on the normal and injured subjects using the leave-one-out classification function of the SPSS statistical software package. This method is a cross-validation of the discriminant in which each case is classified by the functions derived from all cases other than that case.

Once the discriminant function with the highest classification accuracy was determined for each modality and the combined discriminant function, the four discriminant functions were compared based on: specificity, sensitivity and odds ratios. Specificity is defined as the probability of correctly classifying a concussed individual and is calculated as: true positives / false negatives + true positives. Sensitivity is defined as the probability of correctly classifying the absence of a concussion and is calculated as: true negatives / false positives + true negatives. Odds ratio is defined as the likelihood of making a correct classification (an odds ratio greater than 1 indicates that the condition or event is more likely in the first group, here a correct classification) and is calculated as: true positive x true negative / false positive x false negative.

Source Localization

Using the Neuroguide 2.3.7 software combined with the Key Institute's LORETA software program (Pasqual-Marqui, 2002), independent t-tests were used to determine if group differences existed between postures and to determine the anatomical regions of the cortex that differed between groups. All subjects that underwent the 19-channel EEG testing were used to form the groups (31 normal and 30 injured subjects).

Each of the three artifacted EEG files for each subject (sitting, standing, foam) was transformed using the Neuroguide software program into a LORETA individual analysis file. The transformed individual files were then averaged together to form LORETA group analysis files, based on injury classification and posture. Six groups were formed by this process; injured seated, normal seated, injured standing, normal

standing, injured foam, normal foam. Injury groups were then compared based on posture using t-tests.

Planned comparison hypotheses regarding the Brodmann areas affected by concussion were formed prior to running the t-tests. These hypotheses were based on the known correlations between the surface sites and anatomical regions which act as frequency generators in the cortex for those surface sites.

Chapter 4

Results

The data reported in the results section are organized according to four questions of interest. First, is there a difference in the time frames associated with resolution of symptoms measured in different ways; that is neuropsychological test data compared to postural data and EEG data? Second, which of the three testing paradigms (neuropsychological tests, virtual reality and EEG measures) are the most sensitive for injury classification? Third which tests from each modality are the most sensitive since combining these could lead to an improved test battery for use in diagnosis and return to play decision making? Is EEG analysis using low resolution electromagnetic tomographic assessment (LORETA) an effective tool for localizing cortical areas that have been negatively affected by a concussive injury?

Exploratory Data Analysis

Due to the large number of variables inherent in quantitative EEG analysis a data reduction process was used prior to forming the EEG discriminant function. The exploratory data analysis (EDA) used descriptive statistics, specifically power means and the standard error of those means multiplied by 1.645 (90% Confidence Interval).

Variables that overlapped between groups using this analysis were then excluded from inclusion in the EEG discriminant. Tables 4.1 - 4.3 display these descriptive statistics.

Table **4.1**

Table **4.1**: Descriptive statistics for reduction of EEG variables.

Injury		N	Mean		90% C.I.			N	Mean		90% C.I.	
			Statistic	Std. Error	Upper	Lower	Injury		Statistic	Std. Error	Upper	Lower
Norm	T5alphasec	31	55.10	8.97	69.85	40.34	Inj.	30	31.56	5.23	40.16	22.97
	T5beta2sec	31	3.74	0.45	4.48	3.01		30	2.41	0.26	2.83	1.98
	T5beta3sec	31	5.85	0.70	7.00	4.71		30	3.85	0.45	4.60	3.11
	P310Hzsec	31	22.24	4.30	29.30	15.17		30	14.38	2.76	18.92	9.85
	P410Hzsec	31	22.83	4.43	30.12	15.55		30	12.11	2.03	15.46	8.77
	Pz10Hzsec	31	23.48	3.46	29.18	17.78		30	13.58	2.52	17.72	9.45
	T5 alphafoam	31	52.25	8.35	65.97	38.52		30	29.49	3.71	35.60	23.39
	T5 beta2foam	31	4.52	0.47	5.29	3.76		30	2.89	0.27	3.33	2.45
	T5 beta3foam	31	7.23	0.70	8.37	6.08		30	5.38	0.51	6.22	4.54
	P3 10Hzfoam	31	21.55	4.68	29.25	13.85		30	11.50	1.71	14.31	8.69
	P4 10Hzfoam	31	21.69	3.81	27.96	15.42		30	12.38	1.80	15.34	9.42
	O2 10Hzfoam	31	59.55	13.38	81.56	37.53		30	26.84	4.52	34.27	19.41
	T6 10Hzfoam	31	20.16	3.51	25.93	14.39		30	11.36	1.91	14.50	8.22
	Pz 10Hzfoam	31	23.50	3.80	29.74	17.25		30	12.99	2.04	16.35	9.63
	T5alphastec	31	56.92	9.37	72.33	41.51		30	35.08	5.51	44.14	26.03
	T5beta2stec	31	4.11	0.54	4.99	3.22		30	2.68	0.27	3.13	2.23
	T5beta3stec	31	6.69	0.81	8.02	5.36		30	4.40	0.44	5.13	3.68
	P310Hzstec	31	25.03	5.46	34.02	16.04		30	13.55	1.94	16.75	10.35
	P410Hzstec	31	27.11	5.54	36.23	17.99		30	14.61	2.12	18.09	11.13
	Pz10Hzstec	31	29.06	4.93	37.16	20.95		30	14.80	2.23	18.47	11.13
	F3-theta sec	31	13.30	1.08	15.07	11.53		30	12.37	1.26	14.45	10.29
	F4-theta sec	31	13.17	1.11	15.00	11.34		30	12.16	1.22	14.17	10.16
	T3-theta sec	31	6.43	0.50	7.25	5.62		30	6.66	0.82	8.02	5.31
	T4-theta sec	31	5.91	0.59	6.87	4.94		30	5.46	0.60	6.44	4.48
	P3-theta sec	31	16.49	1.69	19.27	13.72		30	13.41	1.51	15.89	10.92
	P4-theta sec	31	15.96	1.73	18.82	13.11		30	13.23	1.58	15.82	10.63

Table **4.2**

Table **4.2**: Descriptive statistics for reduction of EEG variables (cont.).

Injury		N	Mean		90% C.I.		Injury	N	Mean		90% C.I.	
			Statistic	Std. Error	Upper	Lower	Inj.		Statistic	Std. Error	Upper	Lower
Norm	F3-alpha sec	31	18.29	1.97	21.53	15.05		30	17.72	2.56	21.94	13.51
	F4-alpha sec	31	18.03	1.89	21.15	14.92		30	17.68	2.46	21.73	13.62
	T3-alpha sec	31	11.42	1.37	13.67	9.17		30	12.21	2.45	16.25	8.18
	T4-alpha sec	31	10.72	1.34	12.92	8.51		30	10.47	1.58	13.06	7.87
	P3-alpha sec	31	66.74	9.17	81.83	51.65		30	41.84	5.71	51.23	32.46
	P4-alpha sec	31	68.02	9.53	83.70	52.34		30	42.66	5.45	51.61	33.70
	F3-beta1 sec	31	3.46	0.37	4.07	2.86		30	3.12	0.28	3.58	2.65
	F4-beta1 sec	31	3.41	0.36	4.00	2.83		30	3.17	0.29	3.64	2.70
	T3-beta1 sec	31	3.10	0.36	3.69	2.52		30	2.54	0.26	2.96	2.11
	T4-beta1 sec	31	2.76	0.34	3.32	2.19		30	2.34	0.26	2.78	1.91
	P3-beta1 sec	31	10.35	1.89	13.46	7.25		30	6.23	0.85	7.62	4.84
	P4-beta1 sec	31	10.22	1.92	13.38	7.06		30	6.39	0.98	8.00	4.78
	F3-beta2 sec	31	2.46	0.33	3.01	1.91		30	2.18	0.25	2.59	1.77
	F4-beta2 sec	31	2.56	0.41	3.24	1.88		30	2.26	0.28	2.72	1.80
	T3-beta2 sec	31	1.90	0.25	2.31	1.49		30	1.66	0.21	2.00	1.32
	T4-beta2 sec	31	2.02	0.35	2.60	1.44		30	1.62	0.24	2.01	1.24
	P3-beta2 sec	31	3.91	0.46	4.66	3.16		30	2.95	0.34	3.51	2.39
	P4-beta2 sec	31	3.85	0.49	4.66	3.04		30	2.85	0.31	3.37	2.34
	F3-theta foamec	31	14.00	1.03	15.70	12.29		30	13.31	1.28	15.41	11.20
	F4-theta foamec	31	13.62	1.01	15.28	11.95		30	13.21	1.35	15.43	10.99
	T3-theta foamec	31	6.64	0.46	7.39	5.89		30	6.66	0.63	7.70	5.62
	T4-theta foamec	31	5.96	0.47	6.73	5.19		30	5.70	0.61	6.70	4.69
	P3-theta foamec	31	15.44	1.44	17.81	13.07		30	12.86	1.23	14.88	10.84
	P4-theta foamec	31	14.90	1.37	17.15	12.65		30	12.83	1.26	14.91	10.76
	F3-alpha foamec	31	20.77	2.51	24.90	16.65		30	18.78	2.34	22.63	14.92
	F4-alpha foamec	31	20.09	2.43	24.09	16.10		30	18.97	2.42	22.95	15.00

Table **4.3**

Table **4.3**: Descriptive statistics for reduction of EEG variables (cont.).

Injury		N	Mean		90% C.I.		Injury	N	Mean		90% C.I.	
			Statistic	Std. Error	Upper	Lower			Statistic	Std. Error	Upper	Lower
Norm	T3-alpha foamec	31	12.87	1.69	15.64	10.10	Inj.	30	11.85	1.45	14.24	9.46
	T4-alpha foamec	31	10.74	1.22	12.75	8.74		30	10.03	1.33	12.22	7.84
	P3-alpha foamec	31	62.82	9.84	79.01	46.64		30	35.72	3.84	42.04	29.40
	P4-alpha foamec	31	62.49	8.18	75.93	49.04		30	38.02	4.52	45.46	30.58
	F3-beta1 foamec	31	4.02	0.44	4.75	3.30		30	3.56	0.31	4.07	3.06
	F4-beta1 foamec	31	3.91	0.44	4.63	3.19		30	3.61	0.32	4.12	3.09
	T3-beta1 foamec	31	3.96	0.48	4.75	3.17		30	3.35	0.34	3.91	2.78
	T4-beta1 foamec	31	3.68	0.52	4.53	2.83		30	2.88	0.36	3.48	2.29
	P3-beta1 foamec	31	10.21	1.32	12.38	8.03		30	7.45	1.03	9.14	5.76
	P4-beta1 foamec	31	10.39	1.59	13.00	7.77		30	7.69	1.17	9.62	5.77
	F3-beta2 foamec	31	2.60	0.31	3.11	2.09		30	2.39	0.26	2.81	1.97
	F4-beta2 foamec	31	2.56	0.36	3.15	1.97		30	2.39	0.27	2.83	1.94
	T3-beta2 foamec	31	2.72	0.40	3.38	2.07		30	2.34	0.32	2.86	1.82
	T4-beta2 foamec	31	3.11	0.54	4.00	2.22		30	1.93	0.31	2.45	1.42
	P3-beta2 foamec	31	4.30	0.43	5.01	3.59		30	3.16	0.34	3.72	2.60
	P4-beta2 foamec	31	4.12	0.47	4.89	3.34		30	3.09	0.34	3.65	2.52
	F3-theta stec	31	13.55	1.13	15.41	11.69		30	12.66	1.18	14.60	10.73
	F4-theta stec	31	13.29	1.10	15.10	11.48		30	12.77	1.18	14.72	10.82
	T3-theta stec	31	6.46	0.62	7.47	5.45		30	6.64	0.72	7.83	5.45
	T4-theta stec	31	5.98	0.63	7.01	4.95		30	5.69	0.62	6.71	4.67
	P3-theta stec	31	16.43	1.80	19.39	13.47		30	13.34	1.41	15.65	11.03
	P4-theta stec	31	16.07	1.88	19.16	12.99		30	13.27	1.47	15.69	10.84
	F3-alpha stec	31	20.39	2.26	24.11	16.67		30	18.29	2.17	21.85	14.72
	F4-alpha stec	31	19.90	2.11	23.38	16.42		30	18.58	2.24	22.27	14.89
	T3-alpha stec	31	12.83	1.74	15.70	9.96		30	12.35	2.08	15.77	8.93
	T4-alpha stec	31	11.90	1.60	14.53	9.27		30	11.46	1.95	14.66	8.25
	P3-alpha stec	31	70.93	10.18	87.68	54.18		30	43.71	5.24	52.32	35.10
	P4-alpha stec	31	72.57	9.71	88.54	56.60		30	47.82	5.90	57.52	38.12
	F3-beta1 stec	31	3.87	0.46	4.61	3.12		30	3.37	0.28	3.83	2.91
	F4-beta1 stec	31	3.71	0.44	4.45	2.98		30	3.44	0.30	3.93	2.95
	T3-beta1 stec	31	3.62	0.43	4.33	2.92		30	2.92	0.27	3.35	2.48
	T4-beta1 stec	31	3.10	0.38	3.72	2.48		30	2.49	0.26	2.91	2.07
	P3-beta1 stec	31	11.08	1.87	14.16	8.00		30	7.28	0.96	8.85	5.70
	P4-beta1 stec	31	11.34	2.01	14.64	8.04		30	7.26	1.02	8.94	5.59
	F3-beta2 stec	31	2.57	0.35	3.16	1.99		30	2.39	0.28	2.86	1.92
	F4-beta2 stec	31	2.63	0.41	3.31	1.95		30	2.46	0.31	2.97	1.95
	T3-beta2 stec	31	2.01	0.24	2.41	1.61		30	2.00	0.24	2.39	1.61
	T4-beta2 stec	31	2.04	0.28	2.50	1.59		30	1.58	0.21	1.92	1.23
	P3-beta2 stec	31	4.34	0.53	5.21	3.46		30	3.18	0.38	3.79	2.56
	P4-beta2 stec	31	4.19	0.53	5.06	3.32		30	3.06	0.36	3.65	2.46

Group Classification Discriminant Functions Using Different Testing Modalities

i) Neuropsychological (NP) Testing

The Symptom Rating Scale was shown to be a sensitive measure for differentiating between injured and normal subjects when administered within 24 hours of the injury. Table 4.4 shows the descriptive statistics for the neuropsychological tests.

Table **4.4**

Table **4.4**: Descriptive statistics for Normal and Injured groups on neuropsychological tests.

Injury		N	Minimum	Maximum	Mean		Std. Dev.
		Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
Normals	Trails-B > 7days	29	31.0	68.0	41.5	1.6	8.9
	Symbol Digit > 7days	29	53.0	92.0	70.4	1.6	8.7
	SympRate > 7days	15	0.0	12.0	5.1	1.0	4.0
	Symptom Rating 24hrs	29	0.0	39.0	9.2	1.9	10.3
Injured	Trails-B > 7days	23	21.3	60.0	40.8	2.3	10.9
	Symbol Digit > 7days	23	44.0	102.0	67.1	2.5	11.9
	SympRate > 7days	13	0.0	12.0	2.6	1.0	3.8
	Symptom Rating 24hrs	25	6.0	105.0	36.1	5.2	26.1

Table 4.5 displays the significance and group prediction percentages for the Symptom Rating Scale administered at 24hrs, and the combined discriminant formed by the Trails B and Symbol Digit Substitution test administered > 7 days post injury. Predicted groups are based on a comparison to the groups that subjects were placed in when they were admitted to the study. The Symptom Rating Scale administered beyond 7 days post injury did not contribute to the utility of the NP discriminant and was not included; this test will be discussed in isolation later in the results. Tables displaying the

significance of individual tests and coefficients used in the discriminant functions can be found in Appendix 3.

Table **4.5**

Table **4.5**: Neuropsychological discriminant functions (1) > 7 days post injury (2) Symptom Rating Scale administered within 24hrs of injury.

