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The Clinical Value of Oculomotor Assessments Across the Continuum of Concussion

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Abstract

Concussions are complex conditions that are difficult to manage medically. Variations in symptom presentation, intricate neurophysiological processes, and the availability of a variety of possible assessment tools may contribute to this complexity. Clinicians must use a broad approach, employing both subjective symptom assessment and objective assessments to confirm a diagnosis and/or monitor progression and recovery. Oculomotor function after concussion may be an important indicator of injury, given the interconnectedness of oculomotor function, vestibulo-ocular and visual systems, and even cognition. Oculomotor function may be assessed objectively or indirectly using patient-reported symptom checklists as part of subjective assessments. One way of objectively assessing oculomotor function is the observation of saccades: rapid movement of eyes between targets. Two types of saccades were studied: prosaccades, where the eyes move toward a target, and antisaccades, where the eyes move to the mirror opposite location of the target. Antisaccades require inhibition of prosaccades, reflecting a component of executive function. Measuring the reaction time and directional errors of saccades can give insight into the status of some aspects of executive function. Chapter 2 compared objective electroencephalography (EEG) and saccadic eye movements to assess changes in neurological function with accumulated head impacts throughout a season of men's hockey. EEG was sensitive to minor changes in executive function, whereas saccades were not. Subjective measures, such as symptom checklists, provide a standardized protocol for assessing concussion symptoms and severity. Chapter 3 tracked saccades and patient-reported symptom measures to assess changes in the function and symptomology following a 16-week interdisciplinary outpatient rehabilitation intervention for patients with persistent post-concussion symptoms. Improvement in patient function was measured by improved standard outcome measures. These improvements were associated with saccadic eye movement measurements. Chapter 4 investigated the relationship between a patient's initial vestibulo-ocular symptoms and their length of recovery from acute concussion. This study demonstrated that the presence of any vestibulo-ocular symptoms led to 19 times greater odds of not being discharged four weeks after their assessment. This builds on existing research in which patients with vestibulo-ocular symptoms on other diagnostic tests were shown to have delayed recovery. Using the SCAT5 to collect vestibulo-ocular symptoms is easier for clinicians and less provocative for patients. Together these findings show that oculomotor assessments may be useful in hockey athletes with acute concussions and adults with persistent post-concussion symptoms. Further research is needed to determine their utility in subconcussive head impacts.

Keywords

Concussion, mTBI, head impacts, saccade, brain injury, electroencephalogram, SCAT5, hockey, symptoms, rehabilitation, persistent post-concussion symptoms.

Summary for Lay Audience

Our eyes provide us with a constant stream of information about the world around us and our actions within it. The process of controlling our eye movements, known as oculomotor function, is complex and involves communication between many areas of the brain. Oculomotor function may reveal changes in the brain following head impacts and concussions. All contact sports athletes will experience head impacts. Therefore, there is concern about the large impacts that lead to concussions as well as the potential neurological consequences of accumulated head impacts. Most athletes with concussion recover within two weeks, but some individuals experience prolonged symptoms, termed persistent post-concussion symptoms. This thesis investigated the use of oculomotor assessments across the continuum of concussion (subconcussive impacts, acute concussion and persistent post-concussion symptoms). In the subconcussion study, helmet-mounted sensors, rapid eye movements and electroencephalograms were collected before, during, and after the season to evaluate players' brain function. In a separate study, symptom data were retrospectively collected from hockey players in southwestern Ontario to evaluate the relationship between initial vestibulo-ocular symptoms and time to discharge from physician's care. Finally, rapid eye movements were collected before and after a 16-week concussion therapy program for individuals with delayed recovery from concussion. This thesis determined that rapid eye movements are not sensitive enough to detect changes in brain function from subconcussive head impacts. Saccades can measure improvement during therapy for patients with delayed recovery from concussion. Also, initial vestibulo- ocular symptoms are associated with extended time to discharge after concussion for hockey players. These results show that assessing visual symptoms may support prognosis planning for hockey athletes and that eye tracking can monitor recovery for persistent concussion symptoms.

Co-Authorship Statement

Dillon Richards is the primary author of all the chapters contained in this thesis. Dr. James P. Dickey (Professor in the School of Kinesiology, Faculty of Health Science, Western University) co-authored all chapters. Dr. Laura J Graham (Assistant Professor in the School of Physiotherapy, Faculty of Health and Rehabilitation Science) co-authored all chapters.

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Chapter 1

1 Introduction

1.1 Concussion

A concussion is a type of mild traumatic brain injury (mTBI), defined as “a complex pathophysiological process that affects the brain and is induced by biomechanical forces from a direct blow to the head or a blow to the body that transmits these forces to the head”.[1] This pathophysiological process involves diffuse injury within the brain, with the neurons’ axons being injured by the shear stress and tension on axons.[2] This damage can lead to the death of cells, causing an influx of calcium and sodium within the remaining cells and potassium into the extracellular space.[3] Further, glutamate, an excitatory neurotransmitter, is released into the extracellular space.[4] This glutamate increases excitation of the nervous system, utilizing the energy stored in the brain, eventually leading to a metabolic depressive state.[5] These metabolic changes lead to a sequelae of concussion symptoms, and in 10-15% of individuals who sustain a concussion these symptoms will become prolonged or persistent and can be very debilitating.[6]

In Ontario, between 2008 and 2016, there was an average incidence of 1,153 concussions per 100,000 residents.[7] A subset of these reported concussions were sport-related. From 2001 to 2004, Canadians reported consistent numbers of sport-related mTBI (~100/100,000). However, there was a nearly two-and-a-half times increase in reports between 2005 and 2014 (~250/100,000), from which levels have remained stable from 2014 to 2018.[8] Authors explained that this increasing trend may be due to an increased awareness of concussions during this time, possibly due to media coverage.[8] Common signs and symptoms of concussion can be categorized into five clinical domains: somatic, behavioural, cognitive, sleep-related, vestibular and visual/oculomotor.[1] Concussion symptoms may differ between individuals and even between concussions in the same individual.[1] Of those adults who do experience a concussion, most will have full symptom recovery within 14 days[9]. However, the majority of children who experience a concussion are expected to have symptom recovery in 28 days.[1] Athletes experience a similar recovery curve to the non-athletic population[1]; however, it is suggested athletes undergo a standardized 6-step return to play protocol after symptom resolution.[1] Some leagues have integrated this protocol into the rulebook and standard operating procedures (e.g. NCAA NFL rulebook). A recent study of 1751 male and female collegiate athletes with concussion across various sports suggests that 85% of athletes recovered from their concussion and returned to sport within 28 days.[10]

1.2 Subconcussive Impacts

A subconcussive impact is an impact to the head or body that does not result in a diagnosed concussion.[11] While not all athletes will experience a concussion during their career, nearly all athletes will endure subconcussive impacts. In fact, a review of athletes from youth, adult amateur, varsity and professional sport estimated that athletes may experience thousands of head impacts over the course of their respective sport career/participation.[12] It is thought that subconcussive impacts accumulate and cause neuronal damage. Repetitive subconcussive head impacts have been shown to lead to the development of chronic traumatic encephalopathy (CTE).[13] Subconcussive impact accumulation has also been related to an increased risk of developing a mood disorder.[14] Subconcussive impacts frequently occur in ice hockey due to the speed of play and the likelihood of head impacts with other players, the boards, and the ice surface.[15] Many studies have measured changes in physiologic variables resulting from concussive head impacts, including eye tracking,[16] biomarkers,[17–20] vestibular assessments,[21,22] and impact tracking[23,24] in hockey athletes. Helmet-mounted sensors can provide coaches, parents, and clinicians with a wealth of data, including the number of head impacts accumulated.[25,26] The International Ice Hockey Federation estimates that 513,674 Canadians play ice hockey, so it is important that researchers obtain an accurate estimate of head impact accumulation and the resulting effects.[27]

There is evidence that the accumulation of these impacts can have determinantal effects on hockey athletes. Examination of brains donated by hockey players showed that each year of hockey played was associated with a 23% increase in the odds of developing

CTE and a 15% increased likelihood of progressing a stage of CTE.[28] Magnetic Resonance Imaging studies have shown that subconcussive head impact accumulation over a season of hockey leads to increased frontoparietal connectivity, which is suggestive of neural compensation for brain injury.[29] There have been no clinical measures designed to specifically assess clinical changes related to accumulated subconcussive impacts.

1.3 Persistent post-concussion symptoms

Ten to fifteen percent of people with a concussion will have symptoms that persist for months or years post-injury.[6] Symptoms are described as persistent (i.e., persistent post-concussion symptoms: PPCS) when individuals with concussions experience symptoms that persist beyond two weeks in adults or four weeks in children[1] or beyond three months despite care.[6,30,31] PPCS can be very debilitating as the effects may degrade all aspects of the person's life. Patients with PPCS report difficulty with concentration, memory, fatigue and irritability that has changed their regular activities for up to 15 months post-injury.[32] PPCS is an unseen disability, often leading to distress and caregiver burnout[1,33]. PPCS can last for years after an initial injury.[1,34]

PPCS has been associated with physiological impairments in cerebral blood flow[35] and reduced neural connectivity when compared to healthy individuals.[36] Further, there is evidence of reduced white matter integrity in those with PPCS.[37] These physiological changes lead to changes in the visual system, reduction in reaction time, and impaired focus and attention.[34] Several factors increase the likelihood of a patient developing PPCS. A recent clinical decision rule for adults with concussion developed by the Canadian Network of Emergency researchers determined that age, sex, previous multiple mTBI previous concussion within 12 months, history of mental health disorders, prescribed medication, patient reported headache in the emergency department, and cervical sprain all increased the likelihood of a adults developing PPCS.[38] Additionally at one-week follow-up, if a patient reported headaches, sleep disturbance, fatigue, light sensitivity, or scored 21/64 or more on the Rivermead Post-concussion Symptoms Questionnaire, along with a few other factors,[39] they were at an increased risk for developing PPCS 90 days after head injury. The Rivermead Post-Concussion Symptoms

Questionnaire is a patient-reported measure that allows individuals to score if they experience any of a list of 16 common concussion symptoms and the severity (0 = not at all a problem, 4 = severe problem). This clinical decision rule highlighted the importance of identifying symptoms and severity to identify those at risk of developing PPCS. However, these patient-reported measures do not directly measure function. Assessment of the visual/oculomotor and vestibular systems should be part of a complete assessment. Routine assessments would help clinicians monitor recovery and response to treatment for PPCS.

1.4 Concussion Assessment

Clinical assessments can be broadly categorized as subjective or objective. Subjective assessments measure the patient's report of their symptoms and are commonly given in the form of a questionnaire or collected through a standardized interview. There has been debate on the consistency of this information, as each patient will experience and judge their symptoms differently. There is a breadth of research exploring objective measures or biomarkers (e.g., blood tests[40]) and imaging techniques (e.g., Diffuse-tensor MRI[41,42]) to diagnose and track recovery of concussions. However, currently clinical concussion diagnosis relies on patient history and clinical assessment,[1] using a combination of patient-reported measures and clinical assessments of function, such as the Sport Concussion Assessment Tool (SCAT).

