Investigating Vection Responses in Patients with Early Stage Glaucoma

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Abstract

Purpose: Our lab has previously shown that patients with early glaucoma have dysfunctional vection responses. We attempted to explain this finding using a combined index of structure and function (CSFI), originally proposed by Medeiros et al. (OVS 2012;130(9):1107-1116)

Methods: Roll and circular vection were evoked using a back projected screen (Experiment 1) and the Oculus Rift™ system (Experiment 2), respectively. The CSFI, was obtained using clinical data from visual field tests and optical coherence tomography.

Results: In Experiment 1, the log of vection latency was significantly longer for patients with glaucoma ($t(21) = 2.39$, $p < .05$). In Experiment 2, vection latency was significantly longer for the glaucoma group for both stimulus speeds ($F(1,22) = 6.38$, $p = .019$). However, the CSFI was not related to vection latency, duration, or rating (smallest $p = .06$).

Conclusion: In two different studies we replicated the finding that vection responses are longer in patients with glaucoma; however, the CSFI is not related to vection responses.

Dedication

To Marty. Without your support, I could not have made it this far.

You will be missed.

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Introduction

Glaucoma

Description

By 2020, a projected 79.6 million people will be diagnosed with glaucoma worldwide (Quigley & Broman, 2006). Of that population, 11.1 million will completely lose their eyesight, as glaucoma is the second leading cause of irreversible blindness worldwide (Quigley & Broman, 2006; Resnikoff et al., 2004; Kingman et al., 2004). The prevalence of glaucoma in the United States for individuals over the age of 40 was 2.1% between the years 2005-2008, and over 50% of these individuals did not realize that they had glaucoma (Gupta et al., 2016). Self-reported glaucoma prevalence in Canada was found to be around 1.8% between 2002 and 2003 (Perruccio, Badley, & Trope, 2007).

Glaucoma is a progressive optic neuropathy that leads to gradual vision loss, partially due to optic nerve damage and the death of retinal ganglion cells (RGCs) (Quigley, 1999). It can affect one or both eyes, although it is more common to have bilateral glaucoma. The resulting vision loss typically begins in the periphery, while central visual acuity is spared until later stages of the disease. This pattern tends to affect the superior hemifield (corresponding to the inferior retina), forming a paracentral arcuate scotoma that can slowly close in on the fovea (Hart & Becker, 1982). This damage typically occurs in the Bjerrum region, which lies at an eccentricity of around 10 to 20 degrees (Morin, 1979). An arcuate pattern of loss

forms because the RGC axons travel in an arching pathway around the fovea to avoid directly crossing over it.

Research has shown that central vision can also be affected, even in early stage glaucoma (Adams, Heron, & Husted, 1987; Aulhorn & Harms, 1967; Hood et al., 2012). Central vision loss may be underestimated due to the nature of the 24-2 visual field test, which is the most common way to assess the loss of visual function in patients with glaucoma. The test points of the 24-2 are spaced 6 degrees apart, meaning that the central 4 test points (arranged in a square) will not cover the centre-most part of the fovea (Hood et al., 2012). Therefore, the foveal region where up to 30% of all RGCs are located is not taken into account, which may lead to underreported central vision loss (Curcio & Allen, 1990).

Visual Consequences

Glaucoma is a debilitating disease that can affect many aspects of a patient's life. Visual acuity usually remains intact until the later stages, while peripheral vision can be greatly affected. Peripheral vision plays an important role in tasks related to motion perception, orientation, and locomotion, which explains why patients with glaucoma show difficulties with mobility, balance, hand-eye co-ordination, driving, and avoiding falls (Friedman et al., 2007; Popescu et al., 2011; Kotecha et al., 2009; Kotecha et al., 2012; O'Hare et al., 2012; Black et al., 2011). In other words, although these patients can read and perform well on tasks requiring sharp visual acuity, they struggle in many other domains. The decreased ability to

walk without falling is especially worrisome in this patient population, as they are usually senior citizens who are more easily injured. Falls lead to many other complications such as broken bones, which further hinder mobility and overall quality of life.

Glaucoma also has many negative effects on visual perception not necessarily related to peripheral vision loss. Contrast sensitivity, colour perception, and saccadic eye movements are all negatively impacted by glaucoma (Alvarez et al., 1997; Pearson et al., 2001, Lamirel et al., 2012; Kanjee et al., 2012). Some studies suggest that glaucoma not only affects the optic nerve, but that it also alters the visual cortex itself. Reduced volume in the visual cortex and lateral geniculate nucleus (LGN), as well as in nonvisual regions such and the corpus callosum has been shown (Chen et al., 2013; Williams et al., 2013; Gupta et al., 2006, Frezzotti et al., 2014). The corpus callosum is integral for relaying information between the two hemispheres of the brain, implying that glaucoma could have an effect on much more of one's processing ability than initially thought.

It has been suggested that glaucoma preferentially damages the magnocellular visual pathway, which plays a large role in motion detection (Quigley et al., 1987; Anderson & O'Brien, 1997). However, some refute the claim that M cells are more affected, stating that all cell types are affected equally (McKendrick et al., 2007). Although the mechanism behind it is controversial, it is still agreed that these patients have difficulties with motion detection (Trick et al., 1994; Silverman, Trick & Hart, 1990).

The deficits listed above are all very physically and emotionally taxing on patients with glaucoma. It is especially distressing for patients to come to terms with the fact that their gradual loss of vision can only be slowed, not stopped. Patients with glaucoma have an overall lower quality of life and the disease is often co-morbid with major depression, trait anxiety and disturbed sleep (Mills et al., 2009). Gaining a better understanding of glaucoma is an important first step in finding ways to improve the lives of these patients.

Causes and Risk Factors

Intraocular pressure (IOP) is considered to be the main risk factor of glaucoma, although it is not a cause. Normal IOP ranges from 12 – 22 mmHg, where values above this range are considered to be abnormally high. Open angle and closed angle are the most frequent categories of glaucoma. Primary open angle glaucoma (POAG) is the most common form, and it generally occurs when the angle between the cornea and the iris is too narrow, partially blocking the intraocular fluid from draining properly and causing a build up of pressure. The angle may not be narrow in some cases, but glaucomatous damage still occurs. In closed angle glaucoma, the angle is completely blocked, and pressure can continue to build without relief. In these cases, the IOP rises sharply, potentially resulting in irreversible vision loss within hours if not treated. Normal tension glaucoma (NTG) and low tension glaucoma (LTG) also exists, and these patients still suffer vision loss

despite their low IOP. This is why many factors, not just IOP, are important in accurately diagnosing glaucoma.

Glaucoma can also be subdivided into primary and secondary types. Primary glaucomas have no identifiable pathological cause, such as NTG and LTG. Secondary glaucomas have an identifiable cause, such as a physical injury (traumatic glaucoma) or other ocular conditions such as uveitis, pigmentary dispersion syndrome and exfoliation syndrome that can lead to uveitic glaucoma, pigmentary glaucoma, and pseudoexfoliative glaucoma (PXG), respectively. Uveitis is an inflammatory disease of the eye that can result in debris obstructing the trabecular meshwork and increasing IOP. The treatment for uveitis is corticosteroids, which are also known to elevate IOP and may further contribute to glaucomatous damage. Pigment dispersion syndrome is when small pieces of iris pigment flake off and block the drainage canals, raising IOP. Similarly, those with exfoliative syndrome experience the flaking off of small granules from the outer lens, which also causes a blockage. Systemic diseases such as diabetes mellitus can also contribute to developing neovascular glaucoma. Diabetes affects the vascular system, putting the eye under hypoxic conditions, which can lead to RGC death and optic nerve damage. Congenital glaucoma is a more rare form of secondary glaucoma, and it occurs due to an innate dysfunction of the trabecular meshwork, which disrupts proper fluid drainage. In infantile glaucoma, this defect is present at birth, whereas for juvenile glaucoma, it develops around the age of three.

Other risk factors for glaucoma include family history, race, age, myopia, pigmentary dispersion syndrome, and diabetes (McMonnies, 2016). The actual

cause of glaucoma is still widely debated, and many different theories currently exist, with the most prevalent being biomechanical and neurodegenerative theories.

Biomechanical theories of glaucoma aim to explain changes in the eyes—such as increases in IOP—by applying mechanical laws to biological systems. Glaucoma can then be explained in terms of increased IOP causing physical strain on the structures within the eye, leading to vision loss. Having a high IOP will primarily affect the mechanically weakest point of the eye, which is the optic nerve head (Ethier, Barocas, & Downs, 2008; Burgoyne et al., 2005).

This increase in IOP affects not just the optic nerve head, but many other structures. RGC axons are damaged by compression, stretching and shearing forces (Ethier, Barocas, & Downs, 2008). The lamina cribrosa has also been shown to be negatively impacted, with the resulting shearing forces causing large shape deformations (Yan et al., 1994). When these structures change their shape, it can lead to a reduction of blood flow to nearby axons, further damaging RGCs (Quigley et al., 1984; Ethier, Barocas, & Downs, 2008).

The main problem for biomechanical explanations of glaucoma are the many cases of patients with low IOP who exhibit optic nerve damage. It has been proposed that individual biomechanical differences in optic nerve head structure and sensitivity to pressure exist, meaning that some individuals have lower thresholds for the level of IOP necessary to cause harm (Ethier, Barocas, & Downs, 2008; Yan et al, 1994). In fact, it may not just be differences in optic nerve head physiology, but a combined result of different connective tissue geometry, rigidity, and the amount of blood flow (Downs, Roberts, & Burgoyne, 2008).

Berdahl et al. (2008) support the theory that IOP leads to glaucoma, with the caveat that high IOP is only harmful if the cerebrospinal fluid pressure on the other side of the eye is low. If pressure is equalized, the optic disc is not under any strain and the risk of glaucomatous vision loss is minimized. Cases of patients with high IOP would then be protected from vision loss if they also had high cerebrospinal fluid pressure. This theory also explains how patients with LTG may still experience vision loss, as IOP is not the only determinant factor.

Neurodegenerative theories seek to explain glaucoma as a neurological disease that affects not just the eyes, but cortical structures as well. A post-mortem case study by Gupta et al. (2006) showed a patient with neurodegeneration in the optic nerve, posterior LGN, and part of the visual cortex just below the calcarine sulcus. This neural loss correlated with a superior visual field defect that was seen before the patient's death. This was the first study to demonstrate that neurodegeneration beyond the optic nerve occurs in patients with glaucoma. Gupta et al. (2009) later went on to conduct an in vivo study using MRI to further demonstrate LGN degeneration in patients with glaucoma. LGN and visual cortex degeneration has been confirmed by other research groups (Zhang et al., 2012; Zikou et al., 2012; Wang et al., 2016). Activation of the visual cortex also appears to be reduced as glaucoma's severity increases, demonstrating that the neurodegeneration seen in glaucoma is progressive (Murphy et al., 2016).

It is generally thought that RGC death and optic nerve damage occur first, while visual cortex neurodegeneration comes afterwards (Calkins & Horner, 2012); therefore, the deterioration of brain structures past the optic nerve is likely not a

cause of glaucoma, but rather a result of the disease's natural progression via anterograde trans-synaptic degeneration (Calkins & Horner, 2012). For example, patients with early stage POAG do not show any changes in grey matter volume (Li et al., 2012).

There has been an attempt to find commonalities between glaucoma and Alzheimer's disease in order to propose a neurodegenerative theory for the cause of glaucoma. Glaucoma resembles Alzheimer's in many ways, such as the fact that both are chronic, progressive, age-dependent neurodegenerative diseases. McKinnon (2003) refers to glaucoma as an "ocular Alzheimer's disease", suggesting that RGC death occurs due to a similar apoptotic cascade as in Alzheimer's disease. In Alzheimer's disease, the capase-3 protease cleaves an amyloid precursor protein, creating amyloid beta plaques. These plaques are neurotoxic, causing the apoptosis of neurons. A rat glaucoma model showed that RGC death occurred through the same apoptotic cascade as seen in Alzheimer's disease (McKinnon, 2003; McKinnon et al., 2002). Apoptotic RGCs have also been shown to be significantly more present in patients with glaucoma than in age-matched controls (Kerrigan et al., 1997). Apoptosis may cause increases in IOP as death of trabecular network cells can cause the beams to collapse and disrupt the flow of intraocular fluid (McKinnon, 2003; Agarwal et al., 1999).

Detection

RGC loss often happens well before any changes in vision are noted by the patient. Around 35-50% of RGCs can die before visual field tests will begin to show any deficits (Kerrigan-Baumrind et al., 2000; Falkenberg & Bex, 2007; Quigley, Dunkelberger, & Green, 1989). At this point, it is too late to restore vision that has already been lost.

In order to detect glaucoma at an early stage, patients with certain risk factors (such as ocular hypertension, narrow angles, or a family history of glaucoma) are monitored by their clinician. These high risk groups should be seen by their clinician at regular intervals to check for any suspicious developments. In conjunction with screening for risk factors, clinicians also use a battery of tests to diagnose glaucoma and track its progression. There is not a single, determinant factor that is indicative of glaucoma, which is why many attributes need to be taken into account in order to make an accurate diagnosis. These clinical tests can generally be split into measures of structure and function.

Structural diagnostic tests can assess IOP, the level of angle closure, optic disc and optic nerve damage, and the retinal nerve fiber layer thickness (RNFL). Tonometry is used to assess IOP, which is the main risk factor for glaucoma. A small device is placed on the cornea to measure pressure in mm Hg. If the pressure appears high, the angle between the iris and cornea can be measured using gonioscopy to ensure that it is not blocked or too narrow. If the angle is too narrow or completely closed, surgery may be proposed to reduce the IOP.

Optic disc "cupping" is also investigated to look for optic nerve damage using ophthalmoscopy. Pathological cupping occurs when the central area of the optic disc (which is a small pit where the optic nerve exits that has no photoreceptors) increases in size, encroaching on the healthy area of retina that makes up the outer segment of the optic disc. The amount of cupping can also be measured in a ratio of the cup to the disc using a retinal imaging device called optical coherence tomography (OCT). OCT also looks at retinal nerve fiber layer thickness (RNFL), as a thinner layer can indicate RGC death.

Functional tests look at the visual functioning of the patient. Visual field tests are the gold standard for testing peripheral visual function. The visual field test measures the patient's responses to flashing lights to find areas of poor visual functioning. Testing central visual acuity regularly is also important, but problems usually do not arise until moderate to late stage glaucoma.

OCT and visual field tests, which are the main tests used to monitor glaucoma progression, are further detailed in Appendix A.

Treatment

Current pharmaceutical treatments for glaucoma can slow down vision loss, but cannot stop the progression of the disease. Glaucoma-treating eye drops work by either reducing the amount of intraocular fluid production (e.g., beta-blockers) or increasing the rate of drainage within the eye (e.g., prostaglandin-related drugs). IOP is the main target for treating glaucoma, and IOP-lowering drops are effective

even in patients with LTG and NTG. Although IOP is already normal in these patients, further reducing IOP by 30% has been shown to significantly decrease visual field progression (Collaborative Normal-Tension Glaucoma Study Group, 1998).

In cases where IOP cannot be controlled with eye drops alone (such as when the angles are very narrow or closed), surgery is used to create alternative drainage pathways for the intraocular fluid to flow more freely.

The most common IOP-lowering surgery for glaucoma is trabeculectomy. This surgery removes part of the trabecular meshwork and Schlemm's canal, re-directing intraocular fluid through a series of flaps in the sclera to a reservoir or bleb (Weinreb & Crowston, 2005). The flaps are sutured in a way that ensures the intraocular fluid does not flow into the bleb too rapidly and cause it to burst or leak. Removing part of the trabecular meshwork allows for fluid to flow more easily, and the newly created bleb provides an extra space when there is a buildup of fluid in the eye. The bleb is located just under the surface of the sclera, usually hidden behind the upper eyelid. Part of the iris may also be removed during this surgery in an iridectomy, as the iris can potentially block the drainage pathway to the bleb. (Weinreb & Crowston, 2005). Similarly, an iridotomy uses a laser to create a small hole in the iris. Iridectomy or iridotomy can be performed without trabeculectomy, as creating an extra drainage pathway through the iris can also help reduce IOP.