Model	Variables Included	Significance	Predicted Group	Prediction Cross-Val
1.	Trails-B > 7days Symbol Digit > 7days	.391	55.8%	55.8%
2.	Symptom Rating w/in 24hrs	.000	75.9%	75.9%

The Trails 'B'and Symbol digit test combined at > 7 days post injury was a better discriminant than either of these tests administered in isolation. Combined they classified subjects into groups that matched their intake groups 55.8% of the time. This low classification difference was expected based on previous studies that found neuropsychological test differences between injured and normal subjects were not significant at 1-week post injury (Killam et al. 2005; Randolph, 2001)

The Symptom Rating Scale was able to differentiate between injured and normal subjects 75.9% of the time when administered within 24 hours of the injury. In spite of the relative sensitivity of this measure immediately following injury, the effects of a concussion that were detectible using this test resolved relatively quickly making this testing modality ineffective for assessments at approximately 1 week. There was no difference found between groups on the Trails B, Symbol Digit Substitution or Symptom Rating Scale when administered 1 week post injury. Figure 4-1, below, illustrates the finding that the Symptom Rating Scale was able to distinguish between normal and injured subjects only when administered within 24 hours of injury (Figure 4-1).

Figure **4-1**

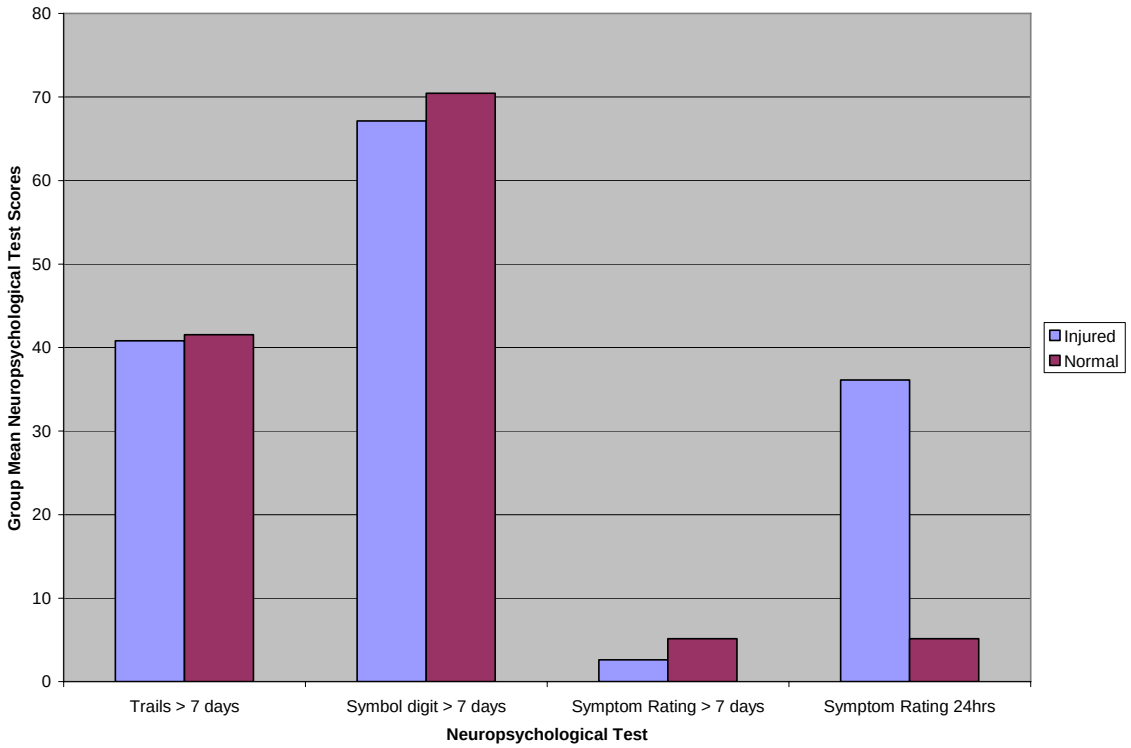

Figure **4-1**: Neuropsychological test scores of normal and injured groups. Only the Symptom Rating Scale administered within 24hrs of injury showed a significant difference between group scores.

As shown in Figure 4-1, the Symptom Rating Scale showed significant group differences when administered within 24hrs of the injury. However, the effectiveness of this testing method was drastically reduced when administered beyond one week post injury. A comparison between the normal individuals and the symptomatically recovered concussed group showed that subjects who have recovered symptomatically from a concussion show less concussion symptoms that normals (Figure 4-2).

Figure **4-2**

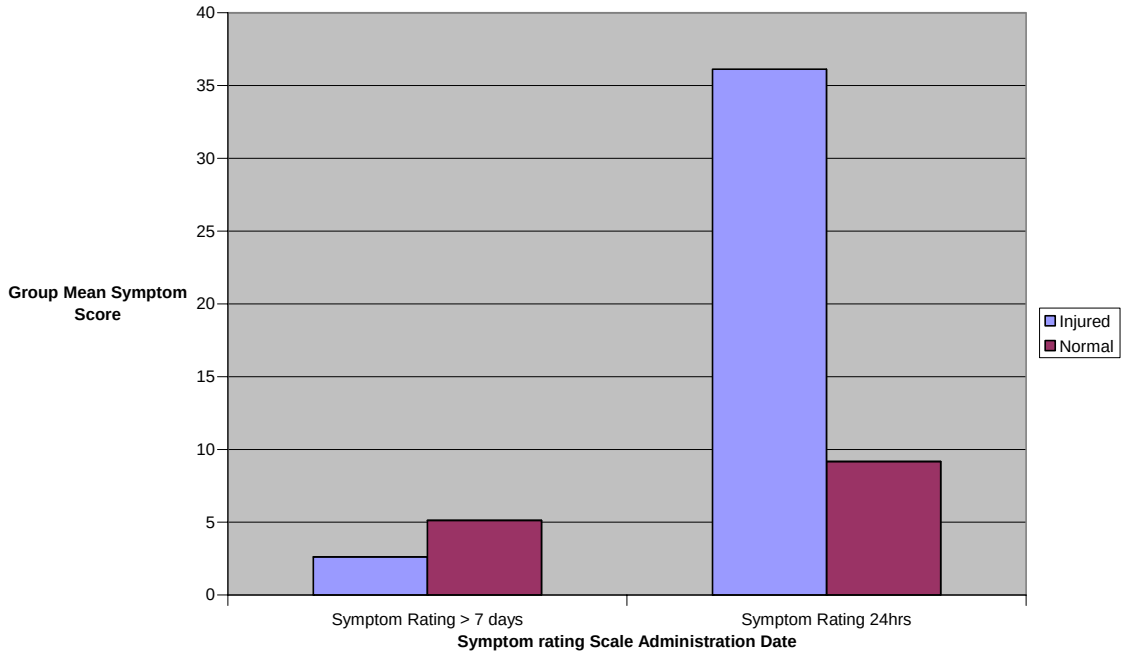

Figure **4-2**: Change in symptom scores for normal and injured groups. Symptom Rating Scale administered > 7 days post injury shows no difference between groups. Symptom Rating Scale within 24hrs show significant difference between groups.

ii) Virtual Reality Testing

Virtual reality (VR) testing was used in order to assess deficits during postural tasks and sensory integration following concussion. Bracing behaviors and the negative effects of concussion on balance have been reported following MTBI (Moss, 2006). The use of virtual reality in posture assessments increased the task difficulty beyond that which is experienced using traditional balance tests, such as standing eyes open or performing self-paced anterior-posterior sway (Slobounov, 2006). Virtual reality also

improved the identification of between group differences when administered more than 7 days post-injury. Table 4.6 shows the decision table that reduced the variables to the one(s) that best classified subjects into the group that matched their study intake group. As with the NP tests predicted groups are based on a comparison to the groups that subjects were placed in when they were admitted to the study and tables displaying the significance of individual tests and coefficients used in the discriminant functions can be found in Appendix 3.

Table **4.6**

Table **4.6**: Decision table for the virtual reality discriminant function reduction.

Model	Variables Included	Significance	Predicted Group	Prediction Cross-Val
1.	.2Hz roll .2Hz all wall .3Hz all wall	.016	78.6%	67.9%
2.	.2Hz all wall .3Hz all wall	.018	75.0%	71.4%
3.	.2Hz all wall	.017	71.4%	71.4%
4.	.3Hz all wall	.022	75.0%	75.0%

Based on the 0.3Hz anterior-posterior moving wall, subjects were correctly classified 75% of the time. This is a misleading statistic, however. Although normal subjects are classified correctly 92% of the time, injured subjects show a high rate of false negatives and are only correctly classified as injured 60% of the time. This finding is discussed further in the results section titled; “Specificity, Sensitivity and Odds Ratio’s of Discriminant Functions”. Our goal is to improve the reliability of safe return to play decisions. The finding of a high number of false negatives indicates that either this VR testing condition is not challenging enough, or that it needs to be paired with other testing

methods that are sensitive in detecting deficits in the athletes who do not show deficits in balance beyond 7 days post injury.

iii) Electroencephalographic (EEG) Testing

Nineteen-channel EEG recordings were taken during an eyes closed seated condition and during two eyes closed standing conditions, namely, bipedal feet together on a firm surface and bi-pedal feet together on a foam surface, as described previously in the Methods section. Following the exploratory data analysis and reduction of EEG variables, 18 EEG variables were placed into the EEG discriminant function and further reduction was performed to find linear combinations of those variables that best separate groups of cases as either injured or normal. Variables were eliminated by removing tests that were not significant contributors to the model as assessed by tests of equality of group means using one-way ANOVA's (Analysis of Variance). A list of the 18 variables included in the original EEG discriminant as well as the tests of equality of group means is found in table 4.7.

Table **4.7**

Table **4.7**: Variables and significance for tests of equality of group means for EEG discriminant with 18 Variables

	Wilks' Lambda	F	df1	df2	Sig.
T5alphasec	.921	5.054	1	59	.028
T5beta2sec	.899	6.623	1	59	.013
T5beta3sec	.912	5.728	1	59	.020
P410Hzsec	.926	4.734	1	59	.034
Pz10Hzsec	.918	5.289	1	59	.025
T5 alphafoam	.907	6.069	1	59	.017
T5 beta2foam	.867	9.032	1	59	.004
P4 10Hzfoam	.925	4.775	1	59	.033
O2 10Hzfoam	.919	5.221	1	59	.026
Pz 10Hzfoam	.910	5.833	1	59	.019
T5beta2stec	.915	5.515	1	59	.022
P3-alpha sec	.919	5.232	1	59	.026
P4-alpha sec	.918	5.247	1	59	.026
P3-alpha foamec	.902	6.423	1	59	.014
P4-alpha foamec	.898	6.732	1	59	.012
P3-alpha stec	.914	5.545	1	59	.022

The discriminant using 18 EEG variables had a cross-validated classification accuracy of 47.5% (table 4.8). Based on the information in table 4.7, the discriminant was reduced and nine variables were kept; T5beta2sec, T5 alphafoam, T5 beta2foam, Pz 10Hzfoam, T5beta3stec, Pz10Hzstec, T5beta3sec, P3-alpha foamec, P4-alpha foamec.

As with the NP and VR tests, predicted groups are based on a comparison to the groups that subjects were placed in when they were admitted to the study and tables displaying the significance of individual tests and coefficients used in the EEG discriminant functions can be found in Appendix 3.

It was expected that there would be amplitude differences between groups in all conditions and that these differences would be greatest in the most difficult task of bipedal stance on the foam surface. These hypotheses were confirmed. Table 4.8 shows the decision process for forming the EEG classification discriminant function using significance and group prediction percentages.

Table **4.8**

Table **4.8**: Decision table for the EEG discriminant function reduction.

Model	Variables Included	Significance	Predicted Group	Prediction Cross-Val
1.	T5alphasec T5beta2sec T5beta3sec P410Hzsec Pz10Hzsec T5 alphafoam T5 beta2foam P4 10Hzfoam O2 10Hzfoam Pz 10Hzfoam T5beta2stec P3-alpha sec P4-alpha sec P3-alpha foamec P4-alpha foamec P3-alpha stec	.483	72.1%	47.5%
2.	T5beta2sec T5 alphafoam T5 beta2foam Pz 10Hzfoam P3-alpha foamec P4-alpha foamec	.067	70.5%	63.9%
3.	T5 beta2foam P4-alpha foamec T5beta2sec P3-alpha foamec	.019	70.5%	65.6%
4.	P4-alpha foamec T5beta2sec P3-alpha foamec	.009	70.58%	67.2%
5.	P4-alpha foamec T5beta2sec	.004	73.8%	70.5%

As was the case with the VR discriminant, the overall cross-validated prediction accuracy of 70.5% using the EEG discriminant does not tell the whole story. Whereas the VR discriminant showed a high number of false negatives, the EEG discriminant (tends to be overly conservative and) shows a high number of false positives. Injured subjects are correctly classified as injured 83% of the time. However, normal subjects are classified as injured 35% of the time, meaning that normals are only classified as normal approximately 65% of the time. This is further discussed in the results section titled "Specificity, Sensitivity and Odds Ratio's of Discriminant Functions". The high number of false positives may be related to the large variability between subjects in EEG power. The overall finding in the literature, in previous work at the Pennsylvania State University and in this study is that concussions cause a reduction in EEG power. Subjects that naturally have low power EEGs (which might, for example, be due to a large skull thickness) would therefore be classified as injured when EEG power is used in isolation as a means of grouping a subject.

Formation of the Combined Modality Discriminant

One of the main aims of this study was to determine if combining tests from across different testing modalities would improve return to play measures. In order to accomplish this we forced the best tests from each of the neuropsychological, virtual reality and EEG testing functions into a combined discriminant and reduced the variables until the discriminant function was found that best separated individuals into normal and injured groups. Since the goal of developing this combined discriminant function was to

improve return to play testing, only tests that advanced the discriminant when administered 7 days post injury or beyond were considered. For this reason, no tests from the neuropsychological testing battery were included in the discriminant as they were not shown to be sensitive at 7 days post injury. Figure 4-3 shows the tests that were included in the combined discriminant and the average group scores for each test. Tables for values used to reduce the discriminant function (tests of equality of group means, classification function coefficients, pooled within-groups matrices and independent samples t-tests) can be found in appendix 3.

Figure **4-3**

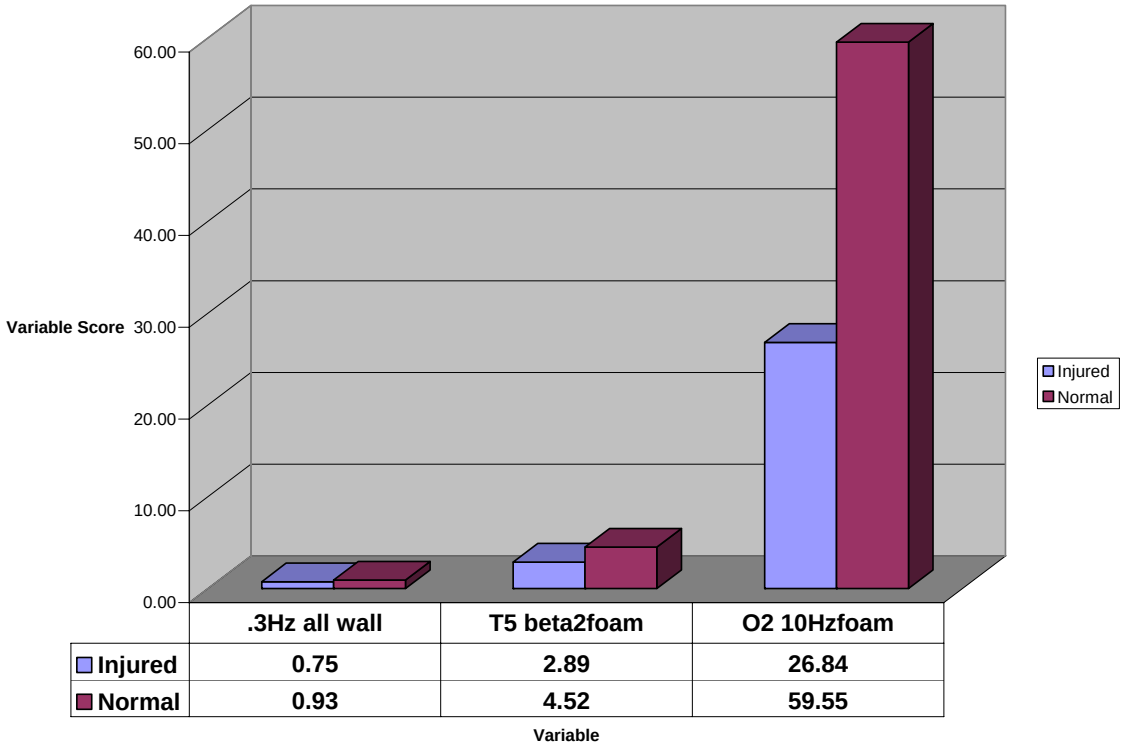

Figure **4-3**: Variables and group scores for the variables in the combined discriminant

Specificity, Sensitivity and Odds Ratio's of Discriminant Functions

Results show that in the case of a mild brain injury the damage to the cortex causes a degradation of accurate responses to external demands. There is also a corresponding change in neuronal functioning. These changes may be reflected in all, but often are found in only one of the following measures: reduced neuropsychological test performance, reduced physical co-ordination and abnormal EEG measures. Following the formation of discriminant functions for each of the three testing modalities and the combined discriminant, we compared the discriminant functions based on their specificity, sensitivity and odds ratios from the cross-validated group predictions. Our aim was to determine which tests detected residual effects of concussion. Therefore we calculated specificity, sensitivity and odds ratios based on comparisons between group membership at the onset of the study and group membership based on the discriminant functions formed in the previous stage of analysis. Specificity is defined as the probability of correctly classifying a concussed individual and is calculated as; true positives / false negatives + true positives. Sensitivity is defined as the probability of correctly classifying the absence of a concussion and is calculated as; true negatives / false positives + true negatives. Odds ratio is defined as the likelihood of making a correct classification (an odds ratio greater than 1 indicates that the condition or event is more likely in the first group, here a correct classification) and is calculated as: true positive x true negative / false positive x false negative. The comparisons between discriminants are shown in table 4.9.

