Investigating the Effect of Mild TBI on the Global Processing of Form and Motion

by

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AUTHOR'S DECLARATION

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners. I understand that my thesis may be made electronically available to the public.

Abstract

Purpose: Individuals with mild traumatic brain injury (TBI) often experience a range of visual symptoms. The cortical processing of visual information involves two parallel streams; the ventral stream (form perception) and the dorsal stream (motion perception). Our purpose was to assess whether processing in the dorsal and/or ventral stream is affected by mild TBI. A range of basic visual functions were also assessed and we investigated the association between each vision measure and Post-Concussion Symptom Inventory PCSI scores.

Methods: Eleven adults with mild TBI (mean age 25.5 yrs, range: 19 – 42, 17 ± 5.2 months post injury), and 25 controls (mean age 27.9 yrs, range: 19 - 38) participated. Global processing of form and motion, as an index of dorsal and ventral stream function, were assessed psychophysically using Glass patterns and random dot kinematograms respectively. Contrast thresholds for coherent motion direction discrimination were also measured. Thresholds were measured twice for each test. Contrast sensitivity (Freiburg test), stereo acuity, near point of convergence, accommodative facility and amplitude, negative and positive fusional vergence and vergence facility were also measured. Mild TBI symptoms were assessed using the Post-Concussion Symptom Inventory PCSI.

Results: Patients with mild TBI demonstrated higher (worse) global form and motion coherence thresholds than controls ($p=0.01$). Global form coherence thresholds in the mild TBI was 25.07%, SD: 5.91 versus the normal 21.23%, SD: 5.37 while global motion coherence thresholds in the mild TBI was 14.38%, SD: 6.67 versus the normal 10.79%, SD: 3.37. Threshold elevations were not due to either the reduced contrast sensitivity or the accommodation and vergence anomalies. The magnitude of the processing deficit did not differ significantly between the global form and motion tasks ($p>0.05$). Contrast thresholds for

motion discrimination did not differ significantly between groups, but there was more between-subject variability in the mild TBI group (mild TBI (1.13%, SD: 0.47) versus the normal (1.20%, SD: 0.038)). There was a significant correlation between contrast thresholds for motion discrimination and PCSI score (R^2= 0.51. p=0.01) in the mild TBI group. PCSI scores were not significantly correlated with global form or motion coherence thresholds. As expected, the mild TBI group were worse that controls for almost all clinical measurements of vision.

Conclusion: Mild TBI affects processing in both the dorsal and ventral cortical processing streams. In addition, our results suggest that mild TBI impairs spatiotemporal contrast sensitivity and that this impairment may contribute to the symptoms of mild TBI.

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Dedication

I dedicate my thesis to my parent's, my wife and my daughter. I could not do this without your support and encouragement. I am lucky and grateful to have you all in my life.

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Introduction and literature review

1.1 Overview

Traumatic brain injury (TBI) caused by trauma to the brain from an external mechanical force is one of the most frequent neurological disorders, and almost 90% of TBIs are considered to be mild (Vos et al., 2012). The term mild TBI is used interchangeably with concussion. Mild TBI is one of the leading causes of disability among the American population with 3.2–5.3 million people suffering from a form of TBI (Corrigan, Selassie, & Orman, 2010). Mild TBI usually occurs when the brain is subjected to an acceleration–deceleration force resulting in disruption of brain function (Elder, Mitsis, Ahlers, & Cristian, 2010). Diagnostic imaging (including CT scans and MRIs) does not show any brain abnormalities such as focal lesions in mild TBI even though mild TBI is associated with a variety of symptoms with different severities (Alexander, 1995). However, advanced imaging techniques, such as diffusion tensor imaging, reveal damage to axons and axonal transport throughout the brain after mild TBI (Alexander, 1995). Therefore, disruption of the brain function in mild TBI may be due to damage of axons of neurons in multiple brain areas.

Although the initial symptoms of patients with mild TBI can seem mild, these symptoms can exert a negative influence on an individual's activities of daily living, such as reading, driving, and moving (Ciuffreda, Suchoff, Marrone, & Ahmann, 1996; Ciuffreda, Ludlam, & Kapoor, 2009). Patients with mild TBI usually manifest several symptoms, such as nausea, dizziness, headaches, difficulty with balance, confusion, disorientation, and light sensitivity (Marar, McIlvain, Fields, & Comstock, 2012). In addition, several vision problems, such as strabismus, photosensitivity, visual field defects, and anomalies of accommodation and vergence, have been well documented (Barnett & Singman, 2015a; Kapoor & Ciuffreda,

2002). Vision problems in patients with mild TBI are usually not related to ocular injury but to impairment in the brain's ability to control the eye or to interpret visual information (Brosseau-Lachaine, Gagnon, Forget, & Faubert, 2008; Kapoor & Ciuffreda, 2002; Lachapelle, Bolduc-Teasdale, Ptito, & McKerral, 2008). For example, it has been reported that individuals with mild TBI have deficits in processing both complex static and dynamic visual stimuli (Brosseau-Lachaine et al., 2008; Lachapelle et al., 2008). Concussion usually causes a variety of signs and symptoms associated with vision, but the exact mechanism of the injury is not fully understood. Therefore, several questions need to be answered. For example, does concussion affect the early processing or the higher cortical processing of visual information, or does concussion affect specific visual processing streams within the brain?

The processing of visual information occurs in different brains areas that can be grouped into two interconnected processing streams: the dorsal and ventral streams. Static visual information tends to be processed within the ventral stream and dynamic visual information within the dorsal stream (Merigan & Maunsell, 1993a). Almost all studies that have investigated the impact of mild TBI on the processing of visual information used stimuli that target the function of only one processing stream (Chang, Ciuffreda, & Kapoor, 2007; Patel, Ciuffreda, Tannen, & Kapoor, 2011). Thus, in the present study, the function of both the dorsal and ventral processing streams was assessed psychophysically using form and motion perception tests to evaluate possible selective impairments of just one stream. In addition, since patients with mild TBI exhibit many different vision problems, it is important to understand the relationship between global visual processing that takes place in the dorsal and ventral streams and other basic visual functions such as visual acuity and stereopsis. Therefore, a range of basic visual functions were also assessed in this study.

1.2 Definition of mild TBI

A clear definition of mild TBI is very important for the interpretation of any study on mild TBI since there is more than one definition with different criteria. This ambiguity in the literature can lead to serious confusion among patients with mild TBI and even to researchers (Bodin, Yeates, & Klamar, 2012). One of the contributing factors to this confusion is a lack of agreement on defining what a mild TBI is. One of the earliest definitions of mild TBI for example was proposed by the Congress of Neurological Surgeons (1966). In that definition, mild TBI was defined as “a clinical syndrome characterized by immediate and transient impairment of neural functions, such as alteration of consciousness, disturbance of vision, equilibrium, etc. due to mechanical forces”. The American Congress of Rehabilitation Medicine (1993) also defined the patient with mild TBI as “a person who has had a traumatically induced physiological disruption of brain function, as manifested by at least one of the following: any period of loss of consciousness; any loss of memory for events immediately before or after the accident; any alteration in mental state at the time of the accident (eg, feeling dazed, disoriented, or confused); and focal neurological deficit(s) that may or may not be transient” (Head, 1993). Also, the World Health Organization (WHO) Collaborating Centre for Neurotrauma Task Force on Mild Traumatic Brain Injury created the following definition for mild TBI: “an acute brain injury resulting from mechanical energy to the head from external physical forces. Operational criteria for clinical identification include (1) one or more of the following: confusion or disorientation, LOC (loss of conciseness) for 30 min or less, posttraumatic amnesia for less than 24 h, and/or other transient neurological abnormalities such as focal signs, seizure, and intracranial lesion not requiring surgery; (2) Glasgow Coma Scale score of 13–15 after 30 min post-injury or later upon presentation for healthcare.”(Linda Carroll, J. David Cassidy, Lena Holm, Jess Kraus, & Victor Coronado,

2004). All these definitions share the basic concept about the mild TBI. However, they differ in the specific details of the injury such as the period of loss of consciousness after the injury.

1.3 Pathophysiology of mild TBI

There is an advance in the understanding of the pathophysiology of mild TBI but the exact mechanisms of injury and the functional disruption of the brain function in mild TBI is not fully understood. It has been suggested that there are different types of mild TBI according to their anatomical localization such as cerebral versus brainstem or according to the biomechanical impact such as rotational versus linear force (McCrory et al., 2005). All these different types of mild TBI can cause two main types of pathophysiologic brain damage due to trauma: diffuse and focal pathology (Blennow, Hardy, & Zetterberg, 2012). Diffuse injury, commonly referred to as Diffuse Axonal Injury (DAI), is primarily caused by sheering and destruction of the axons in brain areas subjected to acceleration/deceleration forces (McCrory et al., 2005; Shaw, 2002). In addition, DAI can include other axonal abnormalities such as transport interruption and swelling of neurons as well as secondary physiological changes. The neural damage can manifest acutely as loss of consciousness or confusion or chronically as Post-Concussion Syndrome PCS (Johnson, Stewart, & Smith, 2013). On other hand, focal injuries are primarily caused by severe direct impacts on the brain that are sufficient to cause intracranial bleeding and subdural hematomas (Blennow et al., 2012). Focal injuries are usually characterized as moderate or severe brain injury according to the severity of the injury. Mild TBI can also result in a neurometabolic cascade including altered cellular metabolism, which accrues immediately after the biomechanical injury (Giza & Hovda, 2001). The neurometabolic changes that occur after mild TBI usually exert widespread effects within the brain, which manifest a variety of clinical signs and symptoms including impairment in memory, attention, and cognition (Giza & Hovda, 2001).

1.4 Visual system

1.4.1 Brief overview of the visual system

When the light inters the eye and reaches the retina, millions of photoreceptors convert the light to electrochemical signals (Schwartz, 2009a). In the retina, visual information is encoded at the level of retinal ganglion cells by small (midget), larger (parasol) and bistratified ganglion cells (Nassi & Callaway, 2009). This visual information is then transmitted through the optic nerve to the lateral geniculate nucleus LGN and then to the primary visual cortex mainly via at least two sub-pathways: the magnocellular (M) and parvocellular (P) pathways (Merigan & Maunsell, 1993a; Yoonessi & Yoonessi, 2011). The magnocellular pathway is thought to receive visual input from parasol ganglion cells while the parvocellular pathway receives input from midget ganglion cells (Nassi & Callaway, 2009). The cells in each pathway have different functional properties. For example, cells in the magnocellular pathway are sensitive to coarse detail (low spatial frequency and high temporal frequency stimuli) while the cells in the parvocellular pathway are sensitive to color and fine detail (high spatial frequency and low temporal frequency stimuli) (Derrington & Lennie, 1984; Merigan & Maunsell, 1993b). These specific functional properties of each pathway make them responsible for encoding specific features of stimuli within the visual filed (Merigan & Maunsell, 1993a). These two pathways also differ anatomically. Cells in the magnocellular pathway have a large cell body and long axons compare with cells in the parvocellular pathway (Michael, 1988). In addition, only 10% of the total population of cells that project to the LGN are magno cells while parvo cells are approximately 70%. There is another pathway in addition to the main two called the koniocellular (K) pathway which receives input mainly form bistratified ganglion cells, but it's function is not fully understood (Yoonessi & Yoonessi, 2011). These pathways remain

segregated within the LGN layers and the input layers of the primary visual cortex (Merigan & Maunsell, 1993b).

The duel stream model of visual information processing proposes that the primary visual cortex receives input mainly via the parvocellular and magnocellular pathways (Figure 1.1) (Merigan & Maunsell, 1993a; Nassi & Callaway, 2009). Beyond the primary visual cortex, there is another segregation of information processing into the dorsal stream (which involves occipito-parietal areas) and the ventral stream (which involves occipito-temporal areas) as shown in Figure 1.1 (Ungerleider & Haxby, 1994). Both of the two processing streams begin in the occipital lobe, and are often referred to as the "what pathway," and the "where pathway". The ventral stream ("what pathway") receives input mainly from the parvocellular pathway, which carries information about shape, form, color, and object identity, to the temporal lobe. On other hand, the dorsal stream ("where pathway") receives input mainly from the magnocellular pathway, which carries information about location, orientation, and movement, to the parietal lobe (Merigan & Maunsell, 1993a). The ventral stream involves cortical areas that are specialized for global form processing while the dorsal stream involves cortical areas that are specialized for global motion processing (Merigan & Maunsell, 1993b).

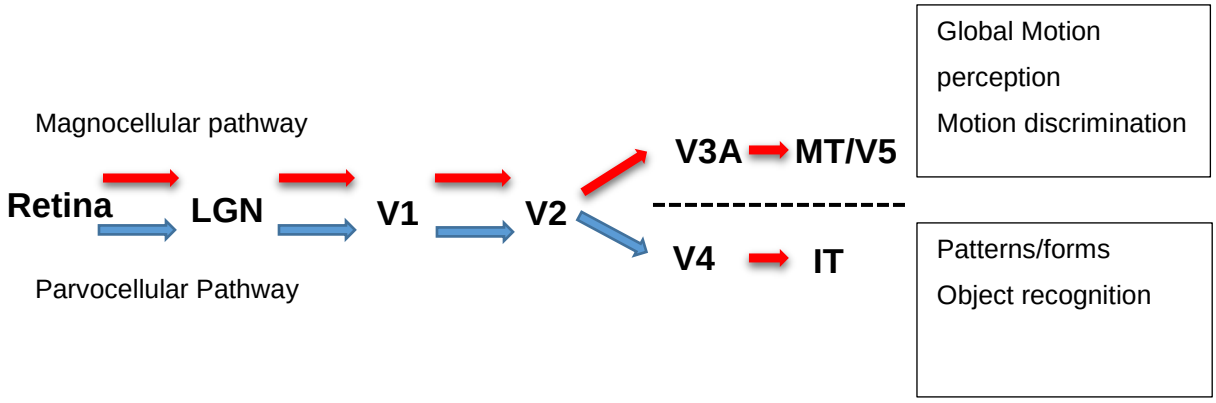


Figure 1.1 A simple schematic of the hierarchical organization of processing stream in the human brain.

1.4.2 Global motion processing

Global motion processing requires the ability to combine local moving elements across space into an overall percept of motion in a noisy environment. The current thought is that the processing of global motion occurs in two different stages along the dorsal stream: the early stage occurs within the primary visual cortex while the second stage occurs within the higher cortical areas (Morrone, Burr, & Vaina, 1995b). The neurons in V1 are sensitive to the direction of luminance-defined (first order) stimuli that move across their receptive field (Morrone, Burr, & Vaina, 1995a). V1 neurons have small receptive fields and often provide ambiguous motion direction signals due to the aperture problem (Marr & Ullman, 1981). Thus, integration of information from multiple small V1 receptive field cells occurs in higher cortical areas to recover the true direction of motion (for example, (Adelson & Movshon, 1982)). Therefore, any abnormalities affecting V1 might have an adverse effect on motion perception. Further downstream, there are extra striate visual areas such as V2, which are sensitive to second-order local motion that is defined by characteristics other than luminance such as contrast, depth, or texture (Smith, Greenlee, Singh, Kraemer, & Hennig, 1998a). In addition, areas V3A and V5/MT are highly sensitive areas for the direction of motion and they integrate input from the motion sensitive neurons in V1 (Wattam-Bell et al., 2010). V3A was identified in humans using fMRI techniques (Braddick et al., 2001a). This cortical area is within the dorsal stream and it is activated during the presentation of different moving stimuli, including random dot kinematograms as shown in Figure 1.2. In V5/MT, most of the neurons have large receptive fields, almost 10 times larger than V1 neurons, and are sensitive to the direction of moving stimuli (Braddick et al., 2001a; Orban et al., 2003). V5/MT plays an important role in motion perception and lesions to this cortical area result in impaired motion perception (Newsome & Pare, 1988). Neurons in V5/MT project to middle superior temporal area MST, which is one

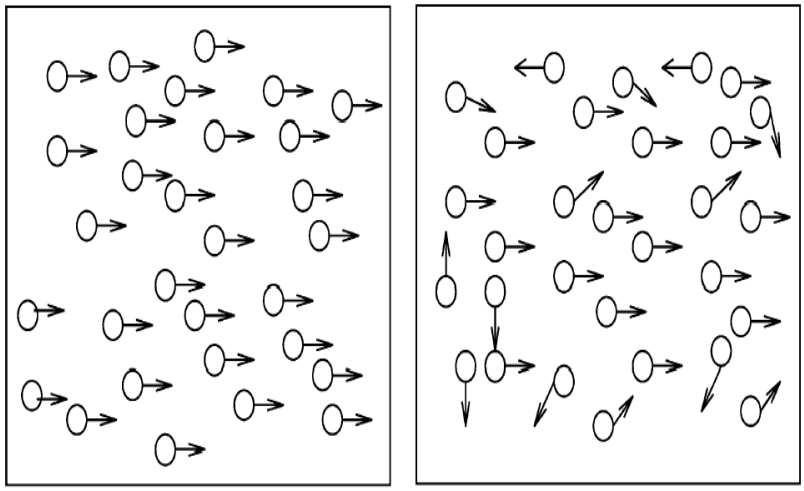
of the higher cortical areas of the dorsal stream. MST neurons are sensitive to complex motion signals, such as rotation and expansion (Britten & van Wezel, 1998).