A shunt or stent is a small, silicone tube that creates an open channel for intraocular fluid to drain into a reservoir called a plate (similar to a bleb) just underneath the sclera (Weinreb & Crowston, 2005). The fluid from the plate is then

gradually absorbed by the conjunctival blood vessels of the eye. This method is not as effective at reducing IOP, and therefore it is not the best choice for those with advanced glaucoma. Shunts or stents may be used as an alternative solution if trabeculectomy fails (Weinreb & Crowston, 2005).

Structure-Function Relationship

There are varying differences in the onset of the deterioration of function (visual acuity and overall visual functioning) and structure (RGC death and optic nerve damage) across patients with glaucoma. In the early stages of the disease, patients may have extensive RGC loss but still maintain 20/20 vision or better when reading (Klein et al., 1995). Due to the relatively high remaining visual function despite the RGC loss, it is not possible to detect glaucomatous abnormalities with visual field tests alone. However, there are some cases where functional changes occur first, or at the same time as structural changes.

As glaucoma advances, visual function appears to deteriorate at a faster rate than structure (Malik & Garway-Heath, 2012). Therefore, the relationship between visual field tests and structural measures (such as neuroretinal rim area) is thought to be curvilinear in nature (Garway-Heath et al., 2002). In other words, RGC loss occurs abundantly in very early stages of the disease, despite the fact that visual field loss is not apparent. In later stages of the disease, RGC loss tapers off and visual field loss occurs at a much more noticeable rate. Many have sought out to find the ideal model to describe how the loss of structure versus function occurs over time.

This is essential for estimating the rate at which glaucoma can progress in patients, allowing for potentially better patient management and treatment.

Harwerth et al. (2010) created a model for linking structural loss to functional loss by looking at a glaucoma disease model in monkeys. He trained the monkeys to perform visual field tests, and enucleated them 2 days after this test to obtain a histological RGC count (Harwerth et al., 2004). His model showed that RGC loss and visual field test sensitivities were linearly related at each eccentricity, when both measures were expressed in logarithmic units (Harwerth et al., 2004). Visual field tests are normally obtained on a logarithmic scale while OCT results use a linear scale. Transforming the data improves the accuracy of the model (Harwerth et al., 2004). These animal studies were crucial for developing an initial framework that could be tested out empirically with histological RGC counts, as opposed to estimates based on OCT results.

Harwerth extended his model to a human population, formulating the Harwerth Non-Linear Model (H-NLM). Instead of a post-mortem histological count, RGCs were estimated based on the thickness of the RNFL around the optic disc from time domain OCT (Harwerth et al., 2004; Harwerth et al., 2010). Since this method does not directly measure the number of RGCs, a topographic map had to be used in order to estimate where the RGC axons and their corresponding bodies lie.
The most recent version of the model includes a correction factor for age and glaucoma severity (Harwerth et al., 2008; Harwerth et al., 2010).

Raza and Hood (2015) later critiqued Harwerth's model, finding RGC estimates that were much greater than what would be expected based on human

histological studies (Curcio & Allen, 1990). The H-NLM estimates RGC counts using only the region of the retina assessed by the 24-2 visual field test, which does not take into account the extreme periphery of the retina. This difference in area may explain why overall RGC estimates are consistently larger when determined with OCT as compared to visual field tests. In addition, the correction factors for age and disease severity may not necessarily increase the accuracy of the model. The H-NLM overestimates the amount of RGC axon loss that typically occurs with age at a rate that's 2 to 4 times greater than human histological reports (Raza & Hood, 2015).

Hood and Kardon (2007) proposed the Hood and Kardon linear model (HK-LM), which is based on an earlier study by Hood et al. (2002) comparing visual sensitivity to multifocal visual evoked potentials. Multifocal visual evoked potentials are objective visual field tests that measure a patient's response to points of light using electrodes placed on the scalp. The RGC layer of the macula is measured directly as opposed to inferring RGC axons from the optic disc. The HK-LM posits that OCT results should have a linear relationship with visual field test sensitivities when both measures are expressed in linear units. The smaller number of assumptions about RGC axons is thought to lead to a model with a higher accuracy. This is possible through a newer form of OCT, frequency-domain OCT.

Unlike the H-NLM model, age or disease severity were not included in the HK-LM model. When directly comparing the two models, the HK-LM was more accurate than the H-NLM when both were run on the same data set of patients and suspects (Raza & Hood, 2015).

The original model Harwerth et al. (2010) developed to describe glaucomatous monkeys was adapted by Medeiros et al. (2012) to create the Combined Index of Structure and Function (CSFI). The CSFI is a weighted calculation using structural and functional data to estimate the amount of RGC loss, compared to the expected number in a healthy individual of the same age. The principle behind the CSFI is that combining structural and functional data should provide a more accurate assessment of glaucomatous disease staging than using the tests separately. The formula behind the CSFI also takes other aspects into account, such as age and visual field eccentricities, as well as changing numerous factors to be applicable to humans as opposed to monkeys. More can be read about the specific calculations used for the CSFI in the Methods section.

However, the results of the CSFI differ from Harwerth's H-NLM, despite the fact that this is where it is derived from. On average, RGC estimates based on OCT results are lower than those obtained from visual field tests (Raza & Hood, 2015). The opposite was seen for Harwerth's H-NLM. This discrepancy may be because the mean axon diameter for humans is 0.5-0.7 μm in histological studies, but Harwerth uses 0.9 μm for his model (Fitz-Gibbon & Taylor, 2012; Swanson & Horner, 2015), which would lead to underestimating the number of RGCs in early stage glaucoma.

Despite the discrepancies in estimating exact RGC numbers, the CSFI has proven itself to be a fairly reliable measure for glaucomatous staging. It can assess the degree of damage in patients with very early stage glaucoma (Tatham, Weinreb, & Medeiros, 2014) and is also more accurate at detecting glaucoma than using structural or functional measures in isolation (Medeiros et al., 2012a).

Our lab has been unable to find clinical measures that explained weaker vection responses in patients with glaucoma (Tarita-Nistor et al., 2014). The CSFI may be a clinical measure that is related to vection responses in these patients.

Vection

Description

Vection is the illusory sensation of self-motion that occurs when a stationary observer views a large, moving scene. The most common real life example of this occurs when someone in a stationary train looks out the window to see the train on the adjacent track begin to move but feels like she/he is actually moving. The feeling that the stationary train is actually the one that is moving is called vection. It is unusual for an entire scene to be moving in nature, so it is more practical for our brains to assume that we are the ones in motion (Howard, 1986). Vection can be subdivided into roll vection (rotation on the roll axis), circular vection (rotation around the yaw axis), and linear vection (forward or backward motion).

The pattern of movement of a large scene across the retina resulting from the relative motion between an observer and their environment is called optic flow (Gibson, 1950). For example, walking forward while looking straight ahead produces optic flow, with the environment appearing to expand from a central point. Optic flow is an important visual cue for determining our heading and maintaining postural stability during locomotion.

Optic flow may also occur when an observer is stationary but is viewing the motion of a scene as it passes by. This is rare in nature but occurs, for example, when we sit on a stationary vehicle (say, a train) while another large vehicle moves beside it. This phenomenon is reproduced in controlled laboratory experiments where seated observers are shown large, moving scenes on a monitor or a headset. In this case, the optic flow field mimics what would be seen by the observer moving through a scene but, during vection, there is no physical self-motion and the vestibular, somatosensory and proprioceptive information can be cancelled by the visual input. When optic flow is the only cue to self-motion, observers experience vection because visual information takes precedence over the vestibular and other inputs that register no real self-motion.

Vection involves a combination of inputs from the visual system, the vestibular system, the somatosensory system and the proprioceptive system (Dichgans et al., 1978). The illusion of vection occurs due to the visual input overriding the vestibular input, causing the brain to interpret the large moving scene as being a result of self-motion instead of the motion of an external image (Palmisano et al., 2011). It is possible to adapt to this sensation after staring at a vection stimulus for an extended period, as the vestibular system will eventually resolve the illusion (Palmisano et al., 2011).

Current fMRI studies show mixed results for precisely which areas of the brain are activated during vection. Vection responses to an optic flow stimuli caused greater activity in the middle temporal cortex, V6, the ventral intra-parietal area, and the parieto-insular vestibular cortex, compared to conditions where vection

responses were not present (Uesaki & Ashida, 2015). These data show some overlap with the results of Wall & Smith (2008) and Kovacs, Raabe, & Greenlee (2008). Wall & Smith (2008) found preferential activation for optic flow that was consistent with cues for egomotion (as opposed to inconsistent with egomotion) in the ventral intra-parietal area and the cingulate sulcus visual area (Wall & Smith, 2008). Vection induced from a three-dimensional optic flow field activated the middle temporal cortex, precuneus, and the dorsal region of the intraparietal sulcus (Kovacs, Raabe, & Greenlee, 2008). The optic flow field displayed a three-dimensional area of dots that appeared to pop out of the screen towards the viewer.

Brandt et al. (1998) showed that during the experience of vection, areas of the vestibular system were suppressed. This would be consistent with the theory that vision dominates, allowing one to feel motion even when the body is remaining entirely still. However, Nishiike et al. (2002) showed both visual and vestibular systems activating in unison—without any vestibular suppression. These various differences in results in terms of which areas are activated may be simply due to differences in methodology and differences in vection stimuli. A consensus has yet to be reached on how the brain triggers the sensation of self-motion, as it involves a complex interplay between various sensory systems.

Response Strength

Peripheral vision plays a large role in motion detection, which is very important in inducing vection responses. Several studies have shown that vection

responses are stronger when a moving display is shown to the peripheral visual field (Held et al., 1975; Johansson, 1977; Keshavarz & Berti, 2014). For example, Brandt, Dichgans, & Koenig (1973) showed that circular vection could be consistently induced by peripheral displays 30 degrees in size, but not by central displays of the same size. Up to 120 degrees of central vision could be obstructed, and participants still reported vection responses. Another study by Tarita-Nistor (2008) also demonstrates this notion. In age-related macular degeneration, patients develop central scotomas, which can be thought of as a natural way to occlude central vision. Much like the healthy participants who still felt vection strongly when shown only peripheral displays in the study by Brandt, Dichgans, and Koenig (1973), Tarita-Nistor et al. (2008) found that patients with age-related macular degeneration experience a stronger sensation of vection compared to controls.

However, other researchers refute the claim that stimulus eccentricity alone modulates vection responses. In attempting to replicate the study by Brandt, Dichgans, and Koenig (1973), Post et al. (1988) showed that vection could be induced by showing a 30 degree display to the centre. This refuted the theory of peripheral dominance for inducing vection responses. Howard and Heckmann (1989) put forth an argument to explain the discrepancy between these two findings, proposing that depth modulated vection responses. They tested this by showing a 54 by 44 degree central motion display either in front or behind of a rotating drum. The near central display produced less than half of the vection response of the far display. Vection responses could also be generated for central vision displays that were only 13.5 degrees. Therefore, motion stimuli that are

farther away and perceived as being in the background produce stronger vection responses. The Brandt et al. (1973) study likely created a foreground-background illusion, making it more difficult to experience vection with the central-only display, as it appeared in the foreground.

It is now accepted that peripheral vision is not the sole factor that results in stronger vection responses. Stimulus eccentricity can interact with other factors such as depth cues to alter the experience of vection. For example, the functional sensitivity hypothesis was proposed by Warren and Kurtz (1992) to explain that central and peripheral vision have different sensitivities to specific types of visual information, which is what leads to a discrepancy in vection response strength. Peripheral vision is thought to be specialized for detecting lamellar flow, in comparison to central vision which is specialized for both lamellar and radial flow (Warren & Kurtz, 1992). Radial flow has a pattern of movement where there is an expansion of points from one central spot. Lamellar flow is composed of vertical motion. Spatial frequency is another factor that affects vection responses, as an interaction was found between the spatial frequency of optic flow and eccentricity (Palmisano & Gillam, 1998). A peripheral stimulus produced the strongest sensation of vection when the stimulus had a high spatial frequency, whereas vection was weakest for a low spatial frequency.

Vection can also be strengthened by altering other factors of the stimulus, such as increasing the speed, or having a more densely populated pattern, up to a certain threshold (Brandt et al., 1973; Seno, Ito, & Sunaga, 2009).

Vection response strength can vary by observer. For example, circular vection responses are stronger in older populations (Paige, 1994). Males tend to experience significantly longer latencies for circular vection than females (Darlington & Smith, 1998). In addition, attention also appears to have an effect on vection, as when shown two opposing stimuli at once, vection is perceived in the direction corresponding to only the attended stimuli (but only when there are no depth cues) (Kitazaki & Sato, 2003). In a previous study, Tarita-Nistor et al. (2014) showed that patients with early stage glaucoma have a significantly weaker sensation of vection compared to controls with healthy vision.

The purpose of this thesis is to explain the presence of weaker vection responses in patients with early stage glaucoma using the CSFI in two experiments.

General Method

Overview

Our lab has demonstrated that patients with glaucoma exhibit a weaker sensation of vection (Tarita-Nistor et al., 2014). However, Tarita-Nistor et al. (2014) could find no clinical tests that explained why these weaker responses occurred.

The following two experiments tested vection responses in patients with early stage glaucoma and controls with normal vision. This study seeks to explain these weaker vection responses in terms of CSFI; an estimate of RGC loss that uses values from both OCT and visual field tests. By drawing information from tests

looking at both structure and function, the CSFI is a useful model for staging glaucoma that draws from both domains instead of just one.

The two experiments have different set-ups for inducing vection, with one being shown on a back-projected screen and the other on the Oculus Rift headset. The projection screen was initially used because it was large enough to cover most of someone's visual field. However, a large number of patients did not experience vection at all using this projection screen, so we used the more immersive Oculus Rift system in Experiment 2 to try to decrease this number.

Inclusion and Exclusion Criteria

The patients were medically treated to normalize their IOP. Mild glaucoma was defined as having central visual acuity at 20/40 or better, visual field mean deviations (MD) no lower than -5 dB, and no pronounced optic disc damage. All patients were undergoing treatment, and had a confirmed diagnosis of bilateral, open-angle glaucoma from their ophthalmologist at the Eye Clinic in Toronto Western Hospital. Controls were excluded if they were suspected of having an undiagnosed case of glaucoma due to family history, high IOP, or other ocular abnormalities. All cases of closed-angle glaucoma, other complicating ocular diseases (such as amblyopia or diabetic retinopathy), diabetes, vestibular system dysfunctions (such as vertigo), neurological diseases, or cognitive impairments were excluded. Any participant with a spherical refraction error worse than ±5 D was also not included.

Recruitment

Patients were recruited via thorough chart reviews at Toronto Western Hospital's Eye Clinic. Patients meeting the study criteria were contacted over the phone and asked if they were willing to participate in a study an hour before their regular appointment at the Eye Clinic. Controls were recruited using flyers posted around Toronto Western Hospital. The flyers provided our phone number so we could screen participants for eligibility via a phone interview before booking an appointment.

All participants provided informed consent (see Appendix C) after the study was described to them in detail. This research project was approved by the University Health Network Research Ethics Board and the Ethics Board of York University, and is in accord with all of the tenets of the declaration of Helsinki.

Clinical Tests

All participants underwent monocular visual field testing using the Humphrey Field Analyzer (model HFA-II 750; Carl Zeiss Meditec, Dublin, CA). The 24-2 Swedish Interactive Threshold Algorithm (SITA) standard was used to assess light sensitivity in decibels at each eccentricity as well as the mean deviations (MD). Visual field tests with fixation losses over 33% or false positive responses over 20% were considered unreliable and therefore discarded.

Using Spectral Domain OCT (model Cirrus; Carl Zeiss Meditec, Dublin, CA), a 200 x 200 optic disc cube protocol scan was taken. This was used to obtain the cup-to-disc ratio, the optic disc area, and the retinal nerve fiber layer (RNFL) thickness.

For patients, we used OCT and visual field results from their most recent visit to the ophthalmologist. If clinical data was older than 6 months from the scheduled date of psychophysical testing, we did not recruit that patient. For controls, these tests were performed before the vection evaluation.

Psychophysical Tests

Best-corrected visual acuity was measured monocularly (OD and OS) using a computerized version of the Early Treatment Diabetic Retinopathy Study (ETDRS) test. In Experiment 2, we used the computerized version of the ETDRS to also test binocular visual acuity. The distance between the viewer and the display was 6 m.