Table **4.9**

Table **4.9**: Comparison of specificity, sensitivity and odds ratio of the discriminant functions for NP, VR, EEG and Combined discriminant.

Discriminant	Specificity	Sensitivity	Odds Ratio
NP	0.57	0.55	1.6
SR 24hrs	0.06	0.9	13
VR	0.6	0.92	18
EEG	0.8	0.61	6.3
Combined	0.93	0.85	77

Based on the results displayed in table 4.9 it may be concluded that, from a clinical standpoint, assessment methods following concussion must reliably test all possible systems that might be differentially affected by concussion in order to retain high specificity and sensitivity. This can be achieved by the use of a combined modality testing function.

Source Localization of Cortical Differences Following MTBI

Based on the differences in amplitude measures between the injured and normal groups it was of interest to determine the anatomical sources of these differences. Low resolution electromagnetic tomographic assessment (LORETA) was thus used to compute the three-dimensional distribution of the electrically active neuronal generators in the brain during the three EEG recording tasks. Planned comparison hypotheses were developed regarding the Brodmann areas that would differ between injured and normal groups based on the surface recordings. Table 4.10 shows a summary of the formed hypotheses and actual results of the LORETA Brodmann area analysis.

Table **4.10**

Table **4.10**: Surface electrode sites for different postures associated with significant group differences plus hypothesized and LORETA generated Brodmann area source locations for injury.

Posture	Surface Elect.	Freq	T-test Group Signif.	Hypothesized B.A.	Actual B.A. (LORETA analysis)
Seated (fig 4-8 & 4-9)	P3	alpha	0.025	40,3,1,2,5,23,13,30	5,40,3,2
	P4	alpha	0.025	40,3,1,2,5,23,13,30	5,40,3,2
	T5	alpha	0.048	40,41,42,39,37,20,30,36	39
		Beta2	0.012		37,20,42,39,36
		Beta3	0.02		37,20
	PZ	alpha	0.016	7,31,30,23,26,29	7,
Bi-pedal firm (fig 4-10)	P3	alpha	0.023	40,3,1,2,5,23,13,30	5,3,240,1
	PZ	alpha	0.01	7,31,30,23,26,29	7
Bi-pedal Foam (fig 4-11 & 4-12)	P3	Alpha	0.014	40,3,1,2,5,23,13,30	5,3,2,1
	P4	alpha	0.012	40,3,1,2,5,23,13,30	5,3,2,1
	T5	alpha	0.017	40,41,42,39,37,20,30,36	40
		Beta2	0.004		39,40,30
	Pz	alpha	0.015	7,31,30,23,26,29	7
	O1	Beta2	0.02	17,18,19,31	19,31
	O2	alpha	0.009	17,18,19,31	31,19,
		Beta2	0.03		19,31,18

Interestingly, the areas with the greatest differences between injury groups were found in the posterior regions. This probably resulted as a function of our subject group. The majority of our concussed subjects suffered an injury by hitting the posterior region of their head (athlete verbal report). Wilberger et al. (2006) also reported that the majority of head injuries in the NFL resulted from oblique and lateral impacts. Many of our athletes, besides being football players, were from sports with similar impact mechanisms such as rugby and hockey. Figures 4-4 through 4-9 are low resolution electromagnetic tomographic images that show the anatomical areas that were most affected by the mild brain injuries in our subjects (Fig. 4-4 seated, 4-5 stand, 4-6 foam all

at 10Hz frequency; Fig. 4-7 seated, 4-8 foam at Beta2 band; Fig. 4-9 foam at Beta3 band). In the figures that follow, blue represents a deficit of the specified frequency band in that specific area of the brain in the injured subject group. Note that the areas correspond to the Brodmann areas (BA) hypothesized and found to be different between groups based on the surface EEG recording (Table 4.10). The LORETA images were generated using pooled data from 31 normal and 30 concussed athletes.

Figure 4-4 shows the differences found in the alpha band between groups in the resting seated condition. These differences were shown to be significant in the posterior regions in the surface EEG recordings at sites PZ (central), P4 (right), P3 (left) and T5 (left). LORETA localized the affected anatomical regions that generate the abnormal power of the 10Hz frequency in the injured subjects. At PZ the difference in 10Hz was generated in the Superior Parietal Lobule of the parietal lobe (BA 7). At sites P3 and P4 the difference between groups was localized to the Superior Parietal Lobule (BA 5), Inferior Parietal Lobule (BA 40) and the Postcentral Gyrus (BA 2 and 3). The difference between groups at T5 was localized to the Inferior Parietal Lobule (BA 39).

Figure **4-4**

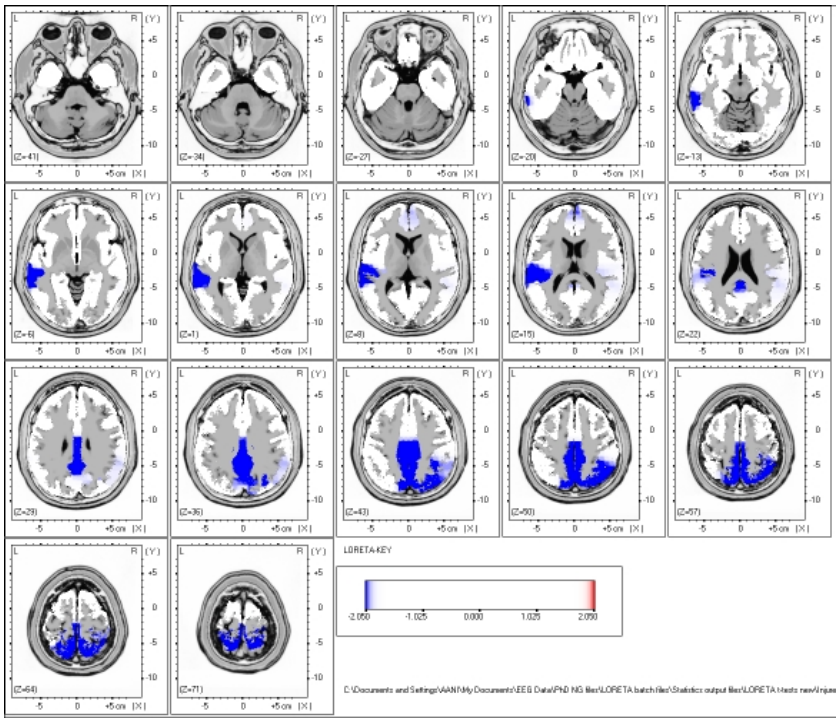

Figure **4-4**: LORETA localized anatomical sources of significant differences between injured and normal groups at 10Hz, seated eyes closed posture.

Figure 4-5 shows the LORETA image slices at 10Hz for the firm surface standing condition. Differences at the surface electrodes were again significant in the posterior region at sites PZ and P3. PZ surface differences were localized to the Postcentral Gyrus (BA 7). Group differences at P3 were localized to the Postcentral Gyrus (BA 5,3,2,1) and the Sub-Gyral of the parietal lobe (BA 40).

Figure **4-5**

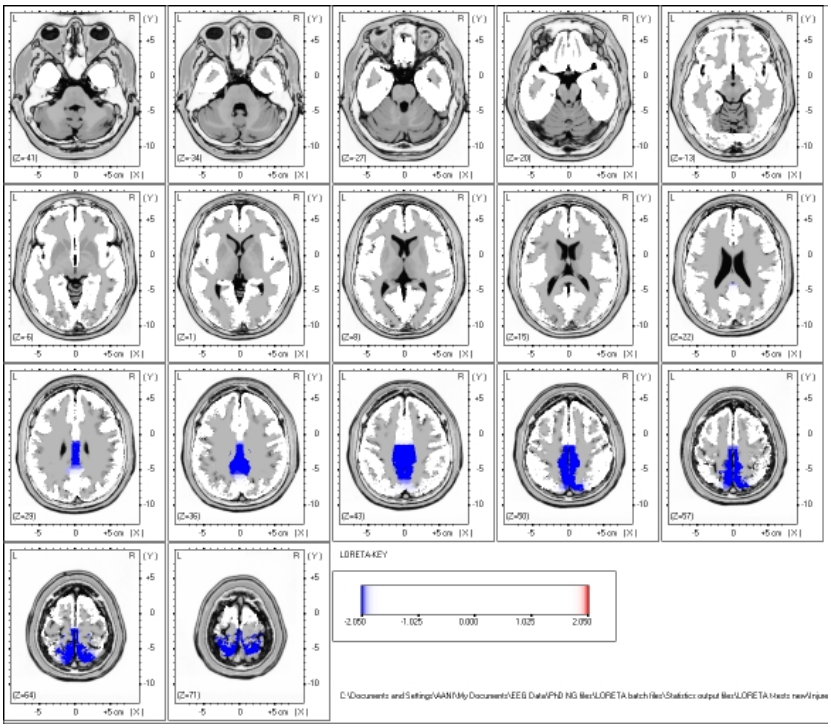

Figure **4-5**: LORETA localized anatomical sources of significant differences between injured and normal groups at 10Hz, eyes closed, bipedal stance on a firm surface posture.

The increased difficulty of the standing condition on the foam surface (Fig. 4-6) showed anatomical differences in the same regions as the firm surface standing condition and the seated resting condition, however, the differences were more pronounced and included Occipital lead O2 (right). The lower power at 10Hz was localized by LORETA to the Postcentral Gyrus (BA 7,5,3,2,1), Paracentral lobule (BA 6,4), Sub-Gyral (BA 40), and at O2 from the Cingulate Gyrus (BA 31) and the Precuneus (BA 19).

Figure **4-6**

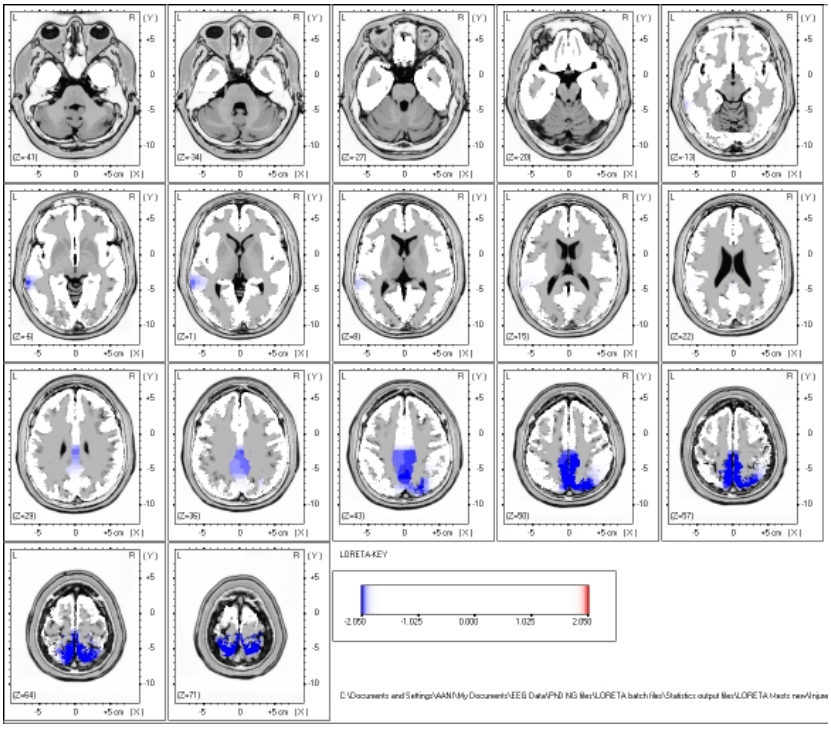

Figure **4-6**: LORETA localized anatomical sources of significant differences between injured and normal groups at 10Hz, eyes closed, bipedal stance on a foam surface posture.

Figures 4-7 and 4-8 illustrate the differences found between groups in the Beta2 frequency band. As with the 10Hz band the injured group again showed significantly less power in the posterior regions in the seated condition and the standing foam condition. No significant differences were found in the standing condition when on the firm surface. The most significant differences in the surface EEG during the seated condition were found at T5. This reduction in power was localized to the Inferior Temporal Gyrus (BA 37,20), Superior Temporal Gyrus (BA 42), Middle Temporal Gyrus (BA 39) and the Fusiform Gyrus of the temporal lobe (BA 36).

Figure **4-7**

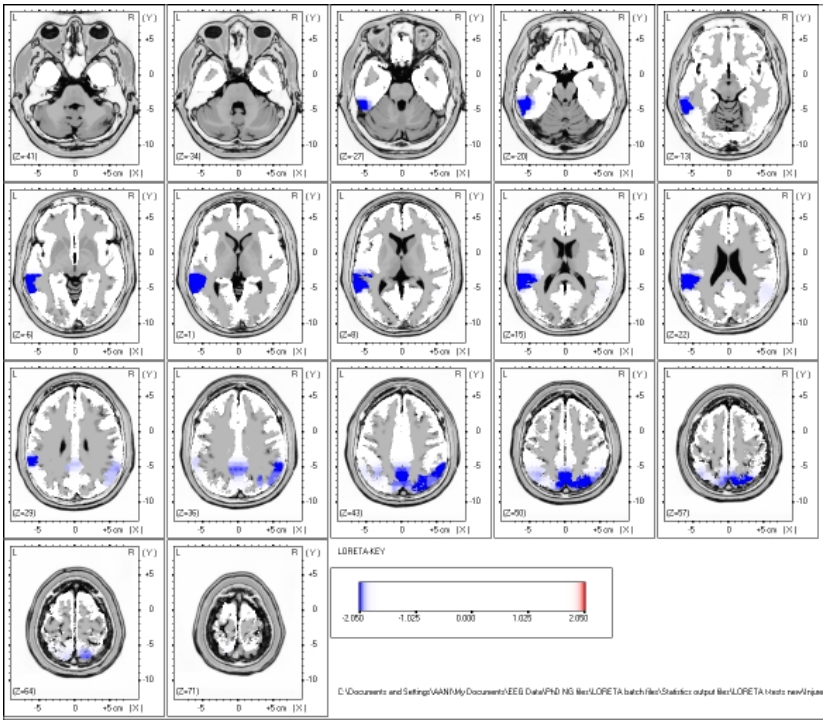

Figure **4-7**: LORETA localized anatomical sources of significant differences between injured and normal groups at 15Hz, seated eyes closed posture.

In the standing foam condition in the Beta2 band (Fig. 4-8) significant differences were found at surface site T5 as well as at sites O1 and O2. The reduction in power at T5

was localized to the Inferior Parietal Lobule (BA 39). Reduced Beta2 power in leads O1 and O2 were contained in the Precuneus (BA 19,31) and Cuneus (BA 18).