Psychophysical techniques are commonly used to assess the global processing of motion as an index of dorsal stream function. In particular, motion perception tasks can be designed to target the function of particular motion processing areas such as V5/MT (Newsome & Pare, 1988; Wilson & Wilkinson, 1998). These tasks typically require the integration of local motion signals in higher cortical areas such V5/MT. The random dot kinematogram RDK is one of the most common psychophysical stimuli used to assess dorsal stream function. RDKs consist of moving dots. A subset of dots move coherently in one direction (horizontal or vertical – the signal dots) and the remaining dots move in random directions (the noise dots; Figure 1.2). The observer judges the direction of coherent motion. Coherent motion thresholds (Newsome & Pare, 1988) are estimated by measuring the minimum signal to noise ratio that enables a particular level of task performance. RDK stimuli can provide a measure of dorsal stream function because they assess global motion processing associated with areas V3A and V5 (Braddick et al., 2001).

Global motion processing also can be assessed using optic flow stimuli (Duffy & Wurtz, 1991). These stimuli are radially moving dots that that travel towards or away from the observer interspersed with other dots that move in random directions. Optic flow is considered as complex motion information that requires further integration of motion information in area MST (Britten & van Wezel, 1998).

All motion integration processes rely on the early processing of motion cues that occurs on V1. Therefore several studies have assessed both the early stage of visual information processing using either temporal contrast sensitivity or the contrast threshold for motion

direction discrimination and the global processing of motion in the same participants (Chakraborty et al., 2015a; Pellicano & Gibson, 2008). Pellicano et al assessed temporal contrast sensitivity, which involves both the magnocelluar pathway within the retino-geniculate area and cortical areas, as well as global motion processing in patients with autism and dyslexia (Pellicano & Gibson, 2008). They reported that patients with autism had intact early stage motion processing while the higher cortical processing associated with the dorsal stream was impaired. In addition, they showed that patients with dyslexia demonstrated impairments for both lower and higher processing of motion. Thus, it is important to assess both early and higher processing stages within the visual system in order to distinguish between focal and widespread deficits. Chakraborty et al reported that the contrast threshold for motion direction discrimination, which targets early cortical processing of motion cues in V1, is independent form the global processing of motion (Chakraborty et al., 2015a). They suggested that integration mechanisms occurring in dorsal stream areas, such as MT/V5, are independent from early visual functions such as contrast sensitivity.



(A) **(B)**

Figure 1.2 A schematic of the random dot kinematogram stimulus with different coherence levels: A: 100% coherence, B: 50% coherence. Figure adapted from (Chen, Nakayama, Levy, Matthysse, & Holzman, 2003)

1.4.3 Global form Processing

Similar to the global processing of motion, global form processing requires the ability to combine local form cues across space into an overall percept of a shape or pattern. The processing of global form information occurs in different regions along the ventral stream similar to the processing of visual motion. In V1, there are cells sensitive to object-based features that fall within their receptive fields such as orientation and color (Schwartz, 2009b). These local form cues from V1 neurons integrate in a higher cortical area called V4, which is part of the ventral stream (Wilkinson et al., 2000). Area V4 is considered to play a primary role in the intermediate processing of global form and the cells in this cortical area are selective to color and form cues but not for direction of motion as shown in Figure 1.1 (Van Essen & Gallant, 1994). Cortical area V4 is sensitive to certain global form patterns such as concentric, radial and hyperbolic forms (Lewis et al., 2002; Wilson & Wilkinson, 1998). Further downstream, there is the inferior temporal lobe (IT), which receives projections from V1 and ventral extra striate areas such as V4. IT is responsible of the processing of complex patterns such as faces (Livingstone & Hubel, 1988; Perrett, Rolls, & Caan, 1982).

Psychophysical techniques involving form detection tasks are commonly used to assess global processing of form as an index of ventral stream function (Newsome & Pare, 1988; Wilson & Wilkinson, 1998). These form detection tasks require the integration of local form cues such as concentric orientation in higher cortical areas such as V4. There are at least two ways in which global processing in the ventral stream has been assessed psychophysically. The first involves a coherent form detection task using stimuli constructed from a set of line

segments. A subset of elements are oriented coherently to form a pattern and the remainder are oriented randomly, Figure 1.3 (Milne et al., 2006). The subject is instructed to discriminate the patterns and the signal/noise ratio of the stimulus is manipulated to measure a coherent form threshold (Milne et al., 2006). Secondly, ventral stream function can be assessed using a coherent form detection task, based on Glass patterns, to measure form coherence thresholds (Lewis et al., 2002). Glass (1969) patterns are considered to be the most ideal stimuli to study the sensitivity to structure in global form (Wilson & Wilkinson, 1998). There are several forms of Glass patterns such as concentric, radial, parallel and hyperbolic (Wilson & Wilkinson, 1998); however, the most commonly used are concentric Glass patterns, Figure 1.4. In the coherent form detection task, there are high contrast dots arranged in pairs that are oriented to form a pattern. Other dot pairs are placed randomly to add noise. Participants are instructed to discriminate between two different glass patterns or one single pattern vs. noise. As in the other global tasks, the signal/noise ratios of the stimuli are varied to measure a coherence threshold.

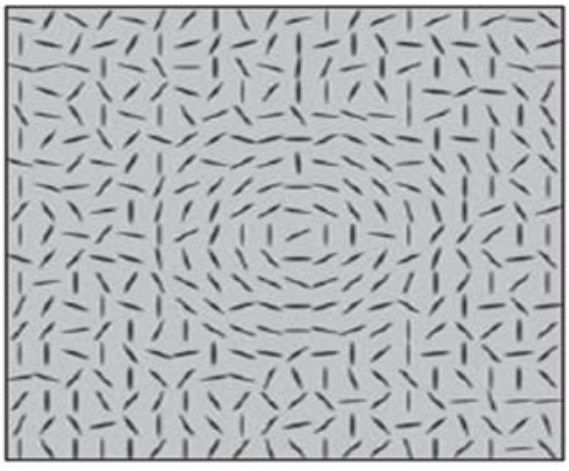
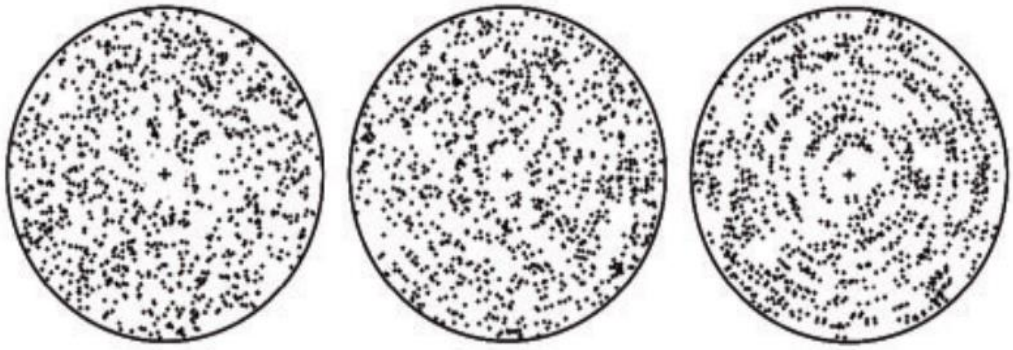


Figure 1.3 Schematic diagram of line segment stimuli stimuli used for a form detection task. Figure adapted from the article Motion perception in preterm children: role of prematurity by Guzzetta and colleges (Guzzetta et al., 2009).



0% 50% 100%

Figure 1.4 Schematic of a concentric glass pattern with different levels of coherence, 100% coherence, 50% coherence and 0% coherence. Figure adapted from the article psychophysics of visual motion and global form processing in autism by Koldewyn and colleges (Koldewyn, Whitney, & Rivera, 2009).

1.5 Function of the dorsal and ventral streams

The functions of the dorsal and the ventral visual streams have been studied extensively, particularly the effects of retino-geniculate pathway lesions on visual function. It has been shown in animal studies that lesions of the magnocellular layers within the lateral geniculate nucleus LGN impair perception of high temporal and low spatial frequency stimuli, supporting the theory that the magnocellular pathway supports processing of these specific stimulus properties (Merigan, Byrne, & Maunsell, 1991; Merigan & Maunsell, 1990). As expected, motion perception is also impaired by lesions to the magnocellular pathway because the dorsal stream primarily receives input from this pathway (Merigan et al., 1991). On the other hand, induced lesions in non-human primates within the parvocellular LGN layers have an effect on visual acuity and static contrast detection, supporting the theory that the parvocellular pathway supports perception of high spatial and low temporal frequency stimuli (Lynch, Silveira, Perry, & Merigan, 1992). In addition, parvocellular lesions have no effect on the perception of motion. Subsequent studies have also shown that there is a complex

interconnection between the two streams, especially in the higher cortical areas (Felleman & Van, 1991; Goodale, 2011; Wang, Sporns, & Burkhalter, 2012).

Developmental studies of the dorsal and ventral streams in humans suggest that the two streams reach adult levels of maturity at different times. According to Gunn and colleges, by the age of 6-7 years the ventral stream fully matures while the dorsal stream continues to develop until the age of 10-11 years (Gunn et al., 2002). In Gunn et al's study, the function of the ventral and dorsal streams was tested psychophysically using global form and global motion detection tasks. The stimulus in the form detection task was constructed from static short line segments, some of which were oriented to form concentric circles while others were oriented randomly. The motion detection task involved variable coherence RDKs with a dot speed of 4°/ sec. There was good agreement between the Gunn et al study and a study conducted by Hadad et al. ((Hadad, Maurer, & Lewis, 2011) in which global motion perception, as index of dorsal stream function, reached maturity before the age of 14 years. In the Hadad et al study, two different dots speeds were used, 4°/sec and 18°/sec. Maturation did not differ between the two speeds but the threshold was lower for the faster moving dots.

In a variety of neurodevelopmental disorders, it has been proposed that not both of the processing streams are damaged, but rather that the dorsal stream is particularly vulnerable to be damaged compared with ventral stream. For example, in Williams syndrome (a genetic disorder associated with cognitive and visuo-motor deficits) there are deficits in the detection of coherent motion, a dorsal-stream function, while the detection of coherent structure, a ventral stream function, remains normal, (Atkinson et al., 1997). A similar pattern of visual deficits has been found in other disorders such as autism and dyslexia (Cornelissen, Richardson, Mason, Fowler, & Stein, 1995; Spencer et al., 2000). Thus, a general "dorsal-stream vulnerability" has been proposed in many different neurodevelopmental disorders.

Several explanations have been proposed for this effect. One explanation is that the magnocellular pathway, which projects to the dorsal stream, has cells with larger cell bodies and longer axons than the parvocellular stream. In addition, there are fewer cells in the magnocellular than parvocellular pathway. Combined, these factors make the dorsal stream more susceptible to damage (Merigan & Maunsell, 1993a; Michael, 1988; Quigley, Dunkelberger, & Green, 1988). This concept might also be applicable the effects of mild TBI on vision.

1.6 Vision disturbances following mild TBI

In mild TBI, there is usually damage to neurons through stretching and shearing of axons. Therefore, a variety of different brain areas and their functions might be adversely affected (Shaw, 2002). As might be expected for a diffuse brain injury, there are several previous studies that have reported normal vision in patients with mild TBI for some visual functions (e.g. visual acuity) but deficits in the others (e.g. contrast sensitivity, binocular vision) (Capo-Aponte, Urosevich, Temme, Rarbett, & Sanghera, 2012). Thus, it is very difficult to describe a specific set of visual impairments that characterizes all mild TBI patients as the pattern of deficits can vary across patients.

Mild TBI can result in a variety of visual dysfunctions including both acute and chronic dysfunctions (Barnett & Singman, 2015a). Patients with mild TBI can present with one or more vision diagnoses including anomalies of accommodation, version, and vergence (non-strabismic or strabismic) as well as photosensitivity and visual field defects (Barnett & Singman, 2015a; Hellerstein, Freed, & Maples, 1995; Kapoor & Ciuffreda, 2002). All of these vision problems can vary in their occurrence and severity from one patient to another.

1.6.1 Accommodation Deficits

Accommodation is the change in curvature of the crystalline lens in order to maintain a clear focused of the image on the retina. According to Ciuffreda and colleagues, 40% of 160 patients with mild TBI manifested accommodative problems including accommodative insufficiency (difficulty focusing at near), accommodative infacility (difficulties in focusing from far-to- near or vice versa), and ill-sustained accommodation (difficulty in maintaining focus for certain period of time) (Ciuffreda et al., 2007; Green et al., 2010). Some patients with mild TBI manifest an accommodative spasm and this might result in pseudo-myopia, and the underlying mechanism of this condition is unclear (London, Wick, & Kirschen, 2003).

1.6.2 Vergence deficits

Vergence eye movement is the simultaneous movement of the two eyes in opposite directions in the horizontal plane in order to maintain binocular alignment. This alignment is very important to maintain binocular single vision. (Mays, Porter, Gamlin, & Tello, 1986). Almost 56% of patients with mild TBI manifested convergence anomalies including convergence insufficiency (CI), convergence excess, and divergence insufficiency (Ciuffreda et al., 2007).

1.6.3 Other visual dysfunctions

Mild TBI can disrupt almost all the aspects of vision and can result in damage to both afferent and efferent visual pathways (Barnett & Singman, 2015a). Damage to the afferent visual pathway can cause visual field defects and decreased contrast sensitivity (Barnett & Singman, 2015a; Kapoor & Ciuffreda, 2002). Visual field deficits are commonly reported after traumatic brain injuries especially in moderate and severe cases but these deficits can be seen in mild TBI also (Kapoor & Ciuffreda, 2002). The visual field deficits can affect any part of the visual field due to a trauma to one specific area within the visual pathway such as the optic nerve, chiasm, optic radiations, or visual cortex (Barnett & Singman, 2015a). Secondly, damage to

the efferent pathway can result in a variety of vision problems such as deficits in pupillary reactions and stereo acuity, as well as strabismus and nystagmus (Barnett & Singman, 2015a).

1.6.4 Visual processing deficits in mild TBI

Most of the studies that have investigated the consequences of mild TBI have concentrated on oculomotor disorders, loss of binocularity, and impaired cognitive functions. However, some studies have assessed the impact of mild TBI on visual information processing, particularly the person's ability to perceive moving objects, or to integrate visual information. Work conducted by (Brosseau-Lachaine et al., 2008) investigated sensitivity to simple and complex visual stimuli in children with mild TBI. They found that the detection threshold for a second-order contrast-defined stimulus (either static or dynamic) was significantly higher in those with mild TBI compared with the normal controls. On the other hand, the threshold for first-order static or dynamic stimuli was normal. In addition, the coherence threshold for radial optic flow stimuli was significantly elevated in mild TBI. Second-order static and dynamic stimuli as well as optic flow stimuli are processed in the higher cortical areas such as V5/MT and MST (Smith, Greenlee, Singh, Kraemer, & Hennig, 1998b) suggesting that there are deficits in higher cortical areas in those with concussion while the lower visual functions remain intact. Patel et al. (2011) measured coherent motion thresholds (CMT) in patients with mild TBI and they reported that there was a significant elevation in CMT in those patients, suggesting that there is deficit in the magnocellular/dorsal pathway. This study is consistent with (Brosseau-Lachaine et al., 2008) because the global motion stimulus is processed mainly within dorsal stream cortical areas including V3 and MT/V5 and both studies reported a deficit in the higher cortical areas within the dorsal stream (Brosseau-Lachaine et al., 2008; Patel et al., 2011).

The effect of mild TBI on the processing of visual information has been studied not only psychophysically but also physiologically. A study by (Lachapelle et al., 2008) assessed different levels of visual information processing (i.e. early and higher levels) in those with mild TBI using visual electrophysiology techniques. In this study, event-related potentials (ERPs) were recorded while viewing different stimuli including pattern reversal, simple motion, and texture segregation stimuli. Those with mild TBI showed an increase in amplitude and a decrease in latency for the texture segregation stimulus suggesting that there is an alteration of the integrative visual processes that occur in higher cortical areas in patients with mild TBI (Brosseau-Lachaine et al., 2008; Lachapelle et al., 2008). There were no significant differences between normal and patients with mild TBI in the amplitude and latency for stimuli that required early processing including pattern reversal and simple motion stimuli. Based on the previous psychophysical and physiological studies, there is early evidence of abnormal integration in the higher cortical areas for both static and dynamic visual information in those with mild TBI.