Both experiments tested vection using a different apparatus and stimulus, which are explained in detail in the Methods section for each experiment. Participants sat in a dark room and viewed a full-field, moving stimulus of white dots on a black background. Participants reported their vection latency and duration by pressing and holding the button of a button-response box. An additional measure of vection was used in each study, such as perceived or actual body tilt (Experiment 1), or a subjective vection strength rating (Experiment 2).

Data Analysis

One of our measures for correlating vection responses to clinical measures in patients with glaucoma was the CSFI, which combines the weighted average of structural (OCT) and functional (visual field) data into an equation to calculate the percentage of RGC loss for each eye (Medeiros et al., 2012; Tatham et al., 2014).

Calculating RGC loss is a multiple step equation that uses various clinical and demographic values.

First, using values from visual field tests (also called Standard Automated Perimetry or SAP), the SAPrgc is calculated. This is a weighted average that uses sensitivity measurements from the visual field test at each eccentricity, to estimate the number of RGCs (see Appendix A for how the visual field values were obtained). An RGC estimate is formulated for each location on the retina, and these are added up to make the total estimate.

$$\boldsymbol{m = [0.054\,x\,(ec\,x\,1.32)] + 0.9} \quad \textbf{(1)}$$

$$\boldsymbol{b = [-1.5\,x\,(ec\,x\,1.32)] - 14.8} \quad \textbf{(2)}$$

$$\boldsymbol{gc = \left\{\frac{[(s-1) - b]}{m}\right\} + 4.7} \quad \textbf{(3)}$$

$$SAP_{rgc} = \sum 10^{\,gc\,x\,0.1} \quad \textbf{(4)}$$

m = slope
b = intercept
gc = ganglion cell quantity (dB)
s = sensitivity (dB)
ec = eccentricity

The values m and b are part of a linear function that plots ganglion cell quantity and the sensitivity value for that eccentricity. Therefore, the SAPrgc is the sum of the RGC estimate for each eccentricity, corresponding to a different area of the retina. This sum, in equation 4, is composed of all 54 points in the visual field

test. Note that ganglion cell quantity and visual field sensitivity are both expressed in db, which is a logarithmic scale, to stay consistent with the logarithmic scale used for visual field results.

Secondly, the OCTrgc is calculated. The OCTrgc is another RGC estimate, but this equation uses primarily structural data obtained from OCT scans. Some functional data from visual field tests are also used.

$$\boldsymbol{d = (-0.007\ x\ age) + 1.4} \quad \textbf{(5)}$$

$$\boldsymbol{c = (-0.26\ x\ MD) + 0.12} \quad \textbf{(6)}$$

$$\boldsymbol{OCTrgc = 10^{\{[log([average\ RNFL\ thickness\ x\ 10870\ x\ d])x\ 10-c]\ x\ 0.1\}}} \quad \textbf{(7)}$$

d = axonal density
c = correction factor
MD = mean deviation (from visual fields)

The axonal density (axons per micrometer squared) estimation takes age into account, since the density of the optic nerve degrades over time. The correction factor is to adjust for the severity of the disease.

Thirdly, the SAPrgc and the OCTrgc values are combined to calculate the weighted RGC count (wrgc). Changes in RNFL thickness (OCT values) are generally much easier to detect than visual field values in early stage glaucoma. Therefore, OCTrgc is weighted higher in patients with early stage glaucoma, while SAPrgc is in advanced glaucoma. The wrgc is a more accurate estimate of the number of RGCs than OCTrgc or SAPrgc alone (Medeiros et al., 2012).

$$\boldsymbol{wrgc = \left(1 + \frac{MD}{30}\right) x\ OCTrgc + \left(-\frac{MD}{30}\right) x\ SAPrgc} \quad (8)$$

The lowest visual field value possible is -30dB, which is why the MD is divided by 30.

Finally, the wrgc has to be transformed to the CSFI, which is the percentage of total RGC loss based on the expected amount of RGCs a healthy person of that age should typically have. In order to do this, Medeiros et al. (2012) had to use estimates for what the expected number of RGCs would be for a healthy individual. A linear regression model was created relating wrgc to age and optic disc area in a control population. The model was then used as a predictor of RGC number based on one's age and optic disc area. The CSFI finds the difference between the wrgc and the expected RGC count (from the linear regression model), and then converts it to a percentage out of 100. Therefore, A CSFI of 25 indicates that 25% of RGCs have died (based on the expected amount of RGCs that should be present). A negative CSFI value indicates a surplus of RGCs compared to the expected amount.

$$\boldsymbol{expected\ RGC\ number = 1301098 - (age\ x\ 9249) + 116070\ x\ optic\ disc\ area} \quad \mathbf{(9)}$$

$$\boldsymbol{CSFI = \left[\frac{expected\ RGC\ number - wrgc}{expected\ RGC\ number}\right] x\ 100} \quad (10)$$

Experiment 1

In this experiment, vection was induced using a large, moving dot pattern displayed on a projection screen. When vection was experienced, this stimulus caused participants to tilt their body in the opposite direction of rotation, allowing us to measure body tilt as an indicator of vection strength. Vection latency and duration was measured as well. In addition, clinical measures were taken in order to calculate the CSFI and determine disease severity.

Participants

We tested 22 (mean age, 70.3 [±6] years) patients with mild glaucoma. 27% (6/22) were female. The mean IOP of both eyes for this group was within the normal range (13.0 [±4] mm Hg). The patient population consisted of two people of Asian descent, and one of African descent, while the rest of the group was white.

In addition, 18 controls with healthy vision were tested. Of those, we used 11 (mean age, 55.5 [±9] years) for the analysis (see Table 2 caption for reasons for exclusion). Thirty-six percent (4/11) were female. Although our initial intention was to collect age-matched data in the control group, we had problems recruiting suitable participants, so exceptions had to be made in order to obtain a large enough sample. As a result of this, the controls were significantly younger than the glaucoma group , $t(21) = 4.40$, $p < 0.001$. Of all the participants, only one control was of African descent, which is a population that is 5-6 times more likely to develop POAG than Caucasians (Tielsch et al., 1991).

Demographic Information

TABLE 1.
Demographic Information of Patients with Glaucoma

				Visual Acuity (logMAR)		IOP	
ID	**Diagnosis**	**Age (years)**	**Gender**	**OD**	**OS**	**OD**	**OS**
G1	POAG	67	M	-0.02	0	15	15
G2	POAG	73	M	-0.04	-0.04	12.5	10
G3	POAG	68	F	-0.1	-0.1	12.5	12
G4	LTG	65	M	-0.1	-0.1	17	13
G5	POAG	74	M	0.2	0	15	16
G6	LTG	64	F	-0.08	-0.08	13	13
G7	POAG	64	F	0.1	0	14	14
G8	POAG	62	M	-0.02	-0.08	16	16
G9	POAG	80	M	0.16	0.24	9	10
G10	NTG	72	M	0	-0.1	10	10
G11	NTG	67	M	0	0	12	12.5
G12	POAG	77	M	0.1	0.26	13	16
G13	POAG	76	F	-0.08	0	8	10
G14	POAG	63	M	0.14	-0.06	16	18
G15	NTG	75	F	0	0	9	8
G16	POAG	69	M	-0.1	0	---	---
G17	POAG	71	M	0.02	0.14	---	---
G18	POAG	70	M	0.14	0.02	14	14
G19	PXG	79	M	0.14	0.42	---	---
G20	PDG	59	M	-0.1	0.34	18	12
G21	POAG	80	M	0	0	---	---
G22	POAG	72	F	0.04	0.06	---	---
MEAN	---	70.32	---	0.02	0.04	13.18	12.91
SD	---	6.08	---	0.10	0.15	2.92	2.75

IOP values were from the date of testing, but this was looked up after the entire study was finished. Unfortunately, some patients no longer had charts available at the clinic at that time, preventing IOP values from being obtained.

TABLE 2.
Demographic Information of Controls

				Visual Acuity (logMAR)	
ID	**Diagnosis**	**Age (years)**	**Gender**	**OD**	**OS**
C1	Normal	45	F	-0.1	-0.1
C2	Normal	46	M	-0.1	-0.1
C3	Normal	72	M	-0.08	-0.08
C4	Normal	62	F	-0.1	0
C5	Normal	57	F	-0.24	-0.1
C6	Normal	58	M	-0.28	0
C7	Normal	58	M	-0.04	-0.02
C8	Normal	56	M	-0.06	0.06
C9	Normal	65	M	-0.04	-0.10
C10	Normal	50	M	0.00	-0.10
C11	Normal	42	F	-0.1	-0.1
MEAN	---	55.55	---	-0.10	-0.06
SD	---	9.13	---	0.08	0.06

Controls did not have their IOP measured, but none of them had been diagnosed with ocular hypertension by their ophthalmologist and were expected to have IOP within the normal range.

TABLE 3.
Demographic Information: Excluded Participants

				Visual Acuity (logMAR)	
ID	**Diagnosis**	**Age (years)**	**Gender**	**OD**	**OS**
CA	Suspect	72	F	0.24	0.14
CB	High Myope	55	F	0.02	-0.06
CC	Normal	52	F	0.12	0.16
CD	Normal	50	M	0.26	0.36
CE	Normal	76	M	0.3	0.22
CF	High Myope	48	F	-0.1	-0.24
CG	Suspect	55	F	0	0
MEAN	---	58.29	---	0.12	0.08
SD	---	11.09	---	0.15	0.20

Only controls had to be excluded from the data analysis.

CA, CG: they were suspected of having previously undetected glaucoma, based on the severity of their clinical tests (see Table 6).

CB, CF: they did not meet our inclusion criteria, as they had refraction outside of ±5 D.

CC, CE: they had visual field data that was too severe for non-glaucomatous participants, as well as fleeting diplopia.

CD: this participant felt panicked during the vection stimulus viewing, and we had to stop the experiment. CD may not have understood several of the other tasks as well.

Clinical Information

TABLE 4.
Clinical Information: Patients with Glaucoma

	MD (db)		RNFL		C/D Ratio		CSFI	
ID	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**
G1	-0.43	-2.25	93	85	0.66	0.65	-2.02	16.05
G2	-0.65	-3.34	78	67	0.73	0.77	17.59	36.82
G3	-1.88	-1.17	92	90	0.64	0.59	10.02	4.47
G4	---	-1.67	115	107	---	0.4	---	-4.34
G5	-2.11	-1.17	82	77	0.73	0.72	20.13	21.55
G6	-3	-1.75	64	60	0.62	0.72	30.76	36.41
G7	0.98	0.27	83	82	0.68	0.65	2.28	7.73
G8	-0.63	-0.61	94	84	0.7	0.65	5.22	14.71
G9	1.09	---	90	94	0.66	0.66	-2.63	---
G10	-0.27	---	74	80	0.76	0.69	24.88	---
G11	-0.08	---	80	70	0.76	0.82	15.50	---
G12	-0.49	-3.5	102	94	0.7	0.66	-6.11	19.12
G13	-1.61	-2.46	91	93	0.59	0.62	9.35	12.00
G14	-1.2	-4.07	96	88	0.68	0.73	2.22	24.64
G15	-1.68	-0.16	89	90	0.64	0.7	10.68	3.38
G16	0.91	-1.66	76	65	0.52	0.45	6.63	25.20
G17	-4.77	0.09	50	69	0.76	0.67	48.34	17.72
G18	0.29	-0.57	76	77	0.69	0.66	13.22	15.25
G19	-4.03	-1.34	79	101	0.71	0.59	30.96	15.67
G20	---	---	61	53	0.76	0.77	---	---
G21	-2.46	0.61	60	81	0.78	0.65	36.17	4.52
G22	---	---	---	---	---	---	---	---
MEAN	-1.16	-1.46	82.14	81.29	0.69	0.66	14.38	15.94
SD	1.63	1.35	15.30	13.73	0.07	0.10	14.53	11.12

MD: values were excluded if the amount of fixation losses or false positives surpassed our cut-off.

RNFL and C/D Ratio: Inaccurate scans were discarded (eg. unable to identify the border of the optic disc, biologically impossible values).

CSFI: If at least one of MD, C/D Ratio, or RNFL could not be used, the CSFI could not be calculated.

TABLE 5.
Clinical Information: Controls

	MD (db)		RNFL		C/D Ratio		CSFI	
ID	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**
C1	0.57	1.79	97	93	0.65	0.67	-2.93	-4.04
C2	0.01	0.2	94	90	0.45	0.47	0.94	5.26
C3	0.44	-0.83	80	73	0.55	0.56	7.32	18.22
C4	-0.71	-0.38	81	83	0.52	0.42	10.65	8.69
C5	1.58	0.51	84	77	0.46	0.55	-0.67	13.99
C6	0.41	-3.26	82	91	0.6	0.32	4.79	12.49
C7	2.61	3.05	106	97	0.46	0.47	-33.86	-23.83
C8	-1.46	-0.88	106	104	0.63	0.6	0.59	-0.96
C9	-0.98	-0.05	97	97	---	---	-4.77	-9.57
C10	0.85	-0.19	91	86	0.69	0.66	-0.59	7.19
C11	0.04	1.24	105	104	0.44	0.5	-7.40	-10.80
MEAN	0.31	0.11	93.00	90.45	0.55	0.52	-2.36	1.51
SD	1.15	1.63	10.17	10.10	0.09	0.11	11.68	12.68

G9: the OCT scan did not accurately assess the borders of the optic disc, preventing the recording of a C/D ratio that was biologically possible.

TABLE 6.
Clinical Information: Unused Data

	MD (db)		RNFL		C/D Ratio		CSFI	
ID	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**
CA	-2.53	-0.85	72	71	0.70	0.71	31.72	27.10
CB	-0.93	-2.04	70	69	0.67	0.44	29.02	29.33
CC	-3.21	-3.63	106	101	0.57	0.61	8.76	14.94
CD	0.38	-0.99	109	103	0.71	0.71	-11.84	-0.03
CE	-5.66	-3.02	84	87	0.65	0.68	33.75	15.92
CF	0.55	0.65	73	74	0.46	0.33	21.21	14.27
CG	-1.49	-2.05	75	72	0.46	0.45	23.37	28.72
MEAN	-1.84	-1.70	84.14	82.43	0.60	0.56	19.43	18.61
SD	2.18	1.44	16.59	14.60	0.11	0.15	16.12	10.62

The reasons for excluding these participants are explained in Table 2. Note that the averages of the excluded controls appear closer to those of the patients.

Apparatus

Vection Test

Participants sat in front of a large, 130 x 130 degree projection screen at a viewing distance of 40cm. A rear projection system was utilized. The stimulus was a high contrast pattern of white dots (with a diameter of 2 deg) on a black background. The dots were in a random pattern with a density of 0.005 dots/deg^2 and they rotated at an angular speed of 45 deg/s. Stimulus rotation was in a clockwise motion, as if staring at a turning wheel from the side, in order to induce roll vection. The stimulus was created in VPixx (VPixx Technologies, Inc, Montreal, Quebec, Canada).

A button-response box was used to measure vection latency and duration. Vection-induced tilt was measured using a specially made tilt sensor attached to a headband. The amount of tilt is determined using one out of three total axes from an accelerometer (Freescale Semiconductors Inc, Austin, TX). The signal from the tilt sensor was sent to a laptop via a USB cable at a rate of 100 Hz. Subjective tilt ratings were obtained using a wooden joystick attached to a protractor that could be moved by the participant to indicate the amount they tilted during a trial.

Procedure

Participants were seated in a dark room in front of the projection screen. An eye patch was worn to cover one eye during each 2 minute trial. Participants were placed at a distance of 40 cm from the screen and instructed not to let their feet or knees touch either the screen or the ground. This was to avoid weakening the illusion of self-motion by making the participant feel anchored.

Participants were told to look straight ahead with a relaxed gaze and not to follow any of the dots with their eyes. In the event that they felt vection, they were told to press and hold a response button for the entire duration of that sensation. If the feeling was intermittent, they could press and release the button several times in accordance with their personal experience. We used the button response box to report vection latency and total vection duration.

A headband-mounted tilt sensor was also worn in order to measure upper body tilt as a more objective vection measure. Viewing the stimulus caused participants to instinctively tilt in the opposite direction, and participants were not

always aware of their own movement. One experimenter was always seated behind the participant to intervene in the event that the body tilt became so large that they were in danger of falling. The maximum tilt and mean tilt was measured for each trial. After each trial was over, participants reported their subjective tilt by moving a joystick on a protractor to estimate the angle of their maximum tilt.