The SCAT was created to be a standardized assessment of sports-related concussion.[1,43] It was developed during the Second Consensus Conference on Concussion in Sport in 2004 and has undergone three revisions, with the SCAT5 being the most recent version, drafted during the Fifth Consensus Conference in 2016[1]. The SCAT5 is comprised of 5 sections: immediate on-field assessment, symptom evaluation, cognitive screening, neurological screening, and delayed recall. The symptom evaluation sub-section assesses 22 symptoms on a 7-point Likert scale, from 0 to 6. Symptom checklists have been shown to have clinical utility in the identification, diagnosis and tracking of recovery in patients[44]. Previous research has used sub-sections of the SCAT5 symptom evaluation to focus on specific aspects of symptom burden and recovery[45]. One primary advantage of symptoms checklists is they assess a patient's symptoms without provoking symptoms that can occur on other measures.[46]

Other common concussion assessments are the Rivermead Post-Concussion Symptoms Questionnaire, Visual Ocular Motor Screen (VOMS) and King-Devick Test. Some assessments that were not originally created to assess concussion have been validated and utilized to assess common aspects related to concussion, such as the General Anxiety Disorder-7 (GAD-7), Headache Impact Test-6 (HIT-6), and Brain Injury Visual Symptom Scale (BIVSS). Each of these measures assesses patient-report of symptoms and symptom severity, but only the VOMS included an assessment of function, specifically the function of the vestibular and ocular-motor systems. Given the prevalence of vision changes after a concussion,[47] explorations of measures that objectively assess ocular-motor function may be an important contribution to the growing body of literature.

Studies have measured changes in oculomotor function due to accumulated head impacts, and the oculomotor system is sensitive to the effects of repetitive subconcussive[18,48–50] head impacts and concussion[51]. Recent research has supported the utility of oculomotor assessment for acute diagnosis of concussion and tracking recovery.[52,53] Specific eye movements, such as saccades, may be useful to assess the function of the various brain areas associated with these eye movements.[52]

1.5 Electroencephalogram

Electroencephalogram (EEG) measures the brain's electrical activity[54], and gives insight into aspects of specific brain functions such as executive function or cognitive processing.[54] Through electrodes placed on the scalp, EEGs can measure changes in the post-synaptic potentials between neurons.[54,55] These potentials relate to the flow of electricity in the brain. This is useful as changes in these potentials are associated with specific neural deficits.[56] EEGs are relatively easy to set up and inexpensive compared to other neurophysiological measurements.[57] EEG has been used to measure complex neuronal processes that fall under the umbrella of executive function, such as attention, memory, and decision-making.[55] EEG has been shown to be sensitive to cognitive changes, with established test-retest reliability and are therefore well suited to assess neurophysiological changes related to concussion and subconcussive impact accumulation.[58] EEGs have a high temporal resolution, such that neuronal activity can be recognized by specific changes in electrical activity following a stimulus.[55]

Event-related brain potentials (ERPs) are waves of this neural electrical activity that relate to a specific task.[59] They are time locked, meaning that ERPs occur at a specific time after the presentation of a stimulus. ERPs provide objective measures of changes of brain function,[17] and may determine the function of cortical pathways.[60] ERPs are related to neural activation, which may provide information that cannot be captured on standardized neurophysiological assessments.[61] An additional benefit of ERPs is that they are resistant to practice effects, improving clinical interpretation from serial assessments.[62]

1.6 P300 and Concussion

One specific ERP of interest to concussion research is the P300. Typically, ERPs are named for their polarity and latency after stimulus presentation. Therefore, the P300 is a positive potential ERP occurring approximately 300 milliseconds after a stimulus. The P300 has been shown to be related to aspects of executive function.[56] There are two subcomponents of the p300, the p3a and p3b, which are related to attention and decision making, respectively.[56] P300 measures have been shown to be altered in concussed individuals, compared with healthy controls.[63] The oddball paradigm is the best-known stimulus to elicit the P300. This paradigm involves the presentation of three stimuli: an infrequent target, a frequent stimulus and distractor stimuli. The presentation of the distractor stimuli elicits the P3a component of the P300.[61] The strength of this response, measured by the electrical amplitude, is thought to measure the engagement of attention.[56] When the infrequent stimulus is presented, a participant must complete a specific task, such as a button push. This elicits the P3b component relating to decision-making, cognitive processing, and memory.[56]

Several studies have used EEG to measure the changes following concussion and subconcussive impacts in hockey.[17] These studies show that concussion in hockey leads to increased amplitudes and longer latencies in the P300 ERP. In contrast, individuals with a concussion showed decreases in processing speed.[17] No studies have measured and compared EEG to functional outcomes such as oculomotor function in hockey athletes.

1.7 Saccades

Changes in eye movements have been used to evaluate brain functions related to cognition and behaviour, and to support determining differential diagnoses in disorders affecting the brainstem, cerebellum, thalamus, basal ganglia and cerebral cortex.[65] Objective tests of oculomotor function may be sensitive markers of cerebral dysfunction after closed head injuries.[64] Saccades are quick eye movements shifting vision to a target, followed by a fixation period where the eyes are still.[65] Saccadic eye movements are relevant to clinicians as they have been shown to measure cognitive changes after concussion.[66–69] Saccades can be measured by their latency, directional errors and positional accuracy.[70] The latency of saccades is the time taken to initiate eye movement after the onset of a stimulus. Latencies vary from 100 ms to 1000 ms but are usually around 200 ms.[65]

Prosaccades are reflexive saccadic eye movements that orient our eyes towards a stimulus in our field of view. Antisaccades are produced by voluntary control and are cognitively driven eye movements in response to a stimulus.[71] Due to the more complex processes involved, antisaccades have longer latencies than prosaccades.[72] Individuals with concussions exhibit deficits in executive function related tasks,[51] and antisaccade eye movements are associated with aspects of executive function and higher-order brain function. Comparing parameters from prosaccades and antisaccades can allow for an objective assessment of cognitive function.[73]

This comparison has demonstrated that athletes with concussions do not exhibit changes in their prosaccade eye movements but do have changes in antisaccades after a concussion.[17] Further research has found slower and less accurate saccades following concussion.[74] When comparing those with a concussion to those with PPCS, prosaccade measures are not changed in either group, but in those experiencing PPCS, there were a greater number of errors when completing antisaccades.[75] This is suggestive that oculomotor measures are related to cognitive deficits such as attention, decision making and inhibition and may be useful in assessing patients with concussion and PPCS.

1.8 Overall Purpose

The overall purpose of this thesis is to evaluate whether oculomotor assessments are useful in the assessment of brain injuries, such as subconcussive impacts, acute concussion, and persistent post-concussion symptoms. This was done through three projects: (1) monitored head impacts accumulated by hockey players in games using helmet-mounted sensors and compared head impact number to oculomotor and EEG measures; (2) compared measures of saccadic eye movements and patient-reported outcome measures in persistent post-concussion symptom patients pre and post 16 weeks of outpatient therapy; (3) evaluated a subset of retrospective intake data from acute concussion patients focusing on subjective assessment of visual and vestibular symptoms to the length of time these patients were seen in clinic.

1.8.1 Chapter 2 Purpose

To measure head impact accumulation in Canadian university male hockey players over a season of play and assess if these impacts are associated with changes in saccade eye movement assessments and ERPs.

1.8.2 Chapter 2 Hypothesis

An increased number of head impacts is associated with increased deficits in cognitive function, measured by saccadic eye movements (increased latency and increased number of directional errors), as well as deficits in neurophysiological ERP measurements (increased amplitudes and latencies).

1.8.3 Chapter 3 Purpose

To determine if adults with PPCS demonstrated objective improvements in saccadic eye movements following 16 weeks of outpatient, intensive brain injury group therapy. Additionally, we sought to determine if these changes were associated with changes in patient-reported outcome measures.

1.8.4 Chapter 3 Hypothesis

Improvements in patient-reported outcome measures are associated with increased oculomotor function as measured by prosaccades and antisaccades.

1.8.5 Chapter 4 Purpose

To assess a subset of self-reported persistent post-concussion symptoms related to the vestibular and ocular systems and determine if the presence of these symptoms was associated with prolonged recovery from concussion.

1.8.6 Chapter 4 Hypothesis

Increased vestibulo-ocular symptom burden is associated with an increased likelihood of a longer time to discharge from outpatient care.

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Chapter 2

Accumulated Head Impacts in University Hockey Players are Associated with Changes in Neurophysiological Function

2 Introduction

Head impacts can be devastating for the careers and lives of injured athletes. As more athletes speak of their experience with head impacts, there has been a recent increase in attention toward these injuries.[1] A concussion may be the most well-known head injury in contact sports. Up to twenty-two percent of hockey players between the ages of ten and twenty-five will experience a concussion playing hockey.[2] While not all athletes will experience a concussion during their career, all athletes sustain subconcussive head impacts. Subconcussive impacts are head impacts that do not result in a diagnosed concussion.[3] Subconcussive impacts are less researched but more common than concussions.[3] Often, these subconcussive impacts do not result in observable concussion symptoms, but they cause damage, such as structural changes in athletes' white matter tracts seen six months after a season of play.[4] Despite their prevalence in sports, little is known about the effect of subconcussive impacts on the neurophysiological function or structure of the brain.