Figure **4-8**

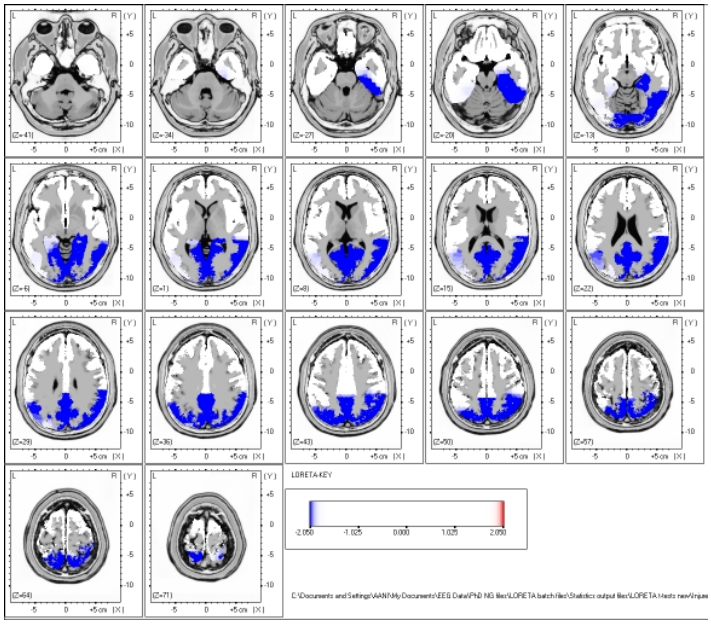

Figure **4-8**: LORETA localized anatomical sources of significant differences between injured and normal groups at 15Hz, eyes closed, bipedal stance on a foam surface posture.

Figure 4-9 shows areas of significant power differences between groups in the Beta3 band. The largest power difference was found in the eyes closed seated resting condition at surface electrode site T5. This was localized by LORETA to the Middle Temporal Gyrus (BA 37) and the Inferior Temporal Gyrus (BA 20).

Figure **4-9**

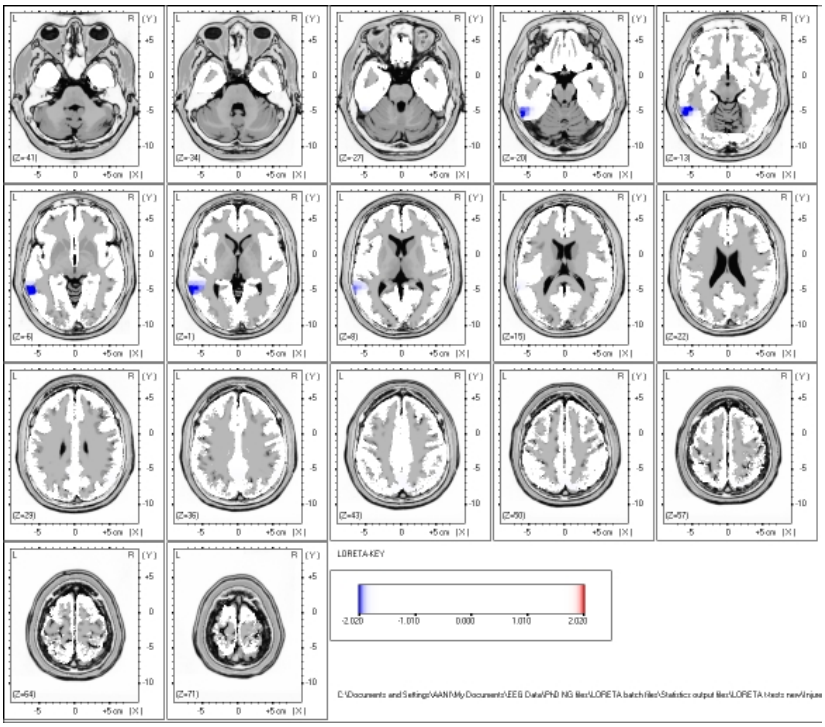

Figure **4-9**: LORETA localized anatomical sources of significant differences between groups at 19Hz, seated eyes closed posture.

Summary

The results of this study revealed: (i) group differences in subjective symptom ratings by athletes in the period immediately following their injury (within 24hrs); (ii) symptom ratings as well as other neuropsychological scores generally tested within

normal limits after one week post injury; (iii) postural and EEG assessments were sensitive instruments for detecting residual deficits beyond one week post injury; (iv) demonstrated that a discriminant testing function that combined multiple testing modalities was more sensitive and reliable for distinguishing between injured and normal subjects than the use of any one testing modality in isolation. Additionally, the use of low resolution electromagnetic tomography was shown to be an effective method by which to localize cortical areas that have been negatively affected by a concussive injury.

Chapter 5

Discussion

The current study compared 30 varsity athletes who had suffered concussions with a control group of 31 athletes who had not had a head injury within the last six months. Our main aim in this study was to compare and contrast the three most accepted concussion assessment tests based on their ability to classify test subjects as either injured or normal. Our secondary aim was to improve concussion return to play testing by reducing the number of false negatives in return to play assessments. To improve the understanding of the brain regions most affected by concussion, differences in the participant's neural resource allocation during postural tasks were assessed Low Resolution Electromagnetic Tomography (LORETA). From the data collected, it was demonstrated that concussion diagnoses and subsequent return to play measures that use only one type of testing modality are insufficient for detecting the many possible negative affects that result from concussion.

In summary, the results showed that neuropsychological testing proved to be an effective testing procedure for assessing concussions within the first 24 hours of injury. However, the effects of the concussion that were detectible using neuropsychological assessments resolved relatively quickly making this testing modality ineffective for assessments at and beyond approximately 1 week. This normalization of neuropsychological testing was expected and is consistent with previous work in this area

that has found resolution of neuropsychological deficits within one week of injury (Collins et al., 2003; Echemendia et al., 2001; Randolph et al., 2005). This symptom resolution based on neuropsychological testing was not necessarily indicative of true injury resolution as demonstrated by the lingering negative effects shown by virtual reality/postural testing and electroencephalographic measures. Virtual reality postural assessments were an effective measurement tool for many subjects who presented functional impairments or sensory difficulties that went beyond the apparent resolution of symptoms as assessed by the symptom rating scale. Electroencephalography was able to detect amplitude differences between the injured and normal subjects. As was the case with the virtual reality testing, the EEG testing modality detected lingering deficits in concussed subjects beyond one week post injury.

Though there was demonstrated utility for each testing method when used in isolation, there was also often a clear mismatch between subject's injury classification when neuropsychological, postural and EEG testing paradigms were compared. This conflict results from the fact that no two concussions are the same in symptomology or pathology and therefore they can be expected to differ in terms of what test will be sensitive in assessing the injury. The use of a testing paradigm that combines the most sensitive tests from each modality is an effective system that resolves the dilemma of differing symptomology and pathology among injuries.

The results of the present study are discussed below in terms of their relevance to global cortical functioning and their importance to the clinical aspects of a concussive injury. In the case of a mild brain injury, functional connections between neurons are disrupted. The effect of this disruption is a shift in the way in which external stimuli and

task demands are dealt with cortically, leading to a resulting degradation of accurate responses to external demands. This disruption in the connections between neurons can be detected by all, but often only one, of the following measures: reduced neuropsychological performance, reduced physical co-ordination or abnormal EEG findings. The resulting clinical implication is that current clinical assessment methods should be expanded to provide a valid and reliable way of testing all possible systems that might be differentially affected by concussion. As a result of the sheer size and complexity of the central nervous system and its potential for a wide range of dynamic changes, one must be wary of any suggested solution to the concussion assessment dilemma that utilizes only one testing approach.

The results from the current study confirm the shift in thinking that is currently taking place in the field of mild brain injury; namely, that concussions are not a transient injury that quickly resolves over a matter of days, but rather, one that has lasting effects that may lead to potentially catastrophic long term outcomes (Slobounov & Sebastianelli, 2006).

Effect of Concussion on Neural Pathways: Long Term Potentiation and Long Term Depression of Synaptic Activity

Before beginning a discussion that relates to the effects of concussion on the human cortex, the intricacies of the neuroanatomy and neurophysiology of this organ must be underscored. The human brain is an incredibly complex system, the likes of which are not paralleled by any other entity known to man. The complexity of the matter is elucidated by knowing that the brain has over 100 billion neurons, each linked to as

many as 10,000 others (Hebb, 1976). Understandings of the links between neuronal workings and mental and physical functioning are only beginning to be understood in spite of centuries of investigation. This complexity is probably the reason that no one unifying pathology has been found that is common to all concussive injuries and is also the probable explanation as to why no two injuries are alike in symptomolgy, pathology or resolution. As the neuropsychologist Donald O. Hebb (1976) stated, "it would be unrealistic to suppose that we will master its [the human brain's] intricacies … it seems quite possible that we will never master them fully, which means also that we may never fully understand the effects of brain injury" (p. 309). Though Hebb's theories are now over thirty years old, his ideas provide a useful framework for understanding the findings of the research under discussion here.

The task of tackling the many complex changes in individual neurons and their subsequent connections that result from mild brain injury is beyond the scope of this discussion. However, the effects of concussion are diffuse and are known to vary between injuries (Powell, 2001; Shaw, 2002). Therefore, any discussion of the effects of concussion must both view the brain as working collectively as a whole and, at the same time, focus on alterations in the integrated workings of localized areas. The discussion that follows is an attempt to illustrate, though not exhaustively, the effects of concussion on human functioning.

In his seminal work "The Organization of Behavior" (1949), Hebb advanced the fields of both neurology and psychology by moving beyond Pavlovian classical conditioning and operant learning's stimulus – response paradigms and creating an integrated model of brain function, learning and the operation of neural plasticity.

Hebb's main tenet was: "When an axon of cell A is near enough to excite cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased" (Hebb, 1949). This has come to be known as Hebbian Theory, in short, the neurons that fire together wire together. In 1973, Stent described the complement to Hebbian Theory, stating "when the pre-synaptic axon of cell A repeatedly and persistently fails to excite the postsynaptic cell B while cell B is firing under the influence of other pre-synaptic axons, metabolic changes take place in one or both cells such that A's efficiency, as one of the cells firing B, is decreased" (Stent, 1973). These theories gave rise to what is today known as neural plasticity.

The work of Rauschecker and Singer (1981) defined three rules which account for the neural mechanism of plasticity: (1) excitatory synaptic connections increase their efficiency when pre-synaptic afferents and post-synaptic target cells are concurrently active; (2) if the post-synaptic cell is active but the pre-synaptic fiber is silent, then synaptic efficiency decreases; (3) synaptic efficiency diminishes slowly over time, if post-synaptic (output) activity is missing. It is possibly this "plasticity" feature of the human neuronal system, more than any other, that is both responsible for the loss of function following mild brain injury as well as the return of function over time.

Plasticity is linked to the phenomena of long-term potentiation (LTP) and long-term depression (LTD). Albensi (2007) described LTP of synaptic transmission as a process that results in a persistent increase in the size of the synaptic component of the evoked response. LTD is the inverse of LTP, it is a weakening of a neuronal synapse that results when the firing of synapse A fails to excite synapse B causing metabolic changes

to take place in one or both cells such that A's efficiency, as one of the cells firing B, is decreased (Stent, 1973). As with any connection, timing is paramount in the development of LTP. As such, it has been demonstrated that "an enhancement of synaptic efficacy is not an inevitable consequence of correlated pre- and post-synaptic activity. Relative timing is of the essence, and, at the same synapse, it is possible to see either LTP or LTD develop" (Cooper, 2005). Magee and Johnston (1980) demonstrated that it was the interplay and specific timing of back-propagating action potentials (bpAP) paired with sub-threshold excitatory post-synaptic potentials (EPSPs) that amplifies dendritic action potentials (AP) and calcium influx, thus inducing LTP. The signals and chemical exchange that are crucial to this proper timing can easily be disrupted by the neurometabolic cascade that results following concussion. As previously discussed, following mild brain injury there is a dramatic increase in Ca++ influx to cortical neurons and an increase in the activation of NMDA receptors. This sudden increase of activity is followed by a spreading depression (Giza & Hovda, 2001). During the days to months following concussion the disruption in the chemical properties of the neurons, and more specifically the alterations in Ca++, it seems reasonable to postulate that there is a disruption in the timing of APs, bpAPs and EPSPs. This disruption most likely leads to LTD and therefore a reduction in the strength and/or number of synaptic connections in the cortex. This change is then reflected in the surface EEG in the days to weeks following concussion. The phenomenon of plasticity has been shown to develop over a period of days. Pascual-Leone et al. (1995) demonstrated that as people learned a new skill using their hand the motor representation of that hand in the cortex increased within a period of 5 days. In the current study EEG measures were taken beyond 7 days post

injury. Differences in EEG measures between groups were shown at this testing time. Based on the findings of Pascual-Leone et al. (1995), it can be argued that cortical changes in our injured group could reasonably have occurred since injury thus accounting for the differences in EEG measures between groups.

Shaw (2002) has done a review of EEG studies following concussion. This review demonstrated a large inconsistency in the specific findings among studies regarding EEG amplitude changes. He concluded that studies in this area demonstrated an initial state of excitability following concussion, but that there was not conclusive evidence that demonstrated a depression in cerebral electrical activity following mild brain injury. There is, however, a major flaw in his review. With the exception of studies that utilized anesthesia, all the studies reviewed recorded EEG within the first few minutes following the concussive blow (these studies reported EEG following concussions induced in rats or monkeys and in boxers immediately after a fight or knock-out). In light of the discussion of LTD, it can logically be argued that the negative effects of concussion that are measurable by electroencephalography may occur over a prolonged period of time, during the subsequent days to weeks following the injury, and would not have been detected by the studies reviewed by Shaw. This was in fact demonstrated by Kolb (1999) who studied dendritic growth in the cortex following lesions. He reported that dendritic growth was not present at day 7 post injury but that there was considerable increase in dendritic length and spine density between day 20 and 60. Pascual-Leone et al. (1995) also supported this notion of cortical change slightly delayed post injury by demonstrating that cortical representation of the hand increased by day 5 during the learning of a new skill with the hand. It is this delay in the changes of

neural mechanisms that might be one of the main factors that contributes to the findings of the many researchers who have successfully applied EEG to concussion assessment. This was indeed the case in our study where EEG changes between injured and normal subjects were shown beyond 7 days post injury. As stated, researchers such as Tebano, Thatcher, Hoffman, Thornton, Thompson, Korn and others, have found reductions in power and functional connectivity to be the most notable alterations in cortical functioning following concussive injury (Hoffman et al., 1995; Korn, 2005; Tebano et al., 1988; Thatcher et al., 1989; Thatcher et al., 1998; Thatcher et al., 2001; Thompson et al., 2005; Thornton, 2003). In the face of cortical disruption, both the chemical balance of cortical neurons and the cortical pathways that link these neurons are damaged giving rise to the diminution of some connections and the strengthening of others. These subsequent changes in cortical connectivity cause interference in the normal functioning of the cortex, the result of which can be manifest in abnormal neuropsychological, postural or EEG responses.

Electrical currents are created, for the most part, from cortical to cortical connections. These currents provide a way of observing and measuring changes, by means of the EEG, that occur as a result of concussion pathology. The differing distances between the columns of pyramidal cells is one of the factors that dictate the frequency of waves that are detected in the surface EEG (Lubar, 1997). Local, regional and global resonant loops differ in the EEG frequencies they produce. Local loops, the activity between adjacent macrocolumns of pyramidal cells and their support cells, appear to be responsible for the higher frequencies. Regional loops, activity between macrocolumns several centimeters apart, produce intermediate frequencies such as alpha

and beta. Global loops, on the other hand, reflect the activity between widely separated areas (such as frontal-parietal and frontal-occipital) and produce the slower frequencies such as delta and theta (Lubar, 1997). Following MTBI the shift that occurs in EEG recordings (e.g. a reduction in the higher frequencies) may result from damage to these resonant cortical loops. Much of the efficiency of thoughts and attention is determined by cortical inhibition that "shuts off" a cell assembly once it has performed its function (Hebb, 1976). Following brain injury the higher frequency of short axon cells, which are thought to be highly inhibitory in function, is disrupted since these small-diameter neurons are highly susceptible to toxins and nutritive lack (Hebb, 1976). This causes a disruption such that there is excess noise in the system leading to less efficient and less precise thought (Hebb, 1976). The disturbance of normal chemical flow following concussion was discussed earlier and can occur in the absence of positive imaging findings by MRI or CT, as is the case in the majority of mild brain injuries. However, the above noted changes in the brain following concussion result in alterations in the electrical activity of the cortex and can be measured by EEG.

The term homeostasis was coined by Cannon in the 1930's. This term was used to describe the maintenance of relatively stable values in the parameters of a system in the face of changing environmental conditions. This notion has since been applied to information processing systems, such as synapses or neural networks, whereby this system is maintained within a dynamic range and the sensitivity of response is kept optimal (Cooper, 2005). Following a cerebral concussion the information processing systems in the cortex are negatively affected due to the degradation of neural connectivity. The system effectively loses its ability to maintain homeostasis, thus

ceasing to function adaptively and is unable to respond appropriately to external task demands. Parallels have been drawn comparing a concussed brain to an aged brain, and the possibility that brain injury can lead to the early onset of brain aging characteristics has been studied (Cooper, 2005; Guskiewicz et al., 2005; Jordan, 2000; Toth, 2005). It was once again the insights of Hebb that very early on drew a correlation between the aging brain and brain injury. In his 1949 publication, "The Organization of Behavior", he noted parallels between brains that had suffered an injury and aging brains. "In both cases there is a loss of brain substance, and it appeared that, while there may be loss of what may be called raw, naked intellectual power, there is also a surprising retention of intellectual function in one's own area of thought". This may have been the first reported link between the now often studied association between mild brain injury and the early onset of Alzheimer's disease or Parkinson's syndrome. The loss of raw intellectual power can be thought of as the ability to form new memories and learn new tasks, while the "retention of intellectual function in one's own area of thought" may be the ability to remember past events and things learned earlier in life. A study by Corkin (1989) also demonstrated this link. By studying veterans in the years following brain injury he noticed a decline in cognitive abilities that had at first been recovered following the injury. Corkin noted that either the neural modifications that had initially allowed for the recovery of function were themselves susceptible to aging, or the processes were similar to the ones normally used for aging. In either case, since the neural modifications had occurred following the brain injury, this adaptation was not able to occur in the normal aging process since the brain is only able to perform this modification once. Additional support was lent to this hypothesis by Kolb (1999). Following brain injury in older rats

he did not observe the favorable behavioral outcome that he had first witnessed in younger rats with the same injury. Concomitant to this lack of behavioral recovery, he noted a failure for the older rats to show synaptic compensation. He supported the theory that functional changes coincide with synaptic changes by demonstrating that both occur in younger rats and neither occurred in older rats. He concluded that the results suggest that "(1) the brain may use similar mechanisms for ageing and recovery from brain injury; and (2) there is a limit to the plasticity of the cortex".

Impairments in learning and working memory are reported as some of the most common neuropsychological symptoms following injury (Bernstein, 2002; McAllister et al., 2001; McHugh et al., 2005). Hebb's general tenet was that synaptic plasticity is related to behavioral change, which was supported by the above discussed experiments by Corkin and Kolb. Although he theorized that there would be synaptic changes in a positive direction (a strengthening of synaptic connections with learning), the reverse is also true, as previously noted by Stent. These neural alterations were revealed in a study by McAllister et al. (2001). MTBI subjects were compared to normal subjects on a working memory task while concomitant fMRI images assessed brain activation. Their findings demonstrated that although measurable task performance outcomes did not differ significantly between groups on any task condition, MTBI subjects demonstrated a different pattern of allocation of processing resources during increased processing loads compared to healthy controls. They suggested that injury-related changes in the ability of concussed subjects to activate or modulate working memory processing resources might underlie some of the memory complaints after MTBI. It is apparent from this study that in order to achieve the same level of output, injured subjects utilize a greater number of

cognitive resources and that a demonstrable change takes place in neural processing following injury. This increase in the recruitment of neural resources during simple tasks leaves less cortical areas available when cognitive load is increased thereby possibly lowering the threshold of maximum processing capacity in injured subjects. Our study demonstrated that following injury athletes were able to perform the neuropsychological testing tasks as well as normal subjects beyond 7 days. This is most likely due to reorganization within the cortex such that these tasks can be performed. Our injured athletes were also able to perform the postural task while standing on a foam surface. EEG recordings taken during this task showed differences in EEG amplitude in the posterior regions between normal and injured subjects. As with the McAllister et al. (2001) study, although the overt task was accomplished, the cortical workings necessary to perform the task were different in injured subjects suggesting that a change has occurred in cortical organization.

Many studies have demonstrated functional recovery in concussed subjects in the days, months, or in more severe cases, years, following injury (Cavanaugh, 2006; Goldburg, 2004; Iverson, 2006; Mainwaring et al., 2005). The "Kennard Principle" is the name given to the finding that recovery of function following motor cortex lesions is greater in youth than it is in similar injuries in adults. Kennard hypothesized that "if some synapses were removed as a consequence of brain injury, others would be formed" and that in the newly developing brain the new pathways would be formed in "less unusual combinations" thereby producing more favorable outcomes. The first portion of the theory regarding the generation of new pathways is supported by much of the previously discussed literature in this section pertaining to plasticity. However, it is now

believed that mild brain injuries in younger, developing brains (although as stated the brain is actually in a constant state of dynamic change through life via LTP and LTD) actually manifest as worse outcomes than injuries sustained by a mature brain. This difference in the recovery of function is hypothesized to be due to a disturbance in the initial organization of neural pathways during the learning of novel tasks, and that there is a greater possibility of recovery in later stages of life since it should take less neural tissue to support certain types of behavior once learned than for initial learning (Kolb, 1999). Regardless of slight differences in each of the forgoing theories, the common thread is once again that neural reorganization after concussion is the mechanism by which functional recovery is possible. This functional recovery is demonstrated in studies such as that of Cavanaugh et al. showing postural improvements, and Iverson et al. who has demonstrated neuropsychological improvements. Assessment methods utilizing multiple testing modalities, such as the ones undertaken in the present study, link the neural changes, as assessed by EEG, with the functional changes, as assessed by neuropsychological and postural testing. This advancement in MTBI testing paradigms allows for the study of the link between synaptic plasticity and behavioral change.

This recovery of function is not to say that the subject is "as good as new", as is evident by the results of the studies on aging by Corkin (1989) and Kolb (1999), the imaging study by McAllister et al. (2001) and the results shown in the present study. Although in both McAllister's and our study, statistically significant differences were not present in neuropsychological testing between groups, both studies revealed cortical differences in processing. In addition, our study showed that complex tasks (an eyes closed standing on foam task) showed greater differences in cortical functioning between

groups than did a simple task (relaxed sitting with eyes closed). Hebb also recognized that the functioning of partially damaged cell assemblies might be less reliable than intact ones, as well as being more easily subject to disruption. This can be viewed as a very early insight into a phenomenon that was not specifically addressed until decades later, namely, second impact syndrome (Saunders & Harbaugh, 1984). Although Kolb did not draw a connection between his findings of dendritic growth following injury and second impact syndrome, there is a clear relationship. Kolb noted that there "might be a limit to dendritic growth". His findings revealed that cells that had once shown an increase in branching in response to injury were unable to show a further increase during learning whereas uninjured subjects did show this increase. He concluded that one can enhance branching either in response to injury or learning, but not both. When the significance of these findings is extrapolated to the phenomenon of recurrent injuries and second impacts, it is clear that the cumulative effects of concussion are most likely real. Neuropsychological testing has been mixed in its findings in this area. So much so that in papers published in 2004 and 2006, Iverson, Lovell and Collins made contradictory claims. The title of the first paper was "Cumulative effects of concussion in amateur athletes" published in *Brain Injury* in 2004. However, only 2 years later in 2006, they published in the *British Journal of Sports Medicine* an article titled "**No** cumulative effects for one or two previous concussions". In both cases the testing paradigm included only neuropsychological testing, specifically the ImPACT program. This demonstrates a discrepancy in outcome measures using a uni-modal testing paradigm. Therefore, it is important to recognize that concussion assessment methods must be multi-modal and should determine the cortical processing that underlies responses to external stimuli.

This will improve the validity of testing and help to ensure the future health of athletes returning to competition.

Clinical Utility of a Combined Modality Concussion Testing Paradigm

The three testing modalities applied in this study (neuropsychological, postural and EEG) have all been supported in the literature as sensitive measures for discerning between concussed and normal individuals (Collins et al., 2003; Echemendia et al., 2001; Guskiewicz et al., 1997; Guskiewicz, 2001; Guskiewicz et al., 2001; Haaland et al., 1994; Ingersoll & Armstrong, 1992; Thatcher et al, 1998; Thatcher et al. 2001; Thompson et al., 2005). As a consequence, they have been implemented and trusted as concussion diagnosis and return to play measures. Despite the empirical support for all three testing modalities, the prevalence and severity of repeat concussions (Guskiewicz et al.,2003; Kontos et al., 2006; McCrae et al., 2005) indicates that currently employed return to play measures, such as symptom resolution (Lovell & Pardini, 2006) or initial severity grading (Cantu, 2006) are either not stringent or not reliable enough.

The results presented in this study are conclusive in demonstrating that differences are present in the classification of athletes, even within the same athlete, depending upon the assessment technique used. At present, mild brain injury severity, as well as return to play assessments, are most often linked to an athlete's performance on neuropsychological tests (Notebaert & Guskiewicz, 2005). Symptom rating is one of the most relied upon tests for screening athletes prior to return to play. In fact, the definition of second impact syndrome hinges on this test since it is defined as "a case in which an

individual still has post-concussive *symptoms* but is allowed to return to sport participation, at which time he or she may be subjected to a second head injury" (Cantu, 2006). It is a grave mistake, however, to base an athlete's readiness for competition on symptom resolution when this does not always reflect lingering pathological abnormalities (i.e. symptom resolution is not necessarily indicative of injury resolution (Thompson et al., 2005). This is not to say that any other one testing modality will be a better indicator of injury resolution. What is indicated by this study is that any one type of testing, when used in isolation, has a relatively large potential for misdiagnosing a concussion and puts the athlete at risk by increasing the chance of a false negative finding. As discussed in the previous section, it is important to link the changes cortical functioning to the behavioral changes taking place. This should be the case in both the deficits that occur in symptoms and functioning immediately following concussion, as well as during the recovery phase.

The results of this study reveal the discrepancy between testing paradigms in their ability to classify subjects as either injured or normal. Neuropsychological testing, more specifically the Symptom Rating Scale, which was shown to be the most sensitive neuropsychological test, had a classification accuracy of 81.5% when administered within 24hrs of the injury. However, the effectiveness of this testing method was drastically reduced when administered beyond one week post injury. The ability of the Symptom Rating Scale to correctly classify injured subjects, who were still abnormal on postural and EEG testing, was only 35.7%. This finding, combined with the high use of the Symptom Rating Scale in concussion and return to play assessments, may have contributed to a previous belief that concussive injuries are "transient" in nature. The

Symptom Rating Scale should, therefore, be considered only as a useful single assessment tool for immediate use following injury. Balance assessment is also an effective tool for assessing concussion in the immediate minutes following injury. A shortcoming of EEG assessments following concussion is their lack of sensitivity close to the time of injury as was revealed by Shaw's (2002) review. A combined testing protocol, such as the one suggested by this study, allows for tests to support each other and therefore improves the reliability of the assessment.

In the moments immediately following injury the Symptom Rating Scale and posture testing would be sensitive measures to diagnose the concussion, whereas EEG alone might lack the necessary sensitivity. In serial assessments, however, the use of EEG testing would be necessary to determine if altered or supplementary cognitive processes were being utilized by the athlete in order to meet the task demands. Although the athlete may score within the normal range on the neuropsychological or postural assessments, the EEG measure would, in most cases, detect these altered cortical patterns. The sensitivity of the EEG measure is also enhanced by increasing the cognitive or physical demands during testing (e.g. standing on a foam surface). This supportive nature of the testing modalities is the key premise behind the sensitivity of a multi-modal testing paradigm.

An interesting finding arose concerning the use of the Symptom Rating Scale. A comparison between normal individuals and a concussed group that have returned to normal should not show significant differences in their symptom scores. However, subjects who have recovered symptomatically from a concussion show better scores on this test than normals. This is probably due to the subjective nature of the test. Athletes

who have been symptomatic report a complete or almost complete absence of symptoms associated with concussion. Subjects who have not incurred a mild brain injury, on the other hand, often report having a mild degree of some of the symptoms associated with concussion. In short, people who are tested using the Symptom Rating Scale after 1 week following a concussion are seemingly "more normal" than people who have never sustained a concussion. Similar "improvements" in test scores have previously been reported as a drawback to this testing modality (De Monte et al., 2005; Macciocch, 1990; Macciocchi et al., 1996; Rosenbaum et al, 2006; Tombaugh, 2006; Wilson et al., 2000). Specifically, it is the practice effects associated with the Symptom Rating Scale that most likely cause this paradox in test results. Practice effects are defined as some improvement in performance between concurrent test sessions based on familiarity with the procedures and/or previous exposure to the assessment (Valovich McLeod et al., 2004). The previous testing session and the familiarity with true symptoms from concussion most likely caused the recovering athletes to compare their symptoms at this second testing session with their symptoms during the first session, within 24 hours of the injury. In contrast, normal athletes taking the test most likely expressed how they were feeling that day, and may have reported feelings not specifically associated with a concussion, but rather symptoms that can result from other factors such as upcoming exams or other personal life stressors.

The addition of two neuropsychological tests that in the past have been considered to be valid assessment tools for concussion (Trails B test and Symbol Digit Substitution test (Randolph, 2005) did not improve NP testing accuracy when administered after a period of one week post-injury. The combination of the three tests produced a

classification accuracy that was correct only half the time. This finding was expected in our study and is consistent with numerous studies that have also shown return to normal on NP testing within one week following injury (Collins et al., 2003; Echemendia et al., 2001; Rosenbaum et al., 2006). This lack of sensitivity in NP testing beyond one week following mild brain injury was also shown in a study by Heitger et al. (2006) who reported "attention, short-term/working memory and general cognitive performance were preserved" at one week following concussion. Furthermore, Randolph et al. (2005) stated that the "effects of concussion on NP test performance are so subtle even during the acute phase of injury (1–3 days post injury) that they often fail to reach statistical significance in group studies. Thus, this method may lack utility in individual decision making because of a lack of sensitivity". They also stated that it has not yet been shown that NP testing is able to detect impairment in players once concussion-related symptoms have resolved. "Because no current guideline for the management of sport-related concussion allows a symptomatic player to return to sport, the incremental utility of NP testing remains questionable" (Randolph et al., 2005). This lack of sensitivity in NP testing was also noted in the previously discussed study by McAllister et al. However, instead of being classified as normal by their NP test results, the overall assessment sensitivity was intact due to the simultaneous brain imaging that took place during the NP tests. Here again is an example of how a multi-modality testing paradigm can improve testing validity by incorporating tests that support each other.

Conclusions

In conclusion, each testing modality demonstrates strengths in some areas but weaknesses in others. Neuropsychological testing is a very powerful tool for concussion assessments in the days immediately following the injury; however, its sensitivity diminishes within one week in the majority of cases. Virtual reality testing is a sensitive tool beyond seven days but showed a high number of false negatives, probably due to our athletic population. EEG measures are highly sensitive beyond seven days post injury but often do not detect injuries immediately post injury. It is for this reason that concussion assessment and return to play measures must incorporate multiple assessment types that support each other and fill in gaps left by single testing paradigms.

Mild Traumatic Brain Injury (MTBI) is a complicated injury requiring proper diagnosis and care. Numerous definitions of concussion have been proposed since it was first recognized. Over the past half century, concussion has predominantly been defined as a "short lasting", "temporary", or "transient" disturbance of neuronal function brought on by a sudden acceleration, deceleration and/or rotation of the head, usually without skull fracture (Shaw, 2002; Wilberger et al., 2006). The demonstrated and discussed inconsistencies in injury resolution dispute this definition since the terms "short lasting", "temporary" and "transient" have been shown to be invalid by recent research; investigations have shown that the effects of a mild traumatic brain injury can persist for months or even years (Slobounov et al., 2006; Thatcher et al., 1989, 1998, 2001). In light of the growing number of findings that demonstrate both functional and pathological differences in weeks to months following concussion, it is time to consider a shift in the

definition of concussion, more diversified testing paradigms and an increase in the recovery period before returning and athlete to competition.

Limitations of the Study

In the case of neuropsychological testing, only the Symptom Rating Scale was able to be administered within 24 hours of the injury. Having all three neuropsychological tests administered at the time of injury would have helped to validate them as sensitive tools early on in the assessment and, therefore, a change in their sensitivity, as was noted with the symptom rating scale, could have been measured. The lack of sensitivity of the trails B test and the symbol digit substitution test may have been present in all post injury measures, however, we were only able to comment on the lack of sensitivity of these tests at approximately one week post injury. Additionally, since NP testing has been shown to be sensitive in previous research a larger battery of NP tests could have possibly led to a more sensitive NP discriminant.

A second limitation resulted from the fact that EEG was not recorded during the VR or NP tests. This would have allowed for the measurement of cortical functioning during tasks that may be sensitive for assessing concussion. As scores improved on the functional tests of VR and NP, this concomitant EEG measurement would have allowed testers to see which brain regions were changing that were responsible for the improvements in performance. In our case we were only able to infer that differences in performance were due to the brain regions that differed in amplitude between groups.

Third, the mechanism of injury was not controlled in this study. Therefore, a reliance on self-report or the report of a trainer was needed to identify the mechanism of injury. Additionally, the lack of control over the forces applied to the brain and the level of injury, forced us to use a wide variety of types of concussive injury. This expanded the possible regions of brain injury and varied the severity of injury between subjects.

Future Research

Current testing upon which return to play decisions are based following a mild brain injury is insufficient to reliably detect the multiple impairments that may be present as a result of concussion. The results of the study and the discussion that followed supported this hypothesis. It is suggested that assessments need to combine tests that support each other and that evaluate the degree of cortical engagement during overt testing prior to making return to play decisions. Future research in the field should further investigate this combination of testing modalities that mutually support each other. This study did not incorporate longitudinal assessments but future studies that track the neural changes that underlie the functional improvements in testing over time would lend further evidence to support the idea of plasticity of the brain following injury. Additionally, tracking changes in regions that are known to be damaged following an injury will allow practitioners to follow recovery from pathology and their functional improvements. Basing return to play decisions on recovery from pathology rather than relying solely on functional changes may reduce the likelihood of a second concussion in athletes.

Second, future research should track the occurrence of second injuries and compare groups that have had underlying neurological recovery that coincides with functional improvement and those that do not. This could further validate the need for imaging (such as EEG, fMRI) during testing and again support the utility of a multi-modal testing paradigm. The addition of a larger battery of NP tests should be incorporated in future research to find tests that may be more sensitive than the ones used in this study. These tests could then be combined with imaging to detect cortical abnormalities while under cognitive task.

A third area of interest for future research would be to investigate whether recovery from second injuries, that occur in the same anatomical location as first injuries, show pathologic changes with functional recovery or whether, as Kolb suggested, there is a limit to dendritic growth. If there is a limit to dendritic growth, and anatomical recovery does not occur in a region following a second injury, then the idea of returning an athlete to competition when they do not show recovery from pathology should be questioned.

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Appendix A

Consent Form

INFORMED CONSENT FOR CLINICAL RESEARCH STUDY

The Pennsylvania State University
(version of use inside the state of Pennsylvania)

Title of Project: The Effects of Mild Traumatic Brain Injury on Neuropsychological Test Scores, Postural Stability and General Brain Function IRB# 14906

Principle Investigators: Semyon Slobounov, Ph.D., James W.G. Thompson

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This is to certify that I, _____, have been given the following information with respect to my participation as a volunteer in a program of investigation under the supervision of Semyon Slobounov. Ph.D.

1. Purpose of the Study: The main purpose of this investigation is to assess the behavioral and neurophysiological (physical brain attributes) indices of mild traumatic brain injury (MTBI), within subjects, on static (not moving) postural stability and general brain function. This experiment is novel in that it will use standard eyes open and eyes closed electroencephalographic (EEG, this is the recording of the electrical activity that the brain produces naturally) recordings and postural assessments during EEG recordings, as well as neuropsychological (the brain's cognitive processing mechanisms) testing pre and post injury within the same subject. It is the expectation of this research group that more meaningful and accurate measures of athlete's readiness for return to play will result.

2. Procedures to be followed: The main purpose of this investigation is to assess the behavioral, neuropsychological and neurophysiological effects of Mild Traumatic Brain Injury on postural stability and general brain function. This experiment is novel in that it will take EEG and balance measures during a manipulation of your visual field and under

normal postural adjustments as well as using standard neuropychological tests (the current gold standard in MTBI testing). EEG measures taken under functional proprioceptive challenges such as these have never been reported in the literature when looking at MTBI. The visual field manipulation will occur by having a 3-D image of a room with striped walls rotating side to side and front to back on a large screen in front of you. It is the expectation of this research group that more meaningful and accurate measures of student athletes readiness for return to play will result. This increase in accuracy for return to play will be due to the fact that when balance and EEG measures for athletes return to normal (as compared to within subjects pre-injury measures and databases currently used in hospitals and private practices based on thousands of subjects who are medically termed to have normal brainwave patterns) while looking at a moving visual field it will be indicative of their ability to function in an athletic environment in which many components of their visual field are moving in relation to each other. Current measures for return to play readiness only measure with respect to a static environment.

The hypothesis is: with the suffering of a MTBI, neurosychological, proprioceptive and neurophysiological components of an individuals brain will be negatively affected as shown by increased poorer neuropsychological test scores, postural instability and EEG patterns which deviate from a normalized database as well as from pre MTBI measures within subject.

The experiment will be divided into 3 parts: one pre-test measure at the onset of the study prior to any concussion you may suffer (will begin upon IRB approval), one post-concussion measure taken within 24-hours of injury and one return to play measure taken after a physician has cleared you for return to play. Upon arrival at the lab, you will remove your shoes and be measured for height and weight. You will then sit in a chair as the EEG electrodes are applied. Your scalp will be cleaned with rubbing alcohol; this is done to remove any oil and dirt residue on the scalp. An elastic cap containing 32 evenly spaced sensors will then be place on the head. The cap completely covers the scalp and the sensors are found from the back of the scalp to the forehead, and from ear to ear. A blunt-ended syringe (absolutely no injections are made) will then be filled with gel. The syringe is used to place the gel between the sensors on the cap and the scalp; this will help insure the researchers collect good clean signals. Two sensors will be placed, one on each ear, and two additional sensors will be placed, one above and one below the left eye. Standard EEG recordings will be taken under the following conditions: eyes open and eyes closed standing, eyes open and eyes closed under normal, everyday postural movements, eyes open and eyes closed seated and under a cognitive math task with eyes open and closed standing and seated. Following the EEG set up you will put on the flock-of-birds vest and stand on the force platform directly in front of the screen. The Flock of Birds vest is a light-weight padded vest (an adjustable personal floatation device purchased from Wal-Mart) with a strip of Velcro down the back. Attached to the Velcro are two flock of birds sensors which measure postural displacement and sway of the standing subject. The force plate measures your postural sway by measuring center of pressure movements based on the pressure displacements of the feet. The measures taken will be EEG using the Neuroscan EEG recording equipment or the Mitsar Corporation EEG equipment, and postural stability using the force plate and the Flock of Birds

sensors and the Balance Error Scoring System (BESS). Once on the force plate in front of the screen with the vest on, you will put on the 3-D glasses used for viewing the screen. You will be asked to remain as stable as possible with your hands at your sides, feet flat on the platform and eyes looking straight ahead. The screen in front of you will have five black and white striped walls (ceiling, floor, left wall, right wall and back wall). Six trials of 25 seconds in duration will occur with the subject in the static position. Each of the trials will have a manipulation of the visual field where the walls will move in various directions and at various speeds of oscillation (back and forth, side to side rotation, anterior/posterior rotation). Following each trial there will be a 10 second break before the onset of the next trial. The BESS consists of 3 postures held for 20 seconds each and each posture is performed twice (total of 6 postures held for 20 seconds each). The postures are; (1) two-footed stance with feet together and eyes closed, (2) one-footed stance on non-dominant foot with eyes closed, and (3) tandem stance with non-dominant foot forward. Each time you deviate from the specified posture within the test period 1 point will be marked. The total points for all postures will be added together to calculate a total score for postural stability.
The EEG recordings will not be linked to any of the other recording equipment, except in the instance of coordinating onsets of recording between the EEG and the force plate. At the completion of the six trials, you will be asked to remove the glasses and vest and step off the platform. The investigator will remove the Quikcap once you are seated.
The neuropsychological tests will be both computerized and paper and pencil administered. The tests consist of memory tests based on word and number sequences. Reaction time tests are a timed response to a visual signal presented on a computer screen.
This is the conclusion of the experiment and then you will be dismissed.

3. Discomforts and risks: Risks to you while participating in this experiment are minimal. There is a chance of dizziness, especially post concussion. Spotters will be used to aid you if you feel dizzy or begin to fall. The experiment will be terminated immediately at your request.

4. Alternative procedures which could be utilized: N/A

5. Time duration of procedures and study: You will spend a maximum of 1 hour per recording session. Data collection for all measures will terminate within one month of the completion of the 2002/2003 competitive season.

6. Statement of voluntary participation: Your participation in this study is voluntary and you may withdraw from this study at any time by notifying the investigator. Your withdrawal from this study or your refusal to participate will in no way affect your care or access to medical services. In the case of equipment malfunction this investigation will be terminated without your consent.

7. Right to ask questions: Any question with respect to the research and the investigation being performed can be directed to the researchers listed at the top of page

1. You may ask whatever questions you may have and all such questions should be answered to your satisfaction. You are free to deny a answer to any specific questions.

8. Medical care: You should understand that medical care is available from the University in the event of injury resulting from research but that neither financial compensation nor free medical treatment is provided. You should also understand that you are not waiving any rights that you may have against the University for injury resulting from negligence of the University or investigators. In the event of a research related injury, any of the people on page 1 can be contacted at the given phone numbers. You may contact the Office for Research Protections , (814) 865-1775 for additional information concerning your rights as a research participant.

9. Compensation: N/A

10. Confidentiality: Names of participants will not be associated with any data and will not be made available to anyone other than the researchers involved in the study. The following may review and copy records related to this research: The Office of Human Research Protections in the U.S. Dept. of Health and Human Services; The Penn State University Biomedical Institutional Review Board (IRB); The Penn State University Office for Research Protections.

11. Benefits: Increased safety and health benefits to persons suffering MTBI due to more sport relevant return to play diagnoses.

This is to certify that I am 18 years of age or older and that I consent to and give permission for my participation as a volunteer in this program of investigation. I understand that I will receive a signed copy of this consent form. I have read this form and understand the content of it.

_____

Volunteer Date

I, the undersigned, have defined and explained the studies involved to the above volunteer.

_____

Investigator Date

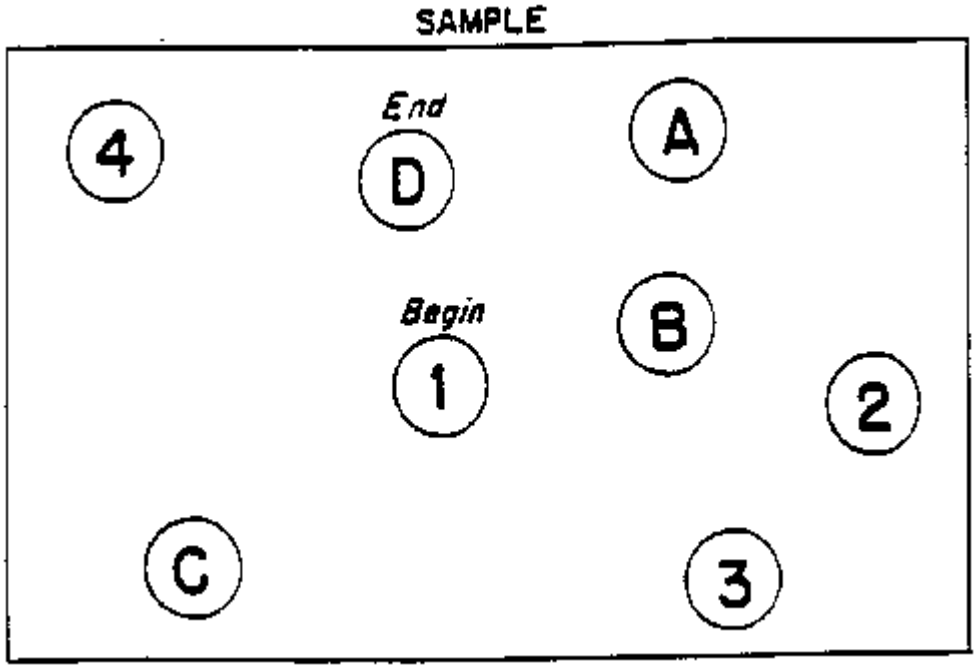
Appendix B

Neuropsychological Tests

TRAIL MAKING TEST – PART B

*"**On this page are some numbers and letters. Begin at number one** [point], **and draw a line from one to A** [point to A], **A to two** [point to 2], **2 to B** [point to B], **B to 3** [point to 3], **3 to C** [point to C], **and so on, in order until you reach the end. Remember, first you have a number, then a letter, then a number, then a letter and so on. Draw the lines as fast as you can. Ready! Go!"***

N.B. **If the athlete makes an error on the sample, correct her/him.**



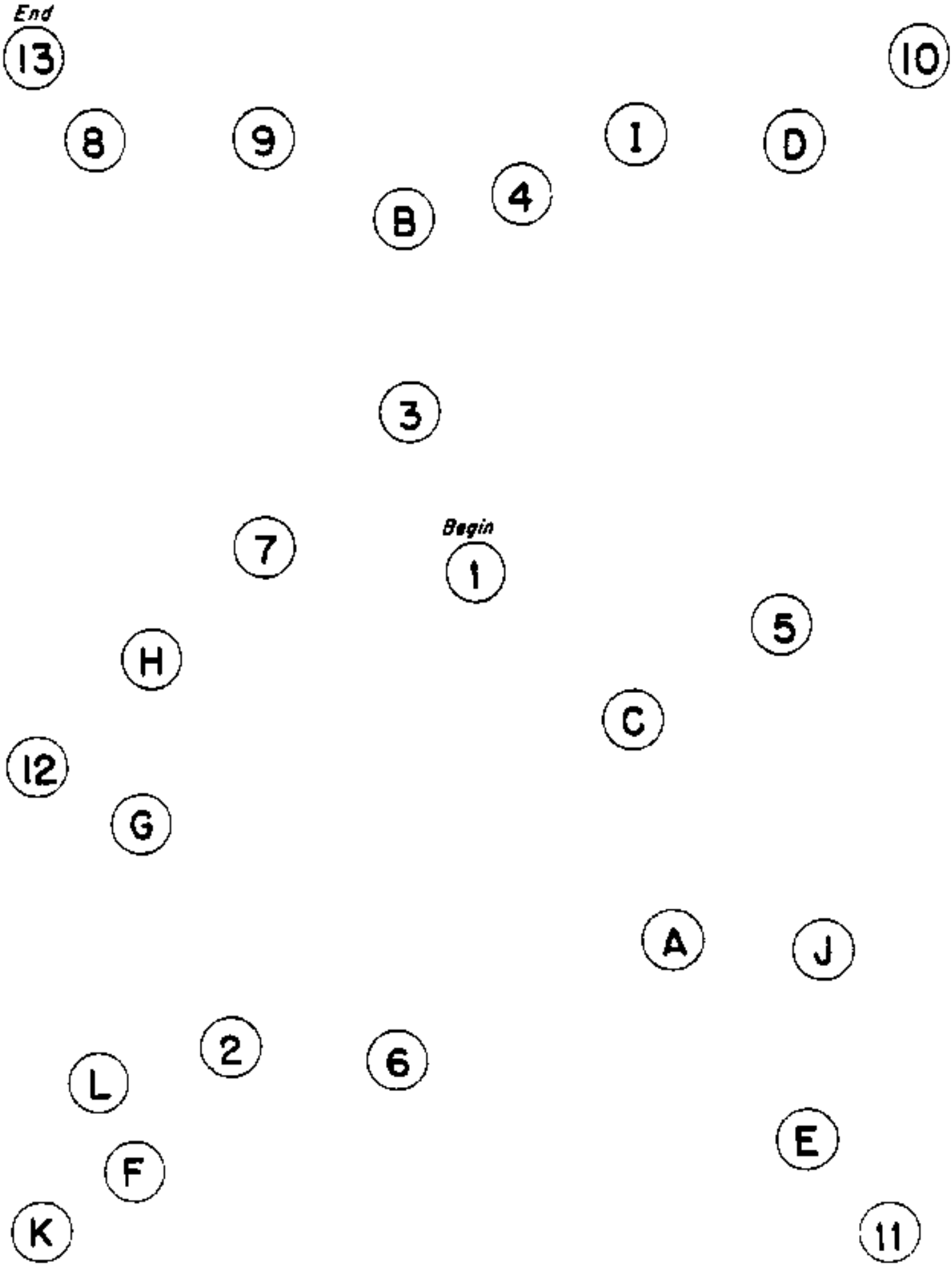
*"**On the other side of this page, I want you to do the same thing. Begin at number 1 and draw a line from 1 to A, A to 2 and so on, until you reach the end. Draw the lines as fast as you can. Any questions?"***

(Turn the page over, indicate where the start is [i.e. "1"] and where the finish is [i.e. 13], then say "Ready! Go!" and start the stopwatch until the athlete reaches the end. Record the time on the sheet in seconds.)

N.B. If the athlete makes an error, call it to his/her attention immediately and have him/her proceed from the point at which the mistake occurred. Do not stop timing.

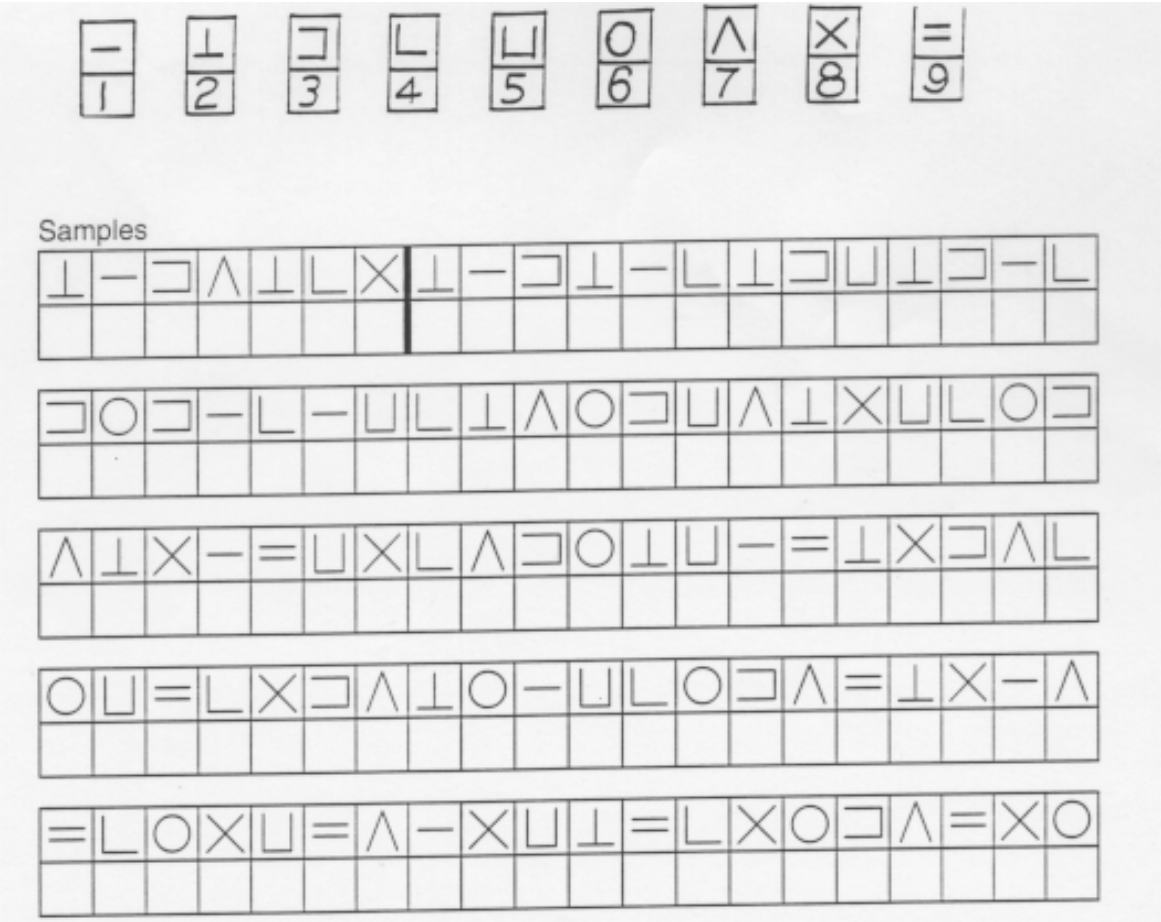
Record the following:

Time: _____ **# of errors:** _____


End
13
10
8
9
I
D
4
B
3
7
Begin
1
5
H
C
12
G
A
J
2
6
L
E
F
K
11

(Examiner's Copy)

KEY



Score @ 60 seconds: _____

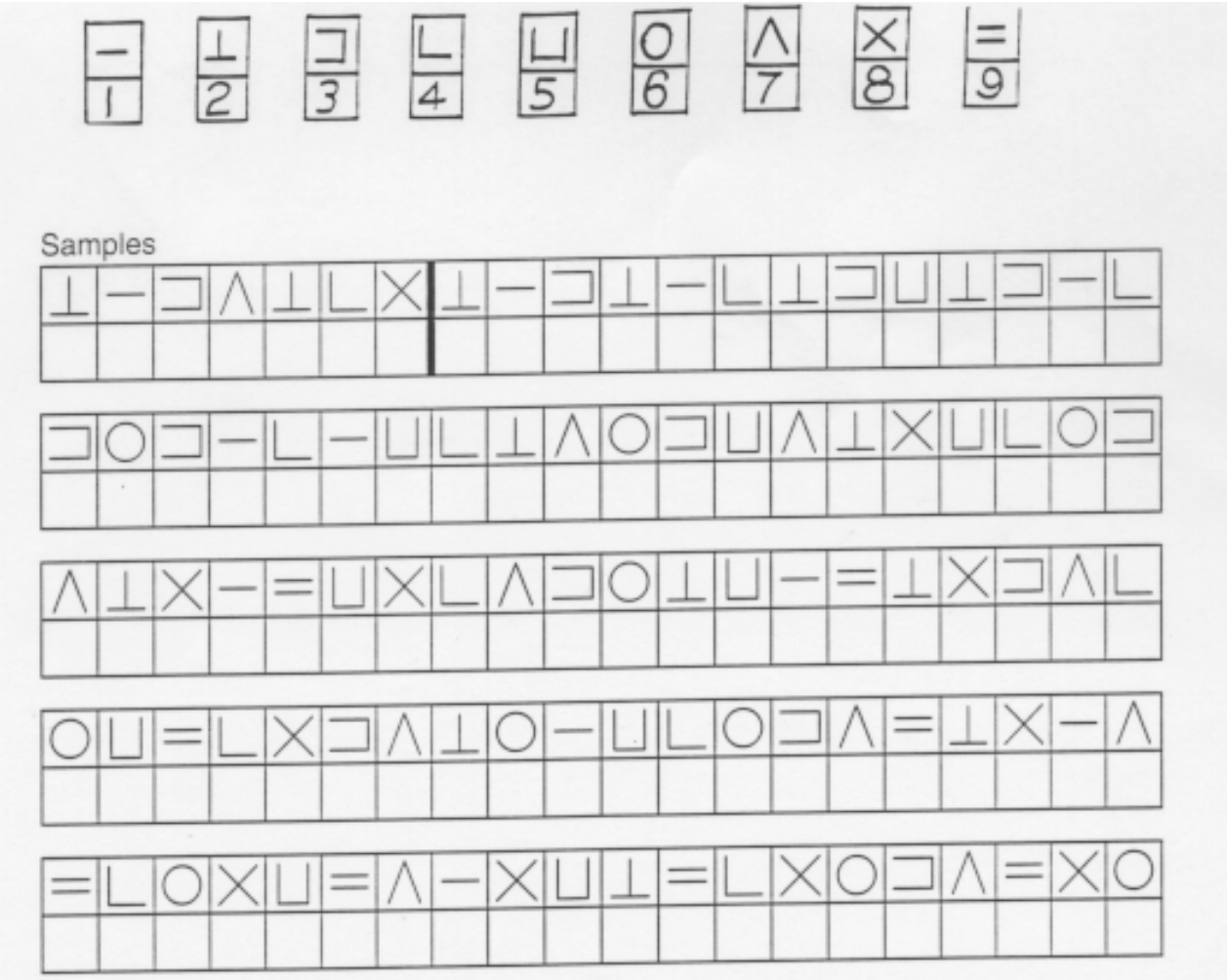
Score @ 90 seconds: _____

Name of Examiner: _____

Signature of Examiner: _____

(Athlete's Copy)

Please detach and give to athlete when administering Symbol-Digit Test.



Symptom Rating Scale

Place this form in front of the Participant and say: **This form lists symptoms that sometimes people have. Please look at this list and tell me if you are experiencing any of these symptoms now.** Have the participant scan the list. If they respond positively to any of these items say: **On a scale of 0 to 6, 0 being none and six being severe, how severely do you feel this symptom is for you currently.** Record their rating on the space provided.

Post - Concussion Symptoms Scale

Name:_____ **Code:**_____ **Date of Concussion:**_____

Rating

None **Moderate** **Severe**

0 1 2 3 4 5 6

Symptoms	Date/Time	Date/Time	Date/Time	Date/Time	Date/Time
Dizziness					
Headache					
Nausea					
Vomiting					
Balance problems					
Trouble falling asleep					
Sleeping more than usual					
Drowsiness					
Low Energy					
Sensitivity to light					
Sensitivity to noise					
More emotional than usual					
Irritability					
Sadness					
Nervous / Anxious					
Numbness or tingling					
Feeling slowed down					
Feeling like "in a fog"					
Difficulty concentrating					
Feeling "Pressure" in head					
Difficulty remembering					
Other:					
Total score					

Appendix C

Results Section Charts & Tables

A) Tests of Equality of Group Means and Classification Coefficients Tables

i) Neuropsychological Variables

Trails B and Symbol digit test > 7 days post injury

Tests of Equality of Group Means

	Wilks' Lambda	F	df1	df2	Sig.
Trails-B > 7days	.999	.071	1	50	.791
Symbol Digit > 7days	.974	1.356	1	50	.250

Classification Function Coefficients

	Injury	
	0	1
Trails-B > 7days	.826	.802
Symbol Digit > 7days	.981	.940
(Constant)	-52.406	-48.624

Fisher's linear discriminant functions

Symptom Rating Scale 24hrs

Tests of Equality of Group Means

	Wilks' Lambda	F	df1	df2	Sig.
Symptom Rating 24hrs	.665	26.245	1	52	.000

Classification Function Coefficients

	Injury	
	0	1
Symptom Rating 24hrs	.025	.097
(Constant)	-.806	-2.449

Fisher's linear discriminant functions

ii) Virtual Reality Variables

VR 3 variables

Tests of Equality of Group Means

	Wilks' Lambda	F	df1	df2	Sig.
.2Hz roll	1.000	.003	1	26	.955
.2Hz all wall	.800	6.508	1	26	.017
.3Hz all wall	.814	5.926	1	26	.022

Classification Function Coefficients

	Injury	
	0	1
.2Hz roll	2686.206	2726.665
.2Hz all wall	-73.817	-79.777
.3Hz all wall	-82.421	-87.462
(Constant)	-1235.512	-1265.540

Fisher's linear discriminant functions

VR 2 variables

Tests of Equality of Group Means

	Wilks' Lambda	F	df1	df2	Sig.
.2Hz all wall	.800	6.508	1	26	.017
.3Hz all wall	.814	5.926	1	26	.022

Classification Function Coefficients

	Injury	
	0	1
.2Hz all wall	26.095	21.640
.3Hz all wall	16.869	13.324
(Constant)	-20.959	-14.125

Fisher's linear discriminant functions

VR 0.2Hz all walls

Tests of Equality of Group Means

	Wilks' Lambda	F	df1	df2	Sig.
.2Hz all wall	.800	6.508	1	26	.017

Classification Function Coefficients

	Injury	
	0	1
.2Hz all wall	31.289	25.743
(Constant)	-15.563	-10.759

Fisher's linear discriminant functions

VR 0.3Hz all walls

Tests of Equality of Group Means

	Wilks' Lambda	F	df1	df2	Sig.
.3Hz all wall	.814	5.926	1	26	.022

Classification Function Coefficients

	Injury	
	0	1
.3Hz all wall	22.851	18.284
(Constant)	-11.347	-7.514

Fisher's linear discriminant functions

iii) EEG Variables

EEG 18 variables

Tests of Equality of Group Means

	Wilks' Lambda	F	df1	df2	Sig.
T5alphasec	.921	5.054	1	59	.028
T5beta2sec	.899	6.623	1	59	.013
T5beta3sec	.912	5.728	1	59	.020
P410Hzsec	.926	4.734	1	59	.034
Pz10Hzsec	.918	5.289	1	59	.025
T5 alphafoam	.907	6.069	1	59	.017
T5 beta2foam	.867	9.032	1	59	.004
P4 10Hzfoam	.925	4.775	1	59	.033
O2 10Hzfoam	.919	5.221	1	59	.026
Pz 10Hzfoam	.910	5.833	1	59	.019
T5beta2stec	.915	5.515	1	59	.022
P3-alpha sec	.919	5.232	1	59	.026
P4-alpha sec	.918	5.247	1	59	.026
P3-alpha foamec	.902	6.423	1	59	.014
P4-alpha foamec	.898	6.732	1	59	.012
P3-alpha stec	.914	5.545	1	59	.022

Classification Function Coefficients

	Injury	
	0	1
T5alphasec	.125	.055
T5beta2sec	-.751	-.567
T5beta3sec	.153	.300
P410Hzsec	-.176	-.151
Pz10Hzsec	.175	.143
T5 alphafoam	-.059	-.024
T5 beta2foam	1.961	1.096
P4 10Hzfoam	.186	.219
O2 10Hzfoam	-.062	-.061
Pz 10Hzfoam	-.122	-.139
T5beta2stec	-.520	-.322
P3-alpha sec	-.249	-.151
P4-alpha sec	.139	.099
P3-alpha foamec	.183	.109
P4-alpha foamec	-.069	-.064
P3-alpha stec	.021	.036
(Constant)	-4.604	-2.447

Fisher's linear discriminant functions

EEG 6 Variables

Tests of Equality of Group Means

	Wilks' Lambda	F	df1	df2	Sig.
T5beta2sec	.899	6.623	1	59	.013
T5 beta2foam	.867	9.032	1	59	.004
Pz 10Hzfoam	.910	5.833	1	59	.019
P3-alpha foamec	.902	6.423	1	59	.014
P4-alpha foamec	.898	6.732	1	59	.012
T5 alphafoam	.907	6.069	1	59	.017

Classification Function Coefficients

	Injury	
	0	1
T5beta2sec	-.335	-.195
T5 beta2foam	1.157	.716
Pz 10Hzfoam	.016	-.001
P3-alpha foamec	.012	.006
P4-alpha foamec	.013	.014
T5 alphafoam	.002	.000
(Constant)	-3.723	-1.864

Fisher's linear discriminant functions

EEG 4 Variables

Tests of Equality of Group Means

	Wilks' Lambda	F	df1	df2	Sig.
T5beta2sec	.899	6.623	1	59	.013
T5 beta2foam	.867	9.032	1	59	.004
P3-alpha foamec	.902	6.423	1	59	.014
P4-alpha foamec	.898	6.732	1	59	.012

Classification Function Coefficients

	Injury	
	0	1
T5beta2sec	-.343	-.193
T5 beta2foam	1.157	.717
P3-alpha foamec	.017	.006
P4-alpha foamec	.016	.014
(Constant)	-3.713	-1.863

Fisher's linear discriminant functions

EEG 3 Variables

Tests of Equality of Group Means

	Wilks' Lambda	F	df1	df2	Sig.
T5 beta2foam	.867	9.032	1	59	.004
P3-alpha foamec	.902	6.423	1	59	.014
P4-alpha foamec	.898	6.732	1	59	.012

Classification Function Coefficients

	Injury	
	0	1
T5 beta2foam	.871	.556
P3-alpha foamec	.017	.006
P4-alpha foamec	.015	.013
(Constant)	-3.666	-1.848

Fisher's linear discriminant functions

EEG 2 Variables

Tests of Equality of Group Means

	Wilks' Lambda	F	df1	df2	Sig.
T5 beta2foam	.867	9.032	1	59	.004
P4-alpha foamec	.898	6.732	1	59	.012

Classification Function Coefficients

	Injury	
	0	1
T5 beta2foam	.843	.547
P4-alpha foamec	.032	.019
(Constant)	-3.593	-1.840

Fisher's linear discriminant functions

iv) Combined Discriminant Function Variables

18 EEG, 3 VR, 2 NP Variables

Tests of Equality of Group Means

	Wilks' Lambda	F	df1	df2	Sig.
.2Hz roll	.987	.284	1	21	.600
.2Hz all wall	.771	6.241	1	21	.021
.3Hz all wall	.763	6.507	1	21	.019
T5alphasec	.981	.412	1	21	.528
T5beta2sec	.755	6.810	1	21	.016
T5beta3sec	.802	5.173	1	21	.034
P410Hzsec	.973	.579	1	21	.455
Pz10Hzsec	.995	.098	1	21	.758
T5 alphafoam	.963	.803	1	21	.380
T5 beta2foam	.655	11.047	1	21	.003
P4 10Hzfoam	.956	.975	1	21	.335
O2 10Hzfoam	.936	1.445	1	21	.243
Pz 10Hzfoam	.974	.556	1	21	.464
T5beta2stec	.774	6.147	1	21	.022
P3-alpha sec	.972	.608	1	21	.444
P4-alpha sec	.958	.920	1	21	.348
P3-alpha foamec	.925	1.699	1	21	.207
P4-alpha foamec	.926	1.685	1	21	.208
P3-alpha stec	.971	.630	1	21	.436
Trails-B > 7days	.981	.415	1	21	.526
Symbol Digit > 7days	.993	.146	1	21	.706

Classification Function Coefficients

	Injury	
	0	1
.2Hz roll	22723.749	23190.779
.2Hz all wall	-818.166	-852.215
.3Hz all wall	-1231.263	-1277.767
T5alphasec	-36.519	-36.834
T5beta2sec	266.869	270.448
T5beta3sec	93.108	93.306
P410Hzsec	-21.865	-22.268
Pz10Hzsec	26.774	28.044
T5 alphafoam	.887	1.142
T5 beta2foam	-181.756	-187.131
P4 10Hzfoam	50.280	50.705
O2 10Hzfoam	13.091	13.123
Pz 10Hzfoam	-42.014	-43.037
T5beta2stec	-85.158	-86.462
P3-alpha sec	52.258	52.920
P4-alpha sec	-11.746	-12.259
P3-alpha foamec	26.966	26.620
P4-alpha foamec	-53.837	-53.633
Trails-B > 7days	4.045	4.193
(Constant)	-10406.564	-10788.875

Fisher's linear discriminant functions

7 EEG, 2 VR Variables

Tests of Equality of Group Means

	Wilks' Lambda	F	df1	df2	Sig.
.2Hz all wall	.800	6.508	1	26	.017
.3Hz all wall	.814	5.926	1	26	.022
T5beta2sec	.683	12.071	1	26	.002
T5beta3sec	.693	11.512	1	26	.002
T5 beta2foam	.575	19.235	1	26	.000
O2 10Hzfoam	.894	3.071	1	26	.092
T5beta2stec	.697	11.278	1	26	.002
P3-alpha foamec	.886	3.352	1	26	.079
P4-alpha foamec	.886	3.332	1	26	.079

Classification Function Coefficients

	Injury	
	0	1
.2Hz all wall	30.781	25.403
.3Hz all wall	28.471	21.203
T5beta2sec	3.222	2.467
T5beta3sec	-.450	-.463
T5 beta2foam	4.731	2.945
O2 10Hzfoam	.133	.086
T5beta2stec	-4.177	-2.944
P3-alpha foamec	.341	.263
P4-alpha foamec	-.359	-.268
(Constant)	-39.963	-22.221

Fisher's linear discriminant functions

Pooled Within-Groups Matrices

		.2Hz all wall	.3Hz all wall	T5beta2 sec	T5beta3 sec	T5 beta2 foam	O2 10Hz foam	T5 beta2 stec	P3 alpha foamec	P4 alpha foamec
Correlation	.2Hz all wall	1.000	.266	-.079	.107	-.090	.112	-.055	.079	.142
	.3Hz all wall	.266	1.000	-.045	.166	-.141	-.019	.019	.056	.074
	T5beta2 sec	-.079	-.045	1.000	.718	.813	.082	.909	.075	.130
	T5beta3 sec	.107	.166	.718	1.000	.576	.033	.641	.098	.144
	T5 beta2foam	-.090	-.141	.813	.576	1.000	.035	.849	.070	.120
	O2 10Hzfoam	.112	-.019	.082	.033	.035	1.000	.175	.832	.871
	T5beta2 stec	-.055	.019	.909	.641	.849	.175	1.000	.159	.201
	P3-alpha foamec	.079	.056	.075	.098	.070	.832	.159	1.000	.950
	P4-alpha foamec	.142	.074	.130	.144	.120	.871	.201	.950	1.000

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% C.I. of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
.2Hz all wall	Equal variances assumed	5.105	.032	2.551	26	.017	.168488	.066046	.032729	.304246
	Equal variances not assumed			2.725	15.846	.015	.168488	.061827	.037317	.299658
.3Hz all wall	Equal variances assumed	6.310	.019	2.434	26	.022	.186338	.076546	.028996	.343681
	Equal variances not assumed			2.559	19.785	.019	.186338	.072804	.034367	.338310
T5beta2 sec	Equal variances assumed	8.073	.006	2.574	59	.013	1.336382	.519274	.297317	2.375446
	Equal variances not assumed			2.596	47.824	.013	1.336382	.514857	.301095	2.371669
T5beta3 sec	Equal variances assumed	3.500	.066	2.393	59	.020	2.002617	.836776	.328232	3.677002
	Equal variances not assumed			2.410	51.302	.020	2.002617	.830967	.334619	3.670615
T5 beta2 foam	Equal variances assumed	9.443	.003	3.005	59	.004	1.632855	.543309	.545695	2.720014
	Equal variances not assumed			3.031	47.785	.004	1.632855	.538679	.549643	2.716067
O2 10Hz foam	Equal variances assumed	11.365	.001	2.285	59	.026	32.708105	14.314638	4.064581	61.351630
	Equal variances not assumed			2.316	36.733	.026	32.708105	14.124701	4.081720	61.334491
T5beta2 stec	Equal variances assumed	8.783	.004	2.348	59	.022	1.428049	.608088	.211267	2.644831
	Equal variances not assumed			2.372	44.411	.022	1.428049	.602031	.215053	2.641046
P3-alpha foamec	Equal variances assumed	7.797	.007	2.534	59	.014	27.104432	10.694431	5.704926	48.503939
	Equal variances not assumed			2.566	38.904	.014	27.104432	10.562800	5.737471	48.471394
P4-alpha foamec	Equal variances assumed	15.026	.000	2.595	59	.012	24.464610	9.428753	5.597718	43.331501
	Equal variances not assumed			2.618	46.658	.012	24.464610	9.343818	5.663637	43.265582

4 EEG, 1 VR Variables

Tests of Equality of Group Means

	Wilks' Lambda	F	df1	df2	Sig.
.3Hz all wall	.814	5.926	1	26	.022
T5 beta2foam	.575	19.235	1	26	.000
O2 10Hzfoam	.894	3.071	1	26	.092
T5beta2stec	.697	11.278	1	26	.002
P3-alpha foamec	.886	3.352	1	26	.079

Classification Function Coefficients

	Injury	
	0	1
.3Hz all wall	29.422	22.245
T5 beta2foam	4.162	2.517
O2 10Hzfoam	.058	.033
T5beta2stec	-2.085	-1.423
P3-alpha foamec	-.007	.001
(Constant)	-22.657	-11.258

Fisher's linear discriminant functions

Pooled Within-Groups Matrices

		.3Hz all wall	T5 beta2foam	O2 10Hzfoam	T5beta2stec	P3-alpha foamec
Correlation	.3Hz all wall	1.000	-.141	-.019	.019	.056
	T5 beta2foam	-.141	1.000	.035	.849	.070
	O2 10Hzfoam	-.019	.035	1.000	.175	.832
	T5beta2stec	.019	.849	.175	1.000	.159
	P3-alpha foamec	.056	.070	.832	.159	1.000

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
.3Hz all wall	Equal variances assumed	6.310	.019	2.434	26	.022	.186338	.076546	.028996	.343681
	Equal variances not assumed			2.559	19.785	.019	.186338	.072804	.034367	.338310
T5 beta2foam	Equal variances assumed	9.443	.003	3.005	59	.004	1.632855	.543309	.545695	2.720014
	Equal variances not assumed			3.031	47.785	.004	1.632855	.538679	.549643	2.716067
O2 10Hzfoam	Equal variances assumed	11.365	.001	2.285	59	.026	32.708105	14.314638	4.064581	61.351630
	Equal variances not assumed			2.316	36.733	.026	32.708105	14.124701	4.081720	61.334491
T5beta2stec	Equal variances assumed	8.783	.004	2.348	59	.022	1.428049	.608088	.211267	2.644831
	Equal variances not assumed			2.372	44.411	.022	1.428049	.602031	.215053	2.641046
P3-alpha foamec	Equal variances assumed	7.797	.007	2.534	59	.014	27.104432	10.694431	5.704926	48.503939
	Equal variances not assumed			2.566	38.904	.014	27.104432	10.562800	5.737471	48.471394

2 EEG, 1 VR Variables

Tests of Equality of Group Means

	Wilks' Lambda	F	df1	df2	Sig.
.3Hz all wall	.814	5.926	1	26	.022
T5 beta2foam	.575	19.235	1	26	.000
O2 10Hzfoam	.894	3.071	1	26	.092

Classification Function Coefficients

	Injury	
	0	1
.3Hz all wall	25.574	19.686
T5 beta2foam	1.858	.949
O2 10Hzfoam	.036	.021
(Constant)	-19.342	-9.697

Fisher's linear discriminant functions

Pooled Within-Groups Matrices

		.3Hz all wall	T5 beta2foam	O2 10Hzfoam
Correlation	.3Hz all wall	1.000	-.141	-.019
	T5 beta2foam	-.141	1.000	.035
	O2 10Hzfoam	-.019	.035	1.000

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
.3Hz all wall	Equal variances assumed	6.310	.019	2.434	26	.022	.186338	.076546	.028996	.343681
	Equal variances not assumed			2.559	19.785	.019	.186338	.072804	.034367	.338310
T5 beta2 foam	Equal variances assumed	9.443	.003	3.005	59	.004	1.632855	.543309	.545695	2.720014
	Equal variances not assumed			3.031	47.785	.004	1.632855	.538679	.549643	2.716067
O2 10Hz foam	Equal variances assumed	11.365	.001	2.285	59	.026	32.708105	14.314638	4.064581	61.351630
	Equal variances not assumed			2.316	36.733	.026	32.708105	14.124701	4.081720	61.334491

B) Classification Tables for Calculation of Specificity, Sensitivity and Odds Ratios

i) NP Discriminants

Trails B & Symbol Digit Substitution > 7 days post injury

Classification Results(b,c)

		Injury	Predicted Group Membership		Total
			0	1	
Original	Count	0	16	13	29
		1	10	13	23
Cross-validated(a)	Count	0	16	13	29
		1	10	13	23

b 55.8% of original grouped cases correctly classified.
c 55.8% of cross-validated grouped cases correctly classified.

Symptom Rating within 24hrs

Classification Results(b,c)

		Injury	Predicted Group Membership		Total
			0	1	
Original	Count	0	26	3	29
		1	10	15	25
Cross-validated(a)	Count	0	26	3	29
		1	10	15	25

b 75.9% of original grouped cases correctly classified.
c 75.9% of cross-validated grouped cases correctly classified.

ii) VR Discriminant: 0.3Hz all walls

Classification Results(b,c)

		Injury	Predicted Group Membership		Total
			0	1	
Original	Count	0	12	1	13
		1	6	9	15
		1	40.0	60.0	100.0
Cross-validated(a)	Count	0	12	1	13
		1	6	9	15

b 75.0% of original grouped cases correctly classified.
c 75.0% of cross-validated grouped cases correctly classified.

iii) EEG Discriminant: P4 alpha foamec, T5 beta2 seated

Classification Results(b,c)

		Injury	Predicted Group Membership		Total
			0	1	
Original	Count	0	20	11	31
		1	5	25	30
Cross-validated(a)	Count	0	19	12	31
		1	6	24	30

b 73.8% of original grouped cases correctly classified.
c 70.5% of cross-validated grouped cases correctly classified.

iv) Combined Discriminant: 0.3Hz all walls, T5 beta2 foam, O2 10Hz foam

Classification Results(b,c)

		Injury	Predicted Group Membership		Total
			0	1	
Original	Count	0	12	1	13
		1	1	14	15
Cross-validated(a)	Count	0	11	2	13
		1	1	14	15

b 92.9% of original grouped cases correctly classified.
c 89.3% of cross-validated grouped cases correctly classified.

VITA

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EDUCATION

PENNSYLVANIA STATE UNIVERSITY — State College, PA
Faculty of Kinesiology (Psychophysiology), PhD (All But Dissertation) — Jan 2002 – Present
M. S. Conferred May, 2004

UNIVERSITY OF BRITISH COLUMBIA — Vancouver, BC
Faculty of Human Kinetics (Major: Health and Fitness, Minor: Commerce) — 1996-1999
B.Sc. (Class A standing)

WORK EXPERIENCE

AMERICAN APPLIED NEUROSCIENCE INSTITUTE — New York, NY
Consulting: Physiology Assessment forPerformance Enhancement — Jan 2006 - Present

TORONTO REHABILITATION INSTITUTE — Toronto, ON
Concussion & Psychophysiology Research Coordinator/Co-investigator — Feb 2005 – Feb 2006

BIOFEEDBACK INSTITUTE OF TORONTO — Mississauga, ON
Quantitative Electroencephalography 19-electrode assessments, — Sept 1999 - Present

PUBLICATIONS & PRESENTATIONS

Co-Presenter: *"Optimizing Performance & Health – Assessment Methods"*
Biofeedback Foundation of Europe (BFE) Annual Conference. February 2007, Berlin, Germany.

Thompson, J.W.G. (2006). *"EEG Changes and Balance Deficits following concussion: One Piece of the Puzzle".* S. Slobounov, W. Sebastianelli. *Foundations of sport-related brain injuries.* Ma., Springer.

Invited Speaker: "*Statistics and Research Design in Biofeedback" & "EEG utility in the Assessment of Brain Injuries"* Biofeedback Certification Institute of America (BCIA) - Neurofeedback Fundamentals Workshop. September, 2006, Ontario, Canada

Thompson, J., Sebastianelli, W., Slobounov, S. (2005). *"EEG and Postural Correlates of Mild Traumatic Brain Injury in Athletes".* Neuroscience Letters, 377, 158-163.

Poster Presentation: "*EEG Correlates of Traumatic Brain Injury in Athletes"*
North American Society for the Psychology of Sport and Physical Activity (NASPSPA)
2004 Annual Meeting: Vancouver, British Columbia, Canada

Invited Speaker: *"Optimal Performance Training for Executives Using Neurofeedback Training"*.
International Society for Neuronal Regulation (ISNR) 2002 Annual Meeting: Scottsdale, Arizona, U.S.A.

RESEARCH AWARDS

The Physicians' Services Incorporated Foundation (PSI).
"*Empirically Validated Return-to-Play Guidelines for Sport-Related Concussions"*
$155,000 (CDN), 2 years, beginning 2005, concludes 2007.