Data analysis

A 2 x 2 [Group (glaucoma, control) x Eye (OD, OS)] mixed factorial ANOVA was run to determine if there was a significant difference in vection responses based on which eye was used. No significant main effect of eye was found (smallest $p = .21$), therefore all further analyses were independent t-tests or Pearson correlations looking at both eyes averaged together. For cases where data from only one eye could be used, the value obtained for that eye was considered to be the average. Only those who experienced vection were included in the analysis, as the vection latency was indeterminate if they never pressed the button. All statistical tests use an α level of .05.

Results

Forty-one percent (n=9) of patients with glaucoma, but only 9% (n=1) of control participants did not experience vection in any of the conditions (i.e., both left eye viewing and right eye viewing). It is interesting that so many patients were completely unable to experience vection, which demonstrates one aspect of the

dysfunctional vection responses of people with glaucoma. All individuals who did not experience vection were excluded from further analysis. The remaining sample contained 13 patients with glaucoma and 10 controls.

The two groups were not age-matched, as the control group was significantly younger than the patients with glaucoma ($t(21) = 4.4$, $p < .001$). Our patient population also had significantly worse average visual acuity, visual field tests, and cup-to-disc ratio.

TABLE 7.
Between Groups (Glaucoma and Control) t-tests

Comparison	df	t	p
Visual Field MD	20	3.82	0.001*
RNFL	21	1.96	0.064
Cup-to-Disc Ratio	21	3.68	0.001*
CSFI	20	2.89	0.009*
Visual Acuity	21	2.27	0.034*
Age	21	4.40	< 0.001*

Our patients had early stage glaucoma, but it was not so mild that they did not have noticeable deficits compared to controls.

Vection Latency

Patients with glaucoma did not have a significantly different vection latency than controls ($t(21) = 1.85$, $p = .08$). However, the data were highly variable in

patients with glaucoma, as the standard deviation was greater than the mean (M = 27.63 s, SD = 30) and there was a positive skew (skewness = 1.67).

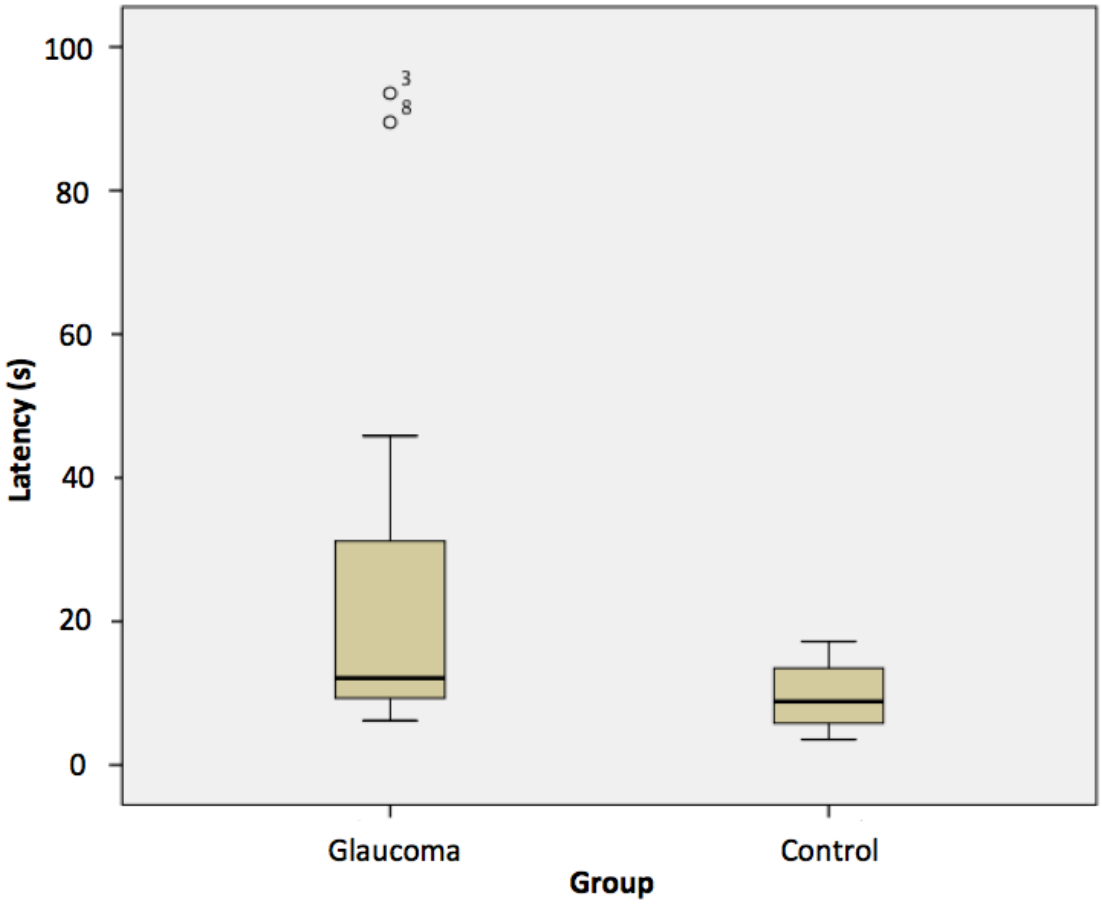

Figure 1. *Box plot of the vection latency of patients with glaucoma and controls. Note the wider spread of the data for the glaucoma group and the two outliers (patients 3 and 8)*

In order to correct for the abnormal spread of our data, we used a log transformation of the vection latency values for both groups. Doing this removed all outliers and reduced the positive skew of the data. This method found that the log of vection latency was significantly longer in patients with glaucoma ($t(21) = 2.39$, $p =$

.03), assuming unequal variances. The mean vection latency for the patients with glaucoma (M = 27.63 s) is just under three times as large as the control group (M = 9.58 s).

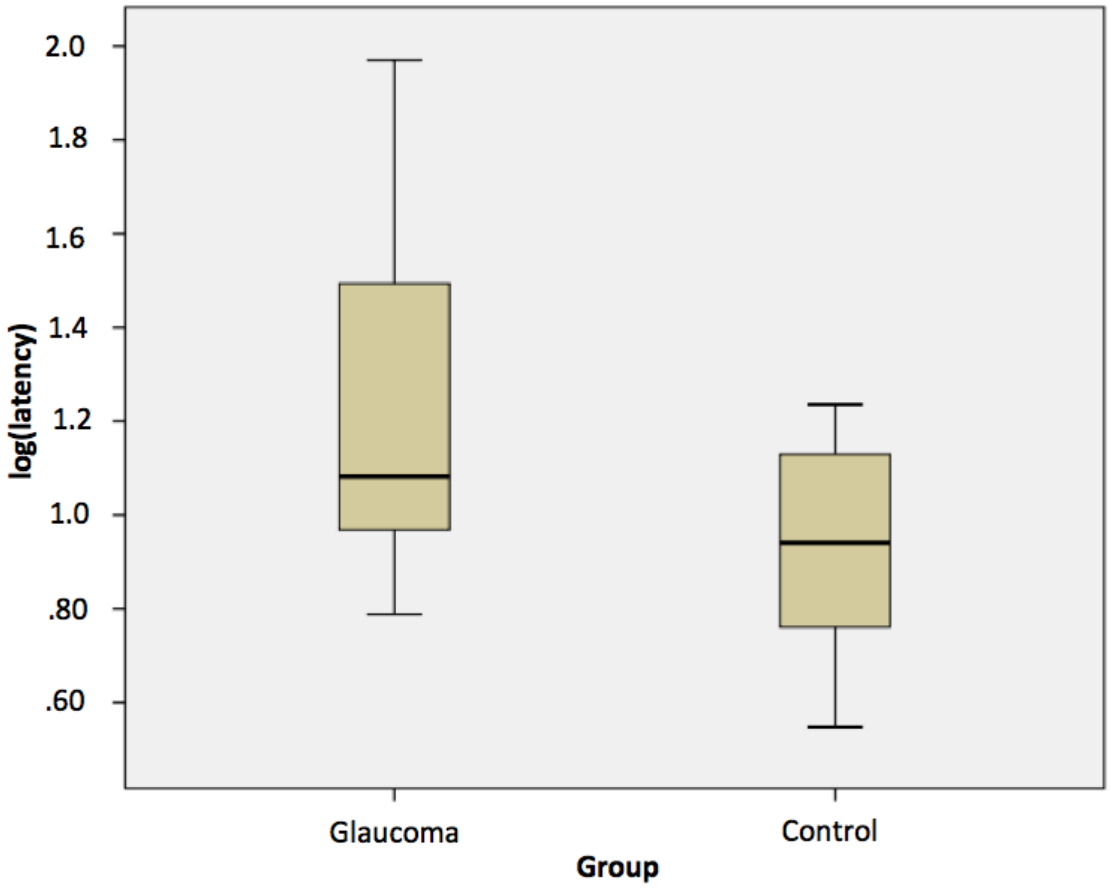

Figure 2. *Box plot showing the log of vection latency of patients with glaucoma and controls.*

Vection Duration

There was no significant difference for vection duration between the two groups ($t(21) = 0.68$, $p = .50$).

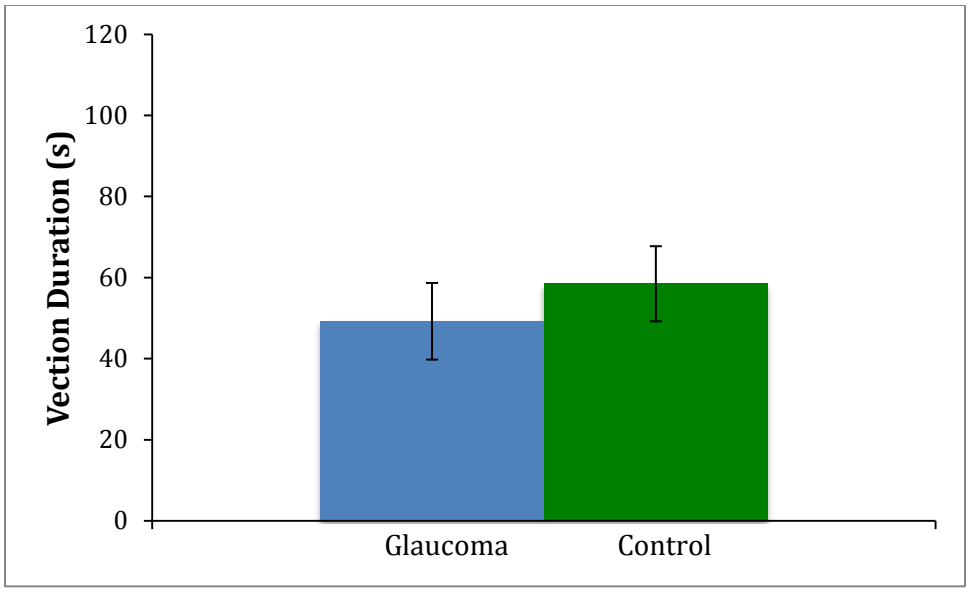

Figure 3. *Vection duration with standard error bars*

Tilt

Objective tilt measures in the glaucoma group also showed no significant difference from controls, including mean body tilt ($t(21) = 0.29$, $p = .78$) and max body tilt ($t(21) = 0.26$, $p = .80$). However, subjective ratings of mean body tilt were significantly lower in patients with glaucoma ($t(21) = 2.12$, $p = .046$).

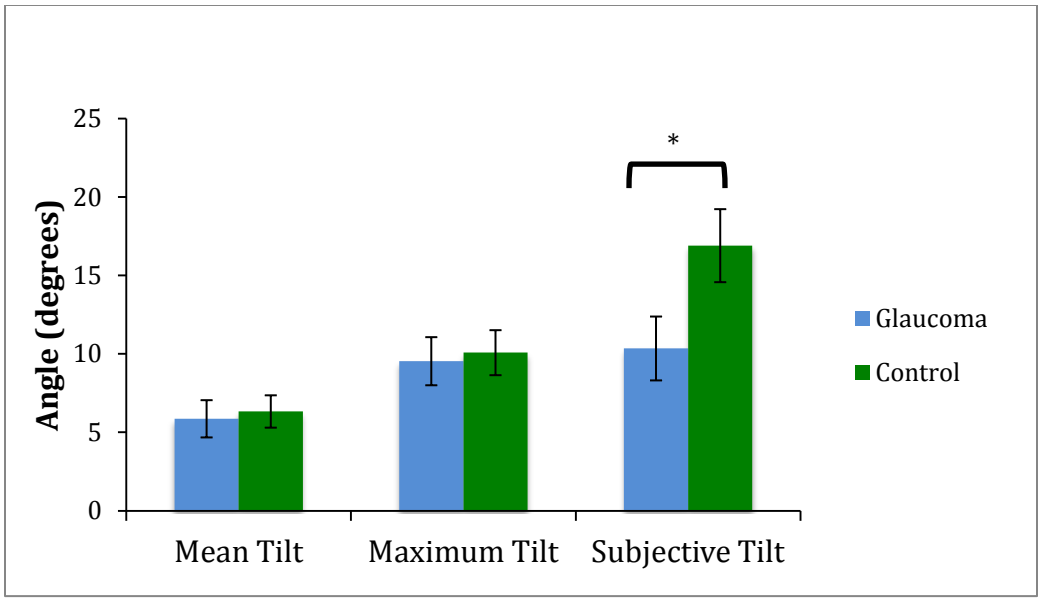

Figure 4. *Different tilt responses of patients with glaucoma and controls.*

Clinical Explanation of Vection Responses

The main purpose of this study was to find an explanation for weaker vection responses in patients with glaucoma. As such, the following clinical measures were related to all the vection and tilt measurements in patients with glaucoma: CSFI, RNFL, cup-to-disc ratio, visual acuity, and visual field MD. There was no significant relationship between CSFI and vection latency or vection duration. A significant correlation was found between CSFI and subjective tilt estimates ($r(11) = 0.75$, $p = .004$). These results are contrary to our predictions, as it shows that a higher CSFI (more RGC loss) leads to higher subjective tilt estimates (a stronger sensation of vection). Visual field MD also had a significant, negative correlation with subjective tilt estimates ($r(11) = -0.70$, $p = 0.01$). This was also contrary to our hypothesis, as

high visual field MD (better visual functioning) was related to lower subjective tilt estimates.