Ice hockey has a similar concussion risk as other contact sports.[5] In the NCAA, men's hockey had concussion rates of 0.76/1000 athletes.[6] Yet most head impact research has focused on football. Canadian university football players receive an average of 335 head impacts per season.[7] Comparing head impacts in high school football and hockey athletes, hockey averaged 24.7 hits per hour compared to 40.5 in football.[8] However, the average impact in hockey had a greater average acceleration than in football, 35.0 g and 24.7 g, respectively.[8]

Currently, there are no standardized clinical assessments to monitor changes associated with the accumulation of subconcussive impacts in athletes.[9] Concussion diagnosis is difficult due to the complexity of the various neurological systems that can be affected.[10] Clinicians have an array of subjective assessment tools to aid in their clinical judgment, including the Post-Concussion Symptoms Scale (PCSS),[11] the

Standardized Assessment of Concussion (SAC),[12] and the Sport Concussion Assessment Tool 5th edition (SCAT5).[13] These assessment tools evaluate concussion-related symptoms, including cognitive, vestibular, visual and affective changes.[14] As part of a complete assessment to diagnose concussions, these outcome measures should be combined with objective tools to assess function.[14] Electroencephalogram (EEG) and saccadic eye movement tracking offer two possible objective measures for assessing aspects of neural function. Objective measures of neurological function are appealing as they may provide objective results and are a more direct measure of neurological function.[15–17]

EEGs measure subtle changes in brain function through the brain's electrical activity.[18] These changes often persist beyond what is captured by common clinical assessments[19] but can be important markers of changes in neural function.[20] P300 latency is associated with the speed of stimulus classification.[21] Event-related brain potentials (ERPs) represent neuron voltage changes in response to a specific task or stimulus.[22] ERPs are used by neurologists and psychologists and could offer other clinicians a valuable tool that can provide objective insight into specific effects that subconcussive impacts can have on function.[23] ERPs are averaged signals of specific waves; the P300 is a positive wave evoked 300 ms after the presentation of a stimulus. The P300 ERP measures attention, stimulus recognition and information processing.[24] P300 amplitudes have been shown to be larger in relation to increased effort to a task.[25] Athletes with a diagnosed concussion, and those with accumulated subconcussive impacts, had similar decreases in P300 ERP amplitudes.[26] P300 amplitude reduction is related to impaired inhibitory control[27] and weaker cognitive control.[28] Two other ERPs that are commonly collected with the P300 are the N100 and N200. The N100 ERP is related to auditory processing[29] and N200 is related to visual processing[30] and has been shown to be related to the progression of cognitive impairment. Both N100 and N200 are decreased later in life in those that have experienced a concussion, with repetitive concussion leading to larger deficits.[31]

Eye movement is a complex process involving many brain areas. Visual information is processed by the visual cortex, posterior parietal cortex, frontal eye fields, the dorsolateral prefrontal cortex and areas in the brain stem. These areas are involved in more complex visual processes and by assessing their integrity via eye movement an understanding which area(s) are vulnerable to concussion could be determined.[32] Assessments of eye movement have been suggested as a marker of cognitive function for over a decade.[33] A saccade is a quick eye movement that directs vision to a specific target, followed by a fixation period where the eyes remain fixed. Concussion-related cognitive dysfunction has been measured with saccadic eye movement.[34–37] Saccades can differ in latency, amplitude, velocity, and direction. Saccade latency refers to the time taken for a saccade to begin after a stimulus is presented and ranges from 100 ms to 1000 ms, but a typical prosaccade latency is 200 ms.[38] The features of the target stimulus can impact latency as saccades are slower if the target has a low intensity, low contrast or high spatial frequency.[39,40] The introduction of a gap period between the current fixation target and the appearance of the following target stimulus can also increase saccade latency.[41]

Prosaccades are a type of saccadic eye movements that occurs naturally in response to the appearance of a stimulus in our visual field. Alternatively, antisaccades are generated by suppressing the automatic response to look toward a stimulus and instead producing a saccade in the opposite direction.[42] Due to the higher order processes involved, antisaccades are slower on average compared to prosaccades.[43] Antisaccades reflect a goal-directed shift in eye movement, which recruits a wider neural network that prosaccades, including areas that are responsible for more complex tasks such as executive function, working memory and inhibitory control. Concussion results in longer latency, reduced accuracy and more errors in saccadic eye movement.[44,45] Some individuals have shown changes a month after their concussion.[16] Comparatively prosaccades often recover within a few days following concussion.[46] Due to this difference in recovery trajectory it has been suggested that prosaccades may be useful for acute concussion assessment and antisaccades for longer term recovery.[47] Incurring head impacts in hockey results in reduced prosaccades latency, slower self-paced saccades and deficits in other eye movement measures.[48]

EEG and oculomotor assessments have been studied as important objective assessments to determine presence of concussion. Furthermore, EEG has been demonstrated as an important neurophysiological function reference value or 'brain vital sign' in elite hockey players who have sustained subconcussive hits.[49] However, there is no research examining the use of oculomotor assessments, specifically saccades and antisaccades in hockey players who have sustained subconcussive hits. The purpose of this study was to describe the neurophysiological function of university hockey players before and after subconcussive impacts using EEG and saccades. The four study objectives were (1) to assess if increased number of head impacts is associated with changes in saccadic and EEG neurophysiological assessment; (2) to compare any resulting changes in EEG measurements to saccade-related measurements; and (3) to assess if during a month-long midseason rest period there are improvements in neurophysiological measures. We hypothesized that an increased number of head impacts would be associated with increased deficits in cognitive function, measured by saccadic eye movements (increased latency and increased number of directional errors), and deficits in neurophysiological ERP measurements (increased amplitudes and latencies). This knowledge will aid in developing assessments that can accurately measure the consequences of accumulated head impacts, as well as the possible promotion of impact-free periods during the season of play to improve player brain health.

2.1 Methods

2.1.1 Participants

All position players of the Western University men's varsity hockey team were approached to participate in the study. Western University's Human Subjects Research Ethics Board Approved the protocol. Of the 23 position players on the Western University Men's varsity Hockey team, 22 volunteered to participate in the study, providing written and informed consent. Participants were excluded if they had a diagnosed learning disability, neurological disorder, or were diagnosed with a concussion during the time of this study. The twenty-two players who consented to be in this study were composed of 9 Defensemen and 13 Forwards. These players participated in an average of 15 games of 24 games throughout the season. The players averaged 22 years of age (21-29).

2.1.2 Procedure

All participants had sensors equipped on their helmets to measure the number of head impacts incurred in games throughout the season. Participants completed neurophysiological testing (eVox System, Evoke Neuroscience, New York, USA) and saccade eye movement video oculography at four-time points in the hockey season: preseason baseline during non-contact training camp (August), midseason 1 (November), midseason 2 (January), and postseason (March). All participants completed all assessments at all testing time points.

2.1.3 Horizontal Saccades

Visual stimuli were presented on a custom-made light board. The light board was centered on the participant's midline and placed 55 cm in front of the participant. Light-emitting diodes (LEDs) were embedded in the board and covered with black cloth. A multicolour LED placed midline to the participant at eye level served as the fixation point. Target LEDs were located 15.5° left and right of the central fixation point and served as target stimuli[50]. Participants sat at a table in a well-lit room with their head placed in a head-chin rest throughout data collection. A high-speed digital video camera (GoPro Hero 6, Los Angeles, USA) was placed above the light board to record the participant's eye movement at a frame rate of 240 Hz. Fibre optic cables (Simplex 1.0 mm Industrial Fiberoptics, Tempe, AZ, USA) were secured in the camera's field of view to record the timing of the target light on the video system.

Each trial began with the presentation of the fixation LED to direct the participant's gaze to the center location. The colour of the fixation LED reminded participants about the type of trial. Red and green fixation LEDs indicated prosaccade and antisaccades, respectively. Additionally, players were verbally cued by the researcher when the testing block switched. The target LED was illuminated for 50 milliseconds following a random delay between 1000 and 2000 milliseconds. Players completed blocks of 20 prosaccade and 20 antisaccade trials. The direction of the target stimulus was assigned pseudo-randomly to ensure ten trials in each direction within each block.

2.1.4 Electroencephalogram

Electroencephalogram testing was performed using a portable commercial EEG system (Evoke Neuroscience, New York, New York, USA). An EEG cap was applied to the head of the participant. The cap consisted of 19 electrodes corresponding to the 10-20 International System for electrode placement [51]. The cap was attached to a wireless amplifier, which transferred the signals to the laptop. An electrocardiogram (ECG) electrode was also attached below their left collarbone to monitor heart rate. Finally, two reference electrodes were placed on the participants' earlobes. Electro-gel was applied to the participant's scalp using a blunt needle via holes in the electrode sensors. Via the testing laptop, feedback was given related to the connection between the scalp and the sensor. All sensors had good connections, below ten kOhms, before proceeding. Participants wore earbuds to ensure all instructions were heard clearly and to reduce distractions.

Two five-minute baseline tests were collected, eyes opened and closed, respectively, as well as a ten-minute choice reaction task. All testing occurred in this order. For the two baseline tests, participants were asked to remain as still as possible to reduce artifacts in the data. Participants were instructed to relax and stare at the computer screen for five minutes for the open-eye test. With eyes closed, participants were similarly instructed to relax and face the screen with their eyes closed while staying awake. A choice reaction task, such as the oddball paradigm, is an often-used research paradigm for ERPs. It consists of the presentation of two visual stimuli each have different probabilities of happening. The small blue circle was presented infrequently, and the large blue circle was frequently presented. The frequent target stimulus elicits a P3a ERP which is a strong positive P300 wave. The amplitude of the P3a wave is associated with the engagement of attention, stimulus recognition, and the processing of novelty stimuli[24] When the infrequent stimulus occurs, subjects must give a physical response, a thumb press of a switch. This infrequent target stimulus elicits a P3b ERP, which is another strong positive P300 wave. The amplitude of the P3b wave does not directly measure cognitive performance but is associated with the amount of attentional resources allocated to a task, information processing, and working memory.[24] Additionally a checker board was presented as a visual distractor. The presentation of this image produced the N200 ERP. During this entire process an auditory tone was played through the headphones to elicit the N100 ERP.

2.1.5 Head Impacts

Players' on-ice head impacts during games were recorded using wireless devices, GForce Trackers. Players impacts were also measured for 10 non-contact practices; no impacts occurred during practice. As such, data was not collected for the 10 non-contact practice sessions. The GForce Trackers (GFT; GForceTracker™, Markham, ON) contain a tri-axial gyroscope, a tri-axial accelerometer, and onboard memory to store impact data. A GFT was attached to the outside of the helmet on the rear crown of the helmet via an industrial-strength re-closeable fastener (3M^{TM} Dual Lock^{TM} Re-Closeable Fastener SJ3551 400 Black, 3M Global Headquarters, St. Paul, MN). GFTs were affixed in this location as it was flat and consistent surface between different helmet versions. Helmets were fitted by the team equipment manager. The accelerometer measured linear accelerations of up to 200 g, with 1 g of resolution, on the three axes. The gyroscopes measured rotational velocity up to 2000 °/s, with 1 °/s resolution. The GFTs are programmed to collect impact data at a user-programmed threshold. We chose a threshold of 15 g summative force; this is considered best practice for tracking head impact data[52]. Data was recorded for 40 ms total, 8 ms before the threshold trigger and 32 ms after. The number of head impacts was recorded and represented head impact accumulation; previous research has used impact accumulation without biomechanical measures.[53,54]

2.1.6 Data Analysis

P300, N100 and N200 waves were recorded from the 19-channel sensors fixed in the EEG cap with the ear-attached ground electrodes. Data were sampled at a rate of 250Hz. P300, N100, N200 signals were analyzed for peak amplitude and latency. These data were separated via the Evox system into P3a and P3b sub waves for the P300 EPRs. Amplitude was determined from the difference between baseline and maximum peak amplitude of the ERP. The Evox system calculated ERP latency as the time from stimulus onset to peak ERP amplitude. Artifacts from eye movement and blinks were removed using a proprietary algorithm.

Neurophysiological performance was analyzed using linear mixed models (LMM) in R Studio (v1.1.456, lme4, effectsize, dplyr and agricolae packages). The number of head impacts was used as the independent variable. All data were visually assessed for normal distribution. Candidate models included different combinations of impact, data collection timepoint, age, position and ten neurophysiological test outcomes (including visual latency, visual peak amplitude, auditory latency, auditory peak amplitude, P3a latency, P3a peak amplitude, P3b latency, P3b peak amplitude, prosaccade latency, and antisaccade latency). Four candidate models were created for each of the ten neurophysiological markers. Each model was a combination of when the measurement was taken (time), the number of impacts accumulated by that time of the season (impact), and the interaction between measurement time and accumulated impacts. Models were run to assess the effect of head impacts on the neurophysiological testing measures over the four collection periods. Player was used as a random effect to account for individual variability, and a fifth model without a random effect was used as a null model. Models were then ranked based on Akaike's information criterion (AIC) value. AIC is used to estimate the prediction error of a model and therefore the quality of the linear models. A lower AIC indicates better fit of the model with an AIC value of two being a standard cutoff for further interpretation, Models were created for each neurophysiological variable and then ranked by AIC, starting with the model with the largest AIC and considering the next model, models with an AIC that was two or less units lower than the previous model were considered to be the final model and further analyzed. Model groups where the null model was the best fit, or if the model of best fit had an AIC greater than two, were not further analyzed. Validity of the model for this particular data set was evaluated by assessing normality, linearity and equal variance, and leverage.[55] We assessed changes in neurophysiological function using a two-way repeated measures ANOVA. Effect size for ANOVAs was calculated as Cohen’s F values. Cohen’s F were interpreted as >.10 were very small, 0.10-.24 as small, 0.25-0.39 medium, and > 0.40 as large effects.[56] Tukey’s tests were completed post hoc, to identify which time points were significantly different within each model. All statistical analyses were completed using R (R Studio v1.1.456).

2.2 Results

2.2.1 Head Impact Accumulation

Players accumulated an average of 267 ±116 head impacts (range: 34 to 507) over the course of the 24-game season. The median number of impacts was 265 impacts. Overall, the players accumulated 5879 total impacts over the season, with 3198 in the first part of the season and 2681 in the second part. Summarized impact data is presented in Table 2.1.

Table 2.1 Mean number of head impacts for Canadian Varsity Hockey Players over the course of a season. Each column represents and individual timepoint. Data are presented as mean (standard deviation). All players row expresses the sum total of impacts between each timepoint.

	Average Number of Head Impacts		
	Preseason- Midseason 1	Midseason 2-Postseason	Total
Forwards	168.8 (74.4)	123 (66.6)	291.9 (128)
Defensemen	111.4 (51.6)	120 (48.6)	231.5 (91.9)
All Players	3198	2681	5879

2.2.2 Electroencephalography

Of the 32 candidate models for the ERP data, four were statistically significant when analyzed by two-way ANOVA. Each model fulfilled the assumptions to be an appropriate model for these data. The relationship between impacts and visual latency (N200) was found to be significant, with visual peak ERP amplitudes increasing over time ($p = 0.034$). Post-hoc analysis found no significant differences between time points (p=0.019). There were small effects from time (Cohen's f = 0.14) and impact (Cohen's f = 0.24). Time also had an effect on the auditory latency (N100) ($p = 0.03$). There was a medium effect size from time (Cohen’s f = 0.34). Post-hoc analysis showed a significant difference between midseason 1 and midseason 2 collection points. P3a latency was related to time (*p*=0.003). The effect of this relationship was large (Cohen’s f = 0.42). Tukey’s post hoc showed significant changes between preseason and postseason (*p*=0.007), midseason 1 and postseason(*p*=0.008), and midseason 2 and postseason (*p*=0.03). P3b peak amplitudes were related to time (*p*=0.02) and the combination of time and impact (*p*=0.04). There were no significant differences between data collection timepoints when examined by Tukey’s test. There were medium effect sizes for time (Cohen’s f = 0.37) and time by impact (Cohen’s f = 0.28). Average EEG measures are summarized in Table 2.2.

Table 2.2 Average Event-Related Potential (ERP) measures for Canadian Varsity Hockey Players over the course of a season. Each column represents and individual timepoint. Data are presented at Mean (standard deviation).

	Preseason	Midseason 1	Midseason 2	Postseason
Visual ERP Latency (ms)	195.24 (37.46)	199.00(25.92)	198.71 (28.72)	188.62 (23.69)
Visual ERP Peak Amplitude (mV)	-11.93 (5.94)	-10.82 (5.13)	-9.35(3.99)	-8.63 (5.18)
Auditory ERP Latency (ms)	212.81 (40.93)	226.95 (30.61)	195.48 (43.70)	216.14 (16.15)
Auditory EPR Peak Amplitude (mV)	-8.14 (2.14)	-9.08 (3.25)	-7.30 (5.57)	-9.74 (2.52)
P3a ERP Latency (ms)	427.14 (39.10)	429.19 (27.24)	435.82 (64.07)	481.05(72.13)
P3a ERP Peak Amplitude (mV)	20.63 (8.15)	21.13 (6.96)	18.47 (7.81)	17.89 (5.29)

P3b ERP Latency (ms)	472.19 (61.88)	494.81 (65.18)	468.05 (67.24)	497.82 (42.58)
P3b ERP Peak Amplitude (mV)	13.68(4.25)	17.45 (6.67)	12.88 (5.18)	13.53 (3.35)

2.2.3 Saccades

Of the eight models created using saccadic measures, no models were statistically significant. Prosaccade and antisaccade latencies did not significantly change for players over the season, nor did they change based on the number of impacts accumulated over a season. Average saccadic measures are summarized in Table 2.3

Table 2.3 Saccade measures of Canadian Varsity Hockey Players over the course of a season. Each column represents and individual timepoint. Saccadic errors are measured as the number of errors per 20 trial blocks. Data are presented as mean (standard deviation)

	Preseason	Midseason 1	Midseason 2	Postseason
Prosaccade Latency (ms)	271.84 (32.79)	271.77 (33.37)	260.00 (27.02)	260.76 (28.71)
Prosaccade Error Rate	0.55 (1.06)	0.24 (0.53)	0.00 (0.00)	0.05 (0.21)
Antisaccade Latency (ms)	313.35 (46.11)	307.76 (36.49)	297.88 (25.95)	294.72 (31.39)
Antisaccade Error Rate	1.91 (1.44)	1.76 (1.45)	1.64 (0.95)	1.14 (1.13)

2.3 Discussion

The purpose of this study was to measure head impact accumulation in Canadian university male hockey players over a season of play and assess if these impacts are associated with changes in saccade eye movement assessments and ERPs.

For comparison of our research findings with other studies, our players accumulated an average of 11.125 impacts per game, and found no difference based on player position. A larger study of 41 male and female collegiate hockey players, recorded 19,880 head impacts over 3 seasons, and found no difference based on player position.[54] These players averaged approximately 113 impacts per exposure, the median number of impacts were 287 and maximum of 785.[54] Several studies have presented data about concussions[2,6] and head impact accumulation in hockey[57] and the resultant neural changes in university athletes.[23] This study contributed to that body of literature, where these findings demonstrated changes in EEG, but not in saccadic eye movements.

The EEG data revealed that an increased number of head impacts was associated with decreased visual latency, auditory latency, and P3a ERP latency. Decreased visual latency may reflect either a faster player response time or smaller ERP amplitude. As latency is measured by the time to reach peak amplitude, a smaller peak would take less time to reach maximum or peak amplitude. In our case, the P3a amplitude was decreased along with the P3a latency.

The amplitude of the P3a wave is associated with the focus of attention and novel stimulus identification.[24] P3a latency and amplitude both increased as the number of head impacts increased. This may be related to a decreased efficiency of the attentional system and increased activation of associated brain regions to reach a threshold for a response. The increased amplitude of P3a ERP found in this sample may be due to the association with latency as it will take longer to reach this higher peak. Further the P3b amplitude was shown to have decreased over time. As P3b is related to decision making this may reflect a reduction in the power of these complex systems.[24] A study of forty-seven junior A hockey players over two seasons of play revealed that the impacts accumulated during a season of youth hockey is associated with reductions in EEG measures, including the n100 and p300 ERPs.[31] Of these forty-seven players twelve players were diagnosed with a concussion, these athletes had increased amplitudes and slower latencies on all EEG metrics measures in these studies.[31] The remaining twenty three players that were not diagnosed with a concussion were shown to have no difference in preseason and post season measures of the P300 ERP.[31] However, there were no changes in antisaccade measures in this thesis, despite this task requiring an element of decision making. Accordingly, the deficits that are apparent in ERPs may not be observable by oculomotor measures.

We cannot determine exactly why saccadic eye movements were not associated with the number of head impacts in our sample. One explanation may be that the cognitive changes caused by cumulative impacts were too small to be detected by saccadic eye movements due to the relatively low number of head impacts experienced by these players during the season. An average of 267 impacts may appear high, but football players of similar age at the same institution averaged 336 impacts per player, with some positional groups seeing as many as 555.[7] It may also be important to appreciate that the duration of the hockey season (8 months) was considerably longer than the football season (3 months), and accordingly the average amount of time between impacts was larger in hockey. While evidence from football[58] and soccer[31] has shown a relationship with the number of impacts, this relationship may not be observed in this study as the number of head impacts these players underwent during the season was lower than comparably aged football[58] and slightly younger soccer[59] athletes.

This study was limited by its small and homogeneous sample. Although all but one eligible player was recruited, we recognize this small sample should not yet be used to draw generalizable conclusions for this population. However, the effect sizes for these results indicate that larger scale studies are warranted in the future. Of course, the population of hockey players is diverse; this means that repeated study requires samples representing various ages, abilities, and genders to be representative of the over 500,000 Canadians report playing hockey[60] .

This study supports the body of literature that suggests the accumulation of subconcussive head impacts is associated with changes in neurological function.[9,31,61–65] This study determined that some methods of quantifying neurological function were more sensitive than others. EEG was useful in identifying changes in neurological function associated with the number of head impacts players received during a season of hockey.

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Chapter 3

Saccadic Eye Movement and Standardized Assessment in Recovery from Persistent Post-Concussion Symptoms

3 Introduction

Ontario had 147,815 concussions on average per year from 2008-2016.[1] Mild traumatic brain injury (mTBI), including concussion, is the most prevalent type of traumatic brain injury, accounting for approximately 82.5% of brain injuries.[2,3] Biomechanical forces to the head or body can induce concussions. These forces can occur in motor vehicle accidents, falls, violence, workplace or sporting accidents, and result in the rapid onset of impairments in neurological function.[4] Acute signs and symptoms of concussion may fall within four main categories: somatic, cognitive, affective, and sleep-related.[3] Symptom presentation can vary between individuals due to several factors, including gender, concurrent mental health conditions and concussion history.[5] Most individuals will have symptom resolution within two weeks of their initial injury.[3]

However, 10-15% of people who sustain a concussion experience symptoms for months or years post-injury.[6] Persistent Post-Concussion Symptoms (PPCS) describes individuals with concussions who experience symptoms that persist beyond four weeks in children[3] or two weeks in adults.[6–8] Recently the PPCS diagnosis has been removed from the Diagnostic and Statistical Manual of Mental Disorders.[9] However, the International Classification of Diseases still includes persistent post-concussion syndrome classification.[10] This lack of unity in diagnostic terminology may contribute to confusion amongst the public and healthcare practitioners.[11] These types of inconsistencies contribute to gaps in clinical knowledge regarding the diagnosis and treatment for individuals with PPCS, there is a gap in clinical knowledge on the diagnosis and treatment for these individuals.[12]

An individual's signs and symptoms of concussion dictate their treatment plan, which may include vestibular, cognitive, balance, or visual tasks.[13] BrainEx90 is an interdisciplinary outpatient intervention for long-term concussion rehabilitation established at Parkwood Institute in London, Ontario.[14] Created by mTBI field experts, BrainEx90 involves 16 weeks of combined physiotherapy and occupational therapy in-person treatment for individuals with persistent symptoms following an mTBI.

Saccades are rapid movements of the eyes between focal points, such as moving between words when reading.[15] Clinicians can use saccades as both an assessment and treatment tool. Saccade dysfunction is a common visual disturbance experienced after a concussion.[15] [15] This study includes two types of saccades: prosaccades and antisaccades. Prosaccades occur when an individual looks toward a stimulus. Antisaccades happen when an individual looks in the mirror opposite direction of a stimulus. The production of antisaccades requires the inhibition of reflexive prosaccades, which requires input from higher-order brain areas.[16] Therefore, antisaccades' directional errors and eye movement latency give insight into aspects of executive function.[16] The neural pathways associated with vision span the frontal lobe, basal ganglia, superior colliculus, cerebellum, occipital lobe, and parietal lobe.[15,17] The broad distribution of brain regions in the visual system makes it susceptible to injury. Individuals with persistent post-concussion symptoms show changes to saccadic components, such as significant positional errors and slower eye movement.[18]

Several studies have shown changes in eye movements in patients with PPCS.[19–21] For example, in athletes with PPCS, improved oculomotor measures were correlated to improved symptoms on subjective assessment.[22] These changes in oculomotor function are important as they can give insight into injuries affecting cortical, brainstem or even specific visual pathways following brain injury.[23] These findings support the use of oculomotor measures to measure recovery in those with PPCS and the correlation of improved function and symptomology.

Subjective measures such as the Generalized Anxiety Disorder 7-Item (GAD-7)[24] and the Rivermead Post-Concussion Symptoms Questionnaire (RPQ)[25] are standard instruments clinicians use to evaluate symptoms of concussions and PPCS.[8] The Ontario Neurotrauma Foundation (ONF) recommends the RPQ and the post-concussion symptom scale[8] for the assessment of concussion symptoms. The ONF also recommends using the GAD-7 for the evaluation of anxiety symptomology following a concussion. Further, there is literature to support the comorbidity of PPCS and anxiety.[26] As such, the use of a general anxiety measure allows clinicians to assess these aspects of a patient's symptoms and determine the appropriateness for referral to specialized services for anxiety intervention (e.g., pharmacological or counselling). The Brain Injury Vision Symptom Survey (BIVSS)[27] is a self-reported survey of vision symptoms and has been used to assess concussion symptoms. The Headache Impact Test (HIT-6)[28] assesses the impact that headaches have on a person's ability to function in their home, job, school, and social life. The BIVSS and HIT-6 again do not directly assess concussions. Instead, they give insight into aspects of symptom burden. These assessments evaluate concussion-related symptoms such as headaches, anxiety, and vision changes. These outcome measures should be combined with objective tools to formulate an accurate diagnosis.[29] By comparing these patient-reported symptoms measures to oculomotor function, we may gain insight into how functional ability relates to symptoms of anxiety, headache, or vision changes.

This study aimed to determine if adults with PPCS demonstrated objective improvements in saccadic eye movements after 16 weeks of outpatient, intensive brain injury group therapy. The secondary aim was to investigate if there was a relationship between saccadic eye movements and performance on four patient-reported measures: RPQ, GAD-7, BIVSS, and HIT-6. We hypothesized that improvements in oculomotor function would be associated with patient-reported outcome measures.

3.1 Methods

3.1.1 Participants

Adults who completed the BrainEx90 program between September 2020 and February 2022 at Parkwood Institute in London, Ontario, Canada, were eligible to participate in this study. Inclusion criteria included individuals who were diagnosed with an mTBI, were 18 years of age or older and attended at least twelve of the sixteen 90-minute BrainEx90 sessions at Parkwood Institute in person. Participants were excluded if they participated in fewer than twelve sessions. This study was approved by the Health

Science Research Ethics Board at the University of Western Ontario and Lawson Health Research Institute, and all participants provided informed written consent.

3.1.2 Measurements

As part of standard clinical practice, clients participating in BrainEx90 completed a standardized assessment battery before and after the 16-week intervention. This battery included subjective and objective assessments performed by an Occupational Therapist and a Physiotherapist and patient-reported outcomes measures: GAD-7[24], RPQ[25], BIVSS[27], and HIT-6[28]. For this study, participants also participated in a video-oculography assessment to collect saccadic eye movements at baseline and post-intervention.

3.1.3 BrainEx90 Program

Participants rotated between 5-minute-long activity stations to work on cognition, balance or core stability, cardio, vestibular function, and vision, as well as two longer stations on self-management and targeted education on recovery-related topics, such as anxiety, nutrition, and mindfulness. Participants attended one session per week. Therapists tailored the activities at each station to the participant's symptoms and tolerance. The physiotherapist and occupational therapist also assigned weekly homework to participants and progress activities for each station as appropriate.

3.1.4 Patient-Reported Outcome Measures

The GAD-7[24] is a self-administered participant questionnaire used to assess anxiety and to screen for Generalized Anxiety Disorder. The measure consists of seven items, asking the individual to rate symptom frequency over the last two weeks. Each response is assigned a score from 0 to 3, from least to most severe.

The RPQ[25] is a self-administered questionnaire used to gauge the severity of 16 common post-concussion symptoms. The participants rated their present symptom severity compared to their pre-injury levels on a scale of 0 to 4.

The BIVSS[27] is a self-administered survey that measures vision-related symptoms of mTBI in adults. Participants rated the frequency of each symptom on a 5-point Likert scale.

The HIT-6[28] is a self-administered questionnaire that measures the impact of headaches on one's ability to perform activities of daily living. The 6-item self-report measures the severity of headache pain and the effect on cognitive functioning and psychological distress.

3.1.5 Video Oculography Assessment

Video recordings of prosaccades and antisaccades were collected using a GoPro digital video camera (Hero 6, Los Angeles, USA) and a validated [30] saccade production system. This system consisted of a lightboard with LED lights embedded, a laptop and a camera. The light board was synchronized with the laptop, which ran a timed LED protocol using LabVIEW (National Instruments, Austin, TX). The videos were recorded at 240 frames per second for a time resolution of 4.6 ms. A chin rest was placed 55 cm in front of the light board at a fixed height, with a white light to illuminate the participant's face and eyes. The participants completed 20 trials of prosaccades, starting with the participant fixated on a green LED in the middle of the screen and then looking toward the target LEDs at 15.5 degrees to each side. There was a random delay before each trial between 1000 and 2000 milliseconds. After a 10-second break, the participants were instructed to complete 20 trials of antisaccades fixating on a red LED in the middle of the screen and then looking in the opposite position of the target LED. The operator of the saccade system would vocally remind patients of the change in saccade type. The tests took about two minutes to complete. A separate fibre optic cable was attached to the chin rest, facing the camera. The fibre optic would illuminate synchronously with the target lights. Allowing the camera to capture the onset of the target lights (via the fibre optic cable) and the movement of the participants' eyes. The videos were analyzed using QuickTime Player 7 by manually counting the frames between the fibre optic illumination and pupil movement and converting the number of frames to time. Saccade latency was defined as the time from stimulus onset to first pupil movement. The video examiner also recorded directional errors. A direction error was recorded if the initial pupil movement was not in the appropriate direction, and errors were recorded as the number of errors.

3.1.6 Procedures

Participants' charts were reviewed to collect baseline scores from initial assessments before participating in the BrainEx90 program. A trained researcher collected video oculography recordings in a separate room at Parkwood Institute in London, Ontario, on the participants' first day of the BrainEx90 program. A trained researcher collected patient-reported measurements and Video Oculography again upon completion of the program either on their last or second to last session.

3.1.7 Analysis

Descriptive statistics were analyzed to characterize gender, age, time from injury to referral, and time from injury to starting the intervention. Two-tailed paired t-tests were used to assess the change from pre-therapy measures to post-therapy measures. Linear mixed-effects models were used to predict standard outcome measure performance based on time (pre-and post-BrainEx90) and change in saccadic performance. These models had both fixed and random effects. The models investigated whether prosaccade performance and antisaccade performance best-predicted scores on standard outcome measures after completing BrainEx90. Saccade latency and error rate were entered as fixed effects as they were fixed but unknown parameters in this population. The participant and time were random effects, as it was expected that each participant would have individual variability. Accordingly, the models accounted for the heterogeneity and variability of these data. A model was created for each of the four outcome measures compared to one of the three saccadic measures as a fixed effect. In total, there were 12 models. Prosaccade errors were not included in the analysis are they are not expected to change in chronic mTBI patients.[31] These models were then further analyzed by two-way repeated measures ANOVA. The effect sizes for these ANOVAs were calculated as Cohen's f values, and both point estimates and 95% confidence intervals are presented. Effect sizes were assessed as >0.10 were very small, 0.10-0.24 as small, 0.25-0.39 as medium, and > 0.40 as large effects.[32] All statistical analyses were completed using R (R Studio v1.1.456 lme4, effectsize, and dplyr packages).

3.2 Results

3.2.1 Participants

Eleven participants met the inclusion criteria, including eight females and three males aged 18 to 57. Mechanisms of concussion included motor vehicle accidents (MVA;n=5), falls (n=4), and sport-related concussions (n=2). On average, patients began the BrainEx90 program 15 months after injury, ranging from 10-34 months.

3.2.2 Outcome Measures

All Participants improved in all outcome measures over the 16-week intervention. There was an average improvement on the BIVSS of 2.18, which was statistically significant (p= 0.0002). These changes ranged from 1-4, which are smaller than the minimum clinically important difference (MCID) of 16.5[33]. The GAD-7 had a statistically significant (p<0.001) average improvement of 2.67 points. Ranging from 1-5, only one patient met the MCID for the GAD-7 of 4 points[34]. The HIT-6 improved by 1.82 points on average, which was statistically significant (p= 0.0002). Change values ranged from 1-4, which are smaller than the MCID of 8[35]. Finally, the RPQ had a statistically significant (p<0.001) average score reduction of 5.37. This reduction is greater than the suggested MCID for the RPQ of 4.6 points.[36,37] They ranged from 2-7 points. The data for outcome measures are summarized in Table 3.1.

Table 3.1 Individual Scores from patients on the Generalized Anxiety Disorder 7-Item (GAD-7), Brain Injury Vision Symptom Survey (BIVSS), the Headache Impact Test (HIT-6), and the Rivermead Post-Concussion Symptoms Questionnaire (RPQ) before and after 16 weeks of concussion therapy. Change is calculated as the difference from pre-therapy (pre) to post-therapy (post). Max scores for each test are BIVSS (112), GAD-7 (21), HIT-6 (78) and RPQ (64). Paired t-tests were used to assess the significance of these changes and are summarized by t-value and p value.

	BIVSS					GAD-7		
Patient	**Pre**	**Post**	**Change**		**Patient**	**Pre**	**Post**	**Change**
1	63	60	-3		1	19	17	-2
2	53	50	-3		2	16	11	-5
3	46	45	-1		3	15	12	-3
4	54	50	-4		4	18	17	-1
5	41	40	-1		5	15	12	-3
6	64	61	-3		6	21	18	-3
7	69	68	-1		7	16	14	-2
8	66	62	-4		8	17	14	-3
9	52	51	-1		9	14	11	-3
10	60	58	-2		10	16	13	-3
11	57	56	-1		11	16	13	-3
Mean	56.82	54.64	2.18		**Mean**	16.64	13.82	2.82
SD	8.64	8.24	1.25		**SD**	2.01	2.48	0.98
T Value	5.7869				**t Value**	9.5216		
p Value	0.0002				**p Value**	0.0001		
	HIT-6					**Rivermead**		
Patient	**Pre**	**Post**	**Change**		**Patient**	**Pre**	**Post**	**Change**
1	65	64	-1		1	42	35	-7
2	65	63	-2		2	30	23	-7
3	58	57	-1		3	32	25	-7
4	62	59	-3		4	30	24	-6
5	66	65	-1		5	29	24	-5
6	65	62	-3		6	42	35	-7
7	62	61	-1		7	39	32	-7
8	62	58	-4		8	36	30	-6
9	57	56	-1		9	36	34	-2
10	62	61	-1		10	34	31	-3
11	62	60	-2		11	26	24	-2
Mean	62.36	60.55	1.82		**Mean**	34.18	28.82	5.36
SD	2.87	2.88	1.08		**SD**	5.34	4.87	2.06
t Value	5.5902				**t Value**	8.6244		
p Value	0.0002				**p Value**	0.0001		

3.2.3 Saccades

All participants had significant decreases in both prosaccade (*p*<0.0001) and antisaccade (*p*=0.0043) latencies, and two participants had an increased antisaccade error rate following BrainEx90. Changes in the number of prosaccade errors were not statistically significant (*p*=0.1669), whereas the change in antisaccade errors was significant (*p*=0.0097). The data for saccades are summarized in Table 3.2.

Table 3.2 Individual saccadic measures from patients before and after 16 weeks of concussion therapy. Change is calculated and the difference from pre-therapy (pre) to post-therapy (post). Paired t-tests were used to assess the significance of these changes and are summarized by t-value and p value.

Prosaccade Latency					**Prosaccade Errors**			
Patient	**Pre**	**Post**	**Change**		**Patient**	**Pre**	**Post**	**Change**
1	324.17	234.79	-89.38		1	0	0	0
2	320.32	220.31	-100.01		2	1	1	0
3	276.04	231.21	-44.83		3	0	0	0
4	290.42	220.31	-70.11		4	0	0	0
5	314.91	284.65	-30.26		5	1	1	0
6	325.00	270.24	-54.76		6	3	0	-3
7	321.23	250.23	-71.00		7	0	0	0
8	328.65	254.61	-74.04		8	4	1	-3
9	282.92	263.13	-19.79		9	0	0	0
10	306.46	263.75	-42.71		10	0	0	0
11	308.33	254.79	-53.54		11	0	0	0
Mean	308.95	249.82	-59.13		**Mean**	0.82	0.27	0.55
SD	18.18	20.89	-24.44		**SD**	1.40	0.47	1.21
t Value	8.0226				**t Value**	1.4907		
p Value	<0.0001				**p Value**	0.1669		
Antisaccade Latency				**Antisaccade Errors**				
Patient	**Pre**	**Post**	**Change**		**Patient**	**Pre**	**Post**	**Change**
1	378.29	291.45	-86.84		1	1	1	0
2	390.20	293.45	-96.75		2	3	2	-1
3	325.21	280.42	-44.79		3	2	1	-1
4	344.12	230.23	-113.89		4	3	0	-3
5	305.04	283.96	-21.09		5	1	0	-1

6	379.17	290.23	-88.94		6	2	0	-2
7	354.31	289.32	-64.99		7	2	1	-1
8	434.03	316.18	-117.85		8	6	3	-3
9	286.11	331.48	-45.37		9	2	2	0
10	313.66	296.06	-17.59		10	2	2	0
11	334.90	322.14	-12.76		11	4	4	0
Mean	349.55	293.17	56.37		**Mean**	2.55	1.45	1.09
SD	43.18	26.61	50.91		**SD**	1.44	1.29	1.14
t Value	3.6727				**t Value**	3.1845		
p Value	0.0043				**p Value**	0.0097		

3.2.4 Models

Five of the twelve candidate models were statistically significant when analyzed by two-way ANOVA. The relationship between antisaccade latency and the BIVSS was statistically significant, with BIVSS score decreasing with decreased latency (*p* = 0.002). There was a large effect from antisaccade latency (Cohen f=1.55). The model assessing antisaccade latency and HIT-6 was significant (p=0.03). Antisaccade latency had a large effect in this model (Cohen f=0.95). The relationship between antisaccade latency and the RPQ was statistically significant, with the RPQ score decreasing with decreased latency (*p* = 0.003). There was a large effect of antisaccade latency (Cohen f= 1.35). Improvements in antisaccade error rates were also shown to relate to improvements in the BIVSS (*p* = 0.015). There was a large effect of antisaccade errors (Cohen f= 1.03). Finally, antisaccade error rates were associated with improved HIT-6 scores (*p* = 0.002). There was a large effect of antisaccade errors (Cohen f= 1.38); however, it was not statistically significant. Most models had large effect sizes. Only the models assessing antisaccade errors to GAD-7, Prosaccade latency to GAD-7, and antisaccade latency to GAD-7 had medium, small, and very small effect sizes, respectively. These data are summarized in Table 3.3.

Table 3.3 Summary statistics from linear mixed effects models for oculomotor measures compared to patient reported outcome measures.

Model

	Estimate	Standard Error	p value	Cohen f
		Antisaccade Latency		
BVISS	0.02	0.00	0.00	1.55
GAD-7	0.00	0.01	0.88	0.05
HIT-6	0.02	0.01	0.03	0.95
RPQ	0.03	0.01	0.00	1.35
		Antisaccade Errors		
BVISS	0.84	0.26	0.01	1.03
GAD-7	-0.23	0.25	0.40	0.26
HIT-6	0.75	0.17	0.00	1.38
RPQ	0.70	0.49	0.20	0.42
		Prosaccade Latency		
BVISS	0.04	0.00	0.94	2.51
GAD-7	0.01	0.01	0.57	0.21
HIT-6	0.03	0.01	0.93	1.83
RPQ	0.07	0.02	0.15	2.78

3.3 Discussion

Adults with PPCS demonstrated objective improvements in saccadic eye movements following 16 weeks of an intensive brain injury group therapy program. These patients had statistically significant decreases in prosaccade and antisaccade latencies, and statistically significant improvements in antisaccade error rate. Additionally, we identified that these changes were related to changes in patient-reported outcome measures. The BIVSS was related to changes in antisaccade latency and error rates; RPQ was related to improvements in antisaccade latency; the HIT-6 was related to antisaccade latency and errors. This augments previous research supporting the efficacy of this program to enhance performance on self-identified goals for those with PPCS.[38]

Decreases in antisaccade latency following 16 weeks of intervention were observed in 100% of the participants. This supports previous literature suggesting that post-concussion antisaccade latencies improve following interdisciplinary therapies.[39–41] These improvements may indicate neurophysiological changes or improved symptom management. A decrease in antisaccade latency suggests enhanced function of higher-order brain areas.[42] However, it is difficult to know if these saccade changes are due to the changes in oculomotor-specific pathways or as part of a more complex cascade of healing without a control group. Individuals with a concussion require more cortical activation to complete simple tasks compared to those without a concussion.[43] Therefore, it is also possible that participants' antisaccade latencies may have improved due to the increased efficiency of other systems, such as motor planning.[44] The results of this study suggest that there may be a relationship between oculomotor function and patient symptomology for aspects of PPCS, such as anxiety or headaches. Further research with a larger sample and control group is needed to define this potential association.

All participants demonstrated improved latency, and 81% demonstrated improved antisaccade error rates, despite participants being, on average, 15 months post-injury. These findings align with those of a prospective study of 37 adults with mild traumatic brain injury (mTBI) compared to healthy matched controls, where antisaccade accuracy deficits persisted for a few months post-injury, while latency returned to normal one-week post-mTBI.[45] While both studies demonstrate persistent antisaccade accuracy deficits in persons with PPCS, the current study adds that these deficits can change with intervention, even months beyond date of injury. One explanation for why 19% did not demonstrate improvement may relate to focus on speed over accuracy during testing. This is possible because when describing the task to patients, there was an emphasis on reaction speed, as the test was primarily measuring reaction time. As such directional errors may have occurred due to the patients focus on speed.

Linear modelling of saccadic performance and patient-reported outcome measures demonstrated a few significant relationships. The BIVSS was related to changes in both antisaccade latency and error rates. The RPQ was related to decreases in antisaccade latency. Finally, the HIT-6 was related to antisaccade latency and errors. These findings support previous research that found that difficulty in multiple object tracking was associated with BIVSS and RPQ scores in a sample of 15 adults with mTBI compared to matched controls.[46] In a study of 32 adults with mild to moderate brain injury, authors concluded that performance deficits were more strongly associated with memory changes than symptoms profiles. [47]

A limitation of the current study is the small sample size. The linear modelling might have more clearly demonstrated relationships if data were collected from more participants. Unfortunately, due to COVID-19 pandemic restrictions, outpatient programming, including BrainEx90, was suspended, thus limiting the number of potential participants during the testing window. However, these models showed large effect sizes for this sample, indicating a possible relationship may exist beyond the few significant models.[48] As such, this research should be continued with a focus on larger samples that would have adequate power to assess these associations.

There is limited normative data measuring saccadic latencies in a persistent post-concussion symptom population. Without pre-injury or normative data, it is unclear to what extent each participant's concussion affected their saccadic latency and error rate. A final limitation is an inability to determine a minimally clinically important difference in saccadic latency and error rate. With the 4.16 ms resolution of the high-speed video, it is difficult to definitively state whether any improvements of less than 4.16 ms were meaningful. Additionally, the process of extracting latency measures from the video recordings was time-consuming, limiting the widespread adoption of video oculography. Future research may consider using electrooculography[49] or other devices with higher acuity to capture subtle differences in saccadic latencies and different comparison outcome measures.

Given the cost and administration demands of diagnostic imaging, video oculography assessment of antisaccades could be a more accurate, objective measure for clinical use. However current processing of these data lacks feasibility in a clinical setting due to extensive time demands. Antisaccades may provide clinicians with an objective adjunct measure to support patient-reported symptom questionnaires.[50] Validating antisaccades measurements for use in a clinical setting would allow for the standardization of concussion assessments and forming of normative data in the future. The effect sizes shown in this study support further research into the association of oculomotor measures and patient-reported outcome measures.

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Chapter 4

4 The Clinical Utility of a Vestibulo-Ocular Sub-Component of the SCAT5

4.1 Introduction

Roughly 1 in 450 Canadians 12 or older report sport-related concussions (SRC) as their most disabling injury in the previous year.[1] SRCs result from biomechanical forces upon the head, neck, or body that result in diffuse changes to pathophysiological processes in the brain.[2] A concussion typically results in a cascade of symptoms and neuropsychological disruptions that may affect memory, ocular movement, the vestibular system, attention, and executive functioning. These symptoms often persist for days to weeks following injury. SRCs are common in contact sports and present a challenge for healthcare providers to evaluate and manage.[3,4] Although most athletes recover within 14 days, approximately 10-15% of individuals experience prolonged symptoms.[35,6] Several risk factors predispose individuals with a concussion to prolonged recovery, including age, sex, concussion history, comorbidities and injury-related characteristics such as the severity of acute symptoms and the presence of vestibulo-ocular symptoms.[5–8] The International Ice Hockey Federation reported that 513,674 Canadian hockey players were registered with the federation.[19] Second only to the United States at 551,006 athletes. However, the total number of individuals who participate in ice hockey is slightly greater. Given such a high percentage of Canadians who play hockey, the combination of the cultural significance of the sport and the likelihood of a concussion whilst playing hockey increases the value of research in this area.

The Sport Concussion Assessment Tool 5th edition (SCAT5) is one of the most widely used concussion assessments.[9] The SCAT5 alone cannot confirm a concussion diagnosis.[2] Instead, it is a tool for clinical interpretation. Best practice for the diagnosis of concussion involves a multifaceted approach that includes patient-reported subjective and objective evaluation.[10] Clinicians assessing SRC use standardized assessments evaluating somatic, cognitive, affect, vestibular, and oculomotor symptoms.[4,10] Symptom evaluation is a sub-section of the SCAT5 that evaluates a range of concussion symptoms on a Likert scale.[9] These include somatic, cognitive, affective, vestibular, and visual-oculomotor symptoms. Subdomains of the SCAT, such as those representing cognitive changes, have been used to evaluate the relationship between cognitive symptoms and timeline for return-to-learn in adolescents following sports-related concussion[11]. By further assessing a subset of the SCAT symptoms, clinicians may be able to identify patients requiring specific treatments or those who need an increased frequency of treatment. For example, children and youth athletes with vestibulo-ocular symptoms are more likely to have delayed recovery following concussion.[6,12] This is particularly noteworthy as fifty to ninety percent of patients with concussion report vestibulo-ocular symptoms.[13–15] While there are assessments that are more specific to these systems,[6,16] they often provoke symptoms, because they require the person to perform movements meant to stimulate the vestibulo-ocular system.[17] This is distressing to patients and may limit a clinician's ability to complete a full and detailed assessment without overprovoking these symptoms. In contrast, the ease of use and the breadth of the SCAT5 symptom evaluation section allow most clinicians to use this assessment. If a subset of the SCAT5 symptoms reflects the functioning of the vestibulo-ocular systems, clinicians may more easily identify patients that need vestibulo-ocular therapy, increasing the effectiveness of care.[3,18]

Some patients will experience persistent post-concussion symptoms (PPCS) following a concussion. These symptoms can be difficult to manage[20]. They make it difficult to enjoy many important aspects of life, including hobbies, exercise, social interactions, and employment.[21] While most sports-related concussions recover within 14 days, injured workers appear to have a different disease trajectory.[22] Workers averaged 4.5 weeks for a return to work, with an interquartile range of 8-24 weeks.[22] In addition to difficulties related to concussion symptoms, individuals with PPCS are also more likely to sustain subsequent brain injuries[23] and unintentional injury.[24,25]

Our study aimed to use a subset of the visual and vestibular symptoms in the SCAT5 as a measure of increased vestibulo-ocular symptom burden and assess if this was associated with an increased likelihood of a longer time to discharge. Assessment of the vestibulo-ocular system is often symptom-provoking for patients, making it difficult for emergency and primary practitioners to complete a detailed assessment in one appointment. Using a subset of the SCAT5 symptom evaluation section, we will assess if the symptoms burden from the vestibulo-ocular system is associated with a longer time to discharge in hockey athletes. We hypothesize that increased vestibulo-ocular symptom burden will be associated with an increased likelihood of a longer time to discharge from outpatient care. Study findings may inform prognostication and/or factors associated with prolonged recovery.

4.2 Methods

Retrospective data were collected from a sports medicine clinic in London, Ontario. These clinical data were stored on the REDCap clinical informatics framework. Ethics approval was acquired from the Health Science Research Ethics Board at the University of Western Ontario, and Lawson Health Research Institute Data were retrospectively reviewed for patients who attended the clinics from May 2018 to February 2022. All patients 16 years or older, diagnosed with a concussion by their treating physician, and whose primary sport was hockey were included in the study if their concussion occurred during hockey. Data on patient demographics, SCAT5 measures and the patient's visit history were collected.

4.2.1 Outcome Measures

The clinical data included the Symptom Evaluation section from the SCAT5. This subcomponent of the SCAT5 consists of a checklist of 22 common post-concussion symptoms, scored by the patient during a clinical interview or by the patient before the assessment on a Likert scale ranging from 0 (none) – 6 (severe). From these 22 symptoms, we further analyzed six symptoms that represent the visual and vestibular systems: nausea, dizziness, blurred vision, balance, light sensitivity, and noise sensitivity[26]. These symptoms were chosen as they represent possible vision and vestibular changes and are relevant to the vestibulo-ocular system.

4.2.2 Statistical Analysis

Descriptive statistics were used to characterize demographic and symptom data. The vestibular ratio was calculated as a measure of symptom burden. The vestibular ratio was the severity of the six vestibulo-ocular symptoms (max score 36) divided by the patient's total symptom severity (max score 132). Four chi-square analyses were performed to assess the relationship between vestibulo-ocular symptoms and time to discharge. The first chi square test assessed time to discharge from outpatient care and presence of any single vestibulo-ocular reported symptom. The next chi-square assessed time to discharge from outpatient care and the number of reported vestibulo-ocular symptoms. The third chi-square test assessed time to discharge from outpatient care and patient reported symptom severity as rated on the likert scale. Finally, the ratio of vestibulo-ocular symptoms and time to discharge from outpatient care were compared by chi-square.

4.2.3 Data Analysis

Outcome measures were divided into binary categories based on clinically relevant markers. Participants were divided by the 28-day mark for time to discharge from outpatient care, as most athletes recover within the first four weeks after injury[3]. Participants with any of the six vestibulo-ocular symptoms were included as having symptoms present. To assess the relationship between time to discharge and the number of symptoms, participants were divided by having less than or greater than three symptoms of 6 possible vestibulo-ocular symptoms. Symptom severity was measured as the sum of the participant's symptoms scores on the six vestibulo-ocular symptoms. These symptom severity scores were divided into mild (<12) and moderate/severe (>12) groups. This is based on the mild (1-2), moderate (3-4) and severe (5-6) scores on the SCAT5 Likert scales multiplied by the number of symptoms. A vestibulo-ocular symptom ratio was calculated as the severity of the vestibulo-ocular symptoms divided by the sum of the patient's scores in all 22 symptoms. Players were categorized as having a high or low ratio if they scored above or below the median vestibular ratio, those with the same ratio as the median were considered high ratio. Odds ratios were calculated to measure the effect size of each of the chi-square tests.

4.3 Results

A total of 255 patients who experienced hockey-related concussion were included in the data set. One hundred and ninety-nine of these individuals attended more than one treatment session and were included in the analysis. This group's mean age and standard deviation (SD) were 18.5 years and 8.79, respectively. Males accounted for 64% of participants. 28% of patients had a prolonged course of therapy greater than 28 days, with a maximum of 560 days. All participants had their complete SCAT5 symptom evaluation data set. The participants had an average symptom severity of 29.9 of 132 with a standard deviation of 25.8. 41% of participants had vestibulo-ocular symptoms. Similarly, 49% of participants had less than three vestibulo-ocular symptoms, and 51% had three or more vestibulo-ocular symptoms. 83% of participants had mild vestibulo-ocular symptoms (total severity <12), and 17% had moderate to severe vestibulo-ocular symptom burden. Demographic data are summarized in Table 4.1

Table 4.1 Summary of demographic data.

Characteristic	**Mean**	**Min**	**Max**
Age	18.7	13	66
Sex (F)	81(36%)	-	-
Days In Therapy	25	1	560
Days Injury to Assessment	20	1	583

The chi-square analysis of the presence of any vestibulo-ocular symptoms and time to discharge was statistically significant (p=<0.001), with an odds ratio of 19.24 (95% CI 8.29-44.63) of longer care was if vestibulo-ocular symptoms were reported. The analysis of the number of symptoms and time to discharge was also statistically significant (p=0.003) with an odds ratio of 2.68 (95% CI 1.4-5.14). The chi-squares for mild vs moderate/severe symptoms by time to discharge and vestibulo-ocular ratio by time to discharge were not statically significant. The results of all chi-square analyses are summarized in Table 4.2.

Table 4.2 Summary of Chi Square statistics.

	OR for Prolonged time to discharge	95% CI	*p*
Presence of any vestibulo-ocular symptoms	19.24	8.29-44.63	<0.001
Having three or more vestibulo-ocular symptoms	2.68	1.4-5.14	0.003
Having mild vs moderate/severe symptom burden	1.34	0.6-2.99	0.467
Having a high vestibulo-ocular symptom ratio	1.12	0.6-2.08	0.719

4.4 Discussion

This study used a subset of the vestibulo-ocular symptoms in the SCAT5 to investigate the relationship between initial symptoms and time to discharge. This study determined that the presence of any vestibulo-ocular symptom led to 19 times greater odds of a patient not being discharged by their primary practitioner after 28 days. Using a subset of SCAT5 to screen athletes may improve athlete care and prognostic planning.

The results of this study show that the presence of vestibulo-ocular symptoms captured within the SCAT5 are clinically relevant to patient prognosis. The subset of symptoms that address vestibulo-ocular symptoms were nausea, dizziness, blurred vision, balance, light sensitivity, and noise sensitivity. Interestingly, 59% of participants did not have any of these symptoms at their initial assessment. However, having one or more vestibulo-ocular symptom led to 19 times greater odds of the patient experiencing an extended recovery. Vestibular symptoms are associated with prolonged recovery in children and NCAA athletes.[6,27]

These findings support the literature on prognostic factors of persistent post-concussion symptoms. The Vestibular Ocular Motor Screen is a prognostic indicator of concussion recovery in children.[28] However, when combined with the King-Devick and the C3 Logix Trails A and Trails B, the four tests were more strongly associated with recovery time.[28] Due to the interconnectedness of the oculomotor and vestibular systems, clinicians need to be aware of the contributing factors and the importance of a detailed assessment of each system to effectively communicate expectations for prognosis and tailor treatment for their clients.

Concussion disorders have been grouped into physiological, cervical, mood/cognition-related and vestibulo-ocular.[29] Vestibulo-ocular symptoms are usually reported by the patient as worsening with movements, such as walking or running, being in a moving environment or performing visual scanning or reading. These symptoms are thought to result from injuries to the brain's oculomotor and vestibular systems.[18] The interplay of these symptoms in prolonged recovery is likely complex. However, these symptoms are debilitating as it can be hard to avoid provocative situations. Concussion care is based on reintroducing activity at a level that does not exacerbate symptoms.[2] For example, in a patient with headaches, a clinician may prescribe physical activity to a level of intensity that headaches do not increase more than 1-2 points on a 10-point numeric pain rating scale. Most of the vestibulo-ocular symptoms (dizziness, blurred vision, balance, light sensitivity, and noise sensitivity) are easily provoked, making it difficult to perform typical activities of daily living in order to maintain a normal lifestyle.

Interestingly, the number of symptoms was not strongly associated with recovery. Where having three or more symptoms only increased the likelihood of prolonged recovery 2.7 times, this slowed recovery may be due to the reaggravation of symptoms throughout the day. Similarly, there was no significant effect of symptom severity on the length of therapy. There was also no significant effect of having a high or low vestibular ratio of symptom severity on length of stay. These findings may be due to a few factors. Firstly, the subjective nature of the SCAT5 may affect the accuracy of the data collected. There is evidence that a fraction of athletes may purposefully lower their scores on subjective assessments to return to sports faster.[27] We encourage clinicians to complete a detailed assessment that encompasses subjective and objective measures.

These results indicate that examining a patient's vestibulo-ocular symptoms can be clinically useful in determining a patient's prognosis. This is relevant as the SCAT5 may be the most widely used concussion assessment. By utilizing a common measure but changing the interpretation to focus on the vestibulo-ocular symptoms, clinicians can assess the vestibulo-ocular system without requiring additional training, taking extra time for specialized tests or provoking the patient's symptoms. This is beneficial as it saves both time and money for clinics and the medical system as a whole and has the potential to improve patient outcomes during their recovery by early identification of those at risk of developing persistent symptoms.

The current study has a few important limitations. The data were derived from one clinic within Ontario and were limited to individuals with hockey-related SRCs; therefore, the findings may not be generalizable. It is also important to note that athletes outside this province or the major cities may have differing access to assessment and care. A limitation of this study is the measure of time to discharge. For most patients, stopping treatment does coincide with recovery. However, there are other reasons for no longer attending care, such as moving, financial constraints or changing providers, to name a few. It is possible that some patients discontinued their care for such reasons, but the reason for discharge was not recorded.

Concussion symptoms and prognosis will vary between patients. Identifying specific vestibulo-ocular motor abnormalities and their associated prognosis using the SCAT5 may aid clinicians. The causality of these relationships needs to be evaluated in a prospective study. If a causal relationship is supported, then clinicians using the SCAT5 could assess the vestibulo-ocular symptom subset as a factor in their clinical interpretation of prognosis and client-specific treatment needs.

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Chapter 5

5 Discussion

This thesis aimed to investigate if oculomotor assessments are useful in assessing a range of brain injuries and their symptoms, including subconcussive impacts, acute concussion, and persistent post-concussion symptoms. This thesis revealed three main findings about the usefulness of oculomotor assessments of concussion. Saccades were not associated with head impact accumulation over a season of hockey. Saccades were, however, associated with patient-reported symptoms in individuals with persistent post-concussion symptoms (PPCS) before and after a 16-week intervention. Finally, patients with acute concussion reporting any vestibulo-ocular symptoms were more likely to remain in physician's care beyond 28 days post-injury.

The subconcussive impact study illustrated that there was an association between changes in EEG and impact accumulation. However, there was no association between impact accumulation and saccadic eye movements. This is inconsistent with studies on impact accumulation in football, soccer and other head impact sports,[1–4,] which have found that subconcussive impacts have shown relationships with saccadic eye movements. This difference may be due to the relatively low number of head impacts that the varsity hockey players experienced in this study compared to football[5] and soccer[6] athletes of similar age/ability. For example, a comparison of high school football and hockey athletes determined that hockey averaged 24.7 hits per hour compared to 40.5 in football.[7]. This low volume of head impacts may not have caused enough structural or physiological damage to be detected. The changes in magnitudes of the antisaccade latencies in this study were comparable to studies of men[8] and athletes without concussion.[9,10] EEG, the more sensitive the two objective measures, showed increased head impacts associated with decreased visual latency and P3a ERPs. This reduced latency may indicate a faster response but could simply reflect the reduced time to reach its peak amplitude.[11] The P3a ERP is related to attention.[12] Therefore, an increased P3a latency and amplitude increased with accumulated head impacts may reflect a decrease in the efficiency of attention mechanisms.[5,6,7,11]This study supports the research that suggests the accumulation of subconcussive head impacts is associated with neurological changes;[1–4,13,14] and that saccades may not be sufficiently sensitive to detect change over a single season. These findings support the need for larger, longer prospective studies to determine the clinical utility of using saccades to detect changes in neurophysiological function following accumulated subconcussive hits.

The persistent post-concussion symptom study showed improved saccadic eye movements for a cohort of patients following a 16-week combined therapy program and that changes in saccadic eye movements were associated with changes in patient-reported symptoms. Specifically, the Brain Injury Vision Symptom Survey (BIVSS), Rivermead Post-Concussion Symptoms Questionnaire (RPQ) and the Headache Impact Test (HIT-6) were shown to have a linear relationship with changes in saccadic eye movements. These findings support previous literature that reported post-concussion antisaccade latencies improved with interdisciplinary intervention[15–18] and difficulty tracking multiple objects was associated with symptoms measured by the BIVSS and RPQ.[19] Decreases in antisaccade latency may relate to improved function of the frontal and parietal lobes.[20] However, other research has shown that these improvements could also be due to improved motor planning.[21] One study found deficits in antisaccade accuracy persist for up to 12 months post-injury, while latency returns to normal one-week post-mTBI.[22] The average participant in our study was 15 months post-injury and still showed improvement with intervention. These findings support the need for further study on the clinical utility of using saccadic eye movement assessment in combination with patient-reported measures and the validity and feasibility of using saccadic eye movements as an objective measure compared to more costly and less accessible neuroimaging techniques.[19]

The hockey player symptomology study determined that the presence of vestibulo-ocular symptoms captured within the SCAT5 was clinically relevant to the patient's prognosis. The subset of vestibulo-ocular symptoms studied were nausea, dizziness, blurred vision, balance, light sensitivity, and noise sensitivity. These findings are particularly important as 50–90% of adults with a concussion report vestibulo-ocular symptoms,[23–25] and some studies have shown a relationship between vestibular symptoms and the development of persistent post-concussion symptoms in children and collegiate athletes.[26–29] Many of the current vestibulo-ocular assessments, such as the Vestibular

Ocular Motor Screening (VOMS), provoke or exacerbate symptoms in patients.[25,30–33] Activities of daily living (ADLs) requiring changes in position or eye and head tracking can generate vestibulo-ocular symptoms of concussion.[26] Authors from one study suggested vestibulo-ocular symptoms are the most debilitating because they are the most easily provoked[26–29,34] Light, noise, and vision are a large part of our daily lives. Accordingly, the vestibular and ocular systems are constantly working, thus impacting a person's ability to rest or limit symptom exacerbation, which may tax the brain and slow healing.[27] This chapter showed that patients' vestibulo-ocular symptoms are associated with their prognosis. The novel contribution of this chapter is that it identified that a simple analysis of the SCAT-5 symptom checklist, focusing on the vestibulo-ocular symptoms, provides meaningful information about prognosis without having to perform symptom-provoking objective assessments. This thesis suggests that prolonged recovery from concussion is associated with vestibulo-ocular symptomology in hockey athletes.[35] Uniquely, six of the SCAT5 symptoms were related to prolonged recovery from concussion.

Future studies should focus on prospective research design to firmly establish the utility of oculomotor measures in assessing concussion. This is particularly important for sport-related concussions since athletes have shorter saccade latencies than non-athletes,[9,36] confounding isolated screening tests. A limitation of this research is that Chapter 2 was based on oculomotor data that were collected from a single team over one season of play. Additionally, the head impact sensors triggered recording at a threshold of 15 *g* to prevent recording accelerations from ordinary activities. While this is best practice,[37] decreases the number of measured head impacts compared to studies that used a 10 g threshold.[38] Further, for Chapters 2 and 3, there was a small sample size. Caution should be exercised when extrapolating these findings to other populations. Overall, all data were collected from a medical center in London, so this sample may not represent all areas of Canada. Research indicates that not all Canadians can access high-quality primary and specialized concussion care.[39] Healthcare services for patients living in remote and isolated regions can be limited because of geographical, socioeconomic, and cultural barriers. Furthermore, there is concern that many concussion clinics in Canada do not have access to physicians or the full complement of physician and allied healthcare professionals needed for comprehensive interdisciplinary care.[40,41]

The overall objective of this thesis was to investigate the use of oculomotor assessments across a range of concussion injuries. This thesis demonstrated that oculomotor assessments could detect recovery in PPCS and aid in understanding the prognosis of acute concussion. Vestibulo-ocular symptoms, measured by the SCAT5, were strongly associated with prolonged recovery. However, while P3a latency did change, saccadic eye movements did not change with the head impacts accumulated during varsity hockey season. These results provide some evidence that oculomotor assessments may be useful for clinicians when assessing acute concussion and tracking recovery of PPCS but that saccades might not help evaluate the effects of subconcussive head impact accumulation in varsity hockey. This thesis aimed to help clinicians and athletes better understand the role of oculomotor assessment in concussion care. The results support using these assessments in specific contexts, particularly acute concussion and individuals with persistent post-concussive symptoms. Future research should aim to to improve our understanding of oculomotor measures for patients with concussions.

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