1.7 Summary

Static and dynamic visual information are thought to be processed within two separate visual processing streams; ventral and dorsal. However, it has been reported recently that there is significant interconnection between these two processing stream in different stages. It has been reported that in some neurodevelopment disorders both streams are not affected but rather only the dorsal stream is impaired. Therefore, the concept of dorsal stream vulnerability has been proposed. For example, patients with autism and dyslexia have a deficit in the dorsal processing stream which manifests as impaired global motion perception while the ventral stream remains intact. Based on the existing literature, patients with mild TBI have impaired motion perception suggesting that there is a deficit in the dorsal processing stream. However,

these studies have assessed only the dorsal stream function which rises an important question about whether there is a widespread defect in those with mild TBI that involves both processing streams.

Chapter 2

Research objectives

2.1 Purpose

The main purpose of this thesis is to investigate the global processing of form and motion, as an index of dorsal and ventral stream function, in individuals with mild TBI. In the literature, researchers found that patients with mild TBI have a deficit in the processing of complex visual information and the perception of global motion (Brosseau-Lachaine et al., 2008; Patel et al., 2011). It is known that visual information beyond the primary visual cortex is processed mainly via the dorsal and ventral streams, and both streams can be assessed psychophysically using global form and motion detection tasks (Merigan & Maunsell, 1993b). There is a possibility that performance on the tasks that are used to evaluate the global processing of form and motion might be affected due to blurred vision and reduced contrast sensitivity (discussed in Chapter 4). It has been reported that patients with mild TBI have deficits in accommodation and vergence that can cause blurred near vision due to accommodation insufficiency and accommodation infacility as well as reduced contrast sensitivity. Therefore, the first research question is to investigate whether contrast sensitivity and the status of accommodation and vergence systems affect the performance on the global processing tasks in normally sighted individuals. This research question is addressed in Chapter 4. The second research question that needs to be answered is whether there is a selective impairment of just one processing

stream (either dorsal or ventral stream) in individuals with mild TBI as would be predicted by the dorsal stream vulnerability hypothesis. This research question is described in Chapter 5.

2.2 Research hypotheses

The hypotheses of this thesis project are:

1. Performance on global form and motion processing tasks is independent from contrast sensitivity and the status of accommodation and vergence systems.
2. Individuals with mild TBI have a selective impairment in the dorsal processing stream, which will be manifested as impaired global motion perception and normal global form perception.

2.3 Study design

Both hypotheses 1 to 2 were tested experimentally using a cross sectional design.

Chapter 3

General Methods

This study was a prospective, cross sectional study, which was designed to investigate the effect of mild TBI on the global processing of visual form and motion.

3.1 Recruitment Protocol

The normal participants and the patients with mild TBI were recruited through flyers posted at the optometry clinics at the School of Optometry and Vision Science, University of Waterloo and The Guelph Vision Therapy Center. Interested participants contacted the researchers by either email or phone and the researchers determined their eligibly based on the inclusion and exclusion criteria. In addition, patients with mild TBI were recruited from the databases of the Vision and Motor Performance Lab.

3.2 Inclusion and Exclusion Criteria

Participants were recruited based on the following inclusion criteria:

1. Between 13 and 40 years of age.
2. English speakers able to comply with instructions to complete tasks.
5. Able to provide informed written consent.

Mild TBI group

1. Sustained a concussion at least 3 months prior to study participation.
2. Diagnosed with mild TBI by a clinician.
3. No loss of consciousness (or if any, less than 20 minutes).

4. No post-traumatic amnesia (or if any, less than 24h).

Participants were excluded based on the following exclusion criteria:

1. Self-reported neuropsychiatric condition
2. Binocular visual acuity worse than 6/12
3. Self-reported Seizures or other neurological disorders

3.3 Vision assessments

3.3.1 Global form and motion perception tests

3.3.1.1 Global form perception

Global form perception was tested psychophysically using a form detection task based on Glass patterns (Figure 3.1). The task was used to measure a form coherence threshold.

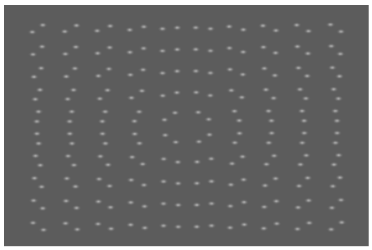
Apparatus

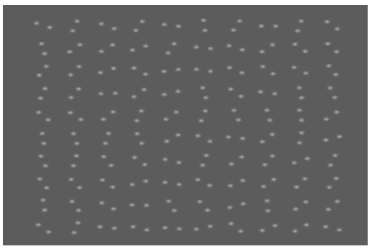
The stimulus was generated by an Apple Macintosh using Psykinematix software. The screen resolution was 1024 x 768 pixels on a 27-inch screen, at the viewing distance of 60 cm. The stimulus was composed of bright pairs of dots presented on a grey background (100 cd/m2) and was presented for 1 second within a rectangular aperture (10° diameter). There were two populations of dot pairs: ‘‘Signal pairs” which were arranged to form a concentric or cross-shaped radial Glass pattern constructed in a manner similar to that described by Wilson and Wilkinson (1998), and “Noise pairs” which were placed randomly within the pattern (Figure 3.1). Form coherence was modulated by varying the ratio of signal to noise dots in the stimulus.

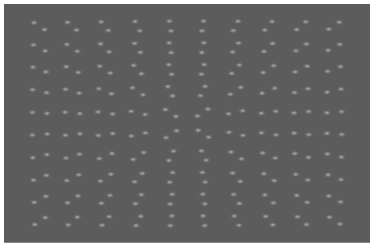
Procedure

Participants used their habitual vision correction during the task. Before starting the global form task, participants completed a familiarization session where the stimulus was presented at 100% coherence. This was followed with the presentation of 3 different reduced coherence levels (80, 70, and 60%). The participant was asked to discriminate between the two different Glass patterns (concentric or cross) by pressing the right arrow on a keyboard for a concentric pattern or top arrow for a radial pattern. Participants had to have an accuracy of at least 75% correct (three correct responses on four trials with the same level of coherence) on each coherence level prior to starting the main global form detection task.

The main task involved a 2-down-1-up adaptive staircase procedure that started at 100% coherence. The threshold was decreased proportionally by 25% for two correct responses and increased by 25% for one wrong response except the first reversal where coherence was decreased by 50%. The staircase converged on the form coherence threshold corresponding to ~80% correct accuracy. The staircase was terminated after 12 reversals and the average of the last 11 reversals was calculated to estimate the form coherence threshold.

(A) 

(B) 

(C) 

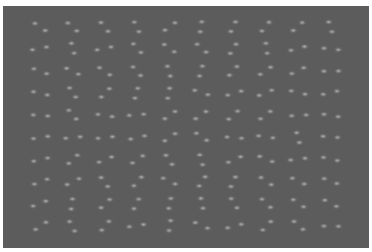
(D) 

Figure 3.1 An example of the global form task stimulus. (A) Concentric 100% coherence level, (B) Concentric 50% coherence level, (C) Radial 100% coherence level, (B) Radial 50% coherence level.

3.3.1.2 Global Motion Perception

Global motion perception was tested psychophysically by using random dot kinematograms (RDKs) to measure motion coherence thresholds.

Apparatus

RDKs were generated by an Apple Macintosh using Psykinematix software. The RDKs were presented on 27-inch screen Apple Macintosh screen with a resolution of 1024 x 768 pixels. RDKs consisted of a 100 dots (circular bright dots presented on a grey background 100 cd/m2) with diameter of 0.24 and a density of 1.27 dot/deg^2. The RDKs were presented for 1 second at a viewing distance of 60 cm within a circular aperture (10° diameter). There was a spatial displacement of the dots in the RDKs every 17 ms in order to achieve a speed of 6°/second. The parameters of the RDKs were chosen based on a previous study that assessed global motion perception in children (Chakraborty et al., 2015b). Signal dots in the RDKs moved either upwards or downwards while noise dots moved in random directions.

Procedure

Participants used their habitual vision correction during the task. Before starting the global motion task, the participant completed a familiarization session during which 100% contrast RDKs were presented with coherence levels of 100, 80, 70 and 60%. Participants identified the direction of the signal dots (up or down). An accuracy of at least 75% correct (three correct responses on four trials with the same level of coherence) for each coherence level was

required before moving on to the main global motion perception task (a schematic of the RDK stimulus is shown in Figure 3.2). A 2-down-1-up adaptive staircase procedure was used to measure a motion coherence threshold in the main global motion task. The staircase began with 100% coherent stimuli. Coherence was decreased proportionally by 25% for two correct responses and increased by 25% for one wrong response except the first reversal where coherence was decreased by 50%. The staircase terminated after 12 reversals and the average of the last 11 reversals was calculated to estimate the coherence form threshold.

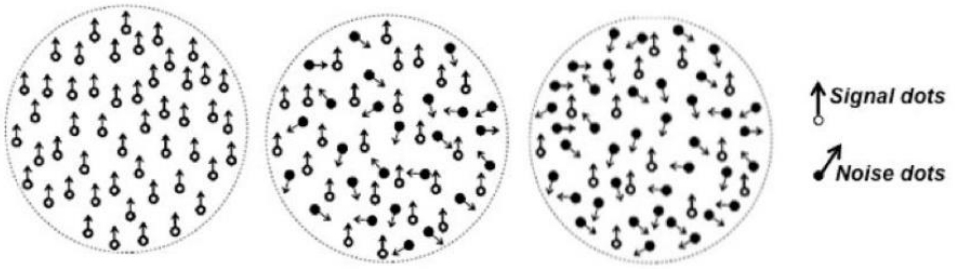


Figure 3.2 A schematic of the random dot kinematogram stimulus with different coherence levels: 100%, 50% and 25% (Chakraborty, 2015: Global Motion Perception in 4.5-year-old Children Born at Risk of Abnormal Neurodevelopment).

3.3.1.3 Contrast sensitivity for motion direction discrimination

The contrast sensitivity threshold for coherent motion direction discrimination was measured in this study to control for the possibly that global motion perception might be affected by deficits affecting lower level visual functions such as contrast sensitivity.

Apparatus

Stimuli used for contrast thresholds were generated using Psykinematix software with parameters identical to the global motion perception task. In this task, RDKs were always presented with 100% coherence and only dot contrast was varied.

Procedures

Participants used their habitual vision correction during the task. RDKs with 100% coherence and 70% contrast were presented to the participant and the motion direction was varied (up/down) until the participant was able to identify the direction of 2 trials correctly. A 2-down-1-up adaptive staircase was then initiated to assess the contrast threshold for motion direction discrimination, whereby dot contrast decreased proportionally by 25% for two correct responses and increased by 25% for a wrong response except the for first reversal where contrast was decreased by 50%. The staircase terminated after 5 reversals and the average of the last 4 reversals was calculated to estimate the contrast threshold**.**

3.3.2 Vision tests

3.3.2.1 Visual acuity

Monocular and binocular distance visual acuity was measured with the participant's distance habitual correction using the Freiburg Vision Test ('FrACT'), an automated procedure for measuring visual acuity, at a distance of 3 meters (Wesemann, 2002). Landolt-Cs were presented on an Apple Macintosh monitor in one of 4 orientations. The participants were asked to respond to the orientation of the Landolt-Cs using a keypad. The ''best parameter estimation by sequential testing'' (PEST) staircase was used to determine the acuity thresholds (in logMAR units). The procedure starts with suprathreshold Landolt-Cs and

optotype size is varied based on participant responses. The Freiburg Vision Test acuity measure has been compared with the tumbling E vision test and there was an agreement of approximately ±1 lines between the two tests (Bach, Reuter, & Lagrèze, 2016). Therefore, Freiburg Vision Test can be used for screening purposes.

Near binocular visual acuity was also measured with the participant's distance habitual correction using Bailey Lovie Near Visual Acuity Chart (Hazel & Elliott, 2002). The near vision chart was viewed from 40cm. The participant was instructed to read from the largest row letter by letter and was asked to guess the letters when they were not sure. Visual acuity was recorded using the by-letter scoring system, where each letter was equal to 0.02 logMAR.

3.3.2.2 Contrast sensitivity

Contrast sensitivity was assessed using the Freiburg Vision Test ('FrACT') with a Landolt ring (a "tumbling C") target (Dennis et al., 2004), presented on an Apple Macintosh screen. In this task, the diameter of the target is kept constant while the contrast was decreased with correct respondses and increased with incorrect responses. The participant used a directional keypad to indicate the orientation of the Landolt C (there were 8 possible directions) and the screen was placed at a distance of 3 m in front of the participant. The contrast threshold was estimated within the FrACT CS test using the PEST (parameter estimation by sequential testing) adaptive method. Contrast sensitivity (CS) was recorded as Log CS.

3.3.2.3 Stereo acuity

Depth perception (stereo acuity) was measured using two different stereo acuity tests. First, the VAC FLY Stereo Acuity Test was used estimate the threshold for local stereopsis using the graded circles within boxes as shown in Figure 3.3 Section 1. This test is designed to measure stereo acuity from 400 to 20 seconds of arc. If the participant could not appreciate

the depth of the circles, the housefly (as shown in figure 3.3 section 2) was used to identify whether the participant had gross stereopsis or not. Stereo acuity was tested at a distance of 40 centimeters and the participant was asked to wear polarized glasses along with his/her habitual correction and identify which circle popped out in each of the blocks

Figure 3.3 VAC FLY Stereo Acuity Test

Secondly, the Randot Preschool Stereo acuity Test was used to estimate the global stereopsis threshold (Figure 3.4). The viewing distance for this stereo acuity test was 40 cm. Participants were asked to name a disparity-defined shapes on each set of test panels or match the shapes to the black-and-white shapes that are printed on the other side of the book. Participants progressed through test panels measuring stereoacuities ranging from 800 to 4 arc sec. The smallest disparity that a participant was able to correctly identify (at least 2 of 3 shapes) was recorded as his/her stereo acuity.

Figure 3.4 3-book Randot Preschool Stereo acuity test.

3.3.2.4 Other Clinical Vision Tests

Other assessments of the status of vision, accommodation, vergence and eye movements were tested and included the following:

The confrontation visual field technique “static, single-quadrant counting” was used to identify any gross visual field defect in the peripheral visual field (Trobe, Acosta, Krischer, & Trick, 1981). In this technique, the participant was asked to count the fingers of the examiner in one particular position while fixating on the examiner’s eye. The examiner presented his fingers around 15 degrees eccentric to participant’s fixation in one the visual field quadrant at a time.

The central visual field was assessed using the Amsler grid test. This test consisted of horizontal and vertical black lines intersecting on a white background, and the participant was asked to fixate on a point in the center of the grid, and then identify if there are areas that were any blurry, absent, or distorted regions (Elliott, 2013).

Pupil reactions were tested using a light source (pen torch) to rule out any relative afferent pupillary defect. The examiner shined a light in front of the participant's eyes while observing the pupil reaction to the light.

A unilateral and alternating cover test was performed to examine for any binocular vision disorders, such as strabismus or heterophoria (Scheiman & Wick, 2008). In this test, the participant was asked to maintain his/her gaze on a fixed target placed at a distance of 3 meters (distance) or at 30 cm (near). The examiner moved a paddle to cover and uncover the participant's eyes to observe any movements. The amount of prism needed to neutralize any strabismus or heterophoria was recorded.

Ocular motility was assessed with the broad H test (Grosvenor & Grosvenor, 2007). In this test, the participant was asked to follow a small target, which was moved by the examiner into different positions of gaze to identify any abnormal eye movements (i.e. restricted eye movement).

The Near Point of Convergence (NPC) was measured using the RAF (Royal Air Force) Ruler (Sharma, 2017). This is an instrument used to assess convergence as well as accommodation and it consists of a four-sided cube attached to a 50 cm long ruler. The RAF ruler was placed in front of the participant's eyes and he/she was asked to fixate on the convergence target (a vertical line with a central dot). The participant was instructed to report when the target

became double while the examiner moved the RAF cube towards the participants eyes. The distance from the eyes where the target became double was recorded in centimeters.

Both positive and negative near fusional vergence amplitudes were measured using a prism bar (American Optometric Association, 2010). This test assesses the amount of prism that can be placed in front of the eyes of the participant before he/she reports a sustained blur. First, the positive fusional vergence amplitude was measure by placing a Base-out prism in front of the participant while he/she fixated on a near target. The prism power was increased until the participant repot sustained blur followed by break and recovery. The amounts of prism when the participant reported blur, break and recovery were recorded in prism power. Secondly, negative near fusional vergence amplitudes were measured by placing a Base-in prism in front of the participant with same procedures the positive fusional vergence amplitude.

Vergence facility was tested using a 12BO/3BI prism flipper to assess a participant's ability to rapidly change vergence without changing accommodation (Elliott, 2013). The participant was asked to wear his/her habitual correction and the examiner placed the prism flipper in front of one eye. The examiner rotated the flipper while the participant read a vertical line of letters from a near chart as soon as they appear clear and single. The result of this test was recorded as number of cycles/minute.

Accommodative Amplitude (AA) was measured monocularly and binocularly using the RAF ruler (push-up method) (Elliott, 2013). The participant was instructed to read the smallest letter

size that they could see on the near chart on the RAF ruler cube when positioned at 40 cm. The examiner then moved the cube slowly towards the participant until he/she notice blur and the distance was recorded in centimeters and then transferred to dioptric power.

Accommodative facility was tested binocularly using a +/−2.00 D flipper to assess the participant's ability to change accommodation without changing vergence (Elliott, 2013). By using near a chart, the participant was asked to look at a letter one line bigger than his/her best corrected visual acuity. The examiner placed a flipper in front of the participant's eyes while looking at the letter and rotating it when the participant reported that the letter was clear. The number of cycles/minute was recorded in which one cycle consisted of clearing both the plus and the minus lenses.

Chapter 4

Global processing of form and motion is independent from contrast sensitivity and the status of accommodation and vergence in normally sighted individuals

4.1 Introduction

The duel stream theory of vision suggests that global form processing occurs primarily in the ventral stream while the processing of global motion occurs primarily in the dorsal stream (Merigan & Maunsell, 1993b; Ungerleider & Haxby, 1994). The ventral stream includes the cortical areas V2, V4, and the inferior temporal cortex, and receives input primarily form the parvocellular pathway (Van Essen & Gallant, 1994). On the other hand, the dorsal stream includes the cortical areas V3a and MT/V5 (Braddick et al., 2001b). The global processing of form and motion requires an integration of local visual information in higher cortical areas. For example, the processing of global motion requires integration of locally moving signals form V1 in higher cortical areas such as MT/V5 (Adelson & Movshon, 1982). Since the local visual information is processed in the primary visual cortex and the global processing of form and motion require an integration of this local information, any deficits in the processing of local visual information may results in abnormal global processing (Adelson & Movshon, 1982; Neumann & Sepp, 1999). Therefore, the impairment of the global processing has at least two possible causes; a deficit in the integration of local visual information in the higher cortical areas or a deficit in the early processing of visual information in V1.

The relationships between global processing and clinical measures of vision such as visual acuity and contrast sensitivity have been investigated in both normally sighted individuals and patients with impaired visual acuity such as amblyopia. For example, Burton et al (2015) investigated the effect of induced bur on the performance of global processing tasks using a

diffuser to blur the stimuli. They reported that the performance of both global form and global motion tasks was impaired with the global form task being more severely affected (Burton et al., 2015). Similarly, in individuals with normal vision, Barton and colleges investigated whether +3.25 diopters of optical bur affected the discrimination of motion direction in random dot kinematograms (Barton, Rizzo, Nawrot, & Simpson, 1996). In their study, the spatial displacement of the dots from one frame to the next was varied while the temporal interval was held constant. They reported that the optical blur adversely affected motion discrimination for small spatial displacements (below 16 arc min, high dot density) and improved it for large spatial displacements. In contrast, another study by (Trick, Steinman, & Amyot, 1995) found that optical bur had no effect on motion discrimination, however the spatial displacement that was used in this study was 24.5 arc min and according to (Barton et al., 1996) the optical bur worsened motion discrimination only for the spatial displacements below than 16 arc min. This suggests that the spatial parameters of the stimulus in motion coherence tasks must be considered for studies involving reduced spatial acuity. Trick et al examined the effect of induced optical blur on the coherence motion threshold using different spherical lens powers. They reported that optical blur of +4 diopters or less had no effect on the coherence motion threshold (Trick et al., 1995). This raises the possibility that performance on the global processing tasks is impaired only by severe visual acuity reductions. Blur-induced reductions in visual acuity can affect other global integration tasks such as motion-defined form identification and texture-defined form identification (Zwicker, Hoag, Edwards, Boden, & Giaschi, 2006).

Stimulus manipulations other than optical bur can also affect the global processing of both form and motion. For example, Burton and colleagues have measured coherence thresholds for form and motion under different lighting conditions (Burton, Wattam-Bell, Rubin, Atkinson,

Braddick, & Nardini, 2016). They found that coherence thresholds were impaired for all the stimuli when the luminance level was decreased with the effect being greater for global form thresholds than global motion thresholds (E. Burton, Wattam-Bell, Rubin, Atkinson, Braddick, & Nardini, 2016b).

Oculomotor problems such as abnormalities of version, vergence, or accommodation are frequently found in the general population (Jang & Park, 2015; Lara, Cacho, García, & Megías, 2001). Accommodative or vergence abnormalities such as convergence and accommodation insufficiency, accommodation infacility, and vergence infacility can result in a variety of symptoms including diplopia and blurred vision (Lara et al., 2001). To our knowledge, the effect of accommodation and vergence dysfunction on global form and motion tasks has not previously been studied. Thus, in this study, the association between performance on global processing tasks and the status of accommodation and vergence was measured.

Impaired global processing that is not due to reduced visual acuity has been reported also. For example, using a static contrast sensitivity test, Shepherd et al reported that impaired performance on a global motion task in patients with migraine may have been due to reduced contrast sensitivity (Shepherd, Beaumont, & Hine, 2012). However, Chakraborty et al found no evidence for a significant relationship between performance on a global motion processing task and contrast thresholds for motion direction discrimination (Chakraborty et al., 2015a). This difference in results is possibly because there were two contrast sensitivity tasks used in each study which target different processing mechanisms (static vs dynamic contrast sensitivity). Therefore, the relationship between the performance on the global processing tasks and contrast sensitivity was also tested in the current study.

4.2 Methods

4.2.1 Participants

Thirty seven participants took part in this study (age between 13 – 36 years old) and 57% of the sample were female. Participants who were recruited for this study had normal corrected Optometry Clinic at the School of Optometry and Vision Science at the University of Waterloo and attended the School to take part in the study. The experimental protocol described in Chapter 3 was used in this study.

4.2.2 Definition of accommodation and vergence dysfunction

A participant was considered as having an accommodation and vergence dysfunction if he or she failed one or more of the following tests.

- A near point of convergence greater than 10 centimeters
- A near vergence facility less than 12 cycles per minute (Scheiman & Wick, 2008)
- A near binocular accommodation facility less than 8 cycles per minute (Scheiman & Wick, 2008)
- A near positive fusional vergence less than 14 prism diopters (blur point) and/or a near negative fusional vergence less than 11 prism diopters (blur point) (American Optometric Association, 2010)
- An accommodation amplitude less than the minimum expected amplitude of accommodation based on this equation: 15 – (0.3*age). (American Optometric Association, 2010)

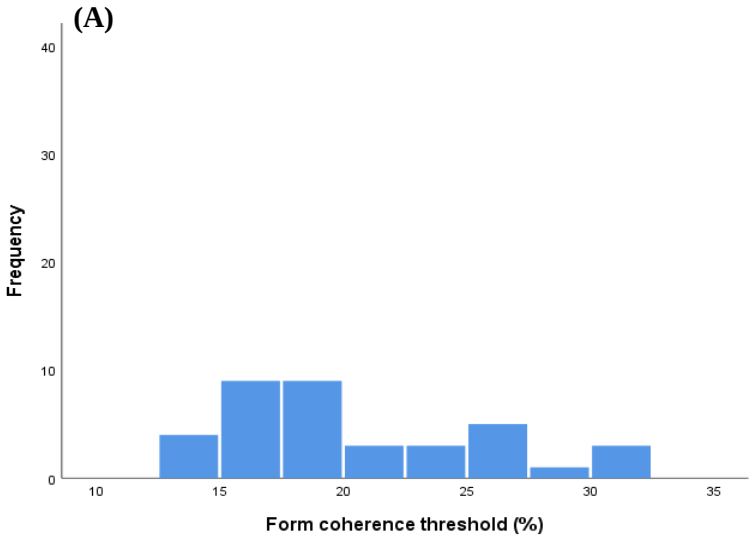
The final outcome for accommodation and vergence status was a dichotomous score of either having or not having an accommodation and vergence problem.

4.3 Analysis

A linear regression model was constructed, using SPSS statistical software, to assess the effect of contrast sensitivity, age and the status of accommodation and vergence on global processing of form and motion. Also the correlation between global processing and age was examined separately for the global form and motion tasks using Person correlations.

4.4 Results

Thirty seven participants aged 13 – 36 years took part in the study. All the participants were able to successfully complete all the psychophysical and the clinical tests and were therefore included in the final analyses. The distributions for form coherence thresholds, motion coherence thresholds and contrast thresholds for motion direction discrimination are shown in Figure 4.1. Form coherence thresholds (Figure 4.1A, mean 20%, range 14% to 32%) and motion coherence threshold (Figure 4.1B, mean 12%, range 6% to 33%) were not normally distributed based on the Shapiro–Wilk normal distribution test. Therefore, log transformation was applied to enable the use of parametric statistical tests. The distribution of the contrast threshold for motion direction discrimination is showed in Figure 4.1C (mean 1.23%, range 0.2% to 1.9%).



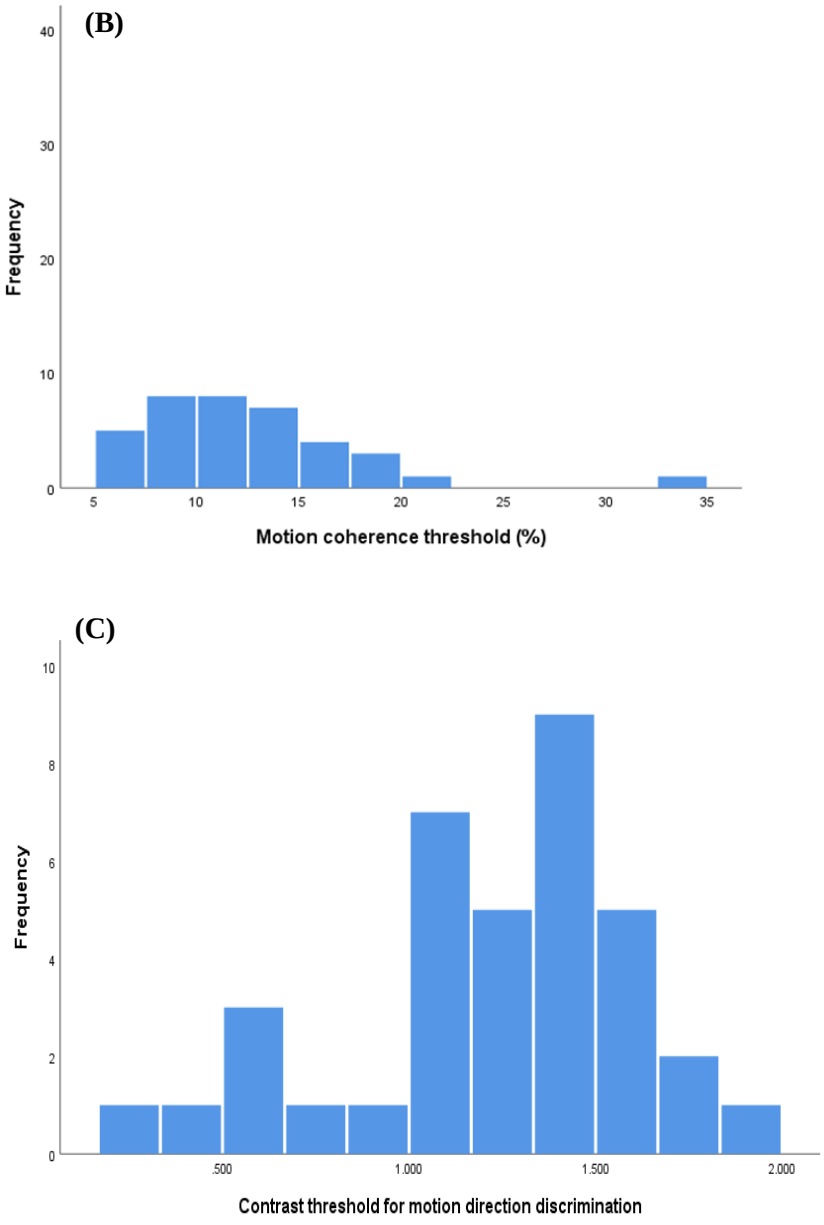


Figure 4.1 Distribution (n = 37) of (A) global form coherence thresholds, (B) global motion coherence thresholds, and (C) contrast threshold for coherent motion direction discrimination.

4.4.1 Relationships among global processing of form and motion, contrast sensitivity, age and the status of the accommodation and vergence system.

Mean log static contrast sensitivity was 2.04 ± 0.22SD with a range of 1.49 to 2.52 while the mean log contrast threshold for motion direction discrimination was 1.23 ± 0.39SD with a range of 0.2 to 1.9 for all participants. The mean age of the participants was 22.46 ± 6.22SD with a range of 13 to 36. There were 20 participants in the sample who had accommodation and vergence dysfunction including convergence insufficiency, convergence infacility, and accommodative infacility. Table 4.1 shows a comparison between participants with and without accommodation and vergence dysfunction.

Table 4.1 Demographic comparison between participants with and without accommodation and vergence dysfunction.

	Normal subjects	**Subjects with accommodation and vergence dysfunction**	**t-test (p value)**
Age, yrs	23.1 ± 6.1 (13 - 33)	22.7 ± 6.7 (13 - 38)	0.633
Distance VA Near VA	-0.17 (± 0.12) -0.12(± 0.09)	-0.21(± 0.10) -0.07(± 0.1)	0.31 0.07
Stereo Acuity Local stereopsis Global stereopsis	 33(± 37) 41(± 4)	 40(± 84) 78(+/- 170)	 0.77 0.37
NPC	5.53 (± 0.09)	7.9 (± 3.69)	0.01
Vergence facility	16.64(± 2.41)	12.6(± 4.22)	0.001
Accommodative facility	10.26(± 3.7)	8.7(± 2.8)	0.16
Positive fusional vergence (blur point)	20.5(± 6)	18.5(± 5)	0.26
Negative fusional vergence (blur point)	24.5(± 2.8)	13.5(± 2)	0.21

Linear regression analyses were conducted and the results are shown in Table 4.2. Form coherence thresholds were not associated with contrast sensitivity, age or the status of accommodation and vergence system. Another linear regression model was constructed as shown in Table 4.3. In this model, the motion coherence thresholds were not associated with contrast sensitivity, contrast threshold for motion direction discrimination, or the status of accommodation and vergence. However, there was strong negative association between motion coherence threshold and age.

Table 4.2 Linear regressions model including contrast sensitivity, status of accommodation and vergence and age (independent variables) for form coherence thresholds (FCT) (dependent variable).

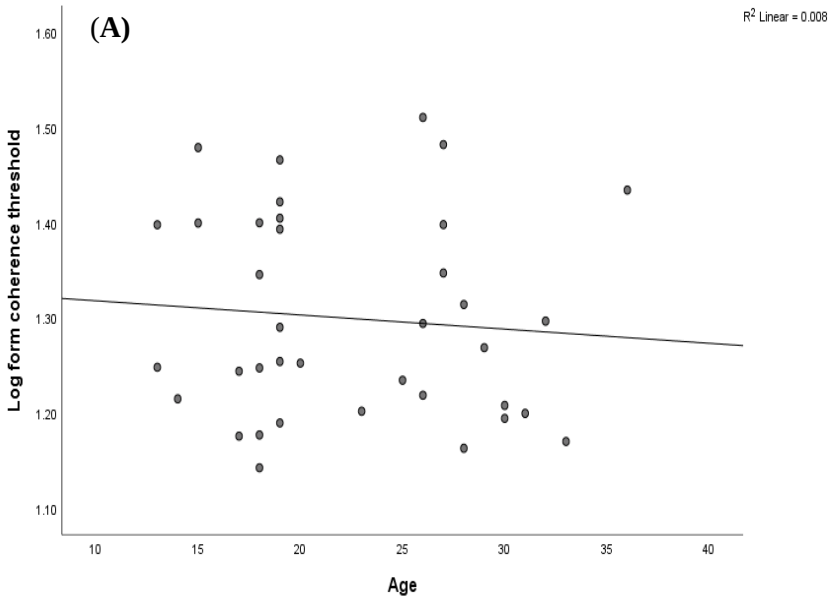
Dependent Variable	**Predictor variable**	**Standardized Coefficient (β)**	**t**	**P value**
FCT	Contrast sensitivity	0.13	0.64	0.53
	Status of accommodation and vergence	-0.14	-0.77	0.45
	Age	-0.14	-0.71	0.48
R^2 for the model= 0.032				

Table 4.3 Linear regression model including contrast sensitivity, contrast threshold for motion discrimination, status of accommodation and vergence, and age (independent variables) for motion coherence threshold MCT (dependent variable).

Dependent Variable	**Predictor variable**	**Standardized Coefficient (β)**	t	**P value**
MCT	Contrast sensitivity	-0.15	-0.89	0.38
	Status of accommodation and vergence	0.03	-0.22	0.83
	Contrast threshold for motion direction discrimination	0.08	0.53	0.56
	Age	-0.43	-2.49	0.018
R^2 for the model= 0.29				

4.4.2 Relationships involving global processing of form and motion

Neither global processing of form or motion were significantly correlated with and distance VA, near VA or stereo acuity ($p>0.05$). In addition, neither form or motion coherence thresholds were correlated with static or motion direction discrimination contrast sensitivity ($p>0.05$). Form coherence thresholds were also not correlated with age ($R^2= 0.008$, $p = 0.61$, Figure 4.2A). However, motion coherence thresholds correlated significantly with age ($R^2= 0.27$, $p = 0.001$, Figure 4.2B). Form coherence threshold was not significantly correlated with motion coherence threshold ($p = 0.89$: Fig. 3.4).



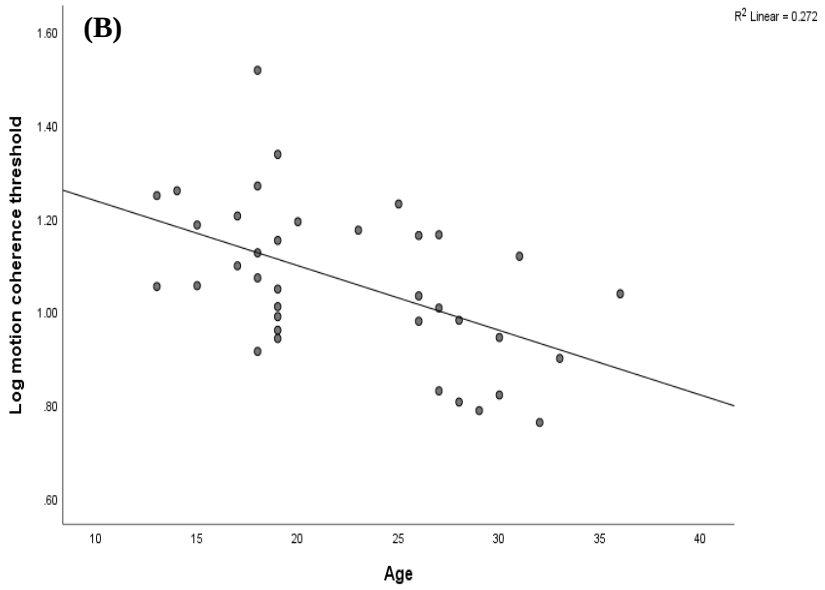


Figure 4.2 Correlations among global form (A) and motion (B) coherence thresholds and age

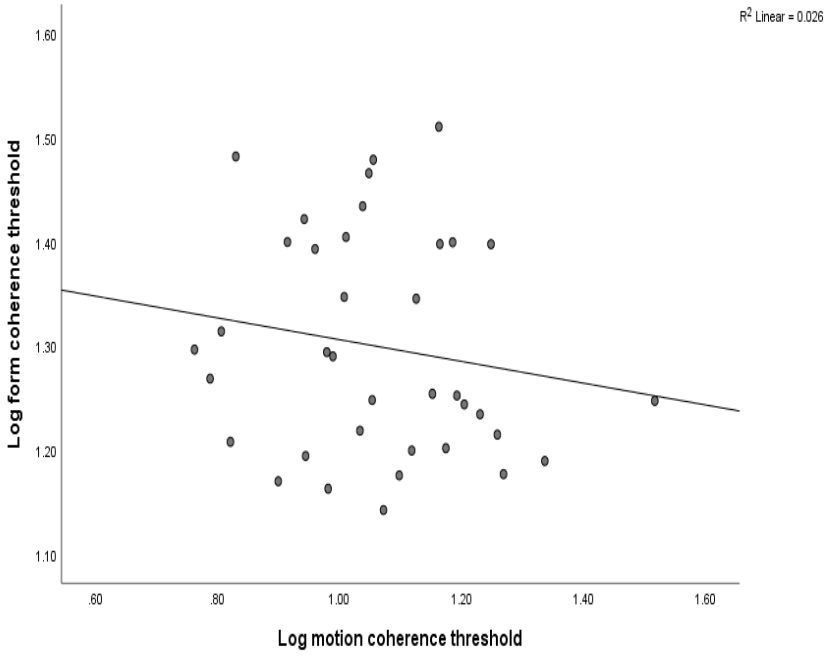


Figure 4.3 Correlation between global form and global motion coherence thresholds.

4.5 Discussion

The aim of this study was to assess whether global processing of form and motion in normally sighted individuals was independent from contrast sensitivity and the status of the accommodation and vergence systems. This question is important since patients with mild TBI have reduced contrast sensitivity and both accommodation and vergence anomalies, which cause blurred vision that can affect performance on global processing tasks (Lara, Cacho, García, & Megías, 2001; Shepherd, Beaumont, & Hine, 2012). In this study, the global processing of form was assessed using global a form detection task based on Glass patterns while global processing of motion was assessed using RDKs. In our sample of normally sighted individuals, we found no evidence for a relationship between the global processing of form or motion and contrast sensitivity (both static and motion based measures) or status of the accommodation and vergence system. Therefore, any impairment of global form or motion perception in mild TBI patients is likely to be due to an impairment of the integration of local visual information in the higher cortical areas if the measures of other visual functions fall within the range we found in our sample of normal participants.

Contrast sensitivity was assessed using two different tasks. First, static contrast sensitivity was assessed using the Freiburg contrast sensitivity test and our results showed no significant association between static contrast sensitivity and performance on either global processing task (form or motion). The absence of a relationship between static contrast sensitivity and motion coherence thresholds is not in agreement Shepherd et al who reported that poor performance on motion tasks in patients with migraine could be due to impaired contrast sensitivity (Shepherd, Beaumont, & Hine, 2012b). The inconstancy between our results and Shepherd et al's study is likely because the contrast sensitivity was tested using two different static contrast sensitivity tests. In the Shepherd et al study, contrast sensitivity was tested

using the Cambridge Low Contrast Gratings while in our study the contrast sensitivity was assessed using Freiburg contrast sensitivity test. Both tests have different spatial frequencies and different methods of measuring the contrast sensitivity (sine wave grating vs. optotype chart). In addition, we tested healthy participants who we would expect to exhibit normal contrast sensitivity.

Secondly, the contrast threshold for motion direction discrimination was measured to assess the early function of the dorsal stream. Our results showed no significant association between the contrast threshold for motion direction discrimination and performance on the global motion task. The absence of a significant relationship between contrast thresholds for coherent motion direction discrimination and motion coherence thresholds has been reported in previous studies (Chakraborty et al., 2015a; Ellemberg, Lewis, Maurer, Brar, & Brent, 2002). For example, Chakraborty et al reported no significant relationship between global processing of motion and contrast sensitivity in 4.5-year-old children born at risk of abnormal neurodevelopment, suggesting that the performance on the global motion task is independent from variation in the contrast sensitivity for motion detection and therefore reflects the function of higher level integration mechanisms (Chakraborty et al., 2015a). Overall, our results suggest that mild reductions in contrast sensitivity are unlikely to influence performance of on the global form and motion tasks. However, we cannot rule out the possibility that pronounced contrast sensitivity reductions could influence global processing task performance.

Similarly, there was no evidence for a relationship between the global processing of form and motion and the status of the accommodation and vergence systems. To our knowledge, this was the first study to address whether there is an association between status of accommodation and vergence system and performance on global processing tasks. Since accommodation anomalies can cause blur symptoms, our findings are consistent with Trick

et al who found no effect of optical blur on the performance of the global motion task (Trick et al., 1995). However, our results are not in agreement with Burton et al who found that both global form and global motion perception are impaired with filter induced blur (Burton et al., 2015). In their study, they used 3 different filters that caused 3 different visual acuity reductions (0.53, 0.88 and 1.2 log MAR near visual acuity). However, in our sample, the worst near visual acuity for a subject with an accommodation and vergence anomaly was 0.01 Log MAR. This suggests that blur is likely to affect performance on global processing tasks only when it causes a substantial near visual acuity impairment.

In our sample, we observed a strong negative association between motion coherence threshold and age. All participants were older than 13 years, and it has been reported in the literature that global motion perception matures before the age of 14 (Gunn et al., 2002). The strong effect of age in our sample is inconsistent with previous studies and there is not clear explanation for this. However, this result indicated that controlling for age is important within our experimental paradigm. Therefore, in the next chapter (Chapter 4) in which the effect of the mild TBI on the global processing of form and motion was studied; the age of the mild TBI and control groups was matched as closely possible. No effect of age was observed for global form coherence thresholds, which is consistence with the previous literature in which global form perception matures by 7 years of age (Gunn et al., 2002).

We found that motion coherence thresholds were not correlated with form coherence thresholds. This suggests that the global form and motion tasks gave thresholds that are independent from one another in normally sighted individuals and possibly reflect independent functions of the ventral and dorsal cortical processing streams respectively. This finding has previously been reported by a functional magnetic resonance imaging (fMRI) study. Braddick et al have reported that form coherence stimuli activate only the higher cortical areas along

the ventral stream while motion coherence stimuli activate the higher cortical areas along the dorsal stream (Braddick, O'Brien, Wattam-Bell, Atkinson, & Turner, 2000).

Chapter 5

Global Processing of Form and Motion in Patients with Mild TBI

5.1 Introduction

In this chapter, the global processing of form and motion, as an index of dorsal and ventral stream function, was assessed in patients with mild TBI and age matched normal controls. In addition, other visual functions such as visual acuity and stereo acuity as well as symptoms of patients with mild TBI were assessed.

5.2 Methods

5.2.1 Participants

There were 36 participants who were recruited for this study, 25 normal controls and 11 patients with mild TBI. The inclusion and exclusion criteria described in Chapter 3.1 were used in this study.

5.2.2 Vision assessment

The same vision assessment described in Chapter 3.3 was used in this study.

5.2.3 Symptoms Assessment

Participants with mild TBI were asked to complete a non-standardized questionnaire designed to obtain information about their medical history (Appendix A). In addition, they were asked to complete a standardized questionnaire ("Post-Concussion Symptom Inventory PCSI", Appendix B), that is used to assess the symptoms of patients with mild TBI. The PCSI questionnaire has rating questions for different symptoms (score 0 – 6) for pre and post-injury, and an overall rating of post-concussion symptoms after mild TBI (score 0 – 4), (Barlow et al.,

2017; Gioia, 2015; Sady, Vaughan, & Gioia, 2014). Scores were calculated by summing across all questions for each participant. The PCSI questionnaire was chosen for this study because it has been used across a variety of ages and it can be used to distinguish between symptomatic and asymptomatic participants.

5.3 Analysis

Statistical analyses were carried out with SPSS statistical software. The Shapiro-Wilk test was used to assess whether data were normally distributed or not. Three analyses were then conducted. Firstly, repeated measures ANOVA was used to compare the differences in both global form and global motion thresholds between the two groups. Secondly, independent samples t-tests (parametric) or Mann-Whitney tests (non-parametric) were used to compare clinical measurements of vision between the two groups. Thirdly, relationships between the mild TBI group's PCSI symptoms and performance on vision measures were analyzed using Pearson correlations.

5.4 Results

Eleven participants with mild TBI (mean age 28 yrs ± 8.56, 17 ± 5.2 months post injury, 64% were females) and 25 age-matched normal controls (mean age 25.48 yrs ± 5.2, 55% were females) took part in this study. All the participants successfully completed the psychophysical measures of global form and global motion perception as well as the clinical measurement of vision. Table 5.1 shows a comparison between the normal participants and those with mild TBI.

Table 5.1 Demographic comparison between normal participants and those who had mild TBI

	Normal controls	**Mild TBI**	**t-test (p value)**
Age (yrs) (mean ± SD)	25.48 (± 5.2)	28 (± 8.56)	0.28
Distance VA Near VA	-0.24 (± 0.06) -0.13 (± 0.09)	-0.20(± 0.10) -0.05(± 0. 09)	0.26 0.02
Log contrast sensitivity	2.13 (± 0.23)	1.95 (± 0.16)	0.03
Stereo Acuity Local stereopsis Global stereopsis	 20.4 (± 1.38) 40 (± 0)	 26.7 (± 10) 60 (± 28.28)	 <0.01 <0.01
NPC	6.6 (± 3.1)	12 (± 9.9)	0.01
Vergence facility	15.32 (± 3.67)	12.7 (± 6.3)	0.13
Accommodative facility	9.8 (± 2.5)	4.9 (± 4.19)	<0.01
Accommodation amplitude difference	4.53 (± 2.9)	-0.04 (± 2.7)	<0.01

All the mild TBI participants had sustained their injury during a motor-vehicle or sporting accident. Mild TBI participants' characteristics are presented in Table 5.2.

Table 5.2 Mild TBI participant characteristics

Mild TBI subject #	Gender/Age	Time since injury (months)	Number of symptoms/20 Total	Total PCSI score/120	Medications
1	Female/19	3	16	80	No
2	Female/40	5	20	86	No
3	Female/40	5	19	46	No
4	Male/23	20	2	4	No
5	Female/26	36	1	1	No
6	Male/21	47	2	2	No
7	Male/22	17	7	15	No
8	Male/22	15	8	25	No
9	Female/24	32	11	27	No
10	Female/29	3	19	74	Yes
11	Female/42	16	19	78	Yes

5.4.1 Comparison of global processing of form and motion and contrast threshold for motion discrimination between mild TBI and normal control groups

The means for both global form coherence threshold and global motion coherence threshold are averaged across the 2 staircases. In the control group, the mean global form coherence threshold was 21.23% (SD: 5.37, range: 14.55 – 32.38%) while global motion coherence threshold was 10.79% (SD: 3.37, range: 5.79 – 17.25%). In the mild TBI group, the mean global form coherence threshold was 25.07% (SD: 5.91, range: 15.96 – 32.69%) while the global motion coherence threshold was 14.38% (SD: 6.67, range: 8.19 – 31.87%). Both global

form coherence threshold and global motion coherence threshold were not normally distributed based on Shapiro–Wilk normal distribution test. Therefore, log transformation was applied in order to normally distribute the data for parametric analysis.

A two-way mixed ANOVA with factors of Group (control vs. mild TBI) and Test Type (global forma vs. global motion) was chosen for analysis of the global processing of form and motion. The results showed a significant main effect of group (F1:34= 7.1, p=0.01). Both form and motion coherence thresholds were higher in the mild TBI group. The interaction between Groups and Test Type was not significant as showed in figure 5.1 (p>0.05). This indicates that the mild TBI group deficit was equivalent for both global perception tasks.

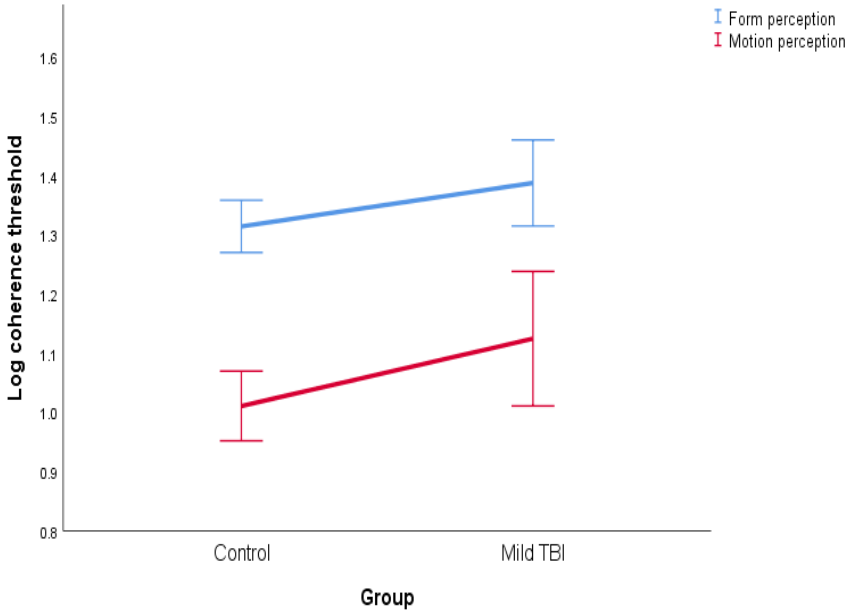


Figure 5.1 From and motion coherence thresholds for the normal and mild TBI groups. Error bars represent 95% Confidence Interval.

Independent sample t-tests revealed no statistically significant differences between participants who had mild TBI and normal controls for contrast threshold for motion direction discrimination as shown in figure 5.2 (t(34)= 0.54, p=0.59). However, there was more

between-subject variability in the mild TBI group versus the controls (compare the confidence intervals in Figure 5.2)

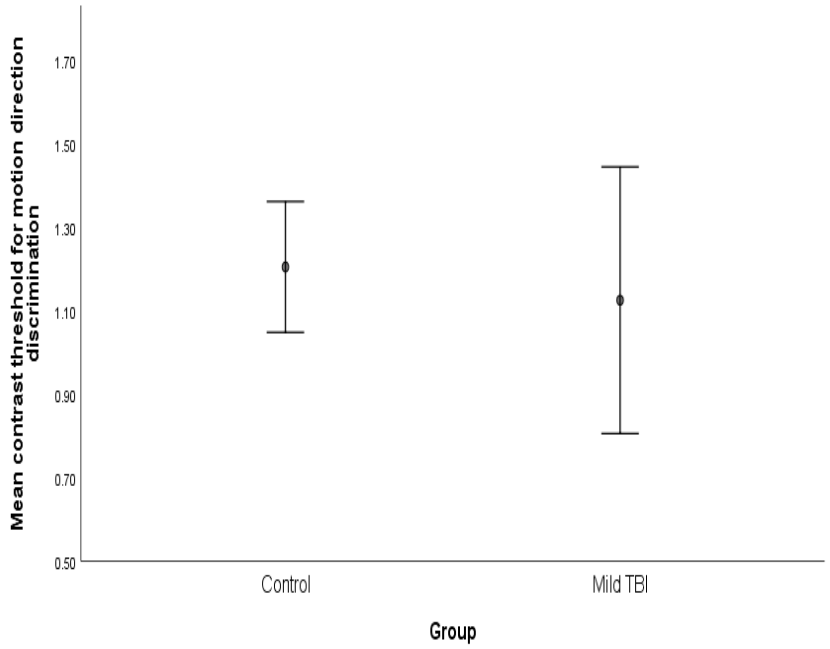
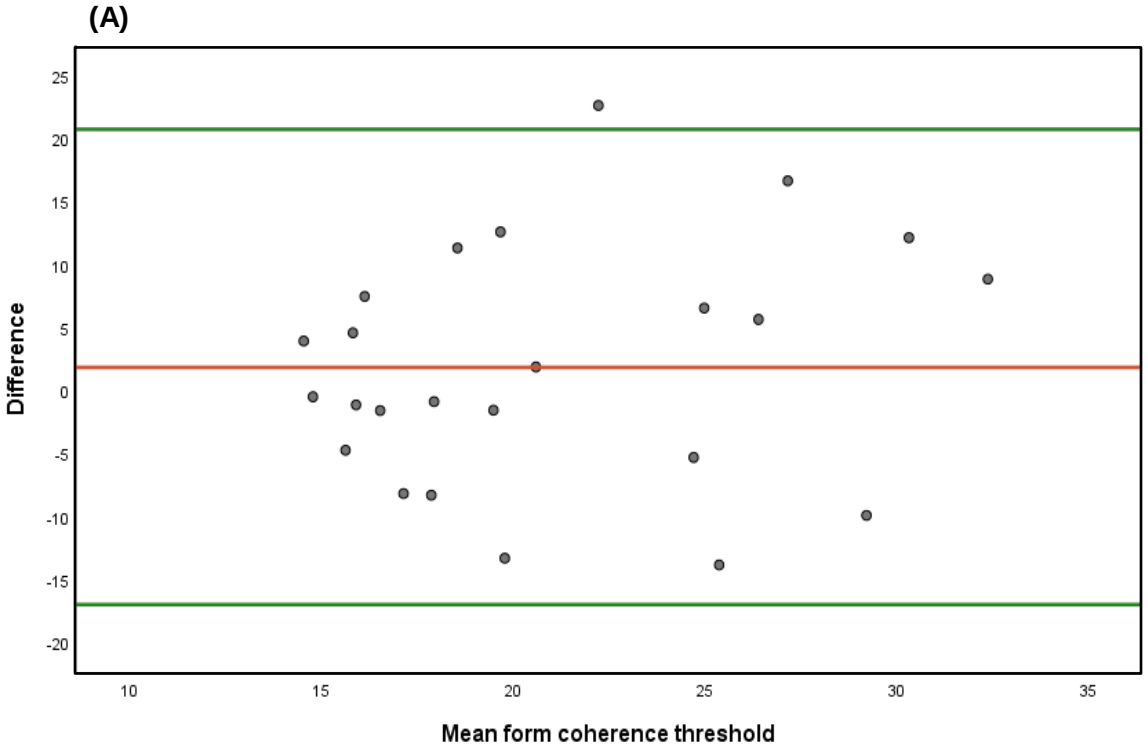


Figure 5.2 Comparison of contrast threshold for motion direction discrimination between mild TBI and normal control groups. Error bare represent 95% Confidence Interval.

5.4.2 Test-retest variability for global form and global motion coherence thresholds in control and mild TBI participants

The two threshold measurements for the global motion and global form tests were compared using Bland Altman analysis. The results for control participants are presented in Figure. 5.3. Each Figure consists of a plot of the difference between the two measurements (threshold 1 vs. threshold 2) against their mean, showing the mean difference (red line) and the limits of agreement (green lines). For the form coherence thresholds in controls shown in Figure 5.3A, the mean difference was 1.86 (95% confidence interval = 5.85 to -2.13) and the limits of agreement were 20.74 to -17.02. The control motion coherence thresholds are shown in

Figure 5.3B. The mean difference was 0.47 (95% confidence interval = 3.11 to -2.17) and the limits of agreement were 12.99 -12.05. In the participants with mild TBI, the form coherence threshold comparison is presented in Figure 5.4A. The mean difference was 4.59 (95% confidence interval = 8.85 to 0.33) and the limits of agreement were 17.27 to -8.09. For motion coherence thresholds shown in Figure 5.4B, the mean difference was 4.13 (95% confidence interval = 7.47 to 0.81) and the limits of agreement were 14.05 to -5.79. Therefore mild TBI patients had larger mean differences but comparable limits of agreement to controls for both global processing measures.



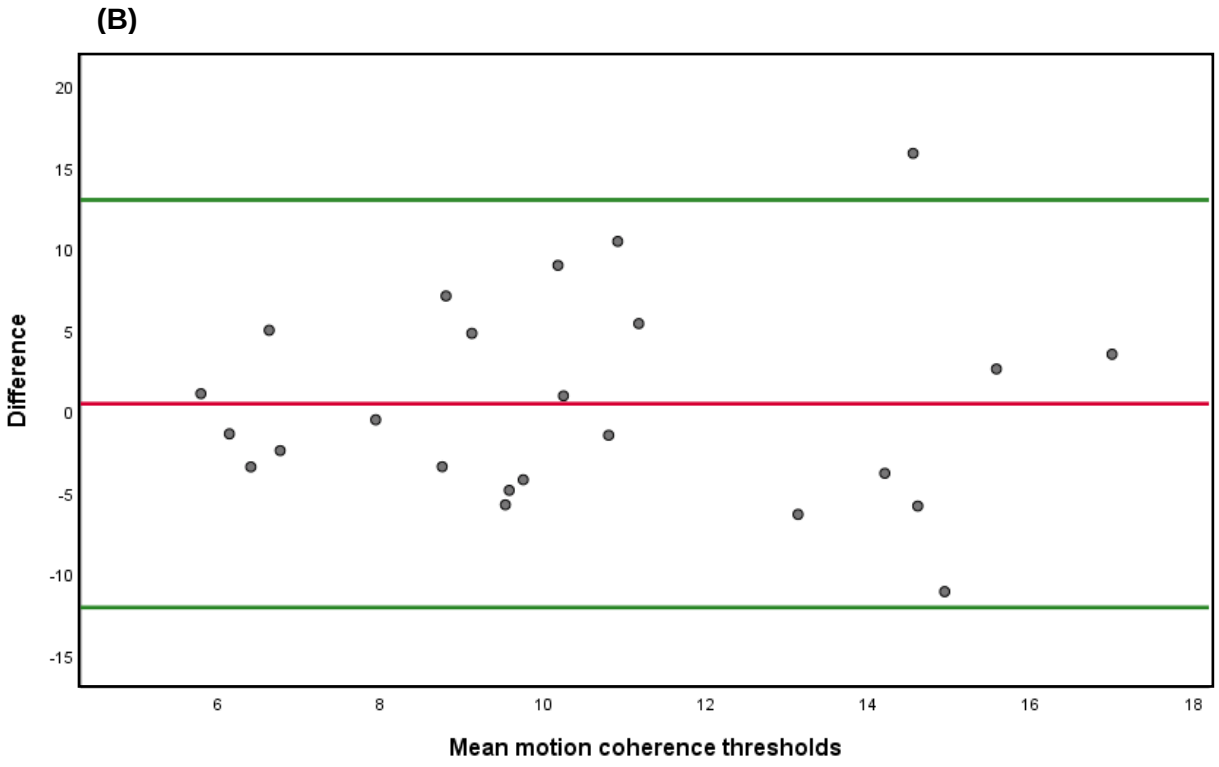
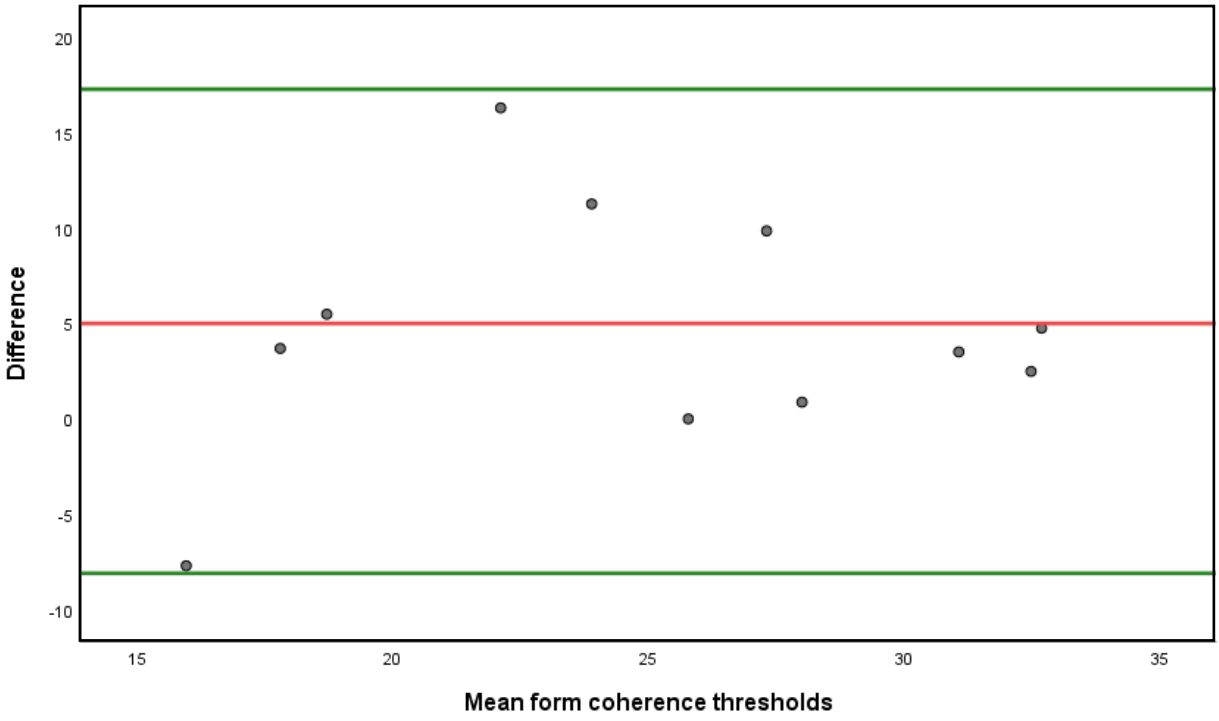


Figure 5.3 Results of the comparisons between the two measurements of global form coherence threshold (A) and global motion coherence thresholds (B) in normal participants.

(A)


Difference
20
15
10
5
0
-5
-10
15
20
25
30
35
Mean form coherence thresholds

(B)

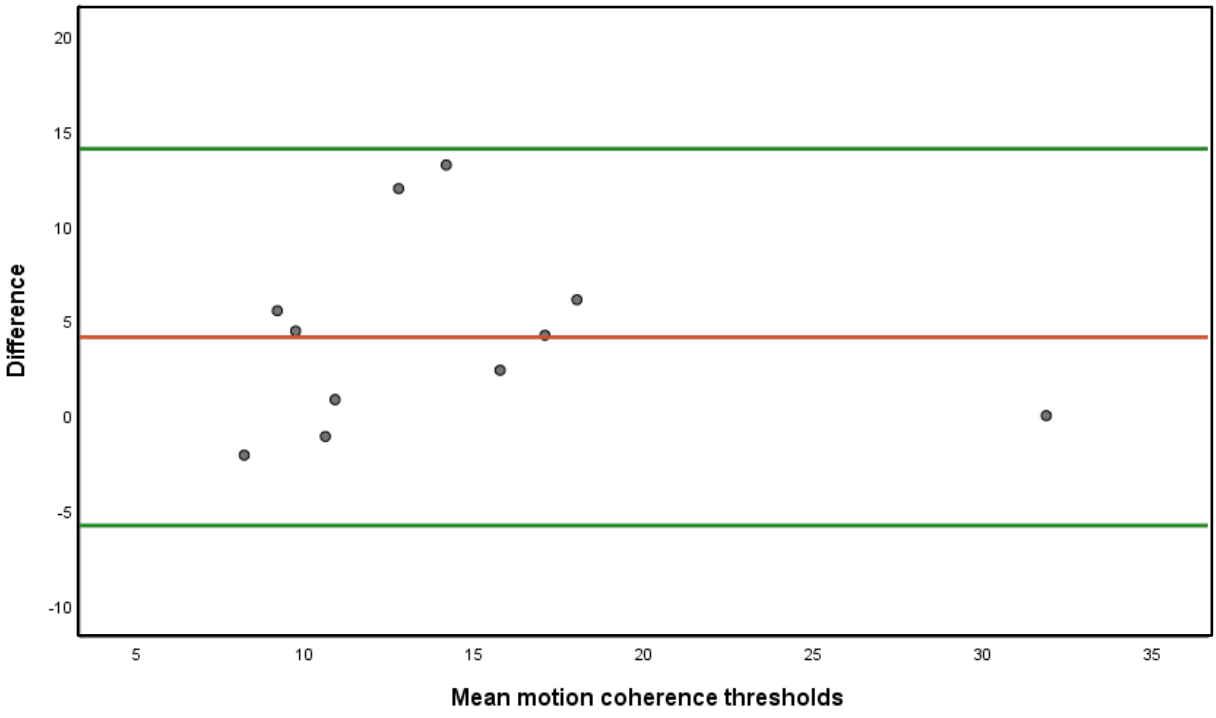
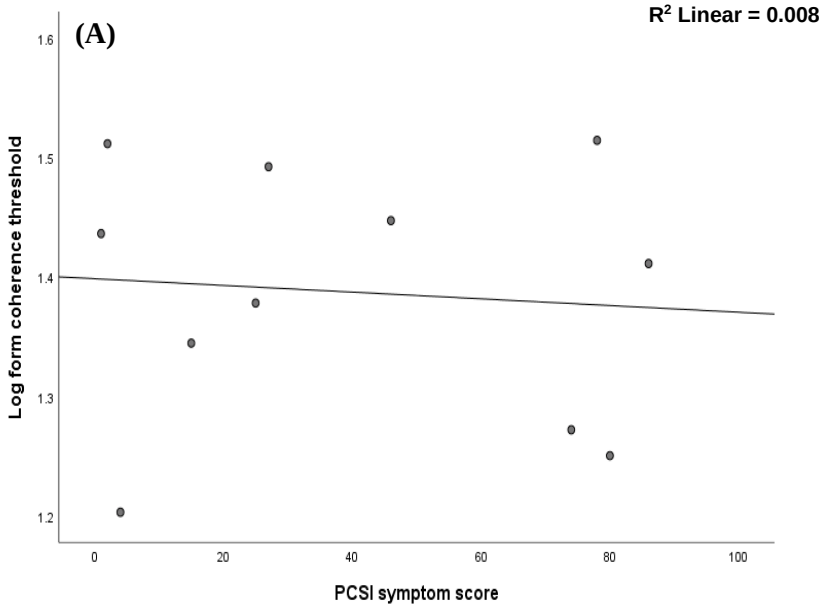
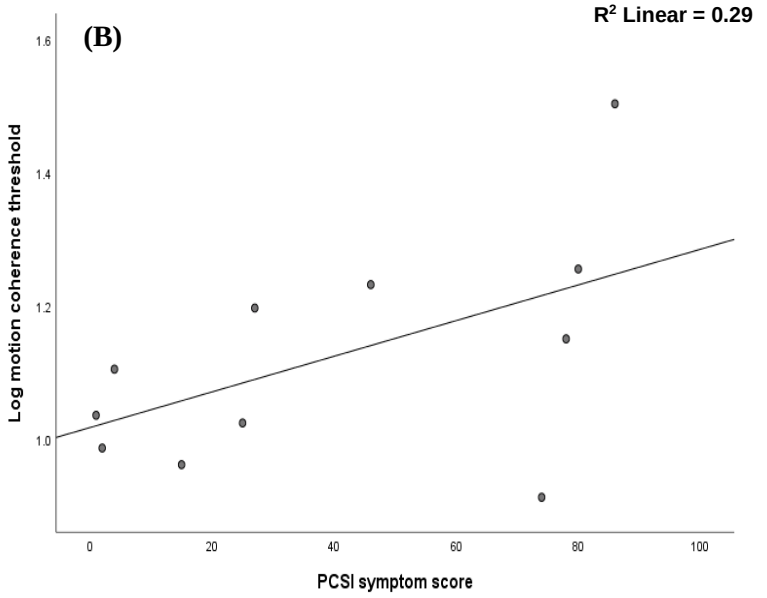

Difference
20
15
10
5
0
-5
-10
5
10
15
20
25
30
35
Mean motion coherence thresholds

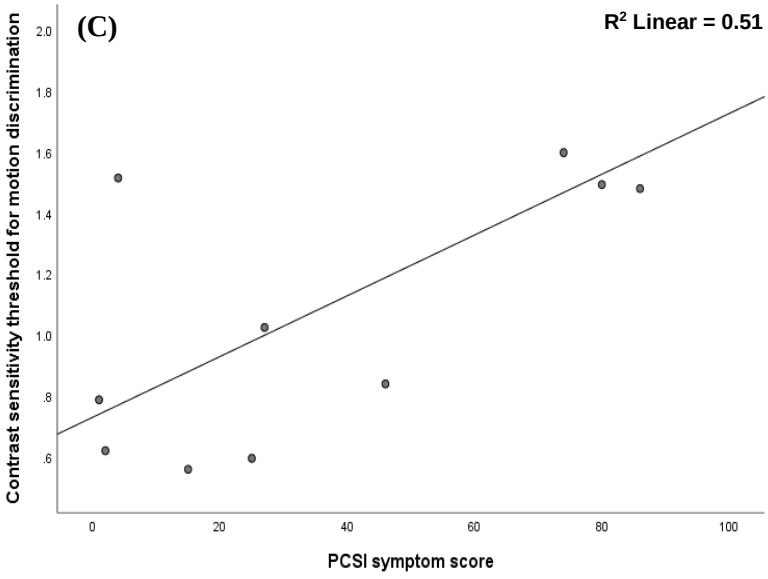
Figure 5.4 Results of the comparisons between the two measurements of global form coherence threshold (A) and global motion coherence thresholds (B) in participants with mild TBI.

5.4.3 Correlations among global processing of form and motion, contrast threshold for motion discrimination and PCSI symptoms score

A secondary analysis was conducted to assess the relationships among the form coherence thresholds, motion coherence thresholds, contrast thresholds for motion discrimination, and concussion symptom scores. There was no significant correlation between PCSI symptom scores and log global form coherence thresholds (R^2= 0.008, p= 0.79, Figure 5.5 A). Similarly, log global motion coherence threshold did not correlate significantly with the PCSI score, although the relationship did approach significance (R^2= 0.29, p= 0.08, Figure 5.5 B). In contrast, there was a significant correlation between PCSI symptom scores and contrast threshold for motion discrimination (R^2= 0.51, p= 0.01) based on Pearson correlation as showed in Figure 5.5 C. In addition, there was significant correlation between PCSI symptom scores and the time since injury (R^2= 0.59, p <0.01; Figure 5.5D).




(B)
R² Linear = 0.29
Log motion coherence threshold
1.6
1.4
1.2
1.0
0
20
40
60
80
100
PCSI symptom score


(C)
R² Linear = 0.51
Contrast sensitivity threshold for motion discrimination
2.0
1.8
1.6
1.4
1.2
1.0
.8
.6
0
20
40
60
80
100
PCSI symptom score

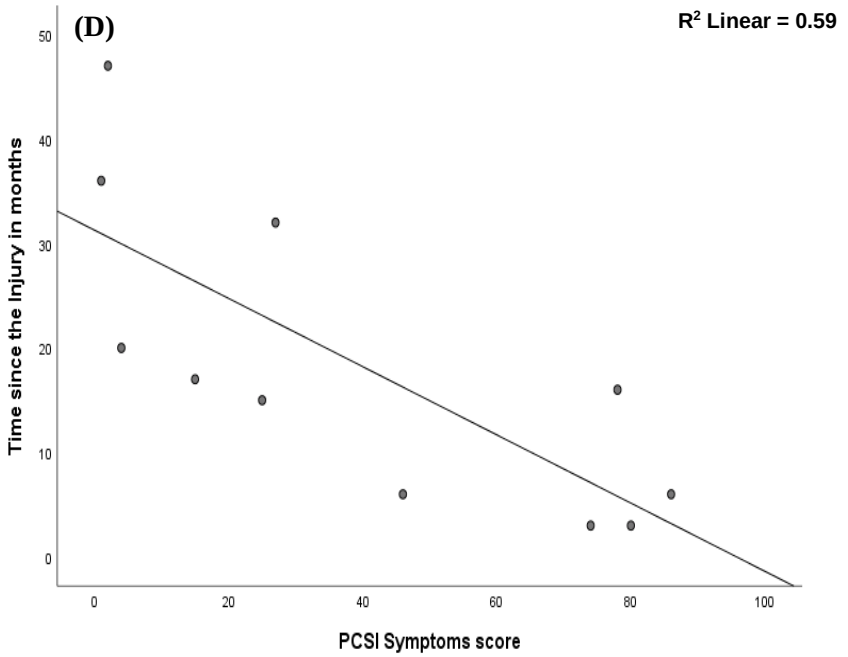


Figure 5.5 Correlations between PCSI symptom scores and log form coherence thresholds (A), log motion coherence thresholds (B), contrast sensitivity for motion discrimination (C), and time since the injury (D).

5.5 Discussion

The main aim of this study was to assess whether patients with mild TBI have a deficit in the global processing of form and motion, as an index of dorsal and ventral stream function. The processing of both global form and global motion involves an integration of local visual cues across large regions of the visual field, and, as such, most likely relies on extra striate processing. The research question of this study is important because the dorsal stream is hypothesized to be particularly vulnerable to damage relative to the ventral stream and to be affected in neurodevelopmental disorders such as autism while the ventral stream remains intact (Pellicano, Gibson, Maybery, Durkin, & Badcock, 2005). Most of the previous studies that have assessed the consequences of mild TBI on the visual system have focused on either clinical measurements of vision that likely reflect processing by early cortical areas (V1) or the

higher processing of visual information such as the sensitivity to complex visual stimuli, for example, global motion stimuli. Unlike previous studies, we did not focus on one aspect of visual information processing, but rather assessed early and higher processing of visual information as well as the symptoms scores of those who sustained mild TBI. In term of higher visual information processing, our results indicate that the global processing of both global form and global motion are affected after the mild TBI. The findings of our study are important since this is the first study that has shown the adverse effect of mild TBI on both processing streams (dorsal and ventral). Our findings are in agreement with (Patel et al., 2011) who reported that there is a significant elevation of the motion coherence threshold in those with mild TBI compared with controls (Patel et al., 2011). In addition, our findings are in good agreement with the Brosseau-Lachaine et al study in which they have found that mild TBI patients have a significant elevation of coherence thresholds for optic flow stimuli that engage higher level dorsal stream areas such as MST (Brosseau-Lachaine et al., 2008). These findings of elevated coherence thresholds for global motion stimuli revealed a specific impairment for patients with mild TBI in their ability to integrate local moving elements into more complex coherence patterns.

The elevated motion coherence thresholds we observed could be explained by abnormal processing within dorsal stream areas such as V3A and MT/V5 or impaired local motion processing due to damage within the magnocellular pathway and/or V1. In this study, we did not include a task that targets early processing within the retino-geniculate areas of the magnocelluar pathway within such as flicker contrast stimuli (Pellicano et al., 2005). However, contrast thresholds for motion direction discrimination were assessed and provided a measure of local motion processing (Chakraborty et al., 2015a). We did not observe any statistically significant differences between the mild TBI and control groups for contrast thresholds for

motion discrimination. This suggests that the impaired motion processing on those with mild TBI is related to an integration deficit of local moving elements rather than abnormal processing of local motion signals.

Similarly, our results show a significant elevation of global form coherence thresholds in the mild TBI group relative to controls. To our knowledge, this study is the first to measure global form processing in individuals with mild TBI. Several studies have reported a deficit in the dorsal processing stream and our results build on this earlier work to reveal a widespread involvement of both processing streams. This widespread deficit of both processing streams might support the thought that there is diffuse axonal injury within the brain in those who sustained mild TBI. In addition, this result raises the possibility that those with Mild TBI might benefit from a variety of rehabilitation therapies including vison therapy.

We observed greater variability in the contrast thresholds for motion direction discrimination within the mild TBI group compared with controls as shown in Figure 5.2. Subsequent analysis suggested that this variation may be associated with PSCI symptom score. In particular, contrast threshold for motion direction discrimination was correlated with the PCSI score (Figure 5.5 C), whereby an increase in the contrast threshold for motion discrimination was associated with an increase in PCSI symptom score. Although our mild TBI group as a whole did not exhibit abnormal contrast thresholds for motion direction discrimination, it appears that elevated thresholds did occur for participants with more pronounced symptoms. The question of whether there is a causal relationship between contrast thresholds for dynamic stimuli and mild TBI symptoms remains to be answered. Our finding is consistent with that of Chang et al who reported a significant relationship between the symptoms reported in patients with mild TBI and critical flicker frequency (CFF) thresholds in which there was increase the CFF threshold with the worse symptoms score (Chang et al., 2007). They suggested that the

relationship between CFF and mild TBI symptoms might be due to a distribution to neural gain sensitivity. In thre present study we found no significant correlation between PCSI scores and either global form or global motion coherence thresholds suggesting that PCSI symptom scores are associated with lower-level visual function rather than performance on higher-level global integration tasks.

Although it has been reported that patients typically recover from 1 to 3 months post injury (McCrea et al., 2009), more that 70% of the participants who sustained mild TBI in our sample still had symptoms. Two participants in the mild TBI group reported in the medical history questionnaire that they were using medication such as antidepressants, and these medications may have affected their visual function (Predictable, 2006).

As expected, participants with mild TBI performed worse than controls on most of the clinical vision tests. First, there was significant reduction in static contrast sensitivity in those with mild TBI compared with controls in our sample even though the worst log contrast sensitivity within the mild TBI group was 1.81 which is considered to be normal in optometric clinical practice (Mntyjrvi & Laitinen, 2001). Since the spatial frequency of the contrast sensitivity test that was used in the current study was low, our finding is in good agreement with Spiegel et al in who reported that there is a shift in the contrast sensitivity function toward high spatial frequencies in those with mild TBI (Spiegel et al., 2016). This suggests that contrast sensitivity for low spatial frequencies is affected in those with mild TBI. Secondly, participants with mild TBI have reduced local and global stereo acuity. Stereopsis is thought to be linked to both dorsal and ventral streams (Neri, 2005; Parker, 2007). The reduction of the stereopsis is possibly attributed to an impairment of both processing streams, which is consistent with our finding of widespread defects in both the dorsal and ventral processing streams. Thirdly, participants with mild TBI performed worse than the normal controls in the NPC, accommodation facility

and accommodation amplitude tests. These findings were reported previously in the same population (Barnett & Singman, 2015a; Barnett & Singman, 2015b; Green et al., 2010; Hellerstein et al., 1995; Kapoor & Ciuffreda, 2002). However, in our sample, the participants with mild TBI performed similarly to the normal control in vergegece facility. This normal performance on the vergence facility might be attributed to the fact that those who sustained mild TBI and participated in this study went through different therapies including vision therapy and their vergence facility had improved due to these vision therapies.

Limitations of the study

The current study has several limitations. One limitation of the study was the small sample size for the mild TBI group. This is due to difficulty in recruiting patients who fit the study inclusion and exclusion criteria and who are willing to participate. For example, one of the study tests was the global motion perception test and many patients with mild TBI report feeling discomfort when viewing visual motion. This makes them not interested in participating in such study. The inclusion of more participants in the future with different age groups will increase the application of these study results to a wider population of mild TBI patients. Another limitation of the current study is that one of the participants who had mild TBI was unable to compete all the clinical vision tests during the study visit, therefore, some of test results were taken from the participant's medical file. Due to the fact that this study had multiple tests and could take up to 90 minutes, additional visual tests such as automated visual fields were not performed. These comprehensive eye tests may provide additional information on the effect of different visual functions on the global processing of form and motion. Lastly, the reaction time for the form and motion tasks was not discussed in this thesis due to the fact that there was no instruction in the protocol of the experiments informing the participants to give their respond as soon as possible.

Chapter 6

Conclusion

The first aim of this thesis (Chapter 4) was to investigate the relationships among the global processing, contrast sensitivity, and the status of accommodation and vergence system. This question is important since the patients with mild TBI have reduced contrast sensitivity as well as accommodation and vergence anomalies. In addition, the analyses addressed the issue of whether the global form and motion tasks were independent from one another. The effect of contrast sensitivity on the performance of both global form and global motion has been addressed previously, however, to our knowledge; there are no previous reports on the influence of accommodation and vergence anomalies on the performance on the global processing tasks. In the literature, there are controversies relating to whether reduced contrast sensitivity and blur, which are some of the symptoms experience by those with mild TBI, have an impact on the performance of global processing tasks. This controversy is possibly due to the fact that each study has used different stimulus parameters for both global form and global motion tasks. We found that global form and global motion coherence thresholds are independent from one another and from contrast sensitivity and the status of accommodation and vergence. This likely because coherence thresholds target the mechanisms that integrate local form or motion signals. Because we used suprathreshold stimuli, these integration mechanisms are relatively robust to normal variations in contrast sensitivity and vergence/accommodation. The lack of a correlation between motion and form coherence thresholds also confirmed that the global motion and global form tasks were independent from one another in controls, in agreement with the duel stream (dorsal/ventral) theory of visual processing.

We also observed a strong association between age and motion coherence thresholds for normally sighted individuals. Therefore, in the study that investigated the effect of mild TBI on the global processing of form and motion, the age of the participants in each group was matched as closely as possible. We are unable to identify an explanation of this correlation.

The Second aim of this thesis (Chapter 5) was to investigate the effect of mild TBI on the global processing of form and motion. In the literature, patients with mild TBI have been found to have impaired motion perception. The dorsal stream vulnerability hypothesis suggests that these deficits might be due to a specific and isolated impairment of the dorsal processing stream. However, to our knowledge, the effect of mild TBI on global form perception associated with the ventral stream had never been previously been studied. We found that mild TBI impaired global motion and form perception equally, indicating a non-specific, widespread effect on higher level processing within the visual cortex. Our finding that both global and local stereopsis was impaired in those who have had a mild TBI compared to controls is consistent with this idea because stereopsis involves both the dorsal and ventral processing streams. Overall this study demonstrates a significant impact of mild TBI on visual integration mechanisms that is not restricted to a single processing stream.

Appendix A

A non-standardized questionnaire designed to obtain information about their medical history

Health History Questionnaire

Date	Participant Code	Age	Study Group

1. When did you have concussion? ___/____/_____ (month/day/year)

2. Have you been taking medications for concussion symptoms? YES_____ NO_____

3. Did you lose your consciousness during the concussion? YES_____ NO_____ If yes, please explain for how long

_____

4. How many concussions have you been diagnosed with excluding this injury:

_____

5. Do you have any significant health problems in which you are taking medications? YES__ NO__ If yes, please explain

_____

6. Have you ever undergone any type of surgeries? YES_____ NO_____ If yes, what type of operation did you have?

_____

7. Have you suffered any other type of head injury? YES__ NO__ If yes, please explain

_____

8. Have you ever experienced seizures? YES_____ NO_____

9. Are you in any way physically ill at this time? YES__ NO__ If yes, please explain

10. Do you currently wear glasses or contact lenses? YES__ NO__

11. If YES to Question 10: How long have you been wearing glasses/ Contact lenses _____ [years/months]

Appendix B

Post-Concussion Symptom Inventory (PCSI-S)
Self-Report Assessment Form
Pre and Post-Injury Report

Participant Code:

Today's date:

We would like to know if you have had any of these symptoms before your injury. Next, we would like to know if these symptoms have changed after your injury. Please rate the symptom at two points in time- Before the Injury/Pre-Injury and Currently.

Please answer all the items the best that you can. Do not skip any items. Circle the number to tell us how much of a problem this symptom has been for you.

0 = Not a problem 3 = Moderate problem 6 = Severe problem

	Before the Injury/Pre---Injury	**Current Symptoms/ yesterday and/or today**
1	Headache	
	0 1 2 3 4 5 6	0 1 2 3 4 5 6
2	Nausea	
	0 1 2 3 4 5 6	0 1 2 3 4 5 6
3	Balance problems	
	0 1 2 3 4 5 6	0 1 2 3 4 5 6
4	Dizziness	
	0 1 2 3 4 5 6	0 1 2 3 4 5 6

5 Drowsiness

0 1 2 3 4 5 6 0 1 2 3 4 5 6

6 Sleeping more than usual

0 1 2 3 4 5 6 0 1 2 3 4 5 6

7 Sensitivity to light

0 1 2 3 4 5 6 0 1 2 3 4 5 6

8 Sensitivity to noise

0 1 2 3 4 5 6 0 1 2 3 4 5 6

9 Irritability

0 1 2 3 4 5 6 0 1 2 3 4 5 6

10 Sadness

0 1 2 3 4 5 6 0 1 2 3 4 5 6

11 Nervousness

0 1 2 3 4 5 6 0 1 2 3 4 5 6

12 Felling more emotional

0 1 2 3 4 5 6 0 1 2 3 4 5 6

13 Felling mentally “foggy”

0 1 2 3 4 5 6 0 1 2 3 4 5 6

14 Difficulty concentrating

0 1 2 3 4 5 6 0 1 2 3 4 5 6

15 Difficulty remembering

0 1 2 3 4 5 6 0 1 2 3 4 5 6

16 Visual problems (blurry, double vision)

0 1 2 3 4 5 6 0 1 2 3 4 5 6

17 Tired or fatigued

0 1 2 3 4 5 6 0 1 2 3 4 5 6

18 Get confused with directions or tasks

0 1 2 3 4 5 6 0 1 2 3 4 5 6

19 Move in a clumsy manner

0 1 2 3 4 5 6 0 1 2 3 4 5 6

20 Answers questions more slowly than usual

0 1 2 3 4 5 6 0 1 2 3 4 5 6

21

In general, to what degree you are acting "differently" than before the injury?

No Difference 0 1 2 3 4 Major Difference

Circle your rating with "0" indicating "Normal" (No Difference) and "4" indicating "Very Different" (Major Difference)

Bibliography

Adelson, E. H., & Movshon, J. A. (1982). Phenomenal coherence of moving visual patterns. Nature, 300(5892), 523.

Alexander, M. P. (1995). Mild traumatic brain injury: Pathophysiology, natural history, and clinical management. Neurology,

American Optometric Association. (2010). Care of the patient with accommodative and vergence dysfunction. Optometric Clinical Practice Guideline,

Bach, M., Reuter, M., & Lagrèze, W. A. (2016). Comparison of two visual acuity tests in school enrolment examinations: Tumbling E test versus Freiburg visual acuity test. Der Ophthalmologe: Zeitschrift der Deutschen Ophthalmologischen Gesellschaft, 113(8), 684-689.

Barlow, K. M., Marcil, L. D., Dewey, D., Carlson, H. L., MacMaster, F. P., Brooks, B. L., & Lebel, R. M. (2017). Cerebral perfusion changes in post-concussion syndrome: A prospective controlled cohort study. Journal of Neurotrauma, 34(5), 996-1004.

Barnett, B. P., & Singman, E. L. (2015). Vision concerns after mild traumatic brain injury. Current Treatment Options in Neurology, 17(2), 5.

Barton, J. J., Rizzo, M., Nawrot, M., & Simpson, T. (1996). Optical blur and the perception of global coherent motion in random dot cinematograms. Vision Research, 36(19), 3051-3059.

Blennow, K., Hardy, J., & Zetterberg, H. (2012). The neuropathology and neurobiology of traumatic brain injury. Neuron, 76(5), 886-899.

Bodin, D., Yeates, K. O., & Klamar, K. (2012). Definition and classification of concussion. In Pediatric and adolescent concussion (pp. 9-19). Springer, New York, NY.

Braddick, O. J., O'Brien, J. M., Wattam-Bell, J., Atkinson, J., Hartley, T., & Turner, R. (2001a). Brain areas sensitive to coherent visual motion. Perception, 30(1), 61-72.

Britten, K. H., & van Wezel, R. J. (1998). Electrical microstimulation of cortical area MST biases heading perception in monkeys. Nature Neuroscience, 1(1), 59.

Brosseau-Lachaine, O., Gagnon, I., Forget, R., & Faubert, J. (2008). Mild traumatic brain injury induces prolonged visual processing deficits in children. Brain Injury, 22(9), 657-668.

Burton, E., Wattam-Bell, J., Rubin, G. S., Atkinson, J., Braddick, O., & Nardini, M. (2016). Cortical processing of global form, motion and biological motion under low light levels. Vision Research, 121, 39-49.

Chang, T. T. L., Ciuffreda, K. J., & Kapoor, N. (2007). Critical flicker frequency and related symptoms in mild traumatic brain injury. Brain injury, 21(10), 1055-1062.

Chen, Y., Nakayama, K., Levy, D., Matthysse, S., & Holzman, P. (2003). Processing of global, but not local, motion direction is deficient in schizophrenia. Schizophrenia Research, 61(2), 215-227.

Ciuffreda, K. J., Kapoor, N., Rutner, D., Suchoff, I. B., Han, M. E., & Craig, S. (2007). Occurrence of oculomotor dysfunctions in acquired brain injury: A retrospective analysis. Optometry-Journal of the American Optometric Association, 78(4), 155-161.

Ciuffreda, K. J., Ludlam, D. P., & Kapoor, N. (2009). Clinical oculomotor training in traumatic brain injury. Optometry & Vision Development, 40(1)

Ciuffreda, K. J., Suchoff, I. B., Marrone, M. A., & Ahmann, E. (1996). Oculomotor rehabilitation in traumatic brain-injured patients. Journal of Behavioral Optometry, 7, 29-38.

Corrigan, J. D., Selassie, A. W., & Orman, J. A. L. (2010). The epidemiology of traumatic brain injury. The Journal of head trauma rehabilitation, 25(2), 72-80.

Derrington, A. M., & Lennie, P. (1984). Spatial and temporal contrast sensitivities of neurones in lateral geniculate nucleus of macaque. The Journal of Physiology, 357(1), 219-240.

Elder, G. A., Mitsis, E. M., Ahlers, S. T., & Cristian, A. (2010). Blast-induced mild traumatic brain injury. Psychiatric Clinics, 33(4), 757-781.

Elliott, D. B. (2013). Clinical procedures in primary eye care E-book Elsevier Health Sciences.

Elliott, D. B. (2013). Clinical Procedures in Primary Eye Care E-Book. Elsevier Health Sciences.

Felleman, D. J., & Van, D. E. (1991). Distributed hierarchical processing in the primate cerebral cortex. Cerebral Cortex (New York, NY: 1991), 1(1), 1-47.

Giza, C. C., & Hovda, D. A. (2001). The neurometabolic cascade of concussion. Journal of Athletic Training, 36(3), 228.

Goodale, M. A. (2011). Transforming vision into action. Vision Research, 51(13), 1567-1587.

Green, W., Ciuffreda, K. J., Thiagarajan, P., Szymanowicz, D., Ludlam, D. P., & Kapoor, N. (2010). Static and dynamic aspects of accommodation in mild traumatic brain injury: A review. Optometry-Journal of the American Optometric Association, 81(3), 129-136.

Grosvenor, T., & Grosvenor, T. P. (2007). Primary care optometry Elsevier Health Sciences.

Gunn, A., Cory, E., Atkinson, J., Braddick, O., Wattam-Bell, J., Guzzetta, A., & Cioni, G. (2002). Dorsal and ventral stream sensitivity in normal development and hemiplegia. Neuroreport, 13(6), 843-847.

Guzzetta, A., Tinelli, F., Del Viva, M. M., Bancale, A., Arrighi, R., Pascale, R. R., & Cioni, G. (2009). Motion perception in preterm children: Role of prematurity and brain damage. Neuroreport, 20(15), 1339-1343.

Hadad, B., Maurer, D., & Lewis, T. L. (2011). Long trajectory for the development of sensitivity to global and biological motion. Developmental Science, 14(6), 1330-1339.

Head, J. (1993). Definition of mild traumatic brain injury. J Head Trauma Rehabil, 8(3), 86-7.

Hellerstein, L. F., Freed, S., & Maples, W. C. (1995). Vision profile of patients with mild brain injury. Journal of the American Optometric Association,

Johnson, V. E., Stewart, W., & Smith, D. H. (2013). Axonal pathology in traumatic brain injury. Experimental neurology, 246, 35-43.

Kapoor, N., & Ciuffreda, K. J. (2002). Vision disturbances following traumatic brain injury. Current Treatment Options in Neurology, 4(4), 271-280.

Koldewyn, K., Whitney, D., & Rivera, S. M. (2009). The psychophysics of visual motion and global form processing in autism. Brain, 133(2), 599-610.

Lachapelle, J., Bolduc-Teasdale, J., Ptito, A., & McKerral, M. (2008). Deficits in complex visual information processing after mild TBI: Electrophysiological markers and vocational outcome prognosis. Brain Injury, 22(3), 265-274.

Lewis, T. L., Ellemberg, D., Maurer, D., Wilkinson, F., Wilson, H. R., Dirks, M., & Brent, H. P. (2002). Sensitivity to global form in glass patterns after early visual deprivation in humans. Vision Research, 42(8), 939-948.

Linda Carroll, J. David Cassidy, Lena Holm, Jess Kraus, & Victor Coronado. (2004). Methodological issues and research recommendations for mild traumatic brain injury: The who collaborating centre task force on mild traumatic brain injury. Journal of Rehabilitation Medicine, 36(Supplement 43), 113-125. 10.1080/16501960410023877

London, R., Wick, B., & Kirschen, D. (2003). Post-traumatic pseudomyopia. Optometry (St.Louis, Mo.), 74(2), 111-120.

Lynch, J. J., Silveira, L. C., Perry, V. H., & Merigan, W. H. (1992). Visual effects of damage to P ganglion cells in macaques. Visual Neuroscience, 8(6), 575-583.

Marar, M., McIlvain, N. M., Fields, S. K., & Comstock, R. D. (2012). Epidemiology of concussions among United States high school athletes in 20 sports. The American Journal of Sports Medicine, 40(4), 747-755.

Mays, L. E., Porter, J. D., Gamlin, P. D., & Tello, C. A. (1986). Neural control of vergence eye movements: Neurons encoding vergence velocity. Journal of Neurophysiology, 56(4), 1007-1021.

McCrory, P., Johnston, K., Meeuwisse, W., Aubry, M., Cantu, R., Dvorak, J., . . . Schamasch, P. (2005). Summary and agreement statement of the 2nd international conference on concussion in sport, prague 2004. British Journal of Sports Medicine, 39(suppl 1), i86.

Merigan, W. H., & Maunsell, J. H. (1990). Macaque vision after magnocellular lateral geniculate lesions. Visual Neuroscience, 5(4), 347-352.

Merigan, W. H., & Maunsell, J. H. (1993a). How parallel are the primate visual pathways? Annual Review of Neuroscience, 16(1), 369-402.

Merigan, W. H., Byrne, C. E., & Maunsell, J. H. (1991). Does primate motion perception depend on the magnocellular pathway? Journal of Neuroscience, 11(11), 3422-3429.

Milne, E., White, S., Campbell, R., Swettenham, J., Hansen, P., & Ramus, F. (2006). Motion and form coherence detection in autistic spectrum disorder: Relationship to motor control and 2: 4 digit ratio. Journal of Autism and Developmental Disorders, 36(2), 225-237.

Morrone, M. C., Burr, D. C., & Vaina, L. M. (1995). Two stages of visual processing for radial and circular motion. Nature, 376(6540), 507.

Nassi, J. J., & Callaway, E. M. (2009). Parallel processing strategies of the primate visual system. Nature Reviews Neuroscience, 10(5), 360.

Newsome, W. T., & Pare, E. B. (1988). A selective impairment of motion perception following lesions of the middle temporal visual area (MT). Journal of Neuroscience, 8(6), 2201-2211.

Orban, G. A., Fize, D., Peuskens, H., Denys, K., Nelissen, K., Sunaert, S., Vanduffel, W. (2003). Similarities and differences in motion processing between the human and macaque brain: Evidence from fMRI. Neuropsychologia, 41(13), 1757-1768.

Patel, R., Ciuffreda, K. J., Tannen, B., & Kapoor, N. (2011). Elevated coherent motion thresholds in mild traumatic brain injury. Optometry - Journal of the American Optometric Association, 82(5), 284-289. 10.1016/j.optm.2010.10.012

Scheiman, M., & Wick, B. (2008). Clinical management of binocular vision: Heterophoric, accommodative, and eye movement disorders Lippincott Williams & Wilkins.

Schwartz, S. H. (2009a). Visual perception: A clinical orientation McGraw Hill Professional.

Sharma, I. P. (2017). RAF near point rule for near point of convergence—a short review. Annals of Eye Science, 2(3)

Shaw, N. A. (2002). The neurophysiology of concussion. Progress in Neurobiology, 67(4), 281-344.

Smith, A. T., Greenlee, M. W., Singh, K. D., Kraemer, F. M., & Hennig, J. (1998a). The processing of first-and second-order motion in human visual cortex assessed by functional magnetic resonance imaging (fMRI). Journal of Neuroscience, 18(10), 3816-3830.

Smith, A. T., Greenlee, M. W., Singh, K. D., Kraemer, F. M., & Hennig, J. (1998b). The processing of first-and second-order motion in human visual cortex assessed by functional magnetic resonance imaging (fMRI). Journal of Neuroscience, 18(10), 3816-3830.

Trick, G. L., Steinman, S. B., & Amyot, M. (1995). Motion perception deficits in glaucomatous optic neuropathy. Vision Research, 35(15), 2225-2233.

Trobe, J. D., Acosta, P. C., Krischer, J. P., & Trick, G. L. (1981). Confrontation visual field techniques in the detection of anterior visual pathway lesions. Annals of Neurology, 10(1), 28-34.

Ungerleider, L. G., & Haxby, J. V. (1994). 'What'and 'where'in the human brain. Current Opinion in Neurobiology, 4(2), 157-165.

Van Essen, D. C., & Gallant, J. L. (1994). Neural mechanisms of form and motion processing in the primate visual system. Neuron, 13(1), 1-10.

Vos, P. E., Alekseenko, Y., Battistin, L., Ehler, E., Gerstenbrand, F., Muresanu, D. F.,Vcsei, L. (2012). Mild traumatic brain injury. European Journal of Neurology, 19(2), 191-198.

Wang, Q., Sporns, O., & Burkhalter, A. (2012). Network analysis of corticocortical connections reveals ventral and dorsal processing streams in mouse visual cortex. Journal of Neuroscience, 32(13), 4386-4399.

Wattam-Bell, J., Birtles, D., Nystrm, P., Von Hofsten, C., Rosander, K., Anker, S., Braddick, O. (2010). Reorganization of global form and motion processing during human visual development. Current Biology, 20(5), 411-415.

Wesemann, W. (2002). Visual acuity measured via the freiburg visual acuity test (FVT), bailey lovie chart and landolt ring chart. Klinische Monatsblatter Fur Augenheilkunde, 219(9), 660-667.

Wilkinson, F., James, T. W., Wilson, H. R., Gati, J. S., Menon, R. S., & Goodale, M. A. (2000). An fMRI study of the selective activation of human extrastriate form vision areas by radial and concentric gratings. Current Biology, 10(22), 1455-1458.

Wilson, H. R., & Wilkinson, F. (1998). Detection of global structure in glass patterns: Implications for form vision. Vision Research, 38(19), 2933-2947.

Yoonessi, A., & Yoonessi, A. (2011). Functional assessment of magno, parvo and konio-cellular pathways; current state and future clinical applications. Journal of Ophthalmic & Vision Research, 6(2), 119.

Zwicker, A. E., Hoag, R. A., Edwards, V. T., Boden, C., & Giaschi, D. E. (2006). The effects of optical blur on motion and texture perception. Optometry and vision science, 83(6), 382-390.

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