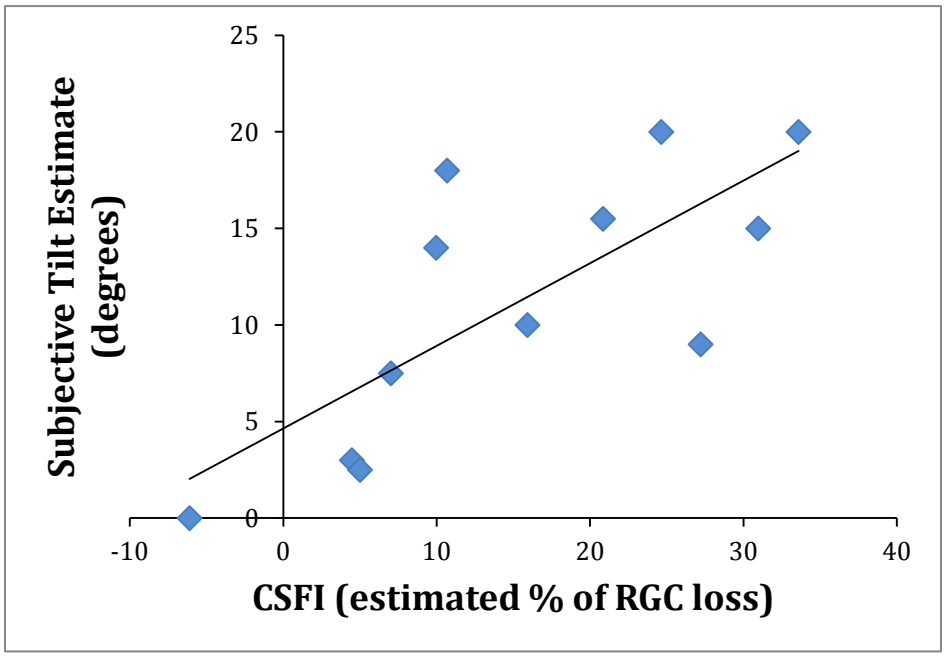

Figure 5*. CSFI and subjective tilt in patients with glaucoma*

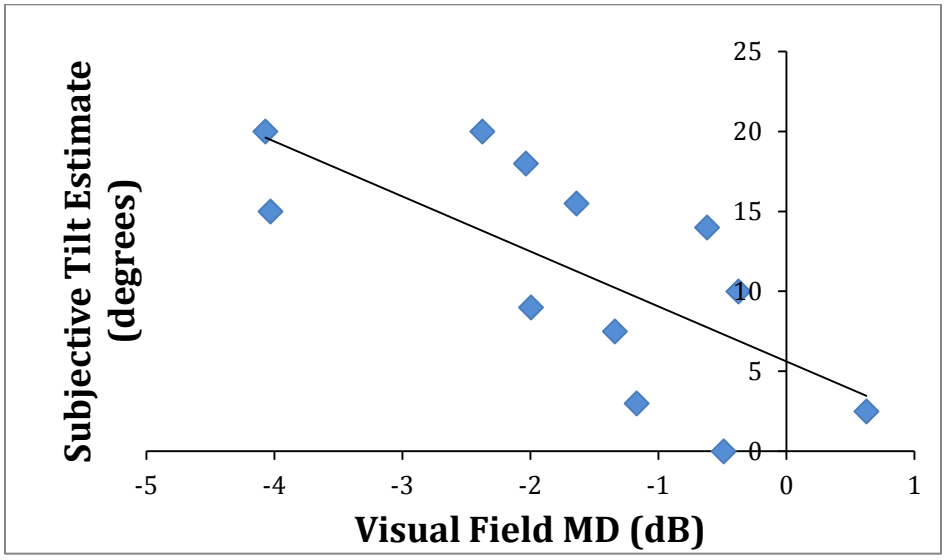

Figure 6. *MD and Subjective Tilt in Patients with Glaucoma*

Experiment 2

Because 40% of patients in Experiment 1 did not experience vection, we used the Oculus Rift – a virtual reality system that displays images on a headset – in order to create a stronger sensation of vection. This headset provides an immersive environment that blocks out external stimuli in a way that was not possible for the projection screen in Experiment 1. This experiment also seeks to relate CSFI to weaker vection responses in patients with glaucoma, but using a stimulus that would ideally be strong enough to induce vection responses in more patients with glaucoma. Vection latency and duration was measured with the same button response box. Body tilt was not measured in this experiment because the stimulus induced circular vection. Instead, participants were asked to rate their subjective vection response on a numerical scale.

Participants

For the group with mild glaucoma, we tested a total of 24 patients. Some patients did not meet our inclusion criteria, so the data of 21 patients (mean age, 71.1 [±5] years) were used (see Table 8 caption for exclusion details). For this group, 38% (8/21) were female. There were two people of Asian descent, and one of African descent, while the rest of the group was white.

The control group had a total of 23 participants with normal vision. We had to exclude those who did not meet our inclusion criteria, leaving us with 17 controls (mean age, 61.5 [±10] years) for the analysis (see Table 8 caption for exclusion details). Our two groups were not age-matched, despite our initial intentions to do

so, as obtaining a large enough age-matched sample was difficult. A t-test showed that the control group was significantly younger than the glaucoma group ($t(21) = 4.4$, $p < .001$). Fifty-five percent (10/18) of the controls were female. Our control group contained three people of Asian descent, and one of African descent, while the rest were white.

Demographic Information

TABLE 8.
Demographic Information of Patients with Glaucoma

				Visual Acuity (logMAR)			IOP	
ID	**Diagnosis**	**Age (years)**	**Gender**	**OD**	**OS**	**OU**	**OD**	**OS**
G1	POAG	74	M	-0.1	-0.1	-0.1	10	10
G2	POAG	65	F	0.1	-0.1	-0.08	14	12
G3	POAG	64	M	0	0	0	18	16.5
G4	POAG	69	M	0	-0.1	0	---	---
G5	NTG	61	F	0.1	0	0.04	16	12
G6	NTG	77	F	0.1	0	0.1	17	14
G7	POAG	73	F	-0.1	0	0	14	13.5
G8	NTG	72	M	---	0	---	12	15
G9	LTG	75	M	0.1	0.1	0.14	13	13
G10	POAG	72	M	0	0.1	0	13	13.5
G11	POAG	75	M	0	0	0.02	6	10
G12	POAG	70	M	-0.1	0	0	13	13
G13	NTG	65	M	0.1	0.1	0.06	10	10
G14	NTG	67	M	-0.08	0.02	-0.06	7	10
G15	POAG	75	F	-0.1	0.44	-0.1	12	13
G16	POAG	68	M	0.12	0.28	0.04	13	8
G17	NTG	73	M	0	-0.1	-0.1	14	12
G18	LTG	69	F	-0.04	---	-0.06	14	14
G19	POAG	74	F	0.14	0.3	0.04	3	10
G20	POAG	80	M	0.14	0.2	0.1	10	14.5
G21	LTG	76	F	0.1	0.1	0	10	10
MEAN	---	71.14	---	0.02	0.06	0.00	11.95	12.20
SD	---	4.86	---	0.09	0.15	0.07	3.66	2.18

TABLE 9.
Demographic Information of Controls

				Visual Acuity (logMAR)		
ID	**Diagnosis**	**Age (years)**	**Gender**	**OD**	**OS**	**OU**
C1	Normal	74	M	-0.1	-0.1	-0.08
C2	Normal	62	F	-0.1	0	---
C3	Normal	56	M	-0.1	-0.1	---
C4	Normal	49	M	0.2	0.2	---
C5	Normal	54	M	-0.1	-0.1	---
C6	Normal	52	F	-0.1	-0.1	---
C7	Normal	54	F	-0.1	-0.1	-0.02
C8	Normal	47	M	-0.3	-0.3	-0.1
C9	Normal	68	F	0.1	0.1	0.06
C10	Normal	70	F	0	-0.1	-0.1
C11	Normal	65	F	0	-0.1	-0.06
C12	Normal	62	M	-0.1	-0.1	-0.1
C13	Normal	49	F	0	0	0.04
C14	Normal	75	F	-0.1	0.1	0.1
C15	Normal	59	F	-0.1	-0.1	-0.1
C16	Normal	71	F	0.4	0	0.02
C17	Normal	79	M	0.2	0.04	0.04
MEAN	---	61.53	---	-0.02	-0.04	-0.03
SD	---	10.08	---	0.16	0.11	0.07

*G8, G18**:** only one eye was tested because the other eye did not meet our inclusion criteria (secondary glaucoma due to a sports injury, or unilateral glaucoma only).*

*G4**:** IOP values were not available in the patient's chart.*

C2-C6: We made an amendment to the protocol part way through and therefore only collected binocular data after the amendment.

TABLE 10.
Demographic Information: Excluded Participants

				Visual Acuity (logMAR)			IOP	
ID	**Diagnosis**	**Age (years)**	**Gender**	**OD**	**OS**	**OU**	**OD**	**OS**
GA	POAG	54	F	0	0.04	0.06	13	15
GB	POAG	73	M	-0.1	-0.1	-0.1	12	11.5
GC	POAG	58	F	-0.08	0.02	0	12	15
MEAN	---	61.67	---	-0.06	-0.01	-0.01	12.33	13.83
SD	---	10.02	---	0.05	0.08	0.08	0.58	2.02
CA	Amblyopia	61	F	-0.04	0.46	---	---	---
CB	Normal	61	F	0.51	0.4	---	---	---
CC	Normal	66	F	0	-0.06	0	---	---
CD	Normal	50	F	-0.1	0	0	---	---
CE	Suspect	60	F	0.14	0.14	0.04	---	---
CF	Suspect	74	F	0.1	0.04	0	---	---
MEAN	---	62	---	0	0	0	---	---
SD	---	7.87	---	0.22	0.22	0.02	---	---

GA, GC: they did not understand many of the tasks. GC also had very poor clinical tests, indicating glaucoma that was closer to the moderate stage.

GB: their visual fields were outside our inclusion criteria.

CA: amblyopia was present in this participant.

CB: visual acuity was outside out inclusion criteria.

CC, CD: they displayed poor comprehension of all tasks, and fell asleep during testing.

CE, CF: they were suspected of having early, undiagnosed glaucoma.

Clinical Information

TABLE 11.
Clinical Information of Patients with Glaucoma

	MD (db)		RNFL		C/D Ratio		CSFI	
ID	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**
G1	-0.93	-0.2	70	81	0.77	0.7	30.48	14.65
G2	2.46	1.83	85	80	0.70	0.66	-7.02	3.90
G3	1.01	0.2	95	86	0.70	0.64	-3.79	8.93
G4	2.83	1.22	76	76	0.71	0.69	14.34	13.96
G5	1.55	0.59	69	59	0.52	0.68	33.96	19.68
G6	-2.5	-0.81	78	93	0.74	0.65	23.60	-2.77
G7	---	-4	88	72	0.78	0.76	---	35.60
G8	---	-1.58	---	93	---	0.52	---	-0.54
G9	-2.7	-0.75	76	73	0.85	0.77	13.30	18.77
G10	-0.49	-1.52	72	71	0.7	0.67	21.37	25.18
G11	0.12	1.57	70	84	0.8	0.71	24.60	4.56
G12	---	---	---	---	---	---	---	---
G13	-1.53	-1.67	63	63	0.67	0.5	34.08	30.24
G14	0.58	0.18	80	85	0.67	0.64	10.99	6.14
G15	1.61	1.34	93	90	0.48	0.44	-19.85	-13.51
G16	0.13	-4.58	70	61	0.72	0.78	22.19	43.99
G17	---	---	72	---	0.67	---	---	---
G18	1.23	---	75	---	0.52	---	14.24	---
G19	-1.1	-0.33	78	90	0.69	0.68	17.03	5.37
G20	0.33	-2.82	76	85	0.6	0.59	6.44	12.26
G21	2.52	1.84	99	87	0.68	0.74	-23.91	1.67
MEAN	0.30	-0.53	78.16	79.39	0.68	0.66	12.47	12.67
SD	1.68	1.91	9.71	10.80	0.10	0.09	17.28	14.42

MD: values were excluded if the amount of fixation losses or false positives surpassed our cut-off.

RNFL and C/D Ratio: Inaccurate scans were discarded (eg. unable to identify the border of the optic disc, biologically impossible values).

CSFI: If at least one of MD, C/D Ratio, or RNFL could not be used, the CSFI could not be calculated.

TABLE 12.
Clinical Information of Controls

	MD (db)		RNFL		C/D Ratio		CSFI	
ID	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**
C1	-0.5	-1.36	78	71	0.57	0.54	11.89	18.94
C2	-0.25	0.07	80	84	0.54	0.45	10.98	6.94
C3	0.96	1.83	86	79	0.66	0.68	7.51	14.95
C4	-0.02	-0.32	91	92	0.61	0.68	6.63	10.84
C5	0.68	1.23	97	99	0.64	0.68	-3.05	-1.88
C6	-2.15	-1	101	101	0.43	0.45	6.13	-0.65
C7	-0.99	0.36	103	98	0.56	0.61	-1.41	-4.66
C8	-0.66	-0.73	99	103	0.55	0.53	-1.02	-5.47
C9	0.64	-0.34	70	66	0.58	0.56	17.25	23.06
C10	0.22	-0.49	82	86	0.28	0.09	2.55	-1.47
C11	-1.35	-4.34	104	111	0.66	0.64	-0.08	9.86
C12	0.02	-0.75	85	85	0.49	0.33	4.97	6.47
C13	-0.63	-1.3	96	93	---	---	---	---
C14	---	-0.26	83	86	0.7	0.57	---	3.28
C15	0.9	1.23	85	79	0.47	0.54	-0.24	8.99
C16	---	-1.75	---	93	---	0.6	---	5.22
C17	3.15	1.65	101	98	0.54	0.55	-23.50	-12.83
MEAN	0.00	-0.37	90.06	89.65	0.55	0.53	2.76	5.10
SD	1.23	1.48	10.32	11.81	0.11	0.15	9.55	9.46

See Table 11 caption for explanation for missing data.

TABLE 13.
Clinical Information of Participants Who Were Excluded

	MD (db)		RNFL		C/D Ratio		CSFI	
ID	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**
GA	0.02	-0.86	69	70	0.64	0.6	25.99	28.85
GB	-8.97	-7.07	68	67	0.58	0.64	48.11	46.31
GC	---	---	---	---	---	---	---	---
MEAN	-4.48	-3.97	68.50	68.50	0.61	0.62	37.05	37.58
SD	6.36	4.39	0.71	2.12	0.04	0.03	15.65	12.35
CA	-0.78	-6.98	98	97	0.53	0.59	-0.28	39.42
CB	-0.13	-0.42	69	86	0.49	0.37	23.22	6.92
CC	-4.50	-6.01	85	72	0.53	0.61	27.34	42.77
CD	-1.00	-0.83	101	106	0.6	0.59	-1.71	-6.07
CE	-3.65	-2.4	98	98	0.67	0.66	20.17	12.02
CF	-3.77	-2.4	79	74	0.7	0.72	31.39	28.92
MEAN	-2.31	-3.17	88.33	88.83	0.59	0.59	16.69	20.66
SD	1.87	2.71	12.80	13.83	0.08	0.12	14.22	19.43

Refer to Table 10 caption for reasons for exclusion.

Apparatus

Oculus Rift

The Oculus Rift (Oculus Rift DK2, Oculus VR, Irvine, CA) is a virtual reality system that displays a stimulus on a headset. The Oculus Rift can create an immersive environment that blocks out most external stimuli in ways a regular monitor cannot. This device allows for lighting and viewing distance to be held at a precisely constant level each time a participant is tested, and has a good test-retest reliability (Foerster et al., 2016). The Oculus Rift has a field of view of 100 degrees diagonally. This system has previously been used to examine vection responses in patients with glaucoma, although this was in the context of balance and fall

prevention (Diniz-Filho et al., 2015). Research has also shown the usefulness of the Oculus Rift for inducing vection in controls (Riecke & Jordan, 2015; Kim et al., 2015).

Procedure

For the vection test, participants wore the Oculus Rift headset with an eye patch covering one eye. The stimulus was a high contrast random-dot pattern. The dots were white on a black background, had a diameter of 1.5 deg, and the pattern had a density of 0.5 dots/deg^2. The dot pattern rotated from left to right, as if displayed on the interior walls of a vertical cylinder. A fast (40deg/s) and slow (20deg/s) version of the stimulus was viewed monocularly (OD and OS) for a total of 4 conditions. Each condition lasted for 2 minutes.

During the viewing period, participants used a response button to report vection latency and duration, by pressing and holding the button when they felt that they were moving. After each condition was over, participants reported their subjective vection strength using a 1-10 scale. A rating of 1 corresponded to the participant feeling as if the dots were moving and they were still (no vection), while a rating 10 corresponded to the participant feeling as if they were moving and the dots were still (full vection).

Data analysis

The results of 2 x 2 x 2 ANOVAs (Group x Speed x Eye) on vection responses revealed that there was no main effect of the viewing eye (smallest p = .49). Since there was no significant different between values obtained with either eye, this allowed all values obtained binocularly to be averaged together. This allowed data analysis to be simplified to 2 x 2 mixed factorial ANOVAs.

The CSFI was related to vection responses using Pearson correlations. The two groups were compared on clinical measurements using independent-samples t-tests. All tests used an alpha level of .05.

Results

Twenty-four percent (N=5) of patients with glaucoma and 11% (N=2) of control participants did not experience vection at all. They were excluded from the following analyses, leaving a total of 15 controls and 16 patients with glaucoma.

Our patients were significantly worse than controls in several clinical measures, such as RNFL, cup-to-disc ratio, and CSFI. Patients were also significantly older than the control group, despite best attempts to age match the two groups. There were no significant differences between the two groups on all the functional clinical measures tested (visual field MD and visual acuity).

TABLE 14.
Independent t-tests between patients and controls

Comparison	df	t	p
Visual Field MD	28	0.01	0.993
RNFL	28	2.91	0.007*
Cup-to-Disc Ratio	27	3.39	0.002*
CSFI	27	2.47	0.020*
Visual Acuity	29	0.87	0.392
Age	29	3.14	0.004*

Table 14. *Patients with glaucoma have functional vision measurements that are not significantly different from controls. It is only when we look at structural measurements that we see indications of glaucomatous damage.*

Vection Latency

A 2 x 2 mixed factorial ANOVA of Group x Speed was run on vection latency, showing main effects of group, as well as speed on vection latency. Patients with glaucoma had significantly longer vection latencies than controls ($F(1,26) = 5.77$, $p = .02$). In addition, the fast condition produced shorter latencies ($F(1,26) = 7.80$, $p = .01$). The interaction between latency and velocity was not statistically significant.

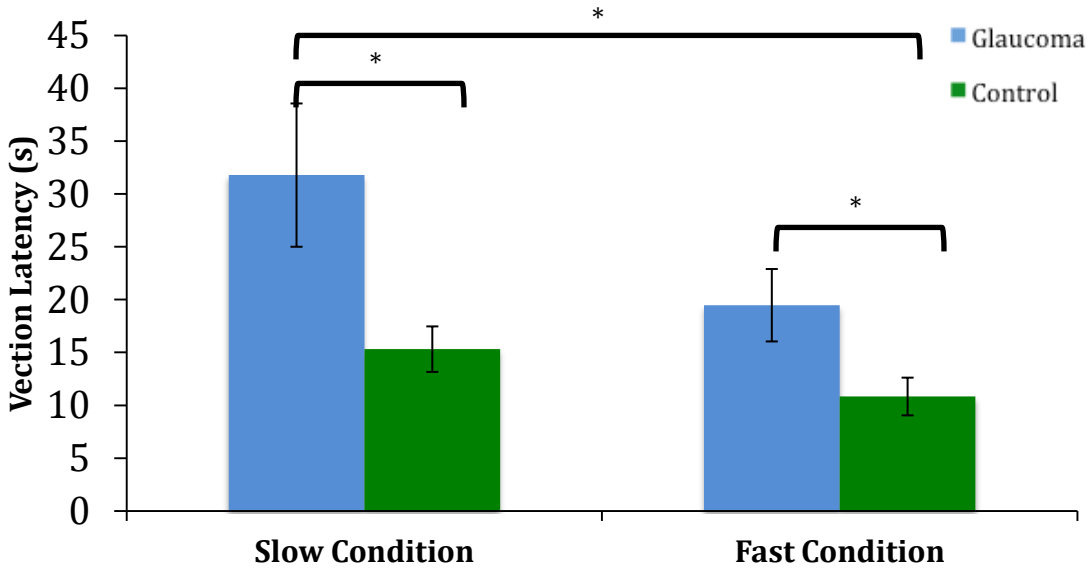

Figure 7. *Vection latency in the slow and fast condition*

In order to compare the statistical analyses of Experiments 1 and 2, a log transformation of the vection latency values was used in a 2 x 2 factorial ANOVA. The results still show a significant main effect of group ($F(1,26) = 13.72$, $p = .001$) and speed ($F(1,26) = 5.96$, $p = .02$) without a statistically significant interaction between these factors.

Vection duration

There was no main effect of group ($F(1,26) = 2.74$, $p = .10$) or speed ($F(1,26) = 1.94$, $p = .18$) on vection duration. There was no interaction.

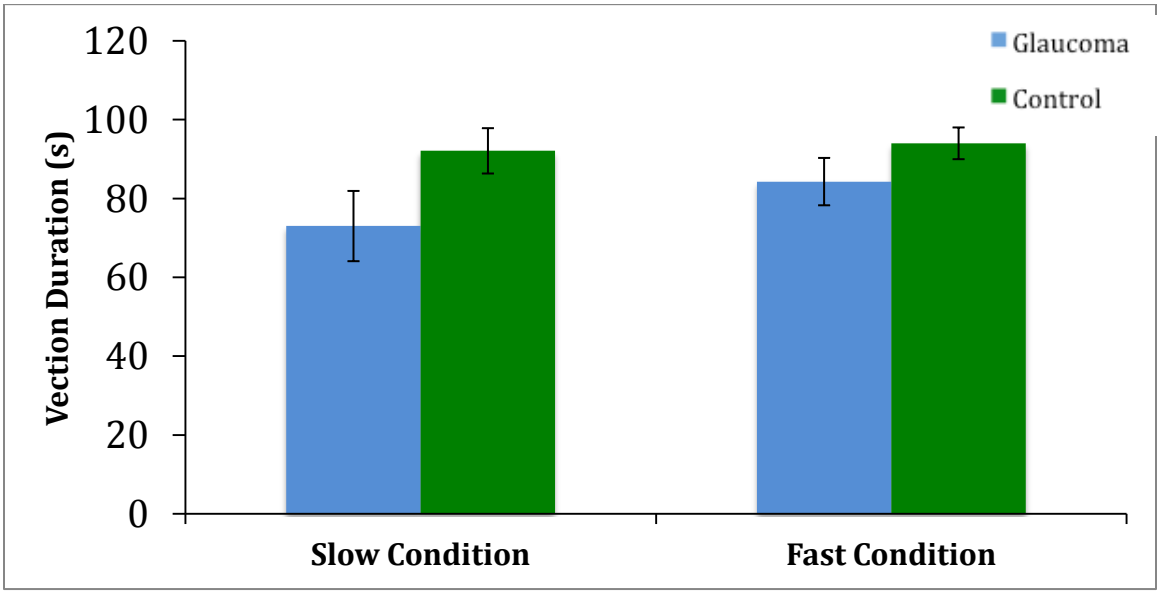

Figure 8. *Vection duration in the slow and fast condition.*

Vection Strength

A main effect was seen for velocity on vection strength ratings, with the faster velocity resulting in higher ratings ($F(1,26) = 22.41$, $p = .005$). There was no interaction.

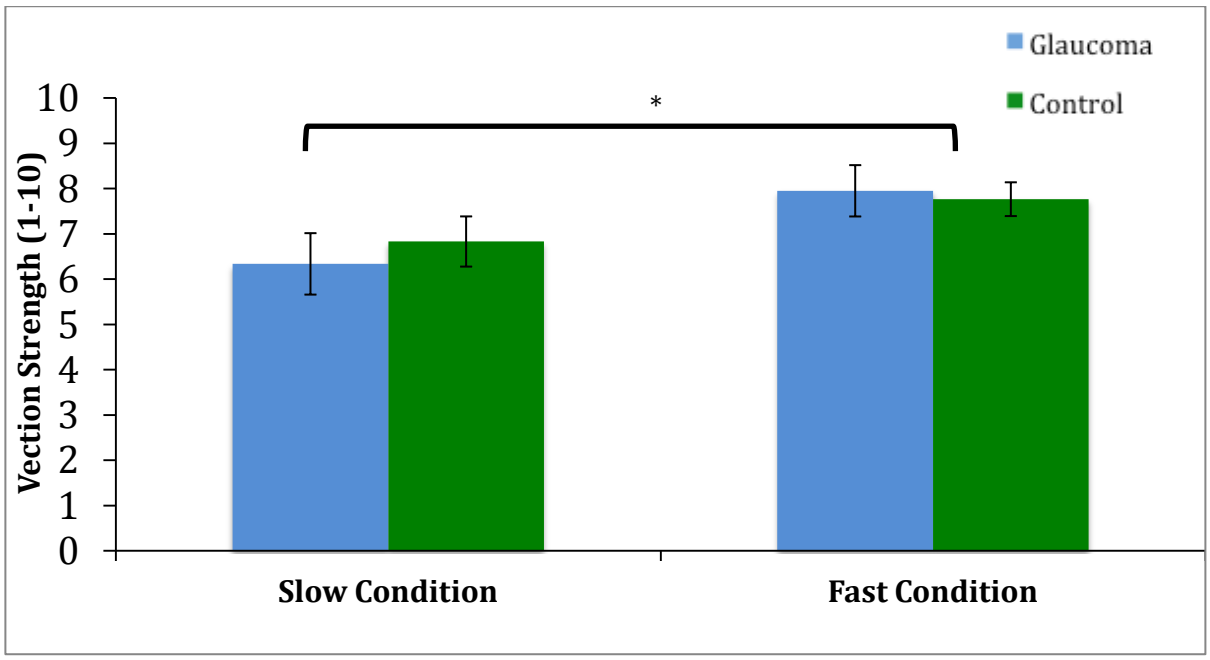

Figure 9*. Subjective vection strength rating in the slow and fast condition.*

Clinical Explanation of Vection Responses

In order to explain these differences in vection responses, we related our vection measurements to all of our clinical tests (particularly, the CSFI) as well as age. However, none of our clinical measures showed significant correlations with

any vection measurements. This was seen for both speeds. Correlations were done separately for the slow and fast condition because some participants may have experienced vection with only one eye in the slow condition and only the other eye in the fast condition. For these cases, we only looked at vection results and clinical data from the eye that experienced vection.

TABLE 15.
Slow condition correlation values in patients

Correlation	df	r	p
MD:Latency	12	-0.130	0.658
MD:Duration	12	-0.151	0.606
MD:Subjective Rating	12	-0.195	0.504
RNFL:Latency	12	-0.256	0.377
RNFL:Duration	12	0.079	0.788
RNFL:Subjective Rating	12	-0.223	0.443
C/D Ratio:Latency	12	-0.260	0.369
C/D Ratio:Duration	12	0.281	0.330
C/D Ratio:Subjective Rating	12	-0.174	0.552
CSFI:Latency	12	0.212	0.467
CSFI:Duration	12	0.012	0.967
CSFI:Subjective Rating	12	0.100	0.734
Acuity:Latency	12	-0.155	0.597
Acuity:Duration	12	0.302	0.294
Acuity:Subjective Rating	12	0.251	0.387
Age:Latency	12	-0.108	0.713
Age:Duration	12	0.443	0.113
Age:Subjective Rating	12	0.241	0.407

None of the correlations reached statistical significance.

TABLE 16.
Fast condition correlation values in patients

Correlation	df	r	p
MD:Latency	13	-0.367	0.178
MD:Duration	13	0.312	0.258
MD:Subjective Rating	13	-0.010	0.972
RNFL:Latency	12	-0.257	0.375
RNFL:Duration	12	0.348	0.204
RNFL:Subjective Rating	12	-0.194	0.506
C/D Ratio:Latency	13	-0.136	0.629
C/D Ratio:Duration	13	0.143	0.611
C/D Ratio:Subjective Rating	13	-0.304	0.271
CSFI:Latency	12	0.301	0.276
CSFI:Duration	12	-0.283	0.327
CSFI:Subjective Rating	12	0.137	0.640
Acuity:Latency	13	0.254	0.361
Acuity:Duration	13	-0.311	0.259
Acuity:Subjective Rating	13	-0.196	0.484
Age:Latency	13	0.043	0.879
Age:Duration	13	-0.170	0.545
Age:Subjective Rating	13	0.195	0.486

None of the correlations in the fast condition reached significance. The degrees of freedom is only 12 for visual field and CSFI comparisons. This is because in the fast condition only, a patient experienced vection in the same eye that had an invalid visual field test (due to high fixation losses). In this case, the "average" for both eyes would only use clinical data of this eye so the other visual field could not be used as a replacement. As such, without that visual field value, CSFI could not be calculated for that patient.

Summary and Concluding Discussion

The results of these two experiments support the original findings by Tarita-Nistor et al. (2014) that vection latency is significantly longer in patients with early stage glaucoma. The fact that we were able to replicate these results twice is compelling evidence for the robustness of this effect. Unfortunately, each study utilized a slightly different stimulus and apparatus, making direct comparisons in vection strength between the three studies impossible.

Experiment 1 and Experiment 2 sought to replicate the difference in vection responses seen by Tarita-Nistor et al. (2014), but the more important aspect was to try to explain why they occur. Patients were measured in a number of clinical measures to attempt to explain these findings.

In Experiment 1, the patients had significant deficits in all clinical measurements except for RNFL thickness. It is understandable that a group with worse vision may not respond well to vection, particularly if they cannot see the stimulus well. However, in Experiment 2, the patients were not significantly different from controls in terms of functional measures of vision (both visual acuity and visual field MD). These patients had no visual deficits, yet they still experienced a notably weaker sensation of vection compared to controls. This suggests that the vection response is potentially affected before it is detectable by function-based clinical tests. It is interesting that patients with such early stage glaucoma have such weakened vection responses, to the point where many do not experience vection at all.

Understanding how these clinical measures affect vection responses is important for elucidating the effects of glaucoma on the visual-vestibular connection. Patients with glaucoma have worse postural stability than controls, as well as a greater likelihood of having fallen in the previous year (Diniz-Filho et al., 2015). The capabilities of the vestibular system appears to be affected by both glaucoma as well as the natural aging process, as individuals rely more on vision for balance as their vestibular system weakens over time (Manchester et al., 1989). Furthering knowledge in this area may help prevent falls in this population. As such, we compared functional and structural clinical measures to vection responses. Experiment 1 showed that both visual field MD and CSFI were related to subjective tilt estimates. However, these correlations were in the opposite direction as expected, suggesting that more glaucomatous damage (detected using both structural and functional tests) lead to stronger vection ratings. Since visual field MD and CSFI did not correlate with actual body tilt, this suggests that participants are highly inaccurate at judging the movement of their own body. For example, compared to their mean tilt (M = 5.82 degrees, SD = 4.28 degrees), patients with glaucoma overestimated the amount they tilted by almost double (M = 10.35 degrees, SD = 7.34 degrees). Participants had to physically move a joystick on a protractor to estimate their tilt, and some participants may not have a good grasp on how the angle on a small protractor corresponds to the angle of their entire upper body. The reason estimates are larger instead of smaller may be because patients with glaucoma have a weaker sense of balance. Patients with glaucoma are three times more likely to have fallen in a given year, compared to age-matched controls

(Kotecha et al., 2012; Haymes et al., 2007). This fear of falling may make these patients more anxious about precarious body positions, leading to overestimations in body tilt. This high level of inaccuracy may reduce the validity of this measure and any correlation that was found with it.

It is important to note that we can already differentiate very mild glaucoma from controls in terms of their vection responses. It appears that vection is either impaired or entirely absent in these patients. However, it is still unclear what precisely causes these weaker responses, as none of our clinical measures were related to them in Experiment 2. It is a puzzling matter.

Perhaps the lack of significant correlations is due to the narrow range of data values. We are only looking at early stage glaucoma, meaning that we were only comparing vection responses to clinical values on the low end of the scale. However, since such a large proportion of patients with even mild glaucoma did not experience vection at all, we avoided more severe cases.

The lack of a correlation between the CSFI and vection responses may also be due to the nature of the CSFI itself. The CSFI groups all RGCs together to calculate gross loss, without separating the cells into their specific subtypes. The CSFI also does not take the accessory optic system into account. This is partocularly important for these experiments, as one of the functions of the accessory optic system is to relay visual-vestibular interactions to the brainstem (Giolii, Blanks, & Lui, 2006). One would expect that a loss of these neurons in particular would lead to weaker vection responses. However, this was not measured by the CSFI, and further

demonstrates the need for an fMRI study to better understand the pathways affected by glaucoma.

It may be that the clinical tests we chose did not capture the reasons for weaker vection responses, and that there must be another clinical measurement that provides an explanation. For example, the cause of these weaker vection responses may be due to glaucoma having an effect on cortical structures. This sort of loss is not readily captured by standard clinical tests for glaucoma such as the visual field test and OCT. Vection is a very complex response that results from conflict between the visual and vestibular system. An area of the visual cortex called V6 has been shown to be preferentially activated during the sensation of vection (Wada, Sakano, & Ando, 2016). However, glaucoma has been shown to damage the visual cortex, which may make it more difficult for the visual system to override the vestibular system to cause the illusion of self-motion (Gupta et al., 2006). Future studies should look into correlating fMRI responses during vection in patients with glaucoma as well as controls with healthy vision. It would then be expected that patients with glaucoma experience less visual cortex activation during vection, which is why their vection response is dampened.

Another possibility is that vection responses were weakened due to reduced contrast sensitivity, which is very common in patients with glaucoma (McKendrick et al., 2007). Contrast sensitivity has been shown to decline in patients with glaucoma even before changes in visual acuity and visual field tests (Ross, Bron, & Clark, 1984; Wilensky & Hawkins, 1989; Regan & Neima, 1984). Therefore, it is possible our patient sample had reduced contrast sensitivity despite having very

early stage glaucoma. Furthermore, contrast sensitivity has been shown to affect vection responses, with lower contrast stimuli producing weaker vection responses in controls at either low or high (but not intermediate) speeds (Holten et al., 2016). A contrast sensitivity test may explain why vection responses were weaker in these patients.

The vestibular system naturally decays with age (Agarwal et al., 2009). This can result in a higher rate of falls as well as a stronger sensation of vection in the elderly (Sattin et al., 1990; Paige, 1994). Both the vestibular and visual system deteriorate with age, however, there is more reliance on the visual system in the elderly (Haibach, Slobounov & Newell, 2008); therefore, vection responses may be stronger in the elderly because visual stimuli can more easily override the vestibular system as the dominant input. However, elderly patients with glaucoma tend to have a loss of peripheral vision. This may explain why vection responses are paradoxically weaker in this older population, as they are relying on vision despite the fact that their peripheral vision is compromised. For example, patients with glaucoma are three times more likely to fall or have issues with locomotion than age-matched controls (Haymes et al., 2007). Tasks reliant on peripheral vision such as these are more negatively affected in patients with glaucoma due to this pattern of vision loss.

Experiment 2 showed a significant main effect for speed on vection latency and subjective vection rating. That is, for the faster speed, vection latency was shorter and the subjective vection rating was higher. This is consistent with the

literature showing that vection strength increases with the speed of the stimulus, up to a certain threshold (Brandt et al., 1973).

Detecting glaucoma at an earlier stage is particularly important for patient prognosis. Glaucoma has been coined “the silent thief of sight”, as it often robs the patient of vision without them being aware of it until it reaches the intermediate to later stages. Once the damage is done, it is irreversible. This is why it’s so important to begin monitoring for glaucoma as soon as possible to minimize the damage. Looking for potential early markers for glaucoma, such as reduced vection responses, could help in the search for developing more efficient screening tools for glaucoma. Even when patients are seen by an ophthalmologist, glaucoma can be undiagnosed in up to 50% of cases (Topouzis et al., 2007). Any addition to the battery of tests used to diagnose glaucoma may help lower this number. The Oculus Rift is very promising as a potential screening device, given its compact size, affordability, portability and ease of use. In this test, it is very clear if there is a sensation of self-motion or not, making it intuitive for both patients and clinicians. Work has yet to be done on whether these results are specific only to glaucoma, but the potential exists for this to be used as a screening device. If this test is successful, catching glaucoma at an earlier stage can lead to earlier treatment and better patient outcomes.

Limitations

Several participants reported feeling "weird" or "floating" instead of typical descriptors of vection. It is difficult to know whether they experienced an entirely different sensation from vection or if they simply did not know how to describe it.

There were a considerable number of patients with glaucoma who did not experience vection in Experiment 1. This may be because the room was visible in the periphery. This would make the stimulus appear in the foreground with the rest of the room in the background. However, stimuli seen as being in the foreground or closer to the viewer tend to reduce vection responses (Post et al., 1988; Howard & Heckmann, 1989). This may be why almost half of our patients with glaucoma were unable to experience vection, as their perception was weakened by the stimulus appearing in the foreground against a stationary background.

The controls were significantly younger than the glaucoma group in both experiments. This may have posed a problem in terms of vection responses, as motion sensitivity tends to decrease with age (Falkenberg & Bex, 2007; Wills & Anderson, 2000). However, we believe this does not invalidate our results as other studies show that induced circular vection (Paige, 1994) and certain types of motion detection (Hutchinson, Ledgeway, Allen, 2014; Betts et al., 2005) actually may become stronger with age. Elderly individuals rely more on their visual system than their vestibular system (Haibach, Slobounov & Newell, 2008), which may cause them to get "tricked" more easily by a vection stimulus into thinking they are actually moving. Since our patients are older, we would then expect them to actually have a stronger sensation of vection, but we found the opposite. As such, we believe

this age difference does not invalidate our results. If anything, it shows just how robust the effect of glaucoma is on reducing vection responses.

Finally, the sample size was rather small for each experiment. It would have been ideal to test the same participants on the projection screen and then the Oculus Rift to increase the number of participants and compare their responses across experiments.

Conclusions

Although our groups were not age-matched, it is still possible to come to the conclusion that patients with early stage glaucoma experience either a weakened sensation of vection, or no vection at all. Even when these patients do not significantly differ from controls in terms of visual field tests or visual acuity, we still see a stark contrast in how vection is experienced. We could not find a correlation between CSFI and vection responses, suggesting that another component of glaucoma is responsible for these weakened vection responses. Future studies can broaden the scope of clinical tests (such as including fMRI or contrast sensitivity tests) to find an explanation for the difference in how these patients experience vection. Furthermore, the vection test on the Oculus Rift may be able to help screen for glaucoma at an early stage, which would improve patient outcomes.

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Appendix A: Visual Fields and OCT

The visual field test is a gold standard clinical test used to assess and track the progression of glaucoma. The patient sits down and places their head on a chinrest; positioned so that one eye is centered with a fixation light. The other eye is covered with a black eye patch. Every time the patient sees a small, flashing light, they press a button. The light will appear in a random location each time. Gradually, the brightness of the lights will decrease until a threshold is reached where they can no longer perceive the light. During the entire testing period, the patient must keep their eyes focused on the fixation light. Along with verbal reminders to maintain fixation, video monitoring of the eye and manual repositioning of the chinrest ensured minimal fixation loss.

The 24-2 SITA-standard test assesses vision on a 54-point grid. As such, it is able to assess both central and non-extreme peripheral vision deficits. SITA-standard is the name of the algorithm, which determines the threshold based on a staircase method. This method is more reliable than the SITA-fast, as it has smaller jumps down in brightness in response to correct answers, although it also takes longer to run. Each eye takes approximately 5 minutes to test.

There is a value at each eccentricity (distance from the centre) assigned in decibels for the dimmest light that person could see. For clinical use, these values are conveniently averaged into the MD (also measured in decibels), which is scaled to the patient's age. A positive value indicates that the patient is performing better than an age-matched, normal population, whereas a negative value indicates the opposite. For example, a score of -3dB means that the patient scored 0.3 log units

less than an age-matched control. The lowest possible value is -30dB. According to the Hodapp-Parish-Anderson (HPA) staging system, mild stage glaucoma is classified as have an MD somewhere around -6 dB, although normal eyes generally score higher than -2 dB (Hodapp et al., 1993; Smith et al., 2014). The severity of glaucoma can also be determined based on clusters of adjacent points that have abnormally low dB values, but this was not used for our method for finding patients with only mild visual field defects (Smith et al., 2014).

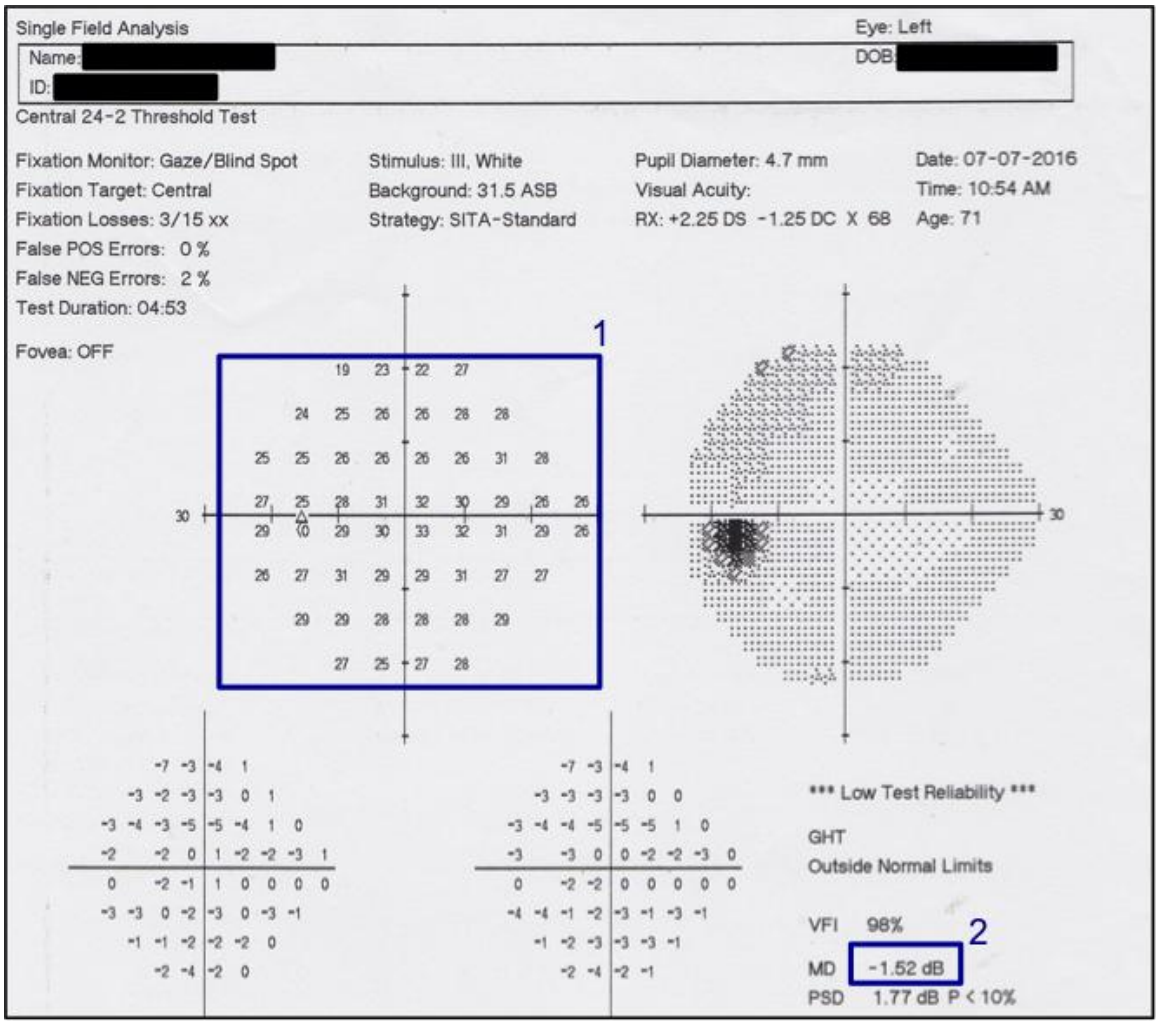

Figure 10. *Visual field test example print-out*

All the visual field information that is used to calculate the CSFI is marked by blue numbers in Figure 10. The grid seen in (1) is essentially a map of retinal sensitivity based on average values from an age-matched control. Values closest to the centre of the axis are representative of the macula and those farthest represent the periphery. High values indicate that the patient is performing well and can perceive very dim lights. The value of <0 is the natural blind spot where the optic nerve exits the eye. The values in the grid are summarized in (2) as the MD, which represents the difference in mean visual sensitivity from the average result of an age-matched population.

OCT is another clinical test commonly used in the screening and monitoring of glaucoma. We used spectral-domain Cirrus HD-OCT, which was currently being used by our patients' clinician to monitor their progress. Spectral domain OCT has been shown to have a better axial resolution, test-retest variability, and sensitivity for the detection of glaucoma than time domain OCT (Drexler et al., 2001). Spectral domain OCT uses light to obtain a cross-sectional image of the retina. There is a reference beam and a sample beam. The sample beam hits the patient's retina and is reflected back in a way that interferes with the reference beam. This interference is then picked up by the OCT, allowing it to form measurements of depth (Drexler et al., 2001). The 200 x 200 Optic Disc Cube scan that we used in both experiments covers a 6mm square grid that is centered around the optic disc.

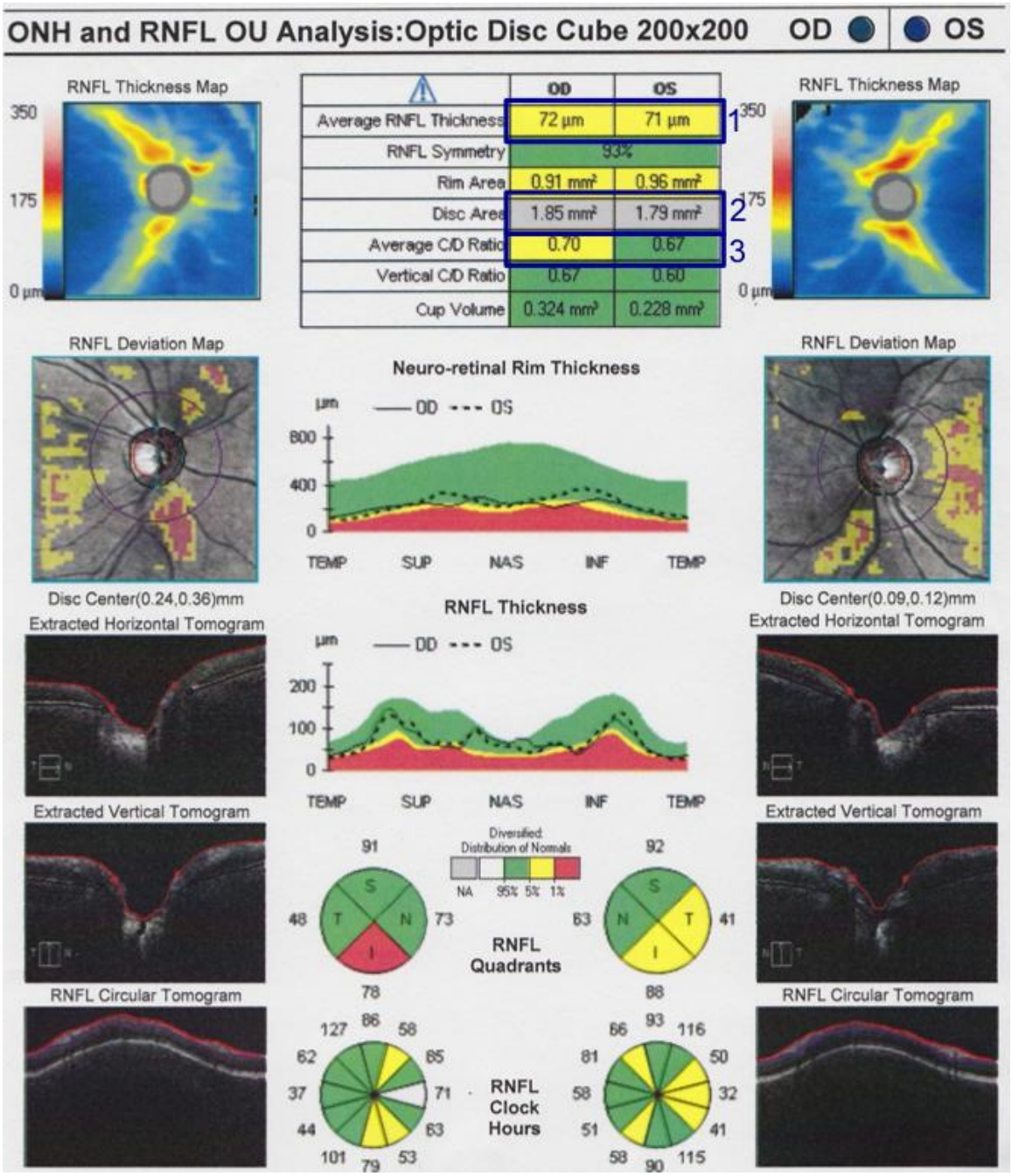

Figure 11. *OCT Example Print-out. The values of an OCT scan are colour-coded based on the (age-matched) probability values of normal. For example, any value in green or white indicates a healthy value within a normal population (p > 0.95) and any value in red is far outside the normal range (p < 0.01).*

The OCT values used to calculate the CSFI and for data analysis are marked by blue numbers in Figure 11. Glaucoma causes the death of RGCs at the RNFL, which thins the retina and can lead to dysfunctional vision. Damage is also often seen at the optic nerve head, which can change the optic disc area. The software of the OCT defines the edge of the disc as where Bruch's membrane ends (Puliafito, 2009). Both RNFL thickness (1) and optic disc area (2) are used to calculate the CSFI. Additionally, we look at the average cup-to-disc ratio (3), although this is not part of the CSFI calculation. The cup-to-disc ratio compares the diameter of the entire optic disc to the "cupping" area inside of it, where the retina forms a small pit for the axons to exit the eye. The cup does not contain nerve fibers. In some cases of glaucoma, the disease progression (usually high pressure) can lead to an increase in the cupping area. A larger cup-to-disc ratio usually implies that there has been glaucomatous damage, as the area of non-functional retina is increasing. However, every individual has their own baseline cup-to-disc ratio, so this average may vary between people. Therefore, a high cup-to-disc ratio may not necessarily be due to glaucoma. It's when the cup-to-disc ratio starts to stray from this baseline level that it becomes a stronger indicator of the progression of glaucoma.

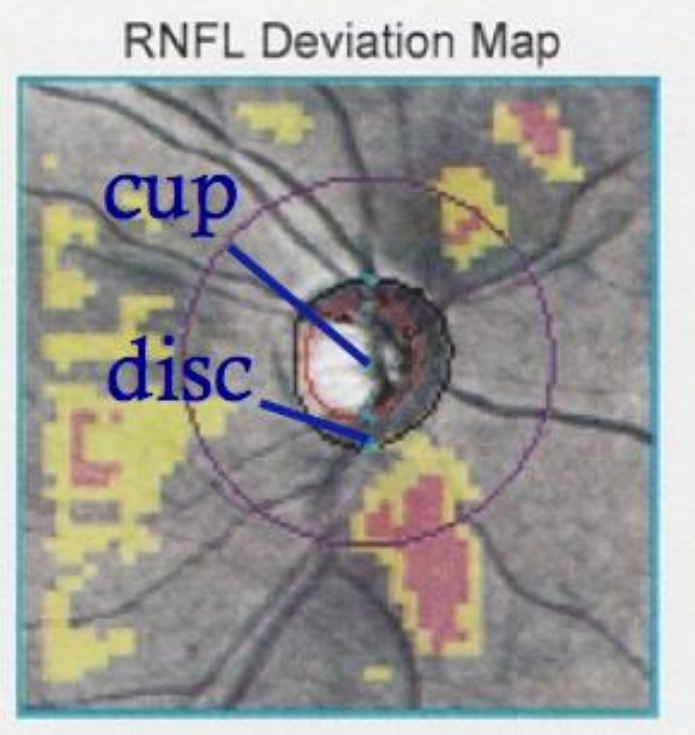

Figure 12. *Close-up of the optic nerve measurement from an OCT print-out. This patient has a moderate level of pathological cupping, as the cup is almost as large as the disc. The inner cup is outlined by a red circle, while the outer border of the optic disc is outlined by a black circle.*

Appendix B

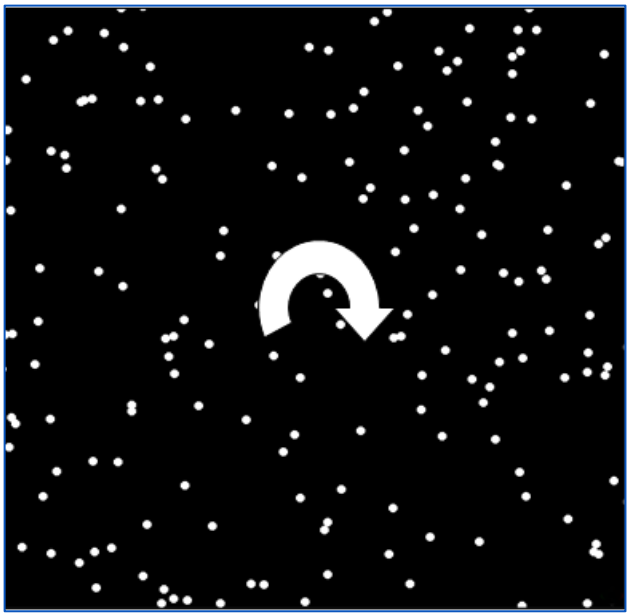

Figure 13. *Experiment 1 stimulus. The random dot pattern rotated around a central point in order to induce roll vection*

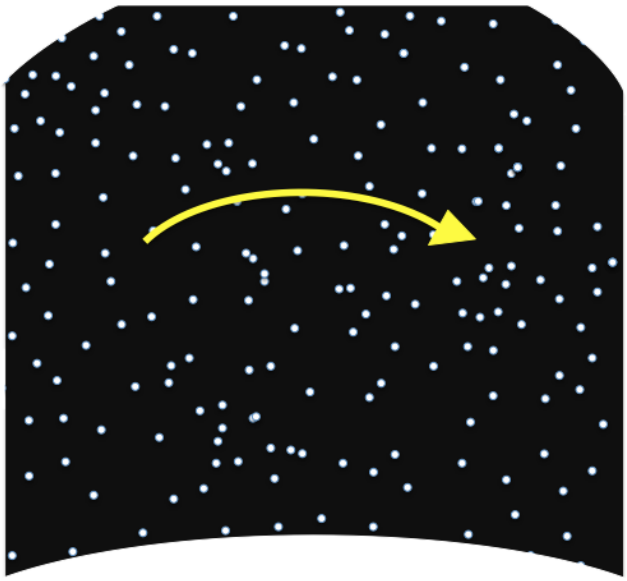

Figure 14. *Experiment 2 stimulus. The random dot pattern was placed on the walls of a virtual cylinder, which rotated around the observer who appeared to be seated in the centre. This induced circular vection.*

Appendix C: Informed Consent

Vision Science Research Program
Toronto Western Hospital

University Health Network
Toronto General Hospital Toronto Western Hospital Princess Margaret Hospital

Consent Form to Participate in a Research Study

TITLE: Self-Induced Motion in Patients with Glaucoma

INVESTIGATORS: Dr. Esther González
Dr. Luminita Tarita-Nistor
Dr. Martin Steinbach
Dr. Graham Trope
Taylor Brin

Introduction
You are being asked to take part in a research study. Please read this explanation about the study and its risks and benefits before you decide if you would like to take part. You should take as much time as you need to make your decision. You should ask the study doctor or study staff to explain anything that you do not understand and make sure that all of your questions have been answered before signing this consent form. Before you make your decision, feel free to talk about this study with anyone you wish. Participation in this study is voluntary.

Background
Glaucoma is the second leading cause of blindness worldwide affecting an estimated 3% of the population over 40 years of age. The scenes that people with glaucoma can see become progressively smaller. We refer to this as a loss of the peripheral vision. Due to the nature of their loss, patients with glaucoma experience difficulties finding places when they walk, and are more likely to fall or to be involved in a car accident than people with normal vision of similar age. Large moving scenes can induce a sensation of self-motion in people with healthy vision. This self-induced motion is called vection and depends on the peripheral vision. The present study investigates whether patients with glaucoma experience vection differently.

Purpose

We do not know whether self-induced motion (vection), which depends on peripheral vision, is affected in people with glaucoma. Therefore, the purpose of this research is to examine the function of peripheral vision by testing if people with glaucoma experience vection in the presence of large, moving scenes. This research will help us understand more about the problems of people with glaucoma.

Procedures

The study will take place at the Ocular Motor Laboratory, located at the Toronto Western Hospital, University Health Network. Testing will be done in one visit and it will last about 40 minutes.

We will examine your sensitivity to experience vection using moving scenes that we will project on a large screen. You will be seated in front of the screen and asked to press a button when you have a sensation that you are moving. After this testing, you will be able to leave.

Risks Related to Being in the Study

There are no additional medical risks due to study procedures. You may experience a slight motion sickness; we will stop any time you feel you are not comfortable.

Benefits to Being in the Study

There are no direct benefits to you from participating in this study. You may benefit from participating in this study by learning how strongly you can experience self-motion. In the future, the information from this study will help people with your condition understand more about their deficits.

Confidentiality

If you agree to join this study, the study doctor and his/her study team will look at your personal health information and collect only the information they need for the study. Personal health information is any information that could be used to identify you and includes your:

- name,
- address,
- date of birth,
- new or existing medical records, that includes types, dates and results of medical tests or procedures.

The information that is collected for the study will be kept in a locked cabinet in a restricted area by the study doctor for 7 years. Only the study team or the people or groups listed at the beginning of this form will be allowed to look at your records. Your participation in this study may also be recorded in your medical record at this hospital.

Representatives of the University Health Network Research Ethics Board may look at the study records and at your personal health information to check that the information collected for the study is correct and to make sure the study followed proper laws and guidelines.

All information collected during this study, including your personal health information, will be kept confidential and will not be shared with anyone outside the study unless required by law. You will not be named in any reports, publications, or presentations that may come from this study.

If you decide to leave the study, the information about you that was collected before you left the study will still be used. No new information will be collected without your permission.

Voluntary Participation

Your participation in this study is voluntary. You can choose not to participate or you may withdraw at any time without affecting your medical care.

In Case You Are Harmed in the Study

If you become ill, injured or harmed as a result of taking part in this study, you will receive care. The reasonable costs of such care will be covered for any injury, illness or harm that is directly a result of being in this study. In no way does signing this consent form waive your legal rights nor does it relieve the investigators, sponsors or involved institutions from their legal and professional responsibilities. You do not give up any of your legal rights by signing this consent form.

Questions about the Study

If you have any questions, concerns or would like to speak to the study team for any reason, please call Dr. Esther G. González or Dr. Luminita Tarita-Nistor or Ms. Taylor Brin.

If you have any questions about your rights as a research participant or have concerns about this study, please call the Chair of the University Health Network Research Ethics Board (REB) or the Research Ethics office number. The REB is a group of people who oversee the ethical conduct of research studies. These people are not part of the study team. Everything that you discuss will be kept confidential.

Consent
This study has been explained to me and any questions I had have been answered. I know that I may leave the study at any time. I agree to take part in this study.

Print Study Participant's Name	Signature	Date

(You will be given a signed copy of this consent form)

My signature means that I have explained the study to the participant named above. I have answered all questions.

Print Name of Person Obtaining Consent	Signature	Date

Was the participant assisted during the consent process? ☐ **YES** ☐ **NO**
If **YES**, please check the relevant box and complete the signature space below:

☐ The person signing below acted as a translator for the participant during the consent process and attests that the study as set out in this form was accurately translated and has had any questions answered..

Print Name of Translator	Signature	Date

Relationship to Participant	Language

☐ The consent form was read to the participant. The person signing below attests that the study as set out in this form was accurately explained to, and has had any questions answered.

Print Name of Witness	Signature	Date

Relationship to Participant

Appendix D: Glossary

Amblyopia: A visual disorder where input from an otherwise physically healthy eye is suppressed at the level of the visual cortex.

Apoptosis: Programmed cell suicide.

Anterograde trans-synaptic degeneration: The death of neurons due to the disruption of signaling from adjacent neurons responsible for input.

Aqueous fluid / intraocular fluid: The fluid located within the eye, which maintains a certain pressure to keep the structure of the eye in tact.

Bruch's membrane: One of the many layers of the retina, it allows for the transport of fluid and structurally supports the other layers.

Calcarine sulcus: A neuroanatomical region that resembles a small fissure, and divides the visual cortex into two portions.

Cerebrospinal fluid: A protective fluid found in the brain and spinal cord.

Conjunctiva: A thin layer of protective mucous that covers the sclera and the inside of the eyelids.

Contrast sensitivity: The ability to distinguish between light and dark.

Corpus callosum: A system of axons that connect the left and right hemisphere of the brain.

Enucleation: The process of removing one or both eyes. This is usually done as a result of some sort of traumatic injury or disease.

Fovea: The area of the retina that has the highest level of acuity. It is located in the centre of the macula, and is used during fixation.

Iris: The coloured part of the eye which changes size in order to let more or less light into the pupil.

Lamina cribrosa: A meshwork that allows optic nerve fibres to pass through and reach the sclera

Lateral geniculate nucleus: This brain structure relays information from the visual pathway to the thalamus.

Lens: The lens of the eye refracts light to allow the viewer to focus at a specific depth. The shape of the lens changes to ensure the object of focus is seen as clearly as possible.

logMAR: A log-based unit to describe visual acuity more precisely than the Snellen chart, although logMAR can also be converted into Snellen.

Macula: An area of high visual acuity in the retina. This area includes the fovea and the surrounding retinal tissue.

Magnocellular pathway: This visual pathway is specific for contrast, spatial orientation, and motion detection.

Neuroretinal rim area: The border around the optic disc where neural tissue is found, just before the physiological cupping area begins.

Ocular hypertension: A condition where pressure inside the eye is unusually high. This can lead to optic nerve damage and/or glaucoma.

Optic nerve: A bundle of axons that carries visual information from the retina to the brain. The area that the optic nerve exits the eye creates a natural blind spot.

Proprioceptive system: A sensory system that provides information about the position of the body in space.

Refractive error: The result of not being able to accurately focus at either near or far distances. Refractive error can be measured in order to obtain an appropriate glasses prescription.

Retinal ganglion cells: This subtype of neurons can be found near the surface of the retina. It is part of a system of cells that transmits visual information from the retina to the brain.

Saccade: A quick eye movement used to change the fixation target.

Schlemm's canal: A circular passage in the eye where aqueous humour flows in order to reach blood vessels on the sclera.

Sclera: The opaque, white region of the eye.

Scotoma: An isolated area where a portion of the visual field has been lost or diminished due to disease or injury.

Somatosensory system: This system provides information about one's immediate environment through touch, pain, temperature, and the movement of the body.

Spatial frequency: The measurement of detail in a stimulus. A stimulus with a high spatial frequency has sharp edges and very fine details, while a low spatial frequency stimulus appears blurry.

Temporal cortex: Part of the cerebral cortex, this region of the brain is thought to be primarily responsible for visual memory, language, and emotion.

Trabecular meshwork: This structure allows for aqueous humour to exit the anterior chamber through Schlemm's canal.

Vestibular system: This system controls balance using a variety of different input, including vision and the sensation of our position from inner ear organs.

Visual cortex: An area of the brain responsible for processing visual information.

Appendix E: Presentations and Publications

Brin, T.A., Tarita-Nistor, L., González, E.G., Trope, G.E., & Steinbach, M.J. Investigating Vection Responses in Patients with Early Stage Glaucoma. *Presented at York University's Brain Behaviour and Cognitive Science Day,* Toronto, Canada, June 2017.

Tarita-Nistor, L., González, E.G., Brin, T.A., & Steinbach, M.J. Disruption of binocular rivalry processes in patients with mild glaucoma. *Presented at the Association for Research in Vision and Ophthalmology*. Baltimore, MA, May 2017.

Brin, T.A., Tarita-Nistor, L., González, E.G., Trope, G.E., & Steinbach, M.J. Investigating the Oculus Rift as a New Device to Study Vection in Glaucoma. *Presented at the Association for Research in Vision and Ophthalmology.* Baltimore, MA, May 2017.

Brin, T.A., Tarita-Nistor, L., González, E.G., Trope, G.E., & Steinbach, M.J. Virtual Reality Vection Responses in Patients with Early Stage Glaucoma. Presented *at York University's Brain Behaviour and Cognitive Science Day,* Toronto, Canada, May 2016.

Tarita-Nistor, L., González, E.G., Brin, T.A., Mandelcorn, M.S., Scherlen, A., Mandelcorn, E.D., Steinbach, M.J. (2016). Fixation stability and viewigng distance in patients with AMD. Optometry and Vision Science, 94(2), 239-245.

Brin, T.A., Tarita-Nistor, L., González, E.G., Trope, G.E., & Steinbach, M.J. Virtual Reality Vection Responses in Patients with Early Stage Glaucoma. *Presented at University of Toronto Ophthalmology and Vision Science Research Day*, Toronto, Canada, May 2016.

Brin, T.A., Tarita-Nistor, L., González, E.G., Trope, G.E., & Steinbach, M.J. Virtual Reality Vection Responses in Patients with Early Stage Glaucoma. *Presented at Krembil Research Day,* Toronto, Canada, May 2016.

Bedell, H.E., Pratt, J.D., Krishnan, A., Kisilevsky, E., Brin, T.A., González, E.G., Steinbach, M.J., & Tarita-Nistor, L. (2015). Repeatability of Nidek MP-1 Fixation Measurements in Patients with Bilateral Central Field Loss. *Investigative Ophthalmology & Visual Science, 56(4),* 1624-2630.

Steinbach, M.J., Brin, T.A., Kisilevsky, E., Tarita-Nistor, L., Trope, G.E., Singer, S., & González, E.G. Vection responses in early stage glaucoma. *Presented at the Canadian Ophthalmological Society Meeting*, Victoria, Canada, 2015.

Brin, T.A., Kisilevsky, E., González, E.G., Tarita-Nistor, L., Trope, G.E., Singer, S., & Steinbach, M.J. Effects of early glaucoma on vection responses. Presented at the Toronto Western Research Institute Research Day, Toronto, Canada, May 2015.

Brin, T.A., Kisilevsky, E., González, E.G., Tarita-Nistor, L., Trope, G.E., Singer, S., & Steinbach, M.J. