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# Concussion

## State-of-the-Art

*Edited by Ioannis Mavroudis*

# Concussion - State-of-the-Art

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# Meet the editor

Dr. Ioannis Mavroudis is a consultant neurologist and Senior Lecturer in Neurology at the University of Leeds, UK. He has extensive research, clinical, and medicolegal experience in functional neurological disorders, traumatic brain injury (TBI), and post-concussion syndrome (PCS). His contributions to these fields have been invaluable, combining clinical acumen, academic prowess, and a deep understanding of the underlying neuroanatomy and pathology. Dr. Mavroudis has gained recognition for his rigorous research in neuropathology, leveraging innovative techniques such as the Golgi method to shed light on central nervous system disorders. His list of published works spans a wide spectrum of topics, including Alzheimer's disease, dendritic alterations, and synaptic pathology. Dr. Mavroudis' research has led to pivotal breakthroughs in understanding PCS and TBI. His publication, "Functional Overlay Model of Persistent Post-Concussion Syndrome," serves as a testament to his dedicated focus in these areas, establishing a new understanding of PCS and its enduring effects. He has authored significant works to promote public understanding and clinical advancement in the field of concussion, such as Concussion: A Patient's Guide to Understanding and Coping (2023) and Concussion - State of the Art (2023). As the academic editor of the latter, Dr. Mavroudis exhibits his commitment to disseminating knowledge and advancing the medical community's grasp of concussion and its aftermath. Dr. Mavroudis has an MD as well as degrees in criminology, forensic medicine, and computing. He also has a Ph.D. in Neuromorphic Computing and Neuronal Morphology. He is a credentialed consultant in concussion management and prevention. He is trained in diagnostic neuropathology, neurophysiology, and psychiatry. He is currently the lead of the Concussion Clinic and the co-director of the Functional Neurological Disorders Clinic. His dedicated exploration of functional neurological disorders and mild traumatic brain injuries, reflected in his clinical work and research endeavors, underscores his comprehensive approach to understanding, diagnosing, and managing these complex conditions.

# Contents

# Preface

*Concussion – State-of-the-Art* is a comprehensive exploration of concussion, a topic of significant importance in the medical field. This book is the culmination of extensive research and collaboration with experts in various disciplines, all dedicated to enhancing our understanding of concussion and its multifaceted impact on individuals and society.

The initial chapters provide an in-depth understanding of the pathophysiology and neuropathology of concussion, laying a solid foundation for the subsequent sections. The book then transitions into a detailed discussion on the physiological and blood biomarkers of concussion, providing valuable insights into the diagnostic and monitoring tools available in the field.

The latter part of the book is dedicated to the rehabilitation of concussion patients, offering a comprehensive guide to the recovery process. It highlights the importance of a multidisciplinary approach in managing concussions and provides practical strategies to optimize patient outcomes.

One of the unique features of this book is its exploration of the impact of concussions on individuals following their release from prison. The final section sheds light on the often-overlooked population of mild traumatic brain injury (mTBI) patients in the criminal justice system, highlighting the need for specialized care and services for this group.

*Concussion – State-of-the-Art* is more than just a book; it is a testament to the ongoing efforts to understand and manage concussion. It is an invaluable resource for clinicians, researchers, and anyone interested in the complex world of concussion.

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Section 1

# Introduction

Chapter 1

# Introductory Chapter: Understanding Concussion – From Immediate Impact to Long-Term Sequelae

*Ioannis Mavroudis*

## 1. Introduction

The field of concussion research has seen remarkable advancements over the past decades. As awareness of the consequences of traumatic brain injuries has grown, so too has our understanding of the complexities of concussion and its sequelae, including Postconcussion Syndrome (PCS). This introductory chapter sets the stage for a comprehensive exploration of concussion, focusing on its definition, the intricacies of PCS, and the ever-present need for further research in this domain.

A concussion, a type of mild Traumatic Brain Injury (mTBI), is typically caused by a blow to the head or a sudden jolt to the body that causes the brain to bounce or twist within the skull. This results in temporary neurophysiological changes and, potentially, neurological symptoms, which can vary widely from person to person and event to event [1].

## 2. Pathophysiology of concussion

Understanding the pathophysiology of concussion is crucial to our interpretation of its effects. A concussion occurs when a force transmitted to the head causes the brain to rapidly accelerate or decelerate, resulting in the brain moving within the confines of the skull. This results in a cascade of neurophysiological events. Upon impact, there is an immediate release of neurotransmitters, which leads to a subsequent ionic flux. This flux affects cellular function, leading to energy imbalance, decreased cerebral blood flow, and changes in metabolism, a state known as 'neurometabolic cascade'. This cascade is thought to be responsible for the myriad of physical, cognitive, and emotional symptoms observed following a concussion [2]. There is a significant recovery period during which the brain is believed to be more susceptible to further injury. This period of vulnerability, combined with the non-specific nature of concussion symptoms, makes management and treatment of concussions a clinical challenge. Understanding these pathophysiological changes not only explains the symptoms following a concussion but also informs why rest and protection from further injury are central to concussion management [3].

## 3. Symptoms of concussion

Concussions can result in an array of diverse and sometimes subtle symptoms, which are generally divided into four categories: physical, cognitive, emotional, and sleep-related. The onset of these symptoms can be immediate or may appear days or even weeks after the injury. Symptoms of a concussion can include headaches, dizziness, fatigue, cognitive impairments such as difficulty concentrating or memory problems, and emotional changes. These symptoms usually resolve within weeks but, for some individuals, they may persist for months or even longer, leading to a condition known as postconcussion syndrome.

Physical symptoms are often the most noticeable and can include headache, dizziness, balance issues, nausea, vomiting, blurred vision, sensitivity to light or noise, and fatigue. There can also be transient changes in neurological function, such as brief loss of consciousness or a state of being dazed or confused immediately after the impact [4].

Cognitive symptoms, while less visible, can be just as debilitating. They include difficulties with memory (particularly short-term memory), concentration, attention, and speed of information processing. These issues can persist and may significantly impact an individual's ability to work or study following a concussion [4, 5].

Emotional symptoms are another vital aspect of concussion and can sometimes be overlooked. Changes in mood, irritability, heightened emotions, anxiety, and depression are commonly reported. It is crucial to recognize these emotional symptoms, as they can have a significant impact on recovery and can often be managed with appropriate support and intervention [4, 5].

Sleep-related symptoms are also common, with individuals reporting changes in sleep patterns such as sleeping more or less than usual, having trouble falling asleep, or experiencing fatigue despite adequate sleep [6].

The complexity and diversity of concussion symptoms underscore the need for a thorough assessment by healthcare professionals trained in concussion management. The constellation of symptoms can also vary significantly from person to person, making individualized care a necessity. Further research is needed to better understand the mechanisms underlying these various symptoms and to develop targeted treatments.

## 4. Postconcussion syndrome

PCS is a controversial diagnosis given its broad and non-specific symptomatology, which can overlap with a range of other conditions, including depression, anxiety, and post-traumatic stress disorder. Postconcussion syndrome (PCS) is a complex disorder characterized by a constellation of symptoms that persist for weeks or months after a concussion. The diagnosis of PCS is typically considered when a patient experiences concussion symptoms that last beyond the usual recovery period, typically defined as beyond three months post-injury. The heterogeneity of PCS symptoms, combined with the lack of universal diagnostic criteria or objective biomarkers, presents a unique set of challenges for clinicians and researchers alike. Despite these challenges, a better understanding of PCS and the development of effective management strategies remain a priority given the significant impact that prolonged symptoms can have on a person's quality of life [7].

Symptoms of PCS closely mirror those experienced immediately after a concussion but they persist beyond the expected recovery timeframe. These symptoms encompass

a range of physical, cognitive, and emotional issues. Physical symptoms like persistent headaches, dizziness, and fatigue are common, as are cognitive problems like difficulty concentrating and memory issues. Emotional symptoms can include depression, anxiety, irritability, and significant changes in mood or personality.

The etiology of PCS is not entirely understood. While some of the symptoms may be related to persistent physiological changes in the brain following a concussion, other symptoms may be influenced by non-physical factors, including psychological responses to the injury and its impact on daily life. This brings us to the concept of functional symptoms in PCS. Functional Neurological Disorder (FND), also known as conversion disorder, involves symptoms that are not consistent with recognized neurological conditions and are believed to have a psychological basis. In the context of PCS, functional symptoms may arise as a reaction to the stress and anxiety associated with the concussion and its aftermath. For instance, a patient might experience non-epileptic seizures, movement disorders, or functional limb weakness, none of which can be explained by the physiological damage caused by the concussion.

Diagnosing and treating PCS, particularly when functional symptoms are present, requires a multidisciplinary approach. It often involves neurologists, psychologists, physiotherapists, and occupational therapists. Treatment may involve not only interventions to manage physical symptoms but also psychological support and therapy to help patients cope with their symptoms and the impact of these symptoms on their daily lives.

The possibility of functional symptoms in PCS underlines the complexity of this disorder and the need for further research to understand its causes, development, and optimal treatments.

The current state of concussion research has yielded vital insights into the pathophysiology, risk factors, and management strategies for concussion and PCS [8]. However, significant gaps remain, and many aspects of these conditions are still poorly understood. We are yet to understand why some people recover quickly from a concussion while others develop persistent symptoms, and how we can predict and influence these outcomes.

## 5. Final thoughts

This book is an endeavor to address these gaps in understanding and to provide a state-of-the-art overview of concussion research. It brings together the work of leading experts in the field, spanning topics from the biomechanics of concussion and advanced neuroimaging techniques, to the complexities of diagnosis and management of PCS, return-to-play decisions, and the legal and ethical implications of concussion in sports and other domains.

We hope that by encapsulating the current understanding and outstanding questions in concussion research, this book will not only serve as a valuable resource for clinicians, researchers, and students, but will also highlight the pressing need for continued research in this domain. After all, it is through ongoing exploration and a constant push for knowledge that we will be able to provide the best care for those affected by concussion and PCS, and effectively reduce the burden of these conditions in the future.

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Section 2

# Diagnosis, Neurophysiology, Neuropathology and Biomarkers

Chapter 2

# Value of Quantitative Electroencephalography in Diagnosis and Management of Mild to Moderate Traumatic Brain Injury: Case Series of 150 Football Players with Multiple Concussions

*John L. Merritt*

**Abstract**

Multiple sports-related concussions have been associated with neurocognitive impairments ranging from a mild dementia to full Alzheimer's disease. Quantifying injuries and associated impairments is important to a diagnosis and management strategy. In addition to a necessary history and physical exam, other testing is always needed to confirm clinical suspicions. Radiology and imaging is often added, but they are often insensitive and nonspecific. An often neglected alternative or addition is electrophysiological assessment. Quantitative EEG, such as eVox, (which we call functional EEG) is one such readily available, objective electrophysiological system that has a large database with which to refer. In our clinic we evaluated a case series of 150 retired former professional American Football players who presented with histories of concussion and persistent symptoms of cognitive impairments. Their evaluations included comprehensive examinations, brain MRI (concussion protocol,) neurocognitive testing, and quantitative electroencephalography (Evoke NeuroScience.). Males, ages 32 to 65 years with professional football careers ranging from 1 to 18 years. Physical exams included ataxia of speech and gait, word finding impairments, nystagmus, pendular reflexes, and abnormal affect. Neurocognitive testing revealed impairments in up to five cognitive domains. MRI (concussion protocol) were positive findings in only 34%. Evoke EEG findings included delayed P300a and P300b, reduced EEG power in regions associated with working memory, and information processing and alterations in heart rate variability. The physical-neurological exam provided some objective findings, but they were often subtle. Brain MRIs were abnormal in only 34%. Neurocognitive testing identified abnormalities in all cases. The Evoke EEG provided electrophysiological abnormalities in all cases. Evoke EEG is sensitive and objective, and adds confirmatory neurophysiological data that correlate tightly with formal neurocognitive impairments and symptoms. Additionally, specific abnormal patterns provided objective rationale for targeted treatment regimens, including neurofeedback and neurocognitive training.

**Keywords:** brain injury, concussion, electrophysiology, biomarkers, biofeedback

## 1. Introduction

The recognition and diagnosis of mild to moderate traumatic brain injury, mTBI, continues to be challenging, even in a world with advanced and expensive technology. Even nomenclature can be perplexing and further confusion occurs when terms like concussion, or post-concussion state are intermixed. The American Congress of Rehabilitation and the World Health Organization have defined clinical criteria but clear diagnoses continue to be elusive and the incidence varies from 200/100,000 to over 700/100,000 [1]. Diagnostic tools are initially associated with radiology. But x-rays and CT scans are overwhelmingly insensitive and MRI and Spect scans are most often negative or nonspecific. A high index of suspicion and neuro-psychological testing are keys, but the latter is often delayed, arduous, complicated by potential tester bias and with much delayed results.

Here we focus on the value of electrophysiological testing in the diagnosis of mTBI, using a readily available system that can be performed in an outpatient clinical setting, The eVox system by Evoke NeuroScience.

Quantitative Electroencephalography, which we call Functional EEG due to its ability to quantify brain waves loci while active physiological functions are underway, has been available in university research settings for over 30 years [2–6]. It was, however, introduced into outpatient clinical settings by commercial entities 12 years ago, such as Evoke Neuroscience of New York, which we used in this study. These commercial systems have standardized the protocols and all results are uploaded to a central processing mainframe system which contains thousands of tests, for age, gender specified reference for comparisons [7].

We added Evoke NeuroScience EEG testing to our clinical testing protocol seven years ago and have found that it's availability in the clinical setting was practical, useful, and provided timely confirmatory electrophysiological data which could aid in the diagnosis, when combined with history, physical examination, and neurocognitive testing. Although our clinical population includes brain injury cases from multiple causes, motor vehicle accidents, falls, infections, hypoxia, here we report the results of a case series of 150 professional football players, with histories of multiple sports-related concussions.

## 2. Methodology

The system consists of an initial, short subjective neurocognitive screener, then application of an individually sized electrode cap with 22 electrodes attached to a laptop computer with the Evoke software. Continuous EEG recordings are made during 5 minutes of rest, with eyes open, followed by 5 minutes rest, with eyes closed, and then 10 minute of continuous recordings as the patient performs tasks from the computer screen. This task includes identifying by pressing a button when a large blue ball appears on the screen during a series of other items appearing on the screen and in one's earpieces. An electrode on the chest over the heart records an EKG rhythm strip during the testing.

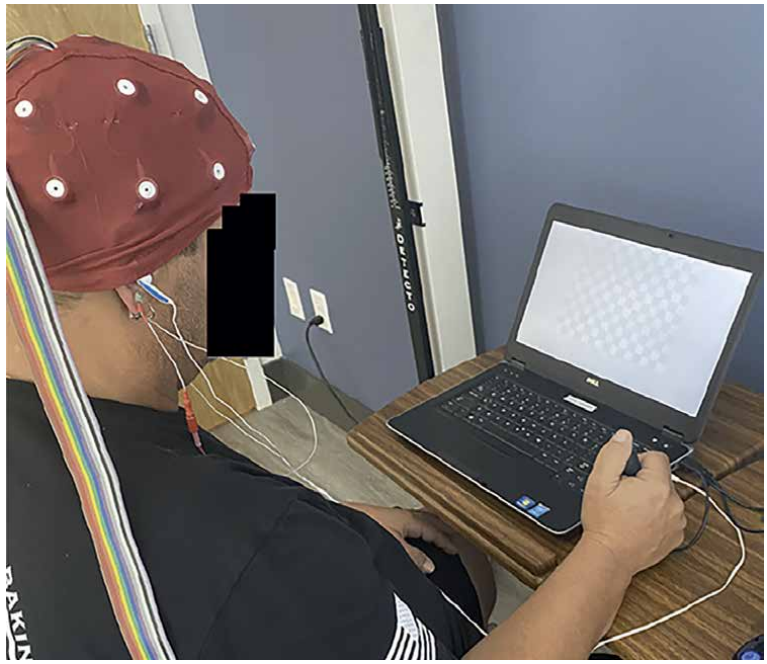


**Figure 1.**
*A subject during testing.*

**Figure 2.**
*Another subject during testing.*

Photos examples during testing.
See (**Figures 1** and **2**).
Objective neurophysiology components obtained from the testing consists of:
Heart-Rate Variability (HRV).
Event-Related Potentials (ERPs).
P300a, P300b, N100
Brain Mapping: Head Maps.
EEG Source Localization: LORETA.
Theta: Beta Ratio.
Peak Alpha Frequency (PAF).

*Examples of these items are illustrated below: in* **Figures 3**–**7**.

As in this Evoke NeuroReport example, objective electrophysiological data is reported after analysis compared to the central mainframe database of over 60,000 examinations.

The Neuropsychological Screener is indeed subjective and repetitive of separate clinical and neuropsychological testings.

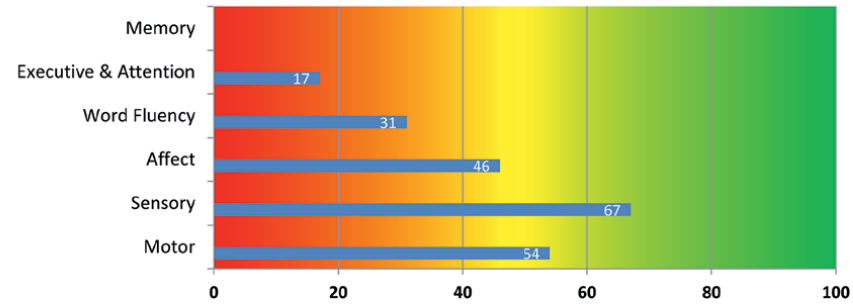
The remaining data are objective.

| | Date of Birth: | | Date of Test: |
|---|---|---|---|
| **Report Code**: | **Age:** 63 yr 1 mo | **Gender:** Male | **Handedness**: Right |
| **Symptoms**: Short term memory loss. More dependant on staff and tech. Mood swings, shortened fuse. PTSD stress while driving. photophobia, hypercusis. Night sweats. Word finding shallenges. | | | |
| **Medications**: Locertin 25mg, Melatonin 29mg HS. ; | | | |

**Neuropsychological Screener**

Score Range: 0 – 100%
Ref Range: >= 60 %

Screener Domain:




Global Score: 57 %

Memory Subtypes

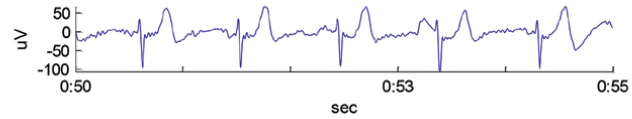
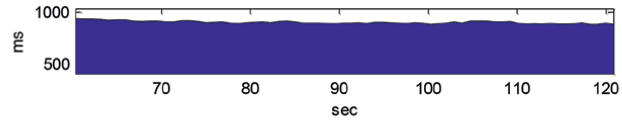
Based on responses to Neuropsychological Screener in the Memory domain

| | |
|---|---|
| **Spatial Navigation** | 100 % |
| **Temporal Orientation** | 88 % |
| **Procedural Actions** | 70 % |
| **Episodic Memory for Places** | 75 % |
| **Face Recognition** | 83 % |
| **Semantic Word Knowledge** | 33 % |

**Figure 3.**
*Neuropsychological screener.*

**Heart Metrics**

**ECG Raw Data Quality Review**

| Data Type | Raw Data Sample |
|---|---|
| **Cardiac Waveform (P-Q-R-S wave)** Image taken from pre-artifacted ECG |   |
| **Heart Rate Variability** |   |

**ECG Heart Metrics**

| Metric | Result | Reference Range |
|---|---|---|
| Heart rate | 67 bpm | 50 - 80 bpm |
| QRS duration | 0.167 sec | 0.06 - 0.12 sec |

**Heart Rate Variability (HRV): Autonomic Nervous System Metrics**

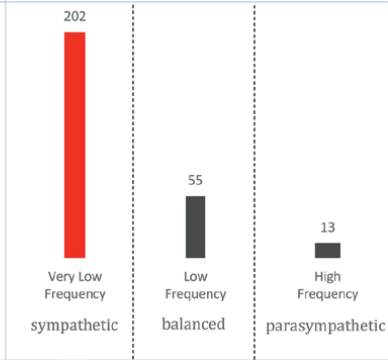
| Metric | Result | Reference Range |
|---|---|---|
| SDNN | 27 ms | 65 - 150 ms |
| Total power | 271 $ms^2$ | >= 800 $ms^2$ |
| HRV Frequency Spectrum: Power ($ms^2$) |   | VLF < LF > HF |

**Figure 4.**
*Heart metrics.*

Heart-Rate Variability (HRV) is an objective evaluation of the autonomic nervous system, which, we remind ourselves, is a brain-controlled process, which is reflected in the variability of the heart rate during the testing. The balance between sympathetic and parasympathetic power in this case shows a high sympathetic dominance. This can be the basis for home-based HRV neuro-biofeedback training, utilizing readily available home-based systems, which can be monitored remotely by the clinician.

Event-Related Potentials (ERPs) document the time elapsed through identified neural circuits related to attention (P300a), information processing (P300b), and visual (N100.) This documents conduction speed through this well described circuit. In this case there is significant prolonged latencies for P300a and P300b, but normal in N100 [8–11].

## Event-Related Potentials (ERPs)

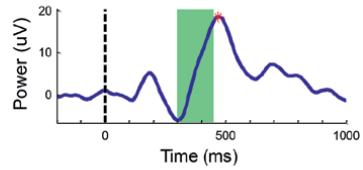
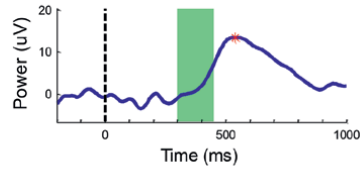
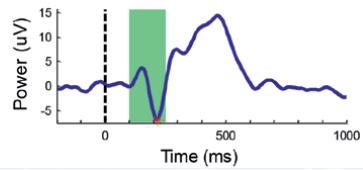
| ERP Component | Electrode Location/ Stimulus | Waveform | Result | Reference Range |
|---|---|---|---|---|
| Attention (P300a) | CZ<br>Checker-board Stimulus |  | Speed: 468 ms<br>Power: 18.6 uV | < 450 ms<br>>= 6 uV |
| Info processing (P300b) | PZ<br>Target Stimulus |  | Speed: 540 ms<br>Power: 13.5 uV | < 450 ms<br>>= 6 uV and >50% P300a power |
| Visual (N100) | O2<br>Checker-board Stimulus |  | Speed: 216 ms<br>Power: -6.9 uV | < 250 ms<br><= -6 uV |

**Figure 5.**
*Event-related potentials (ERPs).*

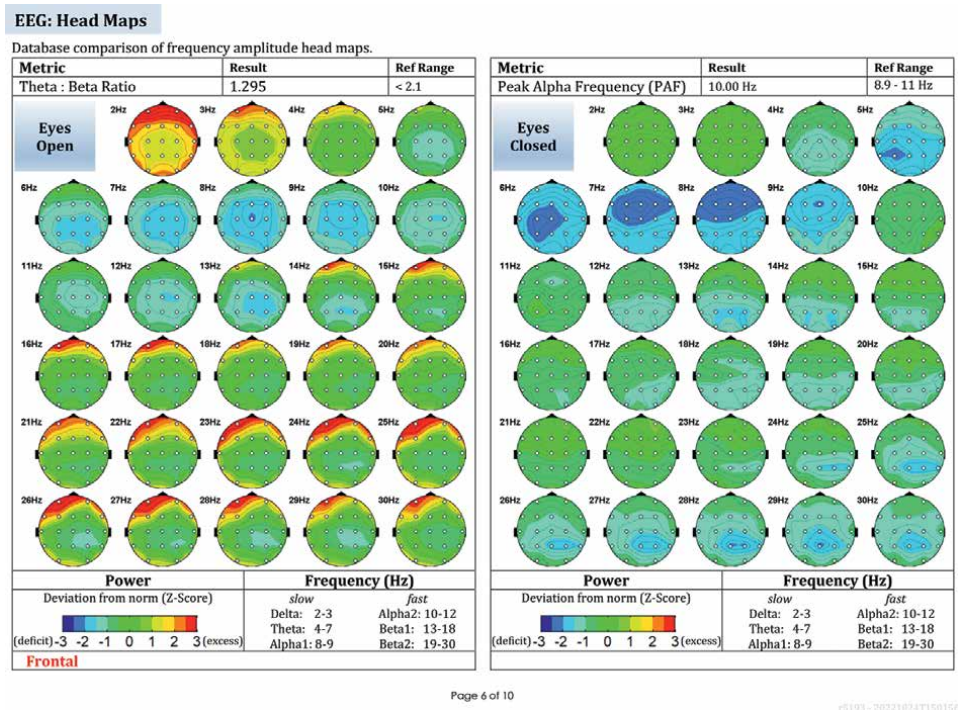



**Figure 6.**
*EEG head maps.*

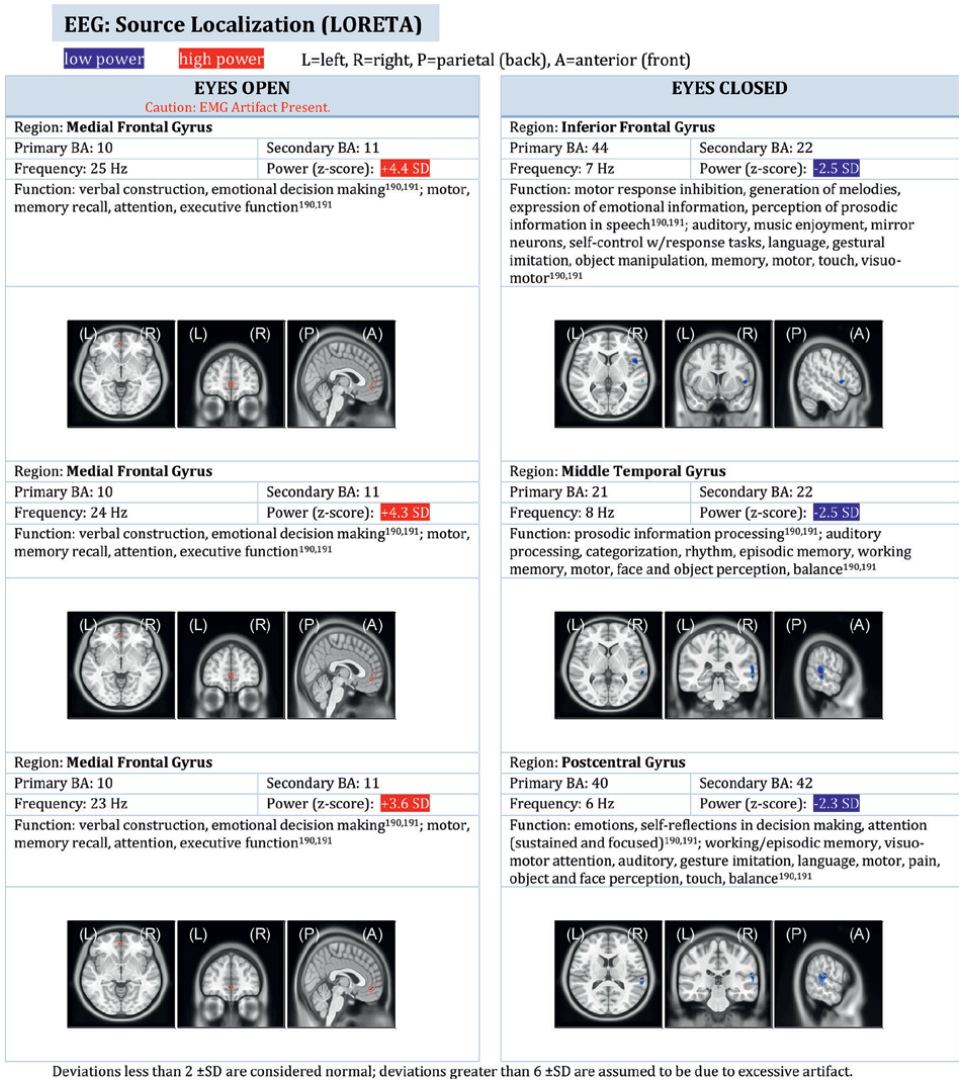



**Figure 7.**
*EEG: Source localization (LORETA).*

EEG Head Maps provide important visual overview of EEG power from brain waves of 2 Hz to 30 Hz, including delta, theta, alpha 1, alpha 2, and beta 1 and beta 2 frequencies, with localization of power over the entire brain, from a top looking down perspective. Deviations in EEG power is illustrated in normal, 1, 2 and 3 standard deviations from normal. In the case illustrated here, there are regional EEG power deviations that can be correlated with regional brain physiology and processes. This information can be optimized by neurobiofeedback training toward specific regions of abnormal EEG power [12].

EEG: Source Localization (LORETA) provides localization of abnormal (excessive high, excessive low) EEG power by localizing to specific Brodmann areas. These anatomical gyri and loci and be then clinically correlated with known neurocognitive functions of these brain regions.

## 3. Results

As expected in American Football alumni all patients were male. Their ages ranged from 32 years to 65 years, with professional football careers ranging from 1 to 18 years, in addition to their college and high school careers. At the time of examination all were ambulatory and 75% were currently employed. Common findings on physical examinations included ataxia of speech and gait ataxia, word finding impairments, nystagmus, pendular reflexes, and abnormal affect. Neurocognitive testing in all cases revealed impairments from mild to marked impairments in up to five cognitive domains. Previously obtained MRI studies (concussion protocol) revealed positive findings in only 34%, with some with scattered areas of gliosis, hemosiderin deposition and focal and global atrophy. Most MRI studies, 66%, even using a concussion protocol, were negative.

Evoke functional EEG findings, however, showed electrophysiological abnormalities in all cases. These included delayed P300a latency under visual attention tasks at the vertex, delayed P300b latency under go-no-go conditions, and slowed response times to visual and cognitive stimuli. There was also commonly low localized frontal and parietal EEG power, reduced neuronal capacity in regions associated with cognition and working memory, abnormal theta/beta ratios, abnormalities in visual, auditory processing, information processing and working memory tracts. Alterations in heart rate variability with reduced vagal activity, sympathetic dominance and baroreflexive activity were prevalent.

## 4. Conclusions

In evaluation of mTBI the physical and neurological examination provides objective findings that are subtle, and significant in only a minority of cases. Brain MRIs with concussion protocol provide positive finding in less than a third of cases and are often non-specific. Formal neurocognitive testing identified abnormalities in all cases, but this may be delayed and remote to busy clinical determinations. In this case series of known concussions, we found that the functional EEG (Evoke Neuroscience) provides valuable, objective electrophysiological data that is without evaluator bias. We note that other, similar systems are also available to practicing brain injury medicine physicians in clinical settings and are not endorsing a specific system, only reporting on our finding with this system. We conclude that such in office electrophysiological technology is currently available and can add confirmatory objective electrophysiological findings that provide meaningful data which correlate with clinical examinations of neurocognitive impairments for mild/moderate traumatic brain injury in a clinical setting. We are currently studying this technology and other technologies in other brain disorders. Additionally, it should be emphasized that even beyond a confirmed diagnosis, identifying abnormal electrophysiological functions also provides specific scientific rationale for targeted treatments and treatment monitoring regimens [13].

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Chapter 3

# Novel Techniques in the Assessment of Sports-Related Traumatic Brain Injury

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## Abstract

Mild traumatic brain injuries (mTBI) or concussions are a substantial health concern, particularly in collision and contact sports. Consequently, there is growing concern regarding the acute and chronic effects of repeated brain trauma. Traditional assessment of mTBI has been based on clinical or computed tomography (CT) assessments followed by a period of in-hospital observation in some cases. These may have significant time and cost implications while potentially exposing patients to ionizing radiation and providing a low sensitivity and specificity. Recent advancements have focused on novel modalities that may potentially predict early and long-term sequelae from mTBI with greater accuracy and provide the optimum personalized treatment plan in collaboration with the athlete. This chapter will outline state of the art in these modalities, from salivary and blood biomarkers imaging and neuropsychology assessments, and discuss their translational applicability to the clinical setting.

**Keywords:** concussion, sports, head injury, neuroimaging, biomarker, return to play

## 1. Introduction

Traumatic brain injury (TBI) is a leading global cause of mortality and morbidity, with an estimated 69 million people globally suffering from TBI annually. The leading mode of injury in TBI is road traffic accidents, with the Western Pacific and Southeast Asia experiencing the highest global disease burden [1]. TBI may be categorized by severity in correlation to the Glasgow Coma Scale (GCS), with 'mild' TBI defined as GCS 13-15, 'moderate' TBI as GCS 9-12, and 'severe' TBI as GCS 3-8. This is clinically relevant as mortality varies from 0.1% in mild TBI to 40% in severe TBI [2, 3], although up to 90% of all TBI is mild [4].

Mild TBI (mTBI), which is used interchangeably with 'concussion', has been further defined with four-point criteria by the American Congress of Rehabilitation Medicine (ACRM) [5]. The management of mTBI varies globally but may involve hospital admission for observation or a CT head scan based on established criteria, such as the Canadian CT head rule [6, 7], with subsequent neurosurgical management if indicated. However, the vast majority of mTBI cases have normal neuroimaging studies, while a normal CT head does not rule out mTBI. Therefore, existing diagnostic pathways may underestimate the degree of tissue insult and subsequent neurological

dysfunction, simultaneously having time and cost implications and potentially subjecting the patient to ionizing radiation [8].

Sports-related concussion (SRC) is a recognized type of TBI, defined by the Concussion in Sport Group (CISG) as 'a direct blow to the head, neck or body resulting in an impulsive force being transmitted to the brain that occurs in sports and exercise-related activities' [9]. The risk is higher in contact sports, such as boxing, American football, ice hockey, association football, rugby, and martial arts, as well as high-velocity sports, such as cycling, motor racing, equestrian sports, rodeo, skiing, and roller skating [10]. SRC may cause acute injuries akin to other modes of TBI. However, there is increasing recognition of the chronic sequelae of SRC, such as chronic traumatic encephalopathy (CTE – usually resulting from repetitive long-term mTBI events) and posttraumatic parkinsonism. Moreover, there is an association with the development of neurodegenerative diseases such as Alzheimer's disease, Motor Neuron Disease (MND), or Parkinson's disease [11]. Increasing awareness of these chronic sequelae has contributed to wider public interest in SRC over the past decade. Thus, optimal assessment and management of SRC is a public health concern.

### 1.1 Current methods of assessing and managing sports-related concussion

At present, there is no objective test to diagnose concussion. Assessment is, therefore, primarily based on clinical assessment and athletes' self-reported symptoms. Consequently, pitchside concussion assessment, investigations, and return-to-play protocols vary between organizations and countries. Commonly used pitchside tools include the Sport Concussion Assessment Tool (SCAT), incorporating clinical measures such as GCS, cognitive assessments such as the Maddocks Score, and a modified Balance Error Scoring System (BESS) [12].

The philosophy in managing SRC traditionally centers around a brief symptom-free period of physical and cognitive rest before allowing the athlete to engage in a graduated return to play [13]. This is usually 1-4 weeks [14]; however, the updated CISG consensus guidelines recommend 'relative rest' including activities of daily living and reduced screen time for up to 2 days following concussion; a return to light-intensity physical activity (e.g., walking) is recommended within 24-48 hours of injury, followed by advancing the duration and intensity of physical activity while monitoring for any recurrence of concussion-related symptoms [9]. Concussion substitutes have been successfully trialled in professional soccer, cricket, and rugby [15–17] to minimize disruption to the sporting spectacle.

However, the reliance on clinical symptoms likely underestimates the impact of SRC on athletes. Athletes may not be aware of the symptoms of SRC and may be motivated to under-report their symptoms to avoid sporting or financial loss [18]. Several assessments require a period of baseline and follow-up testing and formal neuropsychological evaluation, which may not be accessible to sporting clubs with limited resources.

Therefore, a more accurate pitchside and clinical assessment of SRC is needed to provide more individualized care to athletes suffering from this concussion. In this chapter, we will discuss the main emerging domains in the assessment of SRC: biomarkers (blood and salivary), neuro-imaging, and neurocognitive assessment. We will then discuss the implications of these novel modalities on return to play for athletes.

## 2. Biomarkers

Biomarkers are objective, quantifiable characteristics of biological processes [19] and usually refer to measurable biological compounds with a purported or established relationship with a clinical endpoint. An ideal biomarker in SRC would be highly sensitive, specific, easily measurable, and correlate with the clinical syndrome several days after the initial injury, given the practicalities of arranging patient sampling and analysis. Although there has been increasing interest in the field over the last decade, no FDA-approved biomarkers are in routine clinical use. Therefore, in this section, we will review several promising biomarker candidates that may have future utility in the assessment of SRC. Given the comparative inaccessibility in obtaining cerebrospinal fluid (CSF), it is unlikely to be a practical biomarker in SRC and therefore is not further considered in this chapter.

### 2.1 Blood biomarkers

Blood (serum and plasma) biomarkers of SRC – and, more widely, brain injury – must be considered in the context of the biomarker's ability to cross the blood-brain barrier into the systemic circulation, as well as whether the marker is produced extracranially. Nevertheless, several biomarkers have emerged in the literature.

#### *2.1.1 S100β*

S100**β** is a calcium-binding protein responsible for intracellular calcium regulation in astrocytes and is considered a marker of astrocyte injury [20]. It is also found in adipose tissue, muscle, and skin [21]. This marker has been extensively studied in large populations of TBI of all severities, being raised in patients with traumatic cerebral edema and contusions compared to other types of traumatic intracranial hemorrhage. Moreover, S100**β** levels are significantly lower in concussion than all intracranial bleeds [22]. Subsequently, Scandinavian head injury guidelines have included S100**β** as a screening test to obviate the need for CT head in selected patients if sampled within 6 hours of injury [23].

However, results with S100**β** in athletes are mixed. S100**β** has been raised following boxing, running, swimming, association football, ice hockey, and basketball [24] compared to before the sporting activity, which may be partially explained due to its secretion from known extra-cranial sites during exercise. There is also some association with head injury sustained during sporting activity: in one study, increased levels of S100**β** were found following heading and 'acceleration-deceleration' trauma during male professional association football games but was not associated with the high Rivermead postconcussion questionnaire scores taken 24-48 postmatch [25]. Moreover, another study found a significant increase in S100**β** in amateur male boxers who predominantly received punches to the head versus punches to the body, along with increases in Neuron-Specific Elastase (NSE), creatine kinase (CK) and cortisol [26].

Timing of S100**β** sampling is an important consideration, given its concentration peaks up to 1 hour following injury, falling back to baseline up to 6 days following injury [27]. In a recent cohort study of professional rugby players in France, the degree of change of S100**β** (along with NFL) at 36 hours postinjury compared to the preseason baseline was significantly associated with nonresolving concussion, while

the raw concentrations of each biomarker did not demonstrate any significant difference between those with or without nonresolving concussion [28].

In summary, it appears that S100**β** has a positive association with structural abnormalities in patients with SRC, with some association with postconcussion syndrome in the acute stage. Thus, it may have a role in the acute evaluation of SRC.

### *2.1.2 GFAP*

Glial fibrillary acidic protein is a monomeric intermediate protein found in the astroglial skeleton in gray and white matter [20]. It has also demonstrated utility in detecting neuroimaging abnormalities, superior to S100**β** in predicting the presence of traumatic intracranial lesions on CT in patients with mild to moderate TBI [29] and axonal injury on magnetic resonance imaging (MRI) 3 months postinjury in an mTBI population [30].

Although GFAP has been less assessed in the SRC literature, two studies illustrate its potential role as a biomarker. Firstly, a prospective cohort study found a significantly higher concentration of GFAP (alongside NFL) in the CSF of Olympic boxers 1-6 days following a bout and also following a 14-day rest period compared to controls. The one boxer who reported a concussion had the highest GFAP concentration at both time points, suggesting a potential role as a marker of subclinical concussion [31]. Moreover, a large multi-center case-control study of 504 college athletes with concussion found that serum GFAP was significantly elevated acutely following injury up to 7 days following return to play compared to preseason baseline and up to 24-28 h following injury compared to contact and noncontact sports controls. Moreover, GFAP was also significantly elevated in athletes who had a loss of consciousness (LOC) or posttraumatic amnesia (PTA) from the point of injury up to the point of athletes reporting to be asymptomatic and undergoing return to play protocols [32]. Interestingly, the area under the curve (AUC) for GFAP in differentiating between concussed athletes and contact- and noncontact sport athletes was inferior to the SCAT-3 assessment (0.67 to 0.68 vs. 0.94 to 0.95). However, it had a greater AUC in differentiating between concussed athletes with LOC/PTA (0.81 v 0.54 for SCAT-3).

These studies suggest that GFAP may be a marker of the severity of SRC, with some relationship between SRC symptomatology and severity.

### *2.1.3 Tau*

Tau is an intracellular, microtubule-associated protein responsible for assembling axonal bundles. There is a recognition of aggregation and misfolding of tau being responsible for the development of 'tauopathies', a family of neurodegenerative conditions which includes CTE [33]. It has also been found in the liver, kidney, and testes [34]. Tau predicts poor outcomes in severe head injury, akin to S100**β** and GFAP [20], with CSF concentrations of cleaved-tau and total tau having particularly strong associations [35–37]. However, its role in mTBI is more uncertain, where it was shown not to correlate with the long-term outcome (at 3 months) [38], postconcussion syndrome [39], or traumatic intracranial lesions on CT [40].

Moreover, there have also been mixed results in the SRC-related literature. One study in 28 ice-hockey players found total tau (t-tau) levels to be significantly raised in players who suffered a concussion compared to a preseason baseline, along with S100**β**. However, only t-tau levels at 1 h postconcussion were predictive of the length

of resolution of concussive symptoms (AUC 0.91), while high t-tau 144 h post-concussion was associated with the persistence of postconcussion syndrome [27]. However, serum t-tau was found to be elevated in a study of 30 Olympic boxers following a bout compared to 25 controls, even though none of the boxers had a concussion [41]. CSF t-tau was also elevated in this boxer cohort but was not correlated with serum levels [31].

T-tau has also provided mixed results assessed in two large cohort studies: in a 2017 study of 623 collegiate athletes (46 SRC), serum t-tau was found to be significantly higher in SRC and athlete controls compared to nonathlete controls, while elevated t-tau from 6 to 72 h postconcussion was associated with a long return-to-play period (defined as >10 days), with 6-hour t-tau having a high predictive value for a long RTP (AUC 0.81) [42]. In another 2020 study of 1760 collegiate athletes (264 SRC), tau was significantly elevated at 1 h postinjury compared to preseason baseline (along with GFAP and UCH-L1) but returned to baseline after this time point. Moreover, there was no association or predictive value for tau in return to play in athletes who suffered LOC/PTA [32].

The exact significance of elevated tau, therefore, remains to be determined. Like GFAP and S100**β**, it is a marker of brain injury with strong associations in severe TBI, but there is conflicting data in the literature about its utility. This may be explained by methodological differences in the studies concerned, particularly given the 1 h peak of t-tau postconcussion, but more robust data is required.

#### *2.1.4 Other blood biomarkers*

Several other biomarkers have been studied in the literature, including markers of neuronal (neuronal-specific elastase (NSE), brain-derived neuronal factor (BDNF) and UCH-L1), axonal (alpha-II spectrin and neurofilament light) and blood-brain barrier (CSF: serum albumin ratio) dysfunction [43]. High NFL has been correlated with SRC with LOC/PTA even beyond clinical recovery in collegiate athletes [32]. It has correlated with symptom severity, long RTP, and even retirement (if high at 144 h postinjury) for ice hockey players who had PCS symptoms >1 year [44]. This biomarker outperformed tau, S100**β** and NSE and, therefore could be considered a marker of severe PCS.

In summary, blood biomarkers representing various structural components of the CNS have emerged in the literature, with early applications in mTBI and SRC. Of all these, S100**β**, GFAP, tau, and NFL have emerged as leading candidates, and their future diagnostic utility likely lies in the combined use of these markers [32].

### 2.2 microRNAs

In contrast to the biomarkers already discussed, microRNA (miRNA) are smaller, being 19-28 nucleotides in size. They are a class of endogenous, noncoding RNA regulating messenger RNA (mRNA) expression. It is thought that they contribute to the development, differentiation, and synaptic plasticity of neurons, although their function is not fully understood. They are stable at variable pH conditions and resistant to freeze-thawing and enzymatic environmental changes [45]. Over the past decade, there has been increasing research on the utility of miRNA as biomarkers of a range of neurological disorders [46].

Consequently, several research groups have trialed varying panels of miRNA in TBI. One of the first such studies in 2010 found that a combination of serum miR-16,

miR-92a, and miR-765 had a 100% sensitivity and specificity for identifying patients with severe TBI compared to healthy volunteers or orthopedic trauma patients [47]. A further study identified ten miRNA molecules that were upregulated in both mild/moderate TBI and severe TBI [45]. Concentrations of four of these molecules, miR-328, miR-362-3p, miR-451, and miR-486 were also significantly upregulated in the CSF of this cohort, with changes in concentration in eight of these markers being significantly associated with traumatic intracranial lesions on CT scan. AUC >80% for predicting TBI was found in five miRNA molecules, highest in miR-92a (AUC 0.86).

In a cohort study of collegiate American football players throughout a season, serum miRNA concentrations were assessed against indications of concussion, subconcussive impacts, and neurocognitive function [48]. All athletes in this study had a significantly higher concentration of a panel of preselected miRNA biomarkers compared to controls. When considering the Standard Assessment of Concussion (SAC) clinical assessment, five biomarkers had a high predictive value for low SAC scores (<28), with miR-195 having the best predictive value (AUC 0.90). miR-195 was also significantly predictive of concussion in the two athletes (2%) who had suffered this, with an AUC of 0.92, equal to miR-92a. Moreover, neurocognitive scores showed a significant negative correlation with miR-505, miR-30d, miR-92, and miR-151-5p. Worsening balance was significantly correlated with miR 505, miR-30d, miR-151-5p, and worsening reaction times were significantly worsened with miR-20a, miR-505, miR-30d, miR-92, and miR-151-5p.

Another paradigm in the field has been the exploration of salivary miRNA biomarkers. The discovery of neurodegenerative markers such as tau [49], alpha-synuclein and DJ-1 [50] have sparked interest in markers of TBI in saliva. The ease of collecting and storing saliva makes it ideal as a point-of-care test. One group identified five salivary miRNA candidates upregulated in athletes with SRC [51]. One marker, let-7i-5p, had an AUC of 0.86 in predicting SRC.

Interestingly, all miRNA markers were also expressed in all tissues but were highest in the brain. There was also a significantly positive correlation between let-7i-5p and miR-27b-3p and percentile on the Immediate Postconcussion Assessment Cognitive Test (ImPACT) concussion assessment tool. Finally, miR-135b-5p was inversely correlated with the number of concussions. This has progressed to a panel of miRNA (salivary small noncoding RNA – sncRNA) retrospectively and prospectively predicting concussion in a cohort of rugby union players using a panel of 14 sncRNA biomarkers to a high degree of accuracy (AUC 0.96 1 h postgame, 0.93 36-48 h postgame) [52].

The interest in miRNA in SRC has circled back to the civilian population, with a prospective observational cohort study aiming to assess 23 salivary miRNA biomarkers in nonathletes admitted from the emergency department with maxillofacial trauma with a concomitant concussion, compared to those admitted for orthopedic trauma [53].

In summary, microRNA has represented a significant advancement in the diagnosis of SRC, being an easy-to-administer investigation that shows high sensitivity and specificity in diagnosing SRC, with some correlation to neuropsychological measures. Further validation of miRNA is required in longer-term follow-up studies and in return to play scenarios.

### 2.3 Imaging

Imaging forms a key pillar in the investigation of all forms of TBI. There is a general international consensus on the indications for CT head scanning following

acute TBI [23]. However, using these criteria, most cases of mTBI, and by extension SRC, would not undergo a CT scan, and most CT heads would fail to show any acute abnormalities. As seen in the previous section, where there are structural changes in CT, this has been correlated with higher levels of biomarkers of CNS injury and miRNA. This may not be specific in detecting subtle structural and functional imaging abnormalities in an SRC cohort. For this purpose, magnetic resonance imaging (MRI) is an alternative modality that may yield radiological biomarkers in SRC. Currently, American neuroradiology guidelines do not recommend MRI for routine clinical evaluation of TBI, and there are no approved radiological biomarkers [54]. However, there are emerging potential MRI techniques that have yielded biomarkers that may have a role in SRC.

### *2.3.1 Structural MRI imaging techniques*

Diffusion tensor imaging (DTI), volumetric brain imaging, and susceptibility-weighted imaging (SWI) are three techniques that can assess structural changes following TBI. DTI allows the mapping of white matter tracts by evaluating the anisotropic, or preferential, Brownian motion along the tract; this can generate apparent diffusion coefficient (ADC), mean diffusivity, and fractional anisotropy (FA) measurements [55]. FA ranges from 0, implying complete isotropy (unrestricted motion) of water molecules, such as in CSF, to 1, implying complete anisotropy (restricted motion), such as nerve fiber tracts. Most studies on DTI often focus on these quantitative properties in a particular voxel or region of interest (ROI), which contain multiple white matter tracts with differing trajectories, making inferences about individual white matter tracts difficult [56]. DTI has been successfully applied in preoperative planning in epilepsy and brain tumor surgery [57, 58]. In comparison, volumetric brain imaging is generated through 3D T1-weighted imaging sequences, often a standard MRI brain imaging sequence; through these images, gray and white matter may be separated and analyzed [55].

Studies of DTI in mTBI are heterogeneous in methodology, assessing different time points postinjury, comparator groups (controls vs. preinjury baseline), and anatomical ROIs. A review of 100 studies assessing DTI found a reduction in FA in TBI independent of the severity and timing since the injury. Anatomical regions most implicated were the corpus callosum, frontal lobes, internal capsule, and cingulum, which are high FA tracts, and thus possibly more likely to demonstrate a statistically significant change in TBI [59]. Seven of the eight included SRC studies in this review concurred with these DTI findings. Another review of DTI in PCS found that reduced FA and increased mean diffusivity (MD) and radial diffusivity (RD) were associated with the development and severity of PCS [60]. The corpus callosum was again found to be the most affected brain region. DTI changes have also been found in youth American football players with subconcussive head impacts, with a significant correlation between head impacts and reduced FA in two regions (left inferior fronto-occipital fasciculus (IFOF) and the right superior longitudinal fasciculus (SLF) terminal), with greater significance found at the terminals of gray and white matter intersection [61].

In comparison, studies on volumetric brain analysis in mTBI and SRC have consistently shown reductions in brain volume. One study comparing 28 patients one-year following mTBI and 22 controls found a global brain atrophy in the mTBI group greater than the control group, with the bilateral anterior cingulate and left cingulate gyrus isthmus white matter tracts showing a significant reduction in volume

loss, as well as the right precuneal gray matter. Reduction in neurocognitive memory and attention assessments was also correlated with volume loss in the bilateral rostral anterior cingulum white matter, while left cingulate gyrus isthmus correlated with clinical scores of anxiety and postconcussive symptoms [62]. In another study of 50 patients with mTBI, 19 of whom had a posttraumatic headache, those with headaches had significantly reduced gray matter volume in the right anterior parietal and left temporo-opercular regions at 18 months compared to those without posttraumatic headache. There were also several regions of decreased gray matter clusters compared to controls [63]. Volumetric studies in athletes have implicated volume reduction in the thalamus [64] and hippocampus [65]. However, interestingly, a study assessing former college American football players at early midlife (with a mean age of 37.9) found that although repetitive head injury impacts were associated with smaller hippocampal volume, those with professional/graduate degrees did not have a statistically significant reduction in hippocampal volume [66]. This emphasizes the moderating impact of factors such as age and educational attainment, so volumetric studies should be interpreted within this context. Moreover, as in DTI, the comparator population is important, given that there may be normal variation with volumetric brain structures which may not be clinically relevant. Comparison of structural changes in the same athlete pre- and postconcussion appears to be more sensitive in identifying abnormalities [67].

Susceptibility-weighted imaging (SWI) is an MRI technique that is useful for detecting microhemorrhages. Alongside CT, this has been applied in TBI in the diagnosis of diffuse axonal injury [68]. Although noted not to be in a sports-related concussion population, the incidence of microhemorrhages is greater than may first be perceived; in an American cohort study of patients presenting to level 1 and 2 trauma centers with head injury, of which 83% had mTBI, traumatic microhemorrhages were found in 31%. Those with traumatic microhemorrhage were twice as likely to have a disability at 30- and 90-days postinjury, defined as Glasgow Outcome Score $\leq 6$ [69]. Another study following up 30 mTBI patients up to 1 year following their injury found that the presence of microhemorrhages showed worse performance in several cognitive tests in the acute and chronic phase stages, as well as higher symptom severity in the postconcussion symptom scale (PCSS) at 12 months postinjury [70]. However, like other methods of structural MRI evaluation, SWI needs to be considered within the baseline of the patient, as subclinical vasculopathy and amyloid angiopathy may also cause SWI abnormalities. Most literature does not have pre-mTBI imaging; therefore, this may be a confounding factor that may explain some of the abnormalities found. Therefore it may be unclear to what extent such abnormalities were present preinjury, although most athletes are usually younger than the expected age cohort to have such vascular abnormalities [55].

### *2.3.2 Metabolic MRI imaging: MR spectroscopy*

Magnetic resonance spectroscopy (MRS) may act as a 'virtual biopsy' to identify metabolic changes in regions of interest. Commonly studied markers include N-acetyl-aspartate (NAA), a neuronal marker; choline (Cho), a measure of cell membrane turnover; creatine (Cr), a marker of energy metabolism; myoinositol, a glial marker; and glutamate and glutamine (Glx), excitatory neurotransmitters [55]. Several studies have found a decrease in NAA in mild TBI but were equivocal about Cho [54]. In a longitudinal study with serial MR spectroscopy up to 6 months postinjury in 43 patients with mTBI, there was a significantly reduced Cho/Cr ratio

in the thalamus and centrum semiovale in the late subacute stage (mean 37 days postinjury); high Cr in the early subacute stage (mean 5 days postinjury) was positively associated with some neuropsychological metrics at the chronic stage (mean 195 days postinjury), suggesting a possible role in predicting functional outcome [71]. These findings are contrary to our understanding of Cr in metabolic pathways, as this marker is expected to decrease in metabolic crisis states such as SRC. Finally, an MRS study in former NFL American football players found significantly positive correlations between glutamate, glutathione, and myoinositol in the anterior cingulate gyrus and behavioral/mood symptoms, while repetitive head injury was associated with lower parietal white matter creatine [72]. This suggests that repetitive head injury in SRC may lead to reduced cellular energy metabolism, while neuroinflammation may underpin behavioral/mood symptoms.

### *2.3.3 Perfusion-based MRI imaging: Perfusion-weighted imaging and functional MRI*

Perfusion-weighted imaging and functional MRI (fMRI) are two further techniques that have been studied in the SRC literature. Both assess blood flow to regions of the brain to a certain extent, particularly during tasks. The results of these techniques have been mixed, possibly due to the complexity of structural and neurophysiological changes following injury [55]. In a meta-analysis of task-related fMRI studies, the most consistent finding in mTBI was reduced activation in the right middle frontal gyrus, as well as decreased activation in the prefrontal region being associated with cognitive impairment, which may be a result of neuronal injury to the cortex or disruptions to structural connectivity [73]. Within the SRC literature, abnormal resting state fMRI connection cerebellar lobule 5 was found in retired rugby league players [74], while another study of 13 retired NFL players found increased activation of DLPFC and reduced connectivity in the dorsal frontoparietal network while examining executive function [75].

With respect to perfusion imaging, a study of 24 athletes with concussion, followed up to 1 year after return to play, found that cerebral blood flow was elevated in the superior frontal gyrus in the early symptomatic phase, with reduced blood flow in the middle frontal and temporal regions at 1 year [76]. This gives an indication of longer-term changes in the brain following concussion, although the significance of this is currently unclear. Another perfusion study in a group of 15 teenage athletes up to 6 weeks postconcussion found increased cerebral blood flow in the left dorsal anterior cingulate cortex (ACC) and insula, which persisted at the left ACC at 6 weeks. CBF was also higher in the left ACC in athletes with persisting symptoms at 6 weeks postinjury [77]. However, another study in 24 concussed collegiate American football players showed highly significantly ($<0.01$) reduced CBF in the left inferior parietal lobule (IPL), right middle frontal gyrus (MFG), and thalamus in concussed athletes 24-48 h postinjury compared to controls [78]. There were also correlations between clinical and neuropsychological assessments and CBF in numerous brain regions. Finally, a study of concussed American football players against controls demonstrated a significant reduction in CBF at 8 days compared to 24 hours posttrauma in multiple frontal and temporal lobe regions [79], suggesting physiological changes persisted beyond the point of clinical recovery.

In summary, there is an ever-increasing amount of data on MRI imaging in SRC, with some techniques such as DTI analysis of the corpus callosum and fMRI of the right middle frontal gyrus being consistently demonstrated as abnormal in the

aggregated mTBI/SRC literature. However, data on other methods have been mixed, and imaging studies confounded the range of normal variance in neuroimaging techniques. Therefore larger, longitudinal studies with baseline imaging are required to better establish the causative changes in the brain in SRC.

### 2.4 Pitchside and neuropsychological evaluation

Neuropsychologists have become increasingly integrated in the assessment of SRC, and indeed most of the present protocols of SRC management center on detecting cognitive deficits resulting from SRC and monitoring the athlete's recovery. Barth and colleagues first demonstrated using baseline and postconcussion neuropsychological testing that college American football players had measurable cognitive deficits following concussion, which resolved within 5-10 days postconcussion [80]. This progressed to the development of the computerized Immediate Postconcussion Assessment Cognitive Test (ImPACT) [81], which has dominated the sports neuropsychology literature since. Neuropsychological measurements are often used within return-to-play protocols at both the grassroots and professional levels [82].

The traditional model of neuropsychological testing requires 4-6 hours, which is impractical for many athletes, leading to the development of composite assessment batteries, the most prominent of which is the Penn State battery [83], forming the basis of many contemporary concussion protocols. Furthermore, along with the ImPACT assessment, there has been a proliferation of computer neurocognitive assessment devices (CNADs), providing greater access to athletes but at risk of being affected by factors such as response validity, athlete background, or psychometrics, leading to discrepancies with their paper counterparts [84, 85]. To that effect, American neuropsychology bodies released a position statement outlining the best practice for the use of CNADs [86].

Although not strictly a neuropsychological tool, the Sports Concussion Assessment Tool, now in its 6th iteration, has consistently demonstrated the highest sensitivity and specificity out of all pitchside tools in diagnosing SRC (sensitivity 0.83-0.96, specificity 0.81-0.91) [81, 87]. Iterations of the SCAT have included other testing elements with proven efficacy, such as the PCSS, BESS, tandem gait test, and Standard Assessment of Concussion measures. It has been recommended by expert working groups to be used in athletes >13 years of age, with the largest effect sizes occurring <24 hours of injury [81]. The King-Devick test, a measure of visual pathways responsible for planning, initiation, and execution of coordinated saccades/antisaccades, reading, and rapid number naming, has been posited as a useful adjunct alongside the SCAT [88]. While the SCAT may require trained professionals to administer components (e.g., GCS), the King-Devick test has found no difference in scoring between nonprofessionals and professionals [81]. However, a recent meta-analysis found that it has a relatively lower sensitivity (0.77) and specificity (0.82) compared to SCAT, although it noted the quality of evidence to be low, and the test to be predominantly used in male athletes <25 years old, potentially limiting its applicability to other athlete groups [89].

Emerging pitchside assessments include eye tracking and head impact sensors, among others. However, the vestibular/ocular motor screening (VOMS) tool has shown the most promise thus far. This measures response to vestibular/ocular provocation in five domains (convergence, horizontal and vertical saccades, smooth pursuit, horizontal and vertical vestibulo-ocular reflex, and visual motion sensitivity); before the assessment and after each domain, participants are asked about changes in four symptoms (headache, dizziness, nausea, and fogginess) on a 10-point rating scale.

There have been FDA-approved eye-tracking devices that may partially or wholly automate this process, which may be useful in the SRC setting where athletes may not undergo specialist concussion clinical assessment immediately following concussion [90]. It showed high internal consistency (Croenbach's alpha 0.91), with each domain being significantly greater in concussed participants compared to controls. Using a composite model of visual motion sensitivity, vestibulo-ocular reflex convergence distance, the AUC was 0.89 [91]. This has been externally validated in identifying concussions in college athletes within 3 days of injury [92]. It has also been found to have a large effect size in a large cohort of concussed collegiate athletes. However, it had moderate test-retest reliability when comparing preseason baseline to the acute post-concussion phase, alongside other pitchside measurements such as the ImPACT and SCAT3. This suggests that preseason baseline SRC assessments may not be important in identifying clinically significant differences in SRC assessments postconcussion [93].

### 2.5 Conclusions

Sports-related concussion remains, at present, a clinical diagnosis, with clinical assessment tools such as the SCAT being used as adjuncts to assist with the diagnosis. This has been shown to have high sensitivity and specificity, but there is a need to explore different modalities for diagnosing and progressing sports-related concussions. It is clearly a heterogeneous condition, with some markers such as S100**β** and tau being elevated after physical activity and neuroimaging changes, possibly reflecting preinjury or normal variant characteristics. GFAP, tau, and NFL were elevated in athletes who had a prolonged return to play. However, more work is required to monitor the physiological and neuroimaging changes following SRC, their correlation with symptoms and the decision to return to play. This should be done in collaboration between healthcare professionals, athletes, and sporting organizations, such as with the CARE consortium [32]. A future assessment of SRC and return to play may incorporate multi-modality techniques involving validated biological, neuroimaging, and neuropsychological measures. A future assessment of SRC may involve a multimodal assessment involving biological, imaging, and neuropsychological measures [94], and we would encourage future research in the field to be driven toward this.

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Chapter 4

# The Neuropathology of Concussion

*Ioannis Mavroudis, Ioana-Miruna Balmus, Lucian Gorgan and Alin Ciobica*

## Abstract

This review provides a detailed analysis of the pathophysiology involved in traumatic brain injury (TBI), with an emphasis on mild TBI and chronic traumatic encephalopathy (CTE). It explains the dynamic interaction between mechanical trauma and the neuroinflammatory response, especially the crucial role of microglia in post-TBI inflammation. Moreover, the review discusses the significance of dendritic and spinal changes as indicators of a regenerative response. The role of transactive response (TAR) DNA-binding protein 43 and tau protein in the pathogenesis of mild TBI and CTE is assessed, with tau protein changes being a potential biomarker for acute and chronic TBI-related conditions. The study also investigates syndromes commonly found in young athletes, such as second impact syndrome and juvenile head trauma syndrome. The review addresses the complex inflammatory response after mild TBI, focusing on pro-inflammatory and anti-inflammatory mediators, including IL-1, IL-6, TNF-α, and CRP as potential indicators of injury severity and outcome. The review calls for further research to elucidate the exact relationship of these factors in TBI and its long-term effects.

**Keywords:** traumatic brain injury, chronic traumatic encephalopathy, microglia, tau protein, second impact syndrome, inflammatory response

## 1. Introduction

The definition of concussion remains controversial and lacks universal agreement. The 2012 Zurich Consensus Statement on Concussion in Sport proposed that concussion and mild traumatic brain injury (TBI) should be regarded as distinct entities, and defined concussion as a "complex pathophysiological process affecting the brain" that can cause neuropathological damage. However, the statement acknowledged that concussive symptoms typically resolve spontaneously and do not produce imaging abnormalities. In contrast, recent American Academy of Neurology guidelines for sports concussion in 2013 did not differentiate between concussion and mild TBI, defining concussion as "a clinical syndrome of biomechanically induced alteration of brain function, typically affecting memory and orientation, which may involve loss of consciousness." These guidelines noted that the terms concussion and mild TBI are often used interchangeably, highlighting a lack of consensus in their use. Therefore, concussion is currently employed in two distinct ways: (1) to describe a specific

pathophysiological entity with unique diagnostic and management implications, commonly observed in the context of sports injuries; and (2) to describe a constellation of symptoms that arise after different types of TBI [1, 2].

## 2. The pathophysiology of concussion

Concussion and subconcussion injuries are caused by the acceleration and deceleration linear or rotational forces acting on the brain. This results in the elongation and deformation of the brain, causing stretching of neurons, glial cells, and blood vessels and altering membrane permeability. Although all cell compartments and blood vessels are affected by the injury, axons are especially vulnerable as they often extend long distances from the neuronal cell bodies. Axons may be injured even in the absence of the death of the neuron of origin [3, 4].

In addition to structural deformation, acceleration-deceleration forces produce a rapid release of neurotransmitters, influx of calcium, efflux of potassium, and acceleration of the cellular sodium-potassium ($Na^+$-$K^+$) pump to maintain membrane homeostasis, requiring large increases in glucose metabolism. These changes are referred to as the "neurometabolic cascade of concussion."

Post-concussive hypermetabolism in the setting of decreased cerebral blood flow produces a disparity between glucose supply and demand and a cellular energy crisis [5]. Pathological studies of acute concussion and post-concussion syndrome (PCS) have shown multifocal diffuse axonal injury (DAI), microhemorrhage, astrocytosis, and perivascular clusters of activated microglia. The severity of axonal injury is generally parallel to the severity of the TBI, with mild injury producing only microscopic multifocal axonal damage and moderate and severe TBI producing more severe, widespread axonal injury. Mild TBI produces multifocal and perivascular axonal injury in the corpus callosum, fornix, subcortical white matter, and cerebellum, physical changes that may contribute to the severity of symptoms after mild TBI [3, 6]. Focal perivascular accumulations of hyperphosphorylated tau (p-tau) as neurofibrillary tangles (NFTs) and neurites and TDP-43 immunopositive neurites in the white matter have also been found after concussion, suggesting that focal axonal injury may be mechanistically associated with the development of p-tau and TDP-43 pathology. Evidence of microhemorrhage as hemosiderin and hematoidin-laden macrophages may also be present after concussion, indicating loss of microvascular integrity and breach of the blood-brain barrier following mild TBI. Structural changes in the brain after concussive injury, such as DAI and microhemorrhages, are best detected with diffusion tensor imaging (DTI) and susceptibility-weighted imaging (SWI) and are not detectable with conventional structural imaging studies, including computed tomography (CT) scan and magnetic resonance imaging (MRI) [7–10].

## 3. Diffuse axonal injury

Diffuse axonal injury (DAI) is a major neuropathological consequence of TBI and is caused by the acceleration/deceleration forces that shear fragile axons during the trauma [11–14]. Although DAI is more commonly seen in moderate to severe TBI, it can also occur in mild TBI, and its severity is proportional to the deceleration force

[15, 16]. DAI is difficult to identify in patients with TBI using CT and conventional MRI, but novel MRI techniques, such as diffusion tensor imaging (DTI) have been found to be useful for assessing axonal integrity and identifying DAI, particularly in mild TBI patients and athletes with mild sports-related concussive or sub-concussive TBI [17–19]. Histological techniques have shown that DAI can be identified within hours after trauma while being characterized by sequential changes that begin with an acute shearing of axons, disrupted axonal transport with axonal swellings, and secondary disconnection, leading to Wallerian degeneration [11].

Diffuse axonal injury (DAI) with axolemmal disruption leads to calcium influx, neurofilament compaction, and microtubule disassembly. Calcium influx triggers microtubule disassembly, while neurofilament compaction is an early event caused by calpain-mediated proteolysis of neurofilament side arms or phosphorylation [20, 21]. Disruption of calcium homeostasis is the primary regulator of calpain activation, leading to increased intracellular-free calcium, and proteolytic degradation of essential cytoskeletal proteins, such as neurofilament proteins [22, 23].

Diffusion tensor imaging (DTI) is a valuable tool in diagnosing, prognosing, and managing mild TBI. DTI provides information about the microstructure and fiber tract integrity of white matter. Other techniques that may be valuable in evaluating mild TBI include alterations in brain activation through BOLD signals, resting state functional connectivity, magnetic resonance spectroscopy, and SPECT imaging.

Blast injury is becoming an increasingly important form of TBI in civilian and military populations, with the majority of injuries associated with blast exposure. Individuals exposed to blast injury are susceptible to acute and long-term neuropsychiatric and cognitive consequences. Some military veterans with a history of blast exposure show neuropathological changes of chronic traumatic encephalopathy (CTE) during autopsy, while single-blast exposure in wild-type laboratory mice produces neuropathological changes of axonal injury, neuroinflammation, microvascular injury, and abnormal tau pathology, as well as neurobehavioral abnormalities. A post-mortem series of military veterans with documented histories of blast exposure showed focal neuropathological changes of CTE, including cortical foci of perivascular tau pathology, disseminated microgliosis and astrocytosis, myelinated axonopathy, and focal neurodegeneration, very similar to mild CTE pathology found in the brains of athletes with a history of repetitive concussive injury [4]. Also, the clinical symptoms experienced by veterans with blast injury include progressive affective lability, irritability, distractibility, executive dysfunction, memory disturbances, and cognitive deficits [4].

## 4. Microtubule disorganization

Microtubule disorganization may be a direct effect of dynamic axon stretching, leading to immediate breakage and buckling of microtubules post-injury, which triggers progressive microtubule disassembly [24]. This results in the accumulation of organelles that are transported in the axon, and axonal swelling known as axonal retraction balls, leading to eventual disconnection and axotomy [20, 21]. Neuronal damage with axonal bulbs and swellings is most commonly found in the cortical sulci at the interface between gray and white matter [25]. DTI studies have shown that the extent of DAI after mild TBI is related to post-concussion cognitive problems [26].

## 5. The role of microglia

Microglia plays an essential role in the immune system in the brain and mediates the inflammatory response after TBI. Studies in animal models of TBI have shown that activated microglia migrate rapidly toward damaged tissue, forming extended cytoplasmic processes that create a potential barrier between healthy and injured tissues, indicating that microglial activation is a response to axonal damage [27, 28]. This microglial response is associated with the upregulation of both pro- and anti-inflammatory genes, chemokines, and other inflammatory mediators [29]. However, it is still not clear whether modulation of this inflammatory response to brain trauma may have any therapeutic effects. While pharmacological reduction of microglial activation might reduce inflammation and improve neuronal survival, microglial activation might stimulate axonal regeneration after injury [30].

## 6. Dendritic and spinal changes

After TBI, dendritic and synaptic sprouting occurs, leading to increased dendritic arborization and synaptogenesis as part of a regenerative response [31]. Transcription factors c-Jun and ATF-3 have been implicated in axonal regeneration after DAI [32]. Structural proteins, including growth-associated protein GAP-43, have also been associated with neurite sprouting of disconnected damaged axons after the acute phase of TBI [33].

## 7. TDP-43 deposition

TAR DNA-binding protein 43 (TDP-43) may also play a role in mild TBI and CTE pathogenesis. TDP-43 accumulation is a feature of several neurodegenerative diseases, including CTE, AD, and dementia with Lewy bodies. Recent studies have shown that TDP-43 accumulations occur in boxers and American football players with CTE after repeated brain trauma in several gray matter structures, including the brainstem, basal ganglia cortical areas, and subcortical white matter. TDP-43 accumulation after TBI may be part of a physiological injury response, and animal experiments suggest that axonal damage results in an upregulation of TDP-43 expression [34–36].

## 8. The role of tau protein

Tau protein, characterized by a molecular weight ranging between 48 and 67 kDa, serves as a crucial structural component within the axonal cytoskeleton of both the central nervous system (CNS) and peripheral nervous system (PNS) [37, 38]. This microtubule-associated protein is predominantly found in unmyelinated cortical axons, contributing significantly to their structural integrity [39, 40]. Although the expression of tau is mainly observed in the brain, it is also present in extracranial tissues, such as the liver, kidneys, and testis [41]. Historically, research investigating TBI biomarkers has primarily concentrated on total tau (T-tau). However, recent studies have expanded their focus to include phosphorylated tau (P-tau) and cleaved tau (C-tau) as well. Following a TBI, there is a noticeable increase in tau levels within cerebrospinal fluid (CSF) and plasma [42]. Elevated concentrations of tau protein in

CSF have been identified in patients who have experienced TBI, with admission CSF tau levels displaying a correlation with the patients' long-term outcomes [43, 44]. A study analyzing CSF samples from Olympic boxers within one to six days following their bouts revealed a significant increase in tau levels in the boxers' CSF, as compared to healthy control samples [45]. Moreover, higher concentrations of CSF tau were observed in Olympic boxers post-bout, though this was not necessarily linked to the number of head impacts received [46]. Similar findings were reported in a study involving college football players where no correlation was observed between the number of mild TBIs or concussions and tau concentrations. Increased plasma tau levels were also noted following training sessions [47].

In chronic neurodegenerative disorders, such as Alzheimer's disease (AD), CSF T-tau concentrations exhibit a weak correlation with plasma T-tau concentrations [48]. In contrast, a stronger correlation more likely exists in cases of acute TBI, contingent upon injury severity and the subsequent release of T-tau from neurons into both CSF and plasma. Notably, the elevation of tau levels post-TBI tends to persist longer in CSF (weeks) compared to blood (days) [49]. Given the typically low concentrations of tau protein in peripheral blood during both healthy and diseased states, accurate measurement through conventional immunoassays has proven challenging. The advent of ultrasensitive Single molecule array (Simoa) technology has facilitated the precise quantification of T-tau in both plasma and serum [50]. Multiple studies have documented elevated plasma T-tau concentrations in relation to TBI [51], with tau levels generally peaking between 12 and 24 hours after the injury and occasionally persisting at high levels.

The previous studies suggested that tau levels increases following TBI may exhibit both acute and chronic trajectories. While the initial increase in tau levels is indicative of acute neuronal damage, a secondary increase may be associated with chronic neurodegenerative processes and secondary pathologies [52]. Notably, blood tau concentrations have been observed to rise with age [53], and recent findings have reported distinct temporal profiles and substantially higher T-tau levels in female athletes with concussions, as compared to their male counterparts [54]. Furthermore, significant correlations have been found between serum tau concentrations and neurological outcomes in patients who have experienced resuscitated cardiac arrest [55].

In studies involving professional ice hockey players with concussions, plasma T-tau concentrations were elevated one hour post-injury compared to pre-season levels, and accurately predicted return-to-play (RTP) time [56]. Additionally, a study focusing on concussed athletes found that plasma T-tau concentrations six hours after injury correlated significantly with RTP time [57]. Elevated plasma tau levels have also been reported in military personnel exposed to blast injuries within the prior 18 months [50], with higher exosomal tau concentrations being associated with chronic symptoms in military personnel after mild TBI [58]. In a study encompassing TBIs of varying severity, plasma T-tau concentrations successfully differentiated mild TBI cases from controls when samples were collected within 24 hours of injury [59]. Serum tau levels have similarly been identified as significant outcome predictors following TBI [60]. Recent research has demonstrated that acute plasma P-tau concentrations and the P-tau/T-tau ratio outperform T-tau concentrations in predicting TBI outcomes [61]. However, plasma T-tau concentrations upon admission were unable to distinguish between incomplete and complete recovery in cases of single and uncomplicated mild TBIs [62]. Conflicting results have been reported concerning the utilization of C-tau as a fluid biomarker for the acute biochemical diagnosis of mild TBI [62, 63].

## 9. Second impact syndrome and juvenile head trauma syndrome

The second impact syndrome (SIS) and juvenile head trauma syndrome are conditions that affect children and young adults who have suffered minor brain trauma. Juvenile head trauma syndrome refers to the catastrophic or fatal cerebral edema and coma that can result from a single injury in this population. SIS occurs when an athlete experiences a mild head injury or concussion, then suffers a second head injury before the symptoms associated with the first injury have resolved, producing rapid cerebral swelling. SIS typically affects young athletes, particularly males, ranging in age from 10 to 24 years, with a mean age of 17.9 years. Most athletes reported to have SIS were American football players, usually at the high school level, but it has also been reported in association with boxing, karate, skiing, and ice hockey. SIS is thought to result from an abrupt post-traumatic loss of cerebral blood flow auto-regulation and catecholamine release that create a rapid increase in intracranial blood volume and catastrophic cerebral edema. In two-thirds of cases, a thin, acute subdural hematoma has been found on neuroimaging or at autopsy, which may reflect the hyperemic state, in the absence of other major hematomas or space-occupying lesions. The relationship of SIS with juvenile head trauma syndrome or with malignant cerebral edema after mild TBI is uncertain, and both may be manifestations of the same underlying pathophysiology [64].

## 10. The inflammatory response in mild TBI

The inflammatory response is a multifaceted process that involves the activation of various cell types, including microglia and astrocytes, and the release of a multitude of pro-inflammatory and anti-inflammatory mediators [65]. Numerous studies have demonstrated that the inflammatory response is activated early after mild TBI and can persist for several weeks or even months. Inflammatory biomarkers, such as interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP), have been proposed as potential indicators of mild TBI [20, 66, 67]. These biomarkers are elevated in individuals with mild TBI, and their levels have been linked to the severity and outcome of the injury [68]. Inflammation is characterized by the activation of immune cells and the release of inflammatory mediators, such as cytokines and chemokines [69]. In the context of concussion, inflammation has been proposed as a potential contributor to the pathophysiology of the injury and the persistence of symptoms in some individuals [70]. Several studies have investigated the levels of inflammatory biomarkers in individuals with concussions. Some studies have found elevated levels of cytokines, such as IL-6 and TNF-α, in the serum or CSF of individuals affected by concussion events, while others have not observed significant differences in inflammatory biomarker levels between individuals with trauma and controls [71–73].

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Section 3

# Rehabilitation and Management

Chapter 5

# Concussion Rehabilitation

*Valentina Vanessa Re*

## Abstract

Concussion represents one of modern medicine's biggest challenges. As we are gaining more and more information on pathophysiology, diagnosis, and treatment, a lot is still to be cleared. On the side of pharmacology, rehabilitation is the leading treatment for concussion signs and symptoms. From acute to the chronic phase of brain dysfunction, rehabilitation is nowadays providing help to people recover faster and better. In this chapter, we will analyze in depth the key information and evidence supporting current concussion rehabilitation methods and protocols. Through this chapter, we are exploring how aerobic training, vestibular rehabilitation, and oculomotor exercises are working together with the treatment of migraine and neck pain. We also aim to provide the basis and relevance of cognitive rehabilitation and double-task-multifunctional training and the importance of fatigue and mood problem management.

**Keywords:** concussion, rehabilitation, concussion subtypes, vestibular rehabilitation, ocular-motor rehabilitation, neck pain rehabilitation, post-concussion migraine, persistent post-concussion symptoms

## 1. Introduction

A concussion is a mild traumatic brain injury caused by a direct blow to the head, neck, or elsewhere in the body, resulting in an impulsive force being transmitted to the brain. This initiates a neurotransmitter and metabolic cascade, with possible axonal injury, blood flow change, and inflammation affecting the brain [1]. This leads to a brain functional impairment that provokes signs and symptoms, such as headache, neck pain, nausea, balance problems, gait impairment, dizziness, fatigue, sleep disturbances, mood changes, cognitive and focus impairment, less tolerance to cognitive and physical exercise, blurred vision, and visual problems. This is a reversible condition that usually resolves within 2 to 4 weeks, but it can last months or longer [2, 3]. Experiments on rats demonstrate that, during this period of time, brain cells undergo an energy crisis and are more vulnerable to new traumas because of blood flow changes [4–7]. Advanced neuroimaging studies on humans seem to validate these findings [3]. During brain vulnerability period, any additional concussions can lead to an acute more aggressive brain injury, known as diffuse cerebral swelling, or to a progressive subclinical injury summation until massive cell death and encephalopathy, best known as chronic traumatic encephalopathy [8]. United States Centers for Disease Control and Prevention (CDC) have labeled concussion a major public health

issue due to acute and potential long-term effects associated with this injury [9]. Nowadays, many concussions still remain undiagnosed, and above all sport-related concussions [10], but the trend is positive. Over the past decade, knowledge about concussion has increased significantly, with increasing hospital consultations [11] and medical attention.

On actual knowledge, avoiding second-impact exposure and treating concussion with clinical and objective recovery are the key in preventing brain traumatic encephalopathy. That is why it is so important to know how to manage and treat concussions.

## 2. How concussion evaluation is important for rehabilitation

A concussion is a complex heterogeneous injury that presents with a variety of symptoms and clinical findings. The primary goal in concussion evaluation is to characterize the clinical presentation, identify factors of possible prolonged recovery and prescribe a specific treatment plan.

Clinical presentation is different in every concussion by symptom types, intensity, and duration. Researchers have attempted to classify concussions into specific clinical profiles, to help clinicians with prescription and follow-up. Clinical profiles are supported by intuitive evidence, but to date, they are not empirically validated. Nevertheless, they are useful for educational purposes and help in clustering and focusing on current concussion rehabilitation indications. Moreover, it can help in drawing a tailored rehabilitation protocol, which seems promising in concussion recovery, instead of a one-size fits all approach.

Here, we report the main clinical profile classification proposed by the literature.

Collins et al. [12] categorized concussion into five clinical profiles and two modifying factors. It is based on symptoms evaluation and physical examination only; it can be applied from the first week following injury and profiles are not mutually exclusive as the overlap is possible:

1. Vestibular

2. Ocular-motor

3. Cognitive/fatigue

4. Post-traumatic migraine

5. Anxiety/mood

Modifying factors are:

1. Cervical

2. Sleep disturbances

Ellis et al. [13] proposed a classification into three post-concussion disorders and two modifying factors, which can be applied after 3 weeks from injury and it is based on symptoms evaluation, physical examination, and aerobic treadmill testing.

1. Physiological

2. Vestibular-ocular

3. Cervicogenic

Modifying factors are:

1. Mood disorders

2. Migraine

In other studies, even if a classification is not proposed, researchers identify the necessity to have a targeted evaluation and rehabilitation protocols for symptoms, such as headache, insomnia, cognition, mood, balance, vision, and fatigue, if symptoms last more than a month, which recall symptoms identified in the previous classifications.

Clustering patients' symptoms into this clinical profile are helpful for tailored treatment prescription, which we will describe soon in this chapter. A recent review states that individually tailored multimodal interventions have a worthwhile effect in providing a faster return to sport and clinical improvement, specifically in those with persistent symptoms [9, 14, 15]. Collecting a good clinical history is also fundamental. Identification of existing pre-injuries factors that can influence recovery is mandatory.

It has been demonstrated that the natural history of concussion, from 70% up to 85% of cases, is a spontaneous recovery within 2 weeks for adults and 4 weeks for children and adolescents. Patients will experiment with a natural reduction in symptoms by number and gravity through days, without any particular intervention [16, 17]. This means that, after diagnosing a concussion, an observational approach could be part of the treatment process, as Nature is working on its own to promote spontaneous recovery. Nevertheless, it is crucial to know that symptoms and clinical recovery could happen in a shorter time than brain complete function recovery. Preliminary studies have shown that brain normal functioning recovery could last longer than the symptoms perceived [3, 18].

Moreover, we should remember that 15–30% of concussions are going to have a prolonged recovery, and they will need a different approach and treatment. Thus, it is really important for a clinician, to draw up a precise clinical history to help understand if a wait-and-see approach is actionable, or close surveillance and a more active treatment is necessary.

Prolonged post-concussion symptoms (PPCS) and post-concussion syndrome (PCS) are labels used to identify symptoms lasting more than 4 weeks. Researchers are trying to understand recovery trajectories and predict prolonged recovery time as a way to stratify patients for a tailored rehabilitation and treatment protocol.

Nowadays, there are no objective measures to predict prolonged recovery: salivary biomarkers and advanced MRI spectroscopic imaging are promising fields of research, but more studies need to be done before application in clinical settings [3, 19]. Nevertheless, some factors on clinical presentation and history seem, on actual knowledge, to predict recovery time.

Symptoms severity score and overall symptom burden seem to be the most significant predictor of prolonged recovery [10, 20–22], history of previous concussions, sleep disturbances [23], vision and vestibular problem and a history of motion

sickness seems to predict prolonged recovery in children [24], prior diagnosis of mental health problem, as depression, anxiety, bipolar and personality disorder are predictive for prolonged recovery [25], prolonged rest and delay in search for medical attention relate to a longer recovery time too [26].

Physical examination and objective tests are also important to determine a patient's actual impairments and to discover new emerging factors that could predict a longer recovery. For example, cognitive impairment, such as reaction time and visual motor speed performance in neurocognitive testing, relates to prolonged recovery [20, 27].

Once collected all the information, clinicians are ready to give treatment indications and prescribe rehabilitation.

Part of concussion treatment is based on medication, but it will not be discussed, as it goes beyond the aim of this chapter.

## 3. Treatment indication and tailored rehabilitation

### 3.1 Do not harm: avoiding a second impact

First do not harm, state the Hippocratic Oath. Protecting a patient from a second brain impact, especially if close to the one he/she is suffering, is mandatory. As said before after a brain injury, even if mild, the brain lays in a state of vulnerability [1], and a second impact could lead to a Second Impact Syndrome (SIS) or diffuse cerebral edema, with the greatest risk occurring in the first 10 days post-injury [16]. It is particularly true in sport-related concussion because of possible repetitive traumatic events [28], related to sports characteristics. Returning an athlete to play with persistent symptoms may predispose the athlete to a higher risk of a new brain impact injury as concussion decreases the cognitive ability and reaction time, which theoretically diminished an athlete's ability to respond to the demands of the sport. Attention should be paid also to other environments, thus reducing risk exposure to driving, home accidents, or work accidents is recommended until medical clearance.

### 3.2 Observation as the first step of concussion treatment

If clinical history and physical examination are not suggestive of prolonged recovery, an observational approach could be part of the treatment process, as Nature is working on its own to promote spontaneous recovery. As said before, 70–85% of concussions will recover spontaneously, and follow-up could be a good managing decision. Nevertheless, we should also remember that medicine is not an exact science, so follow-up is always recommended.

Usually, behavioral modifications are suggested:

- Regular schedule of sleep and meals.
- Good hydration.
- Do not take drugs or alcohol.
- Do not take medicine if not prescribed.
- If symptoms worsen, go to seek medical attention.

If the clinician is an expert in managing concussion, an active and individualized approach is always recommended, but if patient history and symptoms do not depict a serious clinical presentation, remember that sometimes wrong prescriptions are worse than no prescription.

### 3.3 Rest: is it useful in concussion treatment?

During the acute post-injury period, patients who suffered from concussion usually experience intense symptoms that are worsened by cognitive or physical activity, and assuming that vigorous activity could magnify the underlying energy crisis is reasonable [9, 29, 30]. Moreover, as said before, a second impact during the period of brain vulnerability could lead to more aggressive injury and CTE [31–34]. Literature also demonstrates that delayed reporting and removal from athletic activity following a sports concussion, predicts prolonged recovery [35], meaning that early physical activity could relate to a longer recovery period. These are the main reasons why most clinicians prescribe rest until symptoms improve, and in the previous decade, rest was highly recommended [9].

Nevertheless, it is important to notice that *avoiding contact* during this period and *rest* are two different strategies. If the first one is always recommended as far as the patient remains symptomatic or until medical clearance, the second one is open to different management.

Researchers noted that patients with the highest and lowest levels of activity had worse outcomes and took longer to recover, suggesting that too much or too little physical and cognitive activity could be detrimental to recovery [31].

Strict and prolonged rest in medicine is demonstrated to be of no benefit. It exacerbates symptoms and prolongs recovery [36], and the same thing applies to brain injury [37].

In addition, we should also state that strict rest, meaning no physical or cognitive activity during the time prescribed, forces people who suffer from concussion to avoid sports, social life, and school or work. This has a big impact both on the patient's psychology and on the society [9].

In contrast, there is increasing evidence that early mild noncontact, such as physical activity, does not appear to worsen or cause additional injury and indeed seems to help recovery [9, 17, 37, 38].

So, how is rest beneficial? How much and how long should rest be prescribed?

Evidence from the last 10 years showed that strict rest beyond 2 days will prolong recovery from concussion [37, 39–41], and that symptoms are of greater magnitude.

In agreement with that, the concussion consensus in the sports group set an average rest period of 24–48 hours after a concussion trauma, before starting rehabilitation and progressive return to physical and cognitive activity [2]. During the first few days, rest should not be strict avoidance of physical and cognitive activity [31], but should be dosed, based on the patient's sensitivity to symptom exacerbation. Physical and cognitive activities of daily living are permitted if they do not exacerbate symptoms, absence from school or work is recommended. A patient could sleep and take naps if needed.

### 3.4 Physical activity as a medicine for concussion

Many studies demonstrate that physical activity is the principal intervention in concussion management as it helps in recovering faster and lowering symptoms

intensity [26]. Thus, it is indicated in any concussion case, even if prolonged recovery is not suspected.

If we consider "physical activity" as a medicine, it is important to understand what is the "active ingredient" and how to dose it. "Physical activity" may include aerobic exercise, resistance training, full body exercise, sport-specific exercise, balance and vestibular exercise, visual ocular-motor exercise, postural exercise, multitasking exercise ... and so on.

What is known nowadays is that aerobic exercise and full body exercise, in general, are good interventions for concussion recovery, a sort of "one size fits all" approach, while other types of physical exercise are more specific for concussion clinical subtype profiles. So, in this chapter "physical activity" will be synonymous with "aerobic exercise, resistance training, full body exercise, and sport-specific exercise," while vestibular rehabilitation, balance exercise, motor-ocular exercise, visual rehabilitation, and cervical rehabilitation will be deeply investigated later in this chapter.

It is well established that concussion leads to an altered ionic and cellular homeostasis, that requires more ATP usage to restore the physiological environment. This energy requirement crashes with a setting of reduced cerebral blood flow, resulting in a mismatch between energy supply and demand [32]. The autonomic nervous system is also altered in the concussed patient, and this condition leads to an altered modulation of cardiac function and cerebral perfusion [42, 43].

Introducing aerobic exercise in this setting of the energy crisis is not so straightforward, but at the same time it is well-known that aerobic training could help in autonomic dysfunction recovery [44].

As said before, an average rest period of 24–48 hours after a concussion is recommended, then an initial light aerobic exercise could be initiated, even if symptomatic. The main warning lights that we have in a concussed patient are symptoms. Thus, it is mandatory to count on personal patients' symptoms and feelings and it is important to establish good cooperation with the patient. The active training could be done independently, but it is recommended to be followed by a personal trainer or physiotherapist, who is trained in concussion rehabilitation.

Based on literature findings, here we provide guidance on validated physical exercises for concussion.

### *3.4.1 The graduated return to play protocol (GRTP)*

The fifth consensus statement on concussion in sports creates an easy graduated protocol to return to sport participation [2]. It is based on the progressive introduction of aerobic and resistance training, mixed with sport-specific exercises. For contact sports, returning to full contact practice is permitted after medical clearance. This approach could be applied to any sport.

The characteristics of this approach are based on progressive physical stimulation and evaluation of symptom exacerbation. Every step should last at least 24 hours and if symptoms worsen with the exercise, the athlete should go back to the previous step.

### *3.4.2 GRTP*

- Stage 1. Symptoms-limited activity: Daily activities that do not provoke symptoms and gradual reintroduction of work/school activity.

- Stage 2. Light aerobic exercise: Walking or stationary bike increases heart rate.
- Stage 3. Sport-specific exercise: running or skating drills.
- Stage 4. Harder noncontact training drills, start a progressive resistance training.
- Stage 5. Full contact practice (following medical clearance): Participation in normal training activities.
- Stage 6. Return to sport: Normal gameplay.

Dosing exercise based on symptoms provocation only is a useful method if no assessment tools are disposable. It can be applied to everyone, athletes or not, helping them to increase physical activity. The graduated return to play protocol is obviously particularly indicated for sports concussion, but the underlying symptoms-based approach could be applied also for people who are not athletes, as a "sub-symptoms threshold method" (see below).

For example, we can use the same protocol by using only aerobic exercises, such as walking, running, and cycling. Every step should last at least 24 hours and exercises should be done on a daily basis or 6 days/week and stay at a sub-symptoms' threshold level. On a scale from 0 to10, any new symptoms or symptoms worsening of 3 points out of 10 is considered an "exercise symptoms provocation," and the patient should set his exercise to a lower level, or stop.

The patient should start at a light perceived level of exercise and monitor his symptoms. If no symptoms are provoked, the patient can increase activity level by duration and/or intensity or exercise type and, again, monitor his symptoms. If the exercise provokes symptoms, the patient should set the training at a previous level of exercise for the next 24 hours.

The same pattern could be applied to resistance training.

### *3.4.3 The concussion sub-symptoms threshold approach*

This method is based on the physical activity below the symptoms threshold, which is similar to the previous approach. Nevertheless, it is based on aerobic exercises and a more objective setting and progression.

An initial test should be done to evaluate patient tolerance to aerobic exercise, which has been demonstrated to be lower in concussed patients because of the autonomic dysregulations mentioned before. It is important to set each patient's threshold for symptom exacerbation because the following physical activity is set on a sub-threshold level, and then a new test for progression will follow.

The most popular and validated test is the Buffalo Concussion test. It is done on a treadmill (BCTT) [45] with a progressive increase of aerobic loading, measuring heart rate and symptom exacerbation. In particular, the patient is asked to wear a heart rate monitor and to step on a treadmill. To increase heart rate, the treadmill is tilted progressively, similar to the Balke treadmill test, until aerobic intolerance. The aerobic threshold is set if the maximum heart rate is reached or new symptoms appear or symptoms are worsened by 3 points on a scale out of 10. The patient is then instructed to perform aerobic exercise at 80% of the heart rate threshold for 20 minutes on a daily basis. If the patient is an athlete, it is recommended to exercise at 90% of the heart rate threshold for 20 minutes twice a day. If patients feel

symptomatic while exercising at home, they have to stop and rest and continue the next day at a lower exercise intensity. If not, patients may extend the duration of exercise from 20 to 30 minutes or more, keeping the heart rate steady. A daily symptom diary is recommended to track symptoms exacerbation and exercise progression.

After 1 week a patient could increase heart rate exercise by 5–10% or, if possible, the Buffalo Concussion test should be repeated to set a new symptoms threshold [46, 47].

The test could be performed also on a stationary bike (BCBT) [45].

During the last years, aerobic exercise prescriptions were made easier even in case of a lack of aerobic test or heart rate monitor availability, for more practical use. Test explanations, preset modules, and preset exercise prescriptions are available online, see link below for more information.

BCTT: https://cdn-links.lww.com/permalink/jsm/a/jsm_2020_01_28_haider_19-313_sdc1.pdf

BCBT: https://cdn-links.lww.com/permalink/jsm/a/jsm_2020_01_28_haider_19-313_sdc2.pdf

Aerobic exercise prescription after BCTT or BCBT:

https://cdn-links.lww.com/permalink/jsm/a/jsm_2020_01_28_haider_19-313_sdc3.pdf

Aerobic exercise if HR monitor is not available:

https://cdn-links.lww.com/permalink/jsm/a/jsm_2020_01_28_haider_19-313_sdc4.pdf;

https://cdn-links.lww.com/permalink/jsm/a/jsm_2020_01_28_haider_19-313_sdc5.pdf

Aerobic exercise prescription if no threshold test is performed:

https://cdn-links.lww.com/permalink/jsm/a/jsm_2020_01_28_haider_19-313_sdc6.pdf

### 3.5 Vestibular rehabilitation

If vestibular symptoms are present and a vestibular clinical profile is recognized, a vestibular evaluation and rehabilitation are recommended. Studies evidence that an intervention before 30 days from the injury is indicated [48], but it can be started sooner.

The vestibular system is a complex circuit that detects the motion of the head in time and space and helps to regulate postural stability and balance (vestibulo-spinal reflex), and stabilizes vision (vestibulo-ocular reflex). Disruptions to this system due to concussion are frequent [49], in fact from 23% up to 81% of concussed patients experience dizziness [50].

The reason is likely due to a complex and massive interaction of neurons engaging long pathways, including cortex, brainstem and reticular formation, cranial nerves, and peripheral organs.

Symptoms reported are vertigo, dizziness, impairment in balance, in gait and visual motion sensitivity. Visual motion sensitivity refers to an inability to centrally integrate visual and vestibular information, in particular, in busy environments, such as shopping malls. To make the pathology more complex, this dysfunction may be accompanied by anxiety [51]. Alteration in visual and spatial orientation is identified as a cognitive component of vestibular impairment, as the system is also connected to cortical areas.

Usually, these symptoms are recalled under the term "post-concussion dizziness" or "post-traumatic dizziness," as part of the post-concussion syndrome. It is unclear, to our knowledge, if it is due to functional microstructural abnormalities from the trauma or whether there is an unrecognized labyrinthine cause, or both of them. Autonomic dysfunction could be a potential contributor to post-concussive dizziness, too.

Thus, the necessity of a specific evaluation of the vestibular system, before setting up the rehabilitation program, is mandatory.

If the patient reports spinning vertigo, a labyrinthine cause should be evaluated with specific testing as caloric testing, postural testing, audiometry, and VEMPs, to ensure the correct function of the semicircular canal and otolith organs [49].

If a labyrinthine cause is identified, the treatment aims to resolve the underlying cause. For example, benign paroxysmal positional vertigo (BPPV) should be identified and treated as soon as possible, while possible ruptures of portions of the membranous labyrinth, bleeding, traumatic ischemia, utricular and saccular injuries, and perilymphatic fistula should be addressed to a specialized ENT doctor [49].

If a labyrinthine injury is not identified, the hypothesis of microstructural dysfunction of the brain is reasonable, and symptoms are due to the inability to integrate visual, proprioceptive, and vestibular information. In this latter case, the literature provides some easy and practical tests to assess vestibular and oculomotor function as the Vestibular-Ocular-Motor Screening test [51–53].

Therapies for vestibular impairment are a group of active treatments, including dynamic movements involving head and eye coordination, balance and gaze stabilization exercises. These therapies are based on an expose-recover model involving exercises that stress specific impairments and make symptoms arise in a controlled way to promote recovery.

Rehabilitation interventions were designed to work on vestibular-ocular reflex impairment improving gaze stability and eye-head coordination, thus promoting habituation and adaptation to dizziness symptoms.

Different vestibular rehabilitation techniques may be used based on the symptoms and impairments. Here, we list the main group of clinical impairments and symptoms and the type of physical interventions [50, 54, 55]. Vestibular-ocular reflex (VOR) impairment contributes to dizziness, vertigo, disequilibrium, visual motion sensitivity, unstable sensations, oscillopsia, impaired fixation, visual tracking, instability, and blurred vision [56]. It can be improved by targeted eye-head coordination and gaze-stability training.

- Eye and head coordination exercises are based on holding the eyes on a fixed target while moving the head up and down or side to side. Progression of the exercise is made by symptoms exacerbation and adding complexity to the exercises as it can be done sitting or standing, walking or jumping.

- Gaze stability training is a group of exercises in which the patient is asked to hold the eyes on a target, as above, but the target could be in motion or different targets are proposed, adding smooth pursuit and saccadic eye movement to the previously described exercises.

- Vestibular-ocular reflex cancelation is based on the ability to inhibit vestibular-ocular reflex. The eyes are fixed on a target while moving the head, but the target is moving in the same direction and speed of the patient's head.

- Visual motion sensitivity dysfunction is related to symptoms when exposed to environments with complex visual stimuli. It depends on an altered integration of vestibular and visual information and on the alteration of the optokinetic mechanism (see below). A graded and systematic exposure to visually stimulating environments is often used as a rehabilitative technique to habituate the individual and train the system. In the office visual exposure to rotating and confusing backgrounds are used too.

- Balance dysfunction is based on an altered vestibulospinal reflex or proprioceptive deficits, it can be tested in the office with some practical and easy tests, such as Fukuda, Romberg test, Balance Error Scoring System Tests, or Sensory Organization Test.

- Balance training includes sensory proprioceptive training and dynamic balance training. Progression could be made based on the patients' symptoms by changing position (sitting or standing), changing floor hardness or stability (proprioceptive rocker board or ball), narrowing the base width, standing on one leg, closing the eyes, or confounding glasses may be used to treat impaired postural control. Walking, running, and jumping are used to increase the difficulty and as aerobic stress. Also, head movements could be added.

Many studies have shown that vestibular rehabilitation is effective [57–61].

If post-traumatic dizziness is persistent despite rehabilitation, other causes should be examined as, for example, cervicogenic dizziness, anxiety-related dizziness, post-traumatic migrainous-related dizziness, or a more serious underlying diffuse axonal injury (DAI). DAI is usually reported in more severe traumatic brain injury, but it has to be taken into account as central nervous dizziness is possible and, if clinically suspected, a diffusion tensor imaging or advanced fiber tract MRI has to be considered [49].

### 3.6 Visual and ocular-motor rehabilitation

As for every specific rehabilitation protocol, it is important to collect a good clinical anamnesis and physical examination. It will not be discussed as it is not the aim of this chapter, but abnormal findings will guide in the correct rehabilitation approach. Clinicians should remember that particular abnormal findings in vision and ocular movement, such as visual field loss, cranial nerve palsy, and diplopia, should be investigated with brain MRI, unless made before, to exclude the diagnosis of a major brain injury, instead of a concussion [62]. Especially in patients with prolonged symptoms and recovery.

The visual system is particularly vulnerable to brain traumas because of the numerous brain pathways, cortical areas, and cranial nerves involved in vision. In fact, usually monocular (nuclear and infranuclear) eye movement, best known as ductions, is normal, while binocular (supranuclear) eye movement, such as smooth pursuit, saccades, and optokinetic nystagmus, has pathologic findings. The reason is supposed to be due to a longer neurologic pathway of control, as said before. The alteration could be found also in vestibular-ocular reflex and vergence movements.

Given the fact that concussion is not related to anatomical damages, visual problems are identified as visual dysfunction that could lead to symptoms, such as blurry vision, difficulty in reading, and light sensitivity, which are a common complaints

(35–65%) in post-concussion patients. Visual information processing could also be altered, and thus should be investigated as cognitive impairment [63, 64].

In 2015, a "see to play" protocol was released to help clinicians in rehabilitation prescription for prescription ocular dysfunction, it is based on evaluation and a sort of "one size fits all" treatment, that you can find in the references at the bottom of the page [65].

Below, we report the main pathological findings in visual/oculomotor function in concussed patients and rehabilitation indications for recovery.

- Convergence insufficiency is the reduced ability to converge and is one of the most common concussion visual dysfunctions. It may produce problems with reading, such as diplopia, skipping words or losing one's place, and becoming more easily fatigued while reading [66–68].

    - Convergence insufficiency could be treated with specific exercises. There is a magnitude of exercises in literature, but what seems to be more effective is a combination of office-based exercises and home reinforcement. In particular, office-based exercises should be done by an expert optometrist. The specific indication could be found in the CITT protocol [69] and is based on gross convergence exercises, positive fusional vergence exercises, rump fusional exercises, and jump fusional exercises [69, 70].

- **Accommodation insufficiency** is the reduced ability of the eye to change focus from a distant to a near target and is reported to be as high as 50% in concussed patients. It contributes to binocular visual function and may produce blurry vision with near tasks, as well as headaches, fatigue, and photophobia. It could be associated with convergence insufficiency and pupillary dysfunction [66, 68, 71].

    - **Photophobia** is related to pupillary dysfunction in a suspected imbalance between the parasympathetic and sympathetic systems. It should be treated with a reduction to light exposure (hat or glasses with low-density (20% light reduction) achromatic tint, and neutral gray. Physical exercise is also recommended for a better autonomic balance.

    - **Accommodation dysfunction** could be treated with exercises that enhance accommodation. It could be driven by blurry vision, using various magnitudes of positive/negative lenses in a repetitive manner (flippers) and based on the subject's task performance, the difficulty could be altered by increasing the dioptric power of the lens. Or it could be driven by vergence and proximity. In this case, the exercises could be done monocular or binocular, and progression is made by bringing closer and closer an object asking to focus on it [71].

- **Saccades** are rapid refixation of eye movements from one target to another generated from the frontal eye field. Both vertical and horizontal saccades are important in most visual tasks, including reading. They are found to be abnormal after concussion in as many as 25–33% of children and adolescents [66, 72].

    - Saccades are usually treated by a workout on rapid eye movements, usually, binocular exercises triggering horizontal, vertical, and near-far saccades are

used. Hart chart, visual scanning exercises, reading, or computerized exercises, for example, Sanet Vision integrator or similar are some of the known interventions [70].

- **Smooth pursuit** are complex conjugate, steady, symmetric eye movement that permit one to follow a target, They require attention, anticipation, and working memory, and thus their pathway is a complex interaction between brainstem vestibulo-oculomotor pathways and cortical neurocognitive pathways. In children and adolescents with a concussion the prevalence is from 33 to 66% [66, 73].
    - Smooth pursuit could be worked out by different monocular or binocular exercises, such as thumb rotation, rotating pegboard, tracking objects, or using a computerized approach, such as Sanet Vision Integrator or similar, in sports field strobe glasses could be used [70].
- **Optokinetic nystagmus** is a reflexive eye movement driven by the motion of the visual field on the retina and consists of nystagmus with slow phases in the same direction as the moving stimulus and quick phases in the opposite direction. It is currently believed this reflex is generated through the central processing network integrating visual, vestibular, and proprioceptive information. Symptoms related to optokinetic dysfunction could be related to the best known "visual vertigo" or "visually induced dizziness," dizziness that appears during exposure to environments with complex visual stimuli (e.g., supermarket aisles) [74].
    - Treatment of these symptoms is frequently connected to vestibular rehabilitation discussed before and it is based on an "expose and recover" approach. In-office treatment is usually made in a room free from points of reference and the visual stimulus should reproduce the appearance of the optokinetic disk (optokinetic rotatory disk, or confounding background movements while gaze is maintained on a fixed dot or figure). Usually, real-life exposure to environments with complex visual stimuli is also performed [75].
- **Vestibular-ocular reflex** is a reflexive eye movement in relation to head movement as rotations, tilt, or extension. It is fundamental for gaze stabilization and its dysfunction could lead to different symptoms, such as blurred vision, dizziness, vertigo, balance-related symptoms. Due to the multiple structures involved in these reflexes' pathways, it has a high prevalence in concussed patients.
    - Its rehabilitation has been deeply analyzed in the previous paragraph [56].

Usually, in concussed patients, multimodal exercises are proposed and the result is a mixture of the previously listed exercises, such as saccadic eye movements, visual pursuit, tracking tasks, alternating monocular and binocular tasks, and reading tasks. In addition, visual attention tasks, such as visual-field scanning, attentional grid, and near-far-vision focal shifting, may also be used. Often these tasks involve the use of prisms, special optical lenses, eye cover-ups, penlights, and mirrors. The effectiveness seems to be higher if multiple domain exercises are prescribed [51, 76].

### 3.7 Cervical rehabilitation

Cervical or neck injury can be defined as persistent impairments caused by dysfunction of the somatosensory system of the cervical spine likely caused by strain on the soft tissue.

Most cervicogenic symptoms have been attributed to injury or impairment of the upper cervical spine. The reason is that afferents from the upper cervical spine (C1-C3) are widely interconnected. They carry somatosensory information of head and neck position to the brainstem and the cerebellum, useful for adaptive postural and oculomotor regulation, and to the thalamus and the primary somatosensory cortex, useful for the perception of head and body position.

In fact, their direct interactions with the vestibular nuclei, superior colliculi, and central cervical nuclei help coordinate important reflexes (cervico-ocular reflex and vestibulo-ocular reflex) required for gaze stabilization during functional head and neck movements, and for postural stability (cervicocollic reflex and vestibulocollic reflexes). In addition, interactions with the spinal tract contribute to postural tone regulation (cervicospinal and vestibulospinal reflexes).

During concussion, especially if caused by a whiplash movement, abnormal somatosensory afferents arising from the muscle spindles, nerve roots, and joint and pain receptors of the cervical spine could determine cervicogenic pain, dizziness, disorientation, blurred vision, and balance problems. Aberrant cervical somatosensory information may directly affect the cervical and vestibular reflexes and ocular responses, or may indirectly affect the system by creating mismatched information between abnormal somatosensory cervical information and normal vestibular and visual information. Moreover, cervical afferents interact with the trigeminal sensory afferents through the lesser and greater occipital nerves and could lead to hemicranial pain [77–80].

Cervical spine physiotherapy intervention has been demonstrated to be effective in concussion rehabilitation and symptom improvement [81, 82].

Rehabilitation intervention included manual therapy of the cervical and thoracic spines, cervical neuromotor training exercises, and sensorimotor training exercises. It is important that such a program does not produce an increase in pain or headache, but that some temporary exacerbation of dizziness, nausea, unsteadiness, and/or visual disturbances is acceptable [82].

It is important to perform a good physical examination in order to understand if pain originators, muscle hyperactivation, and nerve sensitization are present and to address rehabilitation. If dizziness is present, it is important to understand if it is originated from the cervical spine by performing specific tests, for example, cervical joint-reposition error test, smooth-pursuit neck-torsion test, head-neck differentiation test, cervical flexion-rotation test, and motor-control assessment of deep cervical flexors and extensors [78].

Cervical pain could be discogenic or due to muscle contraction and nerve sensitization. Manual therapy of the cervical and thoracic spines should be addressed based on physical examination and include a set of manipulative therapy for pain, muscle de-contracture, decreasing unwanted muscle activity, and range of movement improvement and relaxation, which are demonstrated to improve patients' symptoms and joint position sense and dizziness [82, 83].

- Cervical neuromotor training exercises and cervical muscle training have been suggested to improve balance proprioceptive neuromuscular facilitation, for example, activating the deep cervical flexors and scapula stabilizers [82, 84].

- Sensorimotor retraining exercises are a set of specific neuromuscular control exercises to improve cervical joint position sense, head relocation accuracy, and movement sense. It could be trained by using exercises with auditory or visible feedback as a laser fastened to the head to trace patterns on a wall, such as a figure-of-eight. It is important to work also with posture, in particular, by giving ergonomic and postural advice for work sitting position [82].

The best evidence of concussion rehabilitation programs is performing a mixture of vestibular, ocular, and cervical exercises, as they are strictly interconnected [51].

### 3.8 Post-traumatic headache: non-pharmacological treatment

Post-traumatic headache (PTH) is one of the most common sequelae of traumatic brain injury. It is considered a secondary headache defined by the onset of a headache within 7 days following trauma or injury. If the headache persists beyond 3 months, is it defined as a persistent post-traumatic headache. PTH could be associated with somatic symptoms, for example, nausea, vomiting, photophobia and phonophobia, and cognitive and psychological symptoms.

Possible mechanisms of PTH include trauma-induced impairment in descending modulation of pain-modulating systems, neurometabolic changes, and activation of the trigeminal sensory system. We should also remember that Nociceptive input from upper cervical afferents might also converge on the trigeminocervical complex.

It is important to understand if PTH is a tension-type headache, cervicogenic headache, or a migraine, because treatment interventions could differ. ICHD-3 criteria for diagnosing tension-type or migraine are clear. In the diagnosis of PTH, it is also fundamental to reveal the possibility of co-occurring medication-overuse headaches (MOH), which are frequent and have to be addressed.

The heterogeneity of the headache phenotype in PTH might partially be explained by genetic predisposition and a history of headaches [85, 86].

If a headache or migraine clinical profile is suspected then setting a specific treatment is important in concussion rehabilitation.

The approach to the treatment of post-traumatic headache is both pharmacological and non-pharmacological approaches. In this paragraph, we will list the non-pharmacological intervention, as pharmacological treatment is not the aim of this chapter.

- Lifestyle modifications are important to avoid headache triggers. A headache diary is a helpful tool to aid patients in identifying particular triggers and documenting therapeutic responses. Typical lifestyle modifications are: having regular meals and sleep schedule, avoiding alcohol, chocolate, artificial sweeteners, excessive caffeine intake, managing stress, having good hydration, and performing light aerobic exercise [87].

- Other therapies are relaxation training, thermal biofeedback, and cognitive-behavioral therapy. Cognitive-behavioral therapy (CBT) refers to cognitive processes that help in the resolution of psychopathology, particularly emotional pain and dysfunction. It enables patients to develop preventive and acute care strategies, such as trigger identification, modification of maladaptive interrelated thoughts, feelings, and behaviors, surrounding headache, and physiological autoregulation strategies [88].

- Cervical rehabilitation is beneficial in tension-type headache, but also in cervicogenic headache and migraine that have a hyperactivation of the trigeminal system triggered by afferents from the upper cervical spine [89].

### 3.9 Cognitive impairment: indication for rehabilitation

Cognitive complaints following a concussion are frequent and include mental fogginess, feeling to be mentally slow down, difficulties with attention and concentration, and memory problems. They may also be exacerbated by emotional symptoms, such as anxiety, irritability or depression, sleep disturbances, and pain.

Cognitive functions are a group of brain superior functions, including memory, visuospatial orientation, attention, learning, information processing capacity, and reaction time. The most frequently affected domains after a concussion are memory, attention, and visuospatial functions [90, 91].

Cognitive impairments are due to the well-known energy crisis of the brain, which is incapable of providing good interaction between complex neural circuits from different brain areas. In literature, there is also evidence in support of a diffuse axonal injury as an anatomical substrate underlying cognitive dysfunction [90], and depending on the extent and distribution of damage multiple sensory, motor, emotional, and cognitive systems can be affected [92].

Even if most of the studies demonstrate that cognitive impairments are acutely associated with concussion, there is also evidence that usually they improve 2 weeks post-injury. Nevertheless, there is less agreement in the literature on when these deficits completely resolve, and there is evidence that some cognitive deficits can last more than 6 months [93]. Moreover, studies conducted on long-term sequelae in concussed patients reveal that cognitive impairment could arise as a summation of multiple concussions [94].

It is mandatory to remember that during the acute phase of concussion, cognitive symptoms may be due to other concomitant causes, such as visual ocular-motor deficits, which could lead to blurred vision and difficulty in reading and focusing; post-traumatic headache that could be triggered by visual stimuli and so pushing the patient to avoid cognitive activity as a way to reduce pain; vestibular and visual vertigo lead the patient to avoid crowded places and has a high relationship with anxiety, which could arise cognitive issues; vestibular impairments are also related directly to visual and spatial orientation; and finally, autonomic dysfunction could provoke fatigue and difficulty in concentrating.

Knowing this interaction between neurological systems is important to address rehabilitation.

In the acute phase and initial cognitive rest is recommended for 48 hours, then an active approach could be initiated.

Cognitive rest includes reducing reading, computer use, texting, watching television or movies, playing video games, and similar mental activities. Complete cognitive rest is impractical and is not advised [95].

Then, a progressive return to the activity of daily living, return to school and work is recommended, it has to be taken as an “expose and recover” mental exercise, so accommodation could be necessary (see below). Treatment should also focus on the ocular, vestibular, cervical, and autonomic system to reduce cognitive cross-linked symptoms.

If cognitive impairments last longer than 2–4 weeks, a specific cognitive rehabilitation should be activated. If psychological health disorders are coexisting, adding cognitive behavioral therapy is suggested.

- Progressive return to learn and work:

Following a concussion, the active return to school and work is recommended to improve cognitive impairments and thus is a major priority for the recovering patient. Moreover, prolonged absence from school or work environments must be avoided to reduce the risk of secondary adverse social and emotional effects, for example, anxiety and depression [9].

Patients returning to school/work while recovering from concussion benefit from individualized management strategies, as concussion symptoms and cognitive impairments have an impact on academic learning and work performance [9]. Accommodative support and adjustments may be necessary to balance the goals of recovery and return to productivity, but it is also important to ensure that modifications are not prolonged when no longer necessary.

Accommodations for cognitive impairment for example are:

- Gradually school and work reentry, extra breaks or flexible work hours.
- Extra time for test assignment/task completion.
- Enhanced level of supervision, help taking notes, or recording classes/meetings.
- Increase repetition in assignments.
- Break assignments down into smaller pieces and deadlines.
- Provide alternate methods for the student to demonstrate mastery, such as multiple-choice.
- Temporary workload restrictions or placement in a completely different job function.

General accommodations, for example, are:

- Modifications in the school environment to reduce triggers for their symptoms, such as removal from gym or dance class, band/orchestra to reduce visual vertigo or headache, or avoiding bright light or loud noises places.
- Decreased computer work and screen exposure.

Literature proposed different return-to-learn and work strategies, for example the "return-to-learn protocol" proposed by Gioia [96], which is similar to the one used for return-to-play mentioned before in this chapter. Some organizations also released guidelines to help clinicians and school professionals with the management of their concussed students or workers [97, 98].

- Cognitive rehabilitation:

It refers to a set of interventions that aim to improve a person's ability to perform cognitive tasks by *retraining* previously learned skills and teaching *compensatory* strategies.

A neuropsychological assessment is fundamental to identify cognitive strengths and weaknesses and areas of treatment. The neuropsychological assessment is usually done by a neuropsychologist with paper and pencil battery tests. In recent years, many computerized neurocognitive testing, designed for concussed patients are at disposal and if specific training is present, they can be evaluated also by clinicians with different specialties [99, 100].

- Cognitive ***retraining*** is focused on restoring impaired skills through training specific domains and improving general intellectual and executive functioning, attention, memory, and processing speed. Attention exercises engage both visual and auditory skills. Attention and information-processing exercises are designed to enhance information retention and recall, contributing to improvements in memory and processing speed.

- Cognitive ***compensatory*** strategies are the addition of strategies to bypass the cognitive impairment. The key is achieving improved function through the use of an additional tool, for example, using a calendar to remember deadlines, bypassing memory impairments.

- Cognitive-behavioral therapy:

It is a talking therapy that can help patients in managing problems by changing the way they think and behave. It focuses on treating psychological health disorders, including mood, sleep, and anxiety [101].

### 3.10 Fatigue, anxiety, and sleep disorder: how to manage

*Fatigue* is defined as "the awareness of a decreased capacity for mental and/or physical activity, because of an imbalance in the availability, utilization, or restoration of resources needed to perform activities" [102].

In the acute phase post-concussion, more than 70% of patients report excessive fatigue, which can persist for years. It is significantly correlated with anxiety and depression and sleep disturbances [103].

Sleep–wake disturbance and fatigue have been linked also to reduced cognitive functioning [104]. Fatigue and autonomic dysfunction are also correlated [105].

- Fatigue management:

    - Lifestyle modifications are recommended, for example, drinking enough fluids to stay well hydrated, healthy eating habits, getting enough sleep, avoiding known stressors, and avoid alcohol.

    - Physical exercise is helpful in reducing fatigue and sleep disturbances [106].

*Mood and anxiety disorders* are frequent in post-concussed patients. It could be related to previous psychiatric conditions or to other post-concussion impairments,

such as vestibular dysfunction, visual motion sensitivity, migraine and isolation from school work, and social recreational activities.

- Anxiety management depends on symptoms gravity:
    - Mild anxiety could be managed with psychological intervention to gain acknowledgment of the problem, cognitive-behavioral therapy, and behavioral intervention similar to exposure therapy for the treatment of phobias. If psychogenic vertigo is present, vestibular rehabilitation may be recommended.
    - Moderate-to-severe anxiety and particularly if panic attacks are frequent, a psychiatric intervention is also suggested.

*Sleep disorders* reported in post-traumatic brain injury patients include insomnia and hypersomnia syndromes, circadian rhythm disorders, and sleep-related breathing disorders [107, 108]. The pathophysiology may include disruption of neuronal networks involved in the regulation of the circadian rhythm, but it is also related to other post-concussion symptoms, such as pain, headache, or mood disturbances. Studies demonstrate that there is a decrease in melatonin as a possible cause for circadian rhythm alteration. A lack of good-quality sleep is related to fatigue and can affect mood and cognitive functions.

- Sleep management:
    - During the first 48 hours after concussion, sleep is permitted as needed.

After the first few days, avoiding naps and having sleep habits are suggested. For example, having regular bed and wake times and a bedtime routine, such as a warm bath, is helpful. Also, having a healthy sleeping place (dark, clean, tidy, and quiet) is useful. Patients should avoid other activities at bedtime, such as reading, watching TV, or using the computer.

Eating foods containing magnesium, iron, and B vitamins, which could help in producing melatonin, instead of exciting food such as sugar and caffeine 4 to 6 hours before bed, is recommended.

Physical aerobic exercise is suggested everyday, but patient should avoid exercising too close to bedtime.

- Mindfulness therapy and acupuncture could help in some cases.
- Pharmacologic treatment is sometimes recommended if sleep disturbances persist. It could be addressed to treat sleep disorders or the underlying cause as migraine or neck pain.

## 4. Conclusion

A concussion is a heterogeneous and complex syndrome resulting from acute brain trauma. Most of the symptoms reported are related to a brain energy crisis and to disruption in neural circuits. It is considered a reversible condition, even if some

studies demonstrate concussion-related cognitive long-term effects and a suspicion of an underlying diffuse axonal injury is reasonable, as demonstrated in multiple research papers. The summation of a new concussion could lead to phosphorylated tau protein deposits and encephalopathy.

Symptoms usually recover in a brief period, from 2 weeks for adults to 4 weeks for children and adolescents, in almost 80% of cases, but they can last longer. Limiting cognitive and physical rest and setting an early active rehabilitation intervention is the key to a rapid recovery and limiting symptoms chronification.

Progressive cognitive and physical activity in a sub-symptoms threshold manner is the main effective intervention proposed nowadays. In recent years, more individualized rehabilitation is taking place with promising results in concussion management. Clustering patients in different clinical profiles based on individual symptoms lays the foundation for a specific rehabilitation: vestibular, visual ocular-motor, cervical spine, and cognitive rehabilitation are the cornerstone of a tailored intervention. Managing factors, such as mood and anxiety disorder, sleep disturbances, and fatigue, are also fundamental for the achievement of physical and mental well-being.

A concussion is an evolving burning issue and the world of research is moving faster to better understand the importance of concussion clinical profiles, the predictive power of biomarkers, and the effectiveness and timing of treatments.

## Conflict of interest

The author has no conflict of interest.

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Chapter 6

# The Impact of Traumatic Brain Injury on the Receipt of Services Following Release from Prison

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## Abstract

Traumatic brain injury (TBI) is found at substantially higher rates among incarcerated individuals compared to the general adult population. Individuals with TBI report a higher likelihood to experience a range of deleterious outcomes including substance abuse, depression, post-traumatic stress disorder, aggressive behavior, and violence. Thus, a history of TBI is likely to lead to the types of behaviors that will significantly increase the odds of an individual returning to incarceration post-release, as supported by recent research with a cohort of state prisoners. TBI has largely gone unaddressed by prison reentry programs that are integral to rehabilitating individuals returning to the community. Relatively little is known, however, about the effects of TBI on the receipt of services post-release. Additionally, few studies have examined sex differences in the prevalence of TBI in reentry populations. This chapter uses data from a multi-state prisoner reentry program randomized control trial to examine whether individuals with TBI are significantly different than their peers without TBI with respect to a variety of demographic and psychological metrics and in expressions of needs for and participation in services and programming during the transition from incarceration to the community.

**Keywords:** traumatic brain injury, post-traumatic stress disorder, criminal recidivism, mental health, substance abuse

## 1. Introduction

Over the past decade, traumatic brain injury (TBI) has become more widely recognized as a risk factor for criminal justice involvement. While there is no research that provides a causal link between TBI and criminal offending, studies have found TBI among justice-involved individuals to be as high as 10 times that in the general population. Research indicates that between 23–86% of individuals who are incarcerated have a history of TBI [1–4], significantly larger than estimates of TBI in the general population of 8.5% [5]. Like has been observed in adult populations, research has also found large proportions of youth in juvenile justice settings have a history of TBI [6, 7].

TBI is a significant concern among both men and women who are incarcerated. In the general population, epidemiological studies have found TBI rates among men to be almost twice as high as women [8], while the rates of TBI among incarcerated women are the same or slightly higher than their male counterparts [4, 9]. Recent research review articles have pointed to the male bias in TBI research due in large part to the higher incidence of TBI among men in the general population [10–13]. Mollayeva et al.'s analysis of 58 TBI studies that included a focus on sex/gender, found that women were under-represented in most studies and few researchers made hypotheses specific to sex/gender effects [10, 11, 14]. The potential for similarly high rates of TBI among incarcerated individuals warrants attention to the sex differences in this population.

Although there has been little attention devoted to addressing TBI as a risk factor for criminal behavior, there has been extensive focus in the United States since the late 1980s on identifying programs and approaches to assist those returning to the community from prisons and jails to achieve a pro-social future. Reentry services and programming can be characterized as those like cognitive behavior therapy (CBT) that are intended to promote individual change and those like employment services that are practical. To date, much of the evidence suggests that services that focus on individual change may be most effective at reducing recidivism [15–21]. Thus, although the high prevalence of TBI has not been explicitly addressed in reentry efforts, to the extent that programs and services focused on behavioral change and mental health have proven effective in improving outcomes for justice-involved individuals, it is reasonable that there is value in learning more explicitly about the relationships among TBI and service need and receipt during the reentry from incarceration.

After briefly reviewing relevant literature, this chapter describes the 265 individuals who were included in a randomized control trial to examine the impact of a wellness-based prisoner reentry program (5-Key Reentry Program) [22] and who participated in an interview 18-months after release from incarceration. The 18-month interview included the administration of the Ohio State University TBI Identification Method (OSU TBI-ID) [23, 24]. Information on the rate of TBI and a comparison of those with TBI to study participants without TBI on a variety of demographic characteristics is provided. The chapter then statistically examines self-reported receipt of mental health and substance use disorder services over time and whether the receipt of those services is differently impacted by either TBI or sex. The discussion and conclusions section summarizes the key findings and describes plans for future research.

## 2. Literature review

### 2.1 Sex differences in acquiring TBI

TBI results from a blow to the head from an assault, a fall, sporting accident, traffic accidents, or some sort of external force, and often leads to internal bleeding, bruising, and/or a reduced lack of oxygen flow to brain tissues. Men and women acquire TBI-related injuries in different ways. Men are more likely to receive their injuries from being struck by or against an object, interpersonal violence (i.e., fights), motor vehicle accidents, sports-related or workplace injuries, and in military combat; in contrast, women incur TBI more often in falls, concussive impacts, and in incidences of intimate partner violence (IPV) [11, 12, 25, 26].

Women who experience IPV are at great risk for TBI. According to the National Intimate Partner and Sexual Violence Survey, about 41% of women and 26% of men experience IPV in their lifetime [27]. IPV is defined as a pattern of physical violence, sexual violence, psychological aggression, and stalking behaviors inflicted by a current or former intimate [27]. The majority of IPV injuries sustained by women are to the neck, head, face, or strangulation [28]. While there are no epidemiological studies on the rates of TBI among IPV victims, one literature review on TBI from IPV found rates between 35–92% [29]. Jackson et al.'s study of women attending domestic violence support groups found that 92% reported a blow to the head or face and 44% reported loss of consciousness (LOC) [30]. Valera and Berenbaum found 74% of a shelter sample of women exposed to IPV sustained TBI and 50% had a history of multiple TBI [31].

Incarcerated women report high rates of violence and victimization. Three-quarters of women in prison report experiencing IPV, and 70% report experiencing severe physical violence from a parent or caretaker [32]. Colantonio et al. found that incarcerated women with TBI experienced more physical and sexual abuse than those without TBI [33]. Some research also suggests that TBI history increases the odds of reoccurring victimization compared to non-victims and single-event victims [34].

### 2.2 Impact of TBI

While not all individuals who experience TBI will have negative long-term outcomes, many will experience a decline in their daily functioning [35]. TBI may cause problems with various brain functions that can lead to slowed information processing, diminished decision-making capacity, attention disorders and other executive functioning impairments [36–38]. TBI is associated with cognitive impacts, including memory and attention deficits, impulsive behavior, and slowed responses [35]. The long-term social–emotional effects of TBI make individuals vulnerable for the risk factors associated with justice involvement, including aggression, rule-breaking, violence, irritability and risk-taking [37–39].

Research finds that individuals with TBI have a significantly higher occurrence of mental illness, suicide attempts, and poorer quality of life compared to individuals without TBI [5]. TBI in youth is linked to violent behavior, substance use, and mental health problems [35, 40]. Petruccelli et al.'s meta-analysis of research on adverse child experiences (which may include TBI) found strong associations between exposure to childhood violence and poor behavioral health outcomes [41]. Even individuals experiencing mild-TBI are three times more likely to experience depression compared to those without a TBI history [42].

Many TBI injuries are sustained through traumatic events, and some research suggests that PTSD can develop after severe, and even mild TBI [43]. TBI and PTSD have many symptoms in common, including concentration and information processing difficulties, memory problems, irritability, depression, sleep disturbance, nausea, and headaches [44, 45]. Among a sample of female veterans who experienced IPV, those with current IPV-related TBI symptoms were 5.9 times more likely to meet criteria for PTSD symptoms [26]. Given the higher rates of traumatic and TBI experiences, rates of PTSD and TBI co-occurrence are higher among incarcerated populations. Harner found almost half (45%) of the incarcerated women in their sample met criteria for PTSD at the time of the interview, and 23% with severe symptoms [46]. In one of the few large studies examining the relationship between TBI, PTSD, and criminal reoffending, Lattimore et al. found that TBI and PTSD predicted violent offending

but not general criminal behavior [47]. These findings suggest the need for officials to identify individuals with a history of TBI and PTSD and to develop appropriate interventions that could be provided during and after incarceration to reduce the post-release likelihood of violence.

Rates of substance use disorder (SUD) among individuals with TBI is significantly higher than among the general population, with ranges for those with TBI from 37–66% compared to 11% among those without TBI [48, 49]. There is a high co-occurrence of TBI and risky substance use, and while the causal link is unclear, there is evidence that each increases the incidence of the other [50]. Fishbein et al.'s study of TBI and SUD co-occurrence among incarcerated individuals found early TBI predicted early on set and severity of drug use, and earlier drug use predicted greater aggression regardless of TBI [9].

### 2.3 Sex differences in outcomes

Most of the limited research on sex differences in TBI-related symptoms has found that women experience worse functioning symptoms than men [10, 13, 34, 51]. Farace et al.'s meta-analysis of sex differences found that women fare worse on 85% of outcomes, including higher rates of anxiety and depression, concussive syndrome such as dizziness, fatigue, irritability, impaired concentration, insomnia, headache, anxiety, and lower rate of returning to work [13]. Using the Glasgow Outcome Scale-Extended (GOSE), a widely known instrument tool for TBI, Kirkness et al. found that women aged 30 and older had poorer outcomes than younger women and men in all age groups 6 months following the injury, even when controlling for injury severity [51].

While research suggests that TBI is associated with problems during incarceration and post-release, including increasing the risk of reincarceration [1, 47, 52–54], there is limited research exploring sex differences. Wall et al. found women with a history of violence-related TBI were four-times more likely to have physical health problems than women without violence-related TBI [55]. However, they did not find differences in rates of mental health or substance abuse between the groups. Gorgens et al. found that women with TBI on probation have similar recidivism rates to men with TBI, though women without TBI had a lower risk of reoffending than men without TBI [1]. The authors also found that women with TBI were more likely than their male counterparts to have mental illness and substance use disorders [1].

### 2.4 Service utilization by TBI and sex

Research on the role of sex in treatment-seeking behavior is largely mixed. While many researchers have suggested that women are less likely to participate in substance use services than men [56, 57], other research suggests that women are at least as likely or more likely [58–60] to engage in these services. Similarly, some research finds women are more likely to use mental health services than men [61, 62]; while research on specialty psychiatric services shows higher utilization by men [63]. Coxe et al. found that mental service utilization among individuals with a head injury with loss of consciousness was higher for those with military service, a history of drug use, and moderate to severe depression, but no differences were observed by sex [64]. While there is limited research on post-release service utilization for TBI populations, Piccolino and Solberg's study of prison-based services found incarcerated men with high probable TBI used medical and psychological services at significantly higher rates than the low and moderate probable TBI groups and required more crisis services [53].

Overall, TBI is an important factor in the likelihood of success for individuals transitioning from incarceration to the community. However, there has been limited attention to how TBI can impact an individual's receipt of the services aimed at helping them reintegrate into the community. Given this current lack of knowledge, this paper provides an exploratory examination into whether services, specifically targeted for mental health and substance abuse, are impacted by an individual's history of TBI during the 18-months following incarceration, as well as the role of sex in service receipt.

## 3. Methods

### 3.1 Study overview

Data were drawn from individuals recruited into a multistate randomized controlled trial of a behavioral health reentry intervention conducted in two Midwestern states and one southeastern state in the United States. Eligibility for study participation included being 18 years of age or older, incarcerated in a correctional facility study site, approximately 6 months from release from prison, and scheduled for release to a county study site. Upon providing informed consent into the study, participants completed the baseline research interview using computer-assisted interview software. Following completion of the baseline interview, participants were randomized into either a treatment group to receive the 5-Key behavioral health intervention [22] or a comparison group to receive services-as-usual both while incarcerated and following release from prison. Once individuals released into the community, research interviews were conducted with all study participants 1 week later. Additional interviews were conducted at months 8, 14 and 18. Participants received compensation of $40 per follow-up research interview and $5 to update location tracking monthly. No compensation was provided to participants who were incarcerated. Analyses presented here are for the 265 individuals who completed the fourth (T4) follow-up interview at 18 months following release.

### 3.2 Measures

#### *3.2.1 Ohio State University TBI identification method*

A modified version of the Ohio State University TBI Identification Method (OSU TBI-ID) [24] was used to determine history of exposure to TBI. A history of TBI was indicated if the participant endorsed having had a head or neck injury event on any one of the five screener questions from the OSU TBI-ID. If at least one screener question was endorsed, the participant was prompted to answer the question whether they were ever knocked or lost consciousness. If they responded affirmatively, participants were asked if they were knocked out or lost consciousness for 30 minutes or longer. Finally, participants were asked the age when they first injured their head or neck. This assessment was administered at the T4 18-month follow-up interview in the community.

#### *3.2.2 Service assessment for children and adults*

The Service Assessment for Children and Adults (SACA) is a modified version of the Service Assessment for Children and Adolescents [65] that was adapted to ask

about service needs relevant to an individual in the transition from prison to the community. The SACA asked respondents about services in the following nine domains: life skills, mental health, substance abuse, relationships, job readiness, education, physical health, housing, and cognitive. Within each of the service domains, participants were asked whether they needed help in that domain and whether they received help. When an individual endorsed receiving a service, they were asked how many times they received help and whether services were helpful. The domains of mental health and substance abuse were asked at both baseline and follow-up interviews; the remaining seven domains were only asked at follow-up. At baseline, the queries were for any prior need or receipt (i.e., lifetime); at follow-up, the queries were asked relative to the time since last interview.

*3.2.3 Mini neuropsychiatric interview*

Substance use disorder and mental health disorder were assessed with the Mini Neuropsychiatric Interview (MINI) [66]. Participants were assessed for symptoms consistent with major depressive episode, manic episode generalized anxiety disorder, alcohol use disorder, and substance use disorder. The MINI has good test–retest and inter-rater reliability [66] and the MINI has demonstrated effectiveness in correctional settings [67]. All domains of the MINI were administered at the baseline research interview, and alcohol use disorder and substance use disorder were also asked at follow-up.

*3.2.4 Traumatic history questionnaire*

The Trauma History Questionnaire (THQ) is a 25-item measure of lifetime trauma that captures a variety of events, including forced robbery, home break-in, natural disaster, man-made disaster, military combat, close friend/family member murdered, life-threatening illness, intercourse against one's will, and attacked by family member [68]. For each traumatic event, the respondent who answered in the affirmative was asked the number of times the event occurred and the age of the individual at each event. This analysis used a total score from zero to 25 that summed the number of traumatic events endorsed by a participant.

*3.2.5 Childhood trauma questionnaire*

The Childhood Trauma Questionnaire is a 28-item measure of physical abuse, sexual abuse, emotional abuse, physical neglect, and emotional neglect the occurred during the individual's childhood. The total score of each subscale can range between with 5 to 25, with higher scores indicating a higher level of trauma exposure. Cutoffs for moderate–severe exposure are: > = 13 for emotional abuse; > = 10 for physical abuse; > = 8 for sexual abuse; > = 15 for emotional neglect; and > =10 for physical neglect. The CTQ has shown to have strong inter-rater reliability and criterion-related validity [69].

*3.2.6 Demographic information*

Participants were asked at the baseline interview about their race, sex, age, education level, and employment. Race was a three-category variable coded as Black, White, and other. Sex was also a three-category variable of man, woman, and

non-binary. Age was computed based on the date of birth reported by the participant. Education captured an individual's current level achieved and was coded as less than a high school diploma/GED, high school diploma/GED completed, and post-secondary education. Finally, employment asked about the respondent's work situation prior to their incarceration and was coded as unemployed, working full/part-time, or other.

### 3.3 Analytic methods

Analyses focus on respondents who completed a T4 interview, the interview at which the OSU TBI-ID was collected. We first examined how the respondents to the T4 interview compared with the original sample of individuals enrolled at baseline but who did not complete the T4 interview. Bivariate statistics of independent t-tests for continuous measures and chi-square statistics for categorical measures were used to compare the two groups. Within the T4 sample, descriptive statistics are presented overall and stratified by sex and by TBI status. The same bivariate tests were used when comparing service use and need across the interview waves for the T4 sample.

Among respondents completing a T4 interview, fixed effects linear probability models (LPM) were used to estimate within-person changes in service receipt within the mental health and substance abuse domains of the SACA. The analysis sample was further constrained into two, but not mutually exclusive, samples to examine each outcome. For the mental health receipt outcome, analysis was focused on those who indicated a need for mental health services at the baseline interview; similarly, for the substance abuse receipt outcome, analysis only included those with an identified substance abuse need at baseline. Fixed effects LPM allow us to estimate the effects for the full analysis sample by including responders with no change over time in each respective outcome variable. The LPM is shown to have comparable statistical properties to logit models under certain conditions, such as for outcome variable proportions not close to 0 or 1 [70–74]. Moreover, the fixed effects LPM suffers little from the convergence challenges seen with conditional logit, and LPM produces estimates in natural, interpretable percentage point units. Because the fixed effects LPM tests the within-person change in the outcome variable (i.e., mental health or substance use service receipt), each participant effectively acts as their own comparison, which allows for the control of all observed (e.g., sex or race) as well as unobserved time-invariant covariates (e.g., unmeasured health status). Moreover, to further test for between-group difference in within-person change (i.e., by TBI and by sex) we fitted separate models that included interaction terms between each time-invariant covariate and an indicator of time (i.e., 8 months, 14 months, and 18 months with the T1 interview serving as reference). All analysis were completed with Stata version 17.

## 4. Results

### 4.1 Subject characteristics

**Table 1** shows characteristics of the 265 participants who completed the T4 interview at 18-months post-release. Individuals who completed the T4 interview were majority Black (52.08%) and men (83.40%) and reported an average age of 37.79 years old at the baseline interview. Prior to incarceration a majority had been employed (59.25%) and achieved either a high school diploma or GED (72.83%).

| Characteristic | Mean (standard deviation) or percentage (%) | |
|---|---|---|
| | **T4 Completers (*n* = 265)** | **T4 Did not Complete (*n* = 625)** |
| Age | 37.79(11.50) | 37.03(10.61) |
| Sex | | |
| *Women* | 16.60% | 15.22% |
| *Men* | 83.40% | 84.62% |
| Race* | | |
| *Black* | 52.08% | 42.00% |
| *White* | 34.34% | 46.79% |
| *Other* | 13.58% | 11.22% |
| Education Level | | |
| *Less than HS/GED* | 26.62% | 28.89% |
| *HS/GED Completed* | 39.16% | 39.65% |
| *Post-secondary Education* | 34.22% | 31.46% |
| Employment Status* | | |
| *Working (Full or part-time)* | 59.70% | 51.69% |
| *Unemployed* | 28.90% | 41.57% |
| Major Depressive Episode* | 41.13% | 32.80% |
| Manic Episode | 23.02% | 17.60% |
| Alcohol Use Disorder* | 46.42% | 38.88% |
| Substance Use Disorder | 70.94% | 73.12% |
| Generalized Anxiety Disorder* | 18.87% | 13.12% |
| Posttraumatic Stress Disorder | 30.19% | 25.76% |
| Ever needed help for mental health?* | 61.07% | 52.33% |
| Ever received help for mental health? | 56.06% | 45.59% |
| Ever needed help for substance abuse? | 55.30% | 51.85% |
| Ever received help for substance abuse? | 56.44% | 52.01% |
| CTQ emotional abuse* | 10.13(5.30) | 9.36(4.98) |
| CTQ physical abuse | 9.48(4.70) | 8.98(4.72) |
| CTQ sexual abuse | 6.89(4.35) | 6.59(3.96) |
| CTQ emotional neglect* | 11.11(5.08) | 10.45(4.95) |
| CTQ physical neglect | 8.74(4.20) | 8.44(4.21) |
| THQ total score* | 8.17(3.79) | 7.18(3.66) |

**Table 1.**
*Means and percentages of subjects who completed the T4 interview compared to subjects who did not complete the T4 interview (* = $p < 0.05$).*

The sub-sample of T4 responders comprises approximately 29.78% of the original sample of 890 individuals enrolled into the study at baseline. The T4 responders were shown to have significant differences ($p < 0.05$) compared with the sample of study participants who did not complete the T4 interview (**Table 1**) in some categories. Participants who completed the T4 interview reported a higher total score on the trauma history questionnaire (8.17 vs. 7.18) as well as higher scores on both emotional abuse (10.13 vs. 9.36) and emotional neglect (11.11 vs. 10.45) on the childhood trauma questionnaire. T4 responders were also more likely to indicate their race as Black (52.08 vs. 42.00%), and T4 responders reported higher level of major depression (41.13 vs. 32.80%), alcohol use disorder (46.42 vs. 38.88%), and generalized anxiety disorder (18.87 vs. 13.12%). Lastly, T4 responders showed higher levels of need for mental health services prior to incarceration (61.07 vs. 52.33%), and they reported being unemployed prior to incarceration at a statistically lower level (28.90 vs. 41.57%). For all remaining variables, the T4 responders were statistically similar to their counterparts who did not complete the T4 interview.

Members of the T4 sample reported at baseline high levels of lifetime need with help for emotional problems and substance use disorder. Fully 61.07% reported needing help in the past for emotional problems and 55.30% reported needing help for drug and alcohol problems. Most also reported having received help in the past with 56.06% reporting having received help with emotional problems and 56.44% receiving help for drug and alcohol problems.

Nearly one-third (30.2%) of the sample reported having experienced PTSD. The TBI-ID scale wasn't administered at baseline, but individuals reported high levels of physical and emotional trauma. **Table 2** shows the responses to the OSU TBI-ID by sex. Nearly 40% of the respondents reported having been hospitalized following a head or neck injury, with no significant difference between the men and women. Large numbers also reported having head or neck injuries as a result of an accident (35.43%), from a fall or playing sports (39.53%), and from being in a fight or being shot (32.81%)—again the differences in reporting by men and women were not significant. Men were more likely than women to report having been exposed to an explosion or blast (19.91 v. 7.14%; $p < .05$). Of the 146 who reported sustaining head or neck injuries, 88 (60.27%) reported losing consciousness and 39 of those 88 (49.37%) reported losing consciousness for more than 30 minutes. Although women were somewhat more likely to report losing consciousness (68.00 v. 58.68%) and men

| TBI Item | Men | Women | Total |
|---|---|---|---|
| Hospitalization following head or neck injury | 86 (40.57%) | 15 (35.71%) | 101 (39.76%) |
| Head or neck injury in accident | 71 (33.49%) | 19 (45.24%) | 90 (35.43%) |
| Head or neck injury from fall or sports | 81 (38.39%) | 19 (45.24%) | 100 (39.53%) |
| Head or neck injury from fight or being hit, shaken, or shot | 70 (33.02%) | 13 (31.71%) | 83 (32.81%) |
| Near explosion or blast* | 42 (19.91%) | 3 (7.14%) | 45 (17.79%) |
| If injured, knocked out or lost consciousness | 71 (58.68%) | 17 (68.00%) | 88 (60.27%) |
| If knocked out, lost consciousness for 30 minutes or more | 34 (51.52%) | 5 (38.46%) | 39 (49.37%) |

**Table 2.**
*Numbers and percentages of subjects reporting ever experiencing the TBI event by sex (* = $p < 0.05$).*

| Item | Men | Women | Total |
|---|---|---|---|
| Robbed by force or threat of force | 132 (59.73%) | 20 (45.45%) | 152 (57.36%) |
| Robbed without force or threat of force | 103 (46.61%) | 21 (47.73%) | 124 (46.79%) |
| Someone attempted or succeeded in breaking into your home when you were there* | 34 (15.38%) | 13 (29.55%) | 47 (17.74%) |
| Serious accident at work or elsewhere | 137 (61.99%) | 27 (61.36%) | 164 (61.89%) |
| Experienced a natural disaster | 51 (23.08%) | 8 (18.18%) | 59 (22.26%) |
| Experienced a man-made disaster* | 48 (21.72%) | 18 (40.91%) | 66 (24.91%) |
| Seen someone seriously injured or killed* | 173 (78.28%) | 24 (54.55%) | 197 (74.34%) |
| Seen dead bodies (other than funeral) | 128 (57.92%) | 19 (43.18%) | 147 (55.47%) |
| Had close family member or friend murdered* | 165 (74.66%) | 26 (59.09%) | 191 (72.08%) |
| Had spouse, partner, or child die other than by murder or killed by drunk driver* | 55 (24.89%) | 18 (40.91%) | 73 (27.55%) |
| Had a serious or life-threatening illness | 65 (29.42%) | 18 (40.91%) | 83 (31.32%) |
| Made to have sex against your will* | 24 (10.86%) | 21 (47.73%) | 45 (16.98%) |
| Been touched (private parts) under force or threat* | 27 (12.22%) | 25 (56.82%) | 52 (19.62%) |
| Anyone attacked you with a weapon | 119 (53.85%) | 18 (40.91%) | 137 (51.70%) |
| Has anyone attacked you without a weapon and seriously injured you* | 45 (20.36%) | 15 (34.09%) | 60 (22.64%) |
| Has anyone beaten or pushed you hard enough to cause injury* | 55 (24.89%) | 21 (47.73%) | 76 (28.68%) |

**Table 3.**
*Numbers and percentages of subjects reporting ever experiencing selected traumatic events by sex (* = $p < 0.05$).*

were somewhat more likely to report losing consciousness for more than 30 minutes (51.52 v. 38.46%), these differences were not statistically significant.

Select items from the THQ also indicate high levels of lifetime trauma. **Table 3** provides information on the percentage of respondents at baseline who reported ever experiencing specific events. Women reported higher rates of traumatic events for more categories than did men. Women were shown to be exposed to more direct personal crime, such as being beaten (47.73 v. 24.89%) or having their home broken into (29.55 v. 15.38%). Additionally, women reported significantly higher levels of sexual abuse (47.73 v. 10.86%) then did male respondents and experienced more non-violent death within their immediate family and friends (40.91 v. 29.42%). On the flip side, male respondents also reported high levels of lifetime trauma, but it was concentrated in interpersonal violence; particularly, seeing someone killed or injured (78.28 v. 54.55%) as well as having a family member or friend murdered (74.66 v. 59.09%).

### 4.2 Demographic comparison of respondents with TBI versus No TBI at baseline

Among the 265 respondents to the T4 interview, a majority (55.47%) endorsed at least one of the five screener questions for TBI. When comparing those who indicated a lifetime TBI to those participants who did not, significant differences are found (**Table 4**). Individuals with TBI were found to have higher levels of trauma

| Measure | Mean (standard deviation) or percentage (%) | |
|---|---|---|
| | **TBI (*n* = 147)** | **No TBI (*n* = 118)** |
| | *M*(*SD*) / % | *M*(*SD*) / % |
| Age | 38.86(11.17) | 36.46(11.80) |
| Sex | | |
| *Women* | 17.69% | 15.25% |
| *Men* | 82.31% | 84.75% |
| Race* | | |
| *Black* | 41.59% | 65.25% |
| *White* | 43.54% | 22.88% |
| *Other* | 14.97% | 11.86% |
| Education Level | | |
| *Less than HS/GED* | 23.13% | 31.03% |
| *HS/GED Completed* | 38.78% | 39.66% |
| *Post-secondary Education* | 38.10% | 29.31% |
| Employment Status* | | |
| *Working (Full or part-time)* | 62.59% | 56.03% |
| *Unemployed* | 22.45% | 37.07% |
| Major Depressive Episode | 43.54% | 38.14% |
| Manic Episode | 27.21% | 17.80% |
| Alcohol Use Disorder | 50.34% | 41.53% |
| Substance Use Disorder* | 76.19% | 64.41% |
| Generalized Anxiety Disorder* | 23.13% | 13.56% |
| Posttraumatic Stress Disorder | 34.69% | 24.58% |
| Ever needed help for mental health?* | 68.28% | 52.14% |
| Ever received help for mental health? | 59.86% | 51.28% |
| Ever needed help for substance abuse? | 59.18% | 50.43% |
| Ever received help for substance abuse? | 57.82% | 54.70% |
| CTQ emotional abuse | 10.39(5.23) | 9.80(5.38) |
| CTQ physical abuse | 9.68(4.80) | 9.23(4.59) |
| CTQ sexual abuse | 6.95(4.45) | 6.81(4.35) |
| CTQ emotional neglect | 11.21(5.18) | 10.99(4.97) |
| CTQ physical neglect | 8.66(3.93) | 8.83(4.51) |
| THQ total score* | 9.17(3.70) | 6.90(3.52) |

**Table 4.**
*Means and percentages of subjects with TBI compared to subjects without TBI (* = $p < 0.05$).*

as indicated by the THQ total score (9.17 v. 6.90) as well as were more likely to score as having a substance use disorder (76.19 v. 64.41%) and/or a generalized anxiety disorder (23.13 13.56%). Given these reported symptoms by individuals with TBI, it is expected they would also report a higher level of need for mental health services

(68.28 v. 52.14%). Nevertheless, no differences were found in self-reported need for substance use services nor the receipt of either mental health or substance use services. Individuals who screened positive for TBI were more likely to describe themselves as White than individuals without TBI (43.54 v. 22.88%). Employment prior to incarceration was significantly higher for those with TBI compared to their T4 counterparts who did not report TBI (62.59 v. 56.03%).

**Table 5** provides information on the individuals who reported the need for mental health and substance abuse services at baseline. A participant was identified as receiving either mental health or substance abuse services in **Table 5** if they received the service at any point during the 18-month follow-up period. Looking at the results, there is a higher rate of receipt for mental health service (49.38%) among those with a mental health need compared to the rate of receipt for substance abuse service (41.78%) among those with a substance abuse need. Within the TBI subgroup, respondents with TBI reported a higher rate of service receipt for both mental health (51.52 v. 45.90%) and substance abuse (43.68 v. 38.98%) compared to those without TBI. Men with TBI identified a need for substance abuse services at a higher rate (60.53%) than did women with TBI (56.25%); a similar difference is not seen for mental health services. Lastly, women reported a higher rate of receipt than men for both types of services, and the difference was most notable for mental health services versus substance use services (54.29 v. 48.00%).

### 4.3 Impact of TBI and sex on service receipt

Estimation of the fixed effects models began by estimating with a base model that included only the indicators of time to show the average service receipt path over time up to 18 months following reentry. Then, two separate models were estimated that used interactions with time indicators to show how the service receipt path differed by TBI status (Model 2) and sex (Model 3).

Results are presented in **Table 6**. For the models focused on mental health services receipt, no direct effect of time or any of the interaction effects were found to be significant. For the models examining substance use services receipt, there was a

| | **MH service need** | | | | |
|---|---|---|---|---|---|
| | **Overall (n = 160)** | **TBI (n = 99)** | **No TBI (n = 61)** | **Men (n = 125)** | **Women (n = 35)** |
| **MH Service receipt** | 79 (49.38%) | 51 (51.52%) | 28 (45.90%) | 60 (48.00%) | 19 (54.29%) |
| **TBI** | 99 (61.88%) | N/A | N/A | 77 (61.60%) | 22 (62.86%) |
| **Women** | 35 (21.88%) | 22 (22.22%) | 13 (21.31%) | N/A | N/A |
| | SA service need | | | | |
| | Overall (n = 146) | TBI (n = 87) | No TBI (n = 59) | Men (n = 114) | Women (n = 32) |
| **SA service receipt** | 61 (41.78%) | 38 (43.68%) | 23 (38.98%) | 47 (41.23%) | 14 (43.75%) |
| **TBI** | 87 (59.59%) | N/A | N/A | 69 (60.53%) | 18 (56.25%) |
| **Women** | 32 (21.92%) | 18 (20.69%) | 14 (23.73%) | N/A | N/A |

**Table 5.**
*Service receipt by those expressing need at T4 follow-up by TBI and sex.*

| **Mental Health Service Receipt (n = 157)** | | | | | | |
|---|---|---|---|---|---|---|
| | **Model 1: Time Only** | | **Model 2: TBI Interaction** | | **Model 3: Sex Interaction** | |
| Time | *b* | 95% CI | *b* | 95% CI | *b* | 95% CI |
| *8 mos* | .02 | (−.08, .12) | .001 | (−.17, .17) | .05 | (−.06, .16) |
| *14 mos* | .06 | (−.04, .16) | −.001 | (−.17, .17) | .07 | (−.04, .18) |
| *18 mos* | .02 | (−.07, .11) | .02 | (−.14, .18) | .02 | (−.09, .12) |
| TBI Interaction | | | | | | |
| *8 mos x TBI* | | | .04 | (−.17, .25) | | |
| *14 mos x TBI* | | | .09 | (−.12, .31) | | |
| *18 mos x TBI* | | | .0001 | (−.20, .20) | | |
| Sex Interaction | | | | | | |
| *8 mos x Women* | | | | | −.05 | (−.41, .12) |
| *14 mos x Women* | | | | | .01 | (−.32, .21) |
| *18 mos x Women* | | | | | .01 | (−.24, .25) |
| Substance Abuse Service Receipt (n = 143) | | | | | | |
| Time | | | | | | |
| *8 mos* | −.02 | (−.12, .08) | .03 | (−.13, .20) | .01 | (−.10, .12) |
| *14 mos* | −.07 | (−.17, .03) | −.11 | (−.27, .06) | −.04 | (−.15, .07) |
| *18 mos* | −.13* | (−.22, −.04) | −.14 | (−30, .01) | −.11* | (−.21, −.003) |
| TBI Interaction | | | | | | |
| *8 mos x TBI* | | | −.09 | (−.30, .11) | | |
| *14 mos x TBI* | | | .07 | (−.14, .27) | | |
| *18 mos x TBI* | | | .02 | (−17, .21) | | |
| Sex Interaction | | | | | | |
| *8 mos x Women* | | | | | −.20 | (−.46, .07) |
| *14 mos x Women* | | | | | −.15 | (−.41, .12) |
| *18 mos x Women* | | | | | −.14 | (−.39, .10) |

**Table 6.**
*Fixed effects linear probability models: Within-person change in service receipt and time interactions by TBI and sex (* = $p < 0.05$).*

negative effect of time on the receipt of substance use services. As the follow-up time-period increased, the receipt of substance abuse services decreased and at 18 months was 13 percentage points lower compared to the T1 interview at one-week post-release ($b = -0.13, p < 0.05$). None of the interaction terms were significantly associated with substance abuse service receipt in models 2 and 3. However, the decrease in receipt at 18 months remained negative and similar in magnitude to the base model estimates.

## 5. Discussion and conclusions

Research focused on understanding the influence of lifetime experiences of TBI on incarceration and post-incarceration outcomes is in its infancy. However, scientific

discoveries related to the deleterious effects of TBI on lifetime outcomes among athletes and war veterans underscore the importance of this burgeoning body of inquiry. Within a criminal justice involved population, the influence of TBI on individual behavior has high stakes implications for the health and safety of those beyond the justice-involved individual with TBI because criminal behavior frequently impacts the lives of the public. Findings from the current study suggest that additional inquiry is needed into the post incarceration experiences and outcomes for persons with a history of TBI.

The current study results are preliminary yet highly relevant. Rather than assessing TBI during incarceration and at every subsequent time point during post incarceration follow up, we screened for TBI 18 months after release. The screening occurred at that time point not because TBI was a primary focus of the clinical trial, but rather because the participant reports during the study suggested that this additional data point was imperative to understanding reentry results. Because TBI was examined posteriori, we were only able to speak to TBI among those participants retained in the study a year and a half post release. Importantly however, those participants who remained in the study were not the highest functioning, rather statistical analyses indicated that these participants displayed comparatively high needs — suggesting that the study findings reflect the realities of those facing complex issues post incarceration.

Reentry to communities from incarceration is a lengthy experience and the social and behavioral supports needed to fully assimilate into societal expectations of positive and productive living can take a substantial amount of time. Yet, the results from the current study show that the receipt of supportive services declines over time for all reentering participants. And, although the study did not identify statistically significant differences for those who screened positive for a TBI and those who did not at 18-months post-release, this research finding needs further testing because the current study cannot tease out the cumulative impact of TBI because of attrition and the binary (yes/no) nature of the data on service receipt. Most importantly, the research supports what other studies have consistently found – services are needed and important to reentry success and these same services are difficult to access and that the limitations to access are exacerbated overtime.

Future research that is longitudinal in nature that utilizes more detailed measures of cognitive deficits like executive dysfunction can help to pinpoint which symptoms of TBI persist, and the myriad of ways those symptoms may impact how a person progresses through services provided during and after incarceration. Foundational research describing the prevalence and patterns of TBI of formerly incarcerated individuals in the community is still needed as is more causal research that can help to identify treatment targets and intervention components post-release. In turn, reentry services providers can screen for TBI and provide more tailored approaches to individual care with the expectation that such tailored approaches could improve the relatively limited impact that generic reentry approaches have accomplished to date.

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## Conflict of interest

The authors declare no conflict of interest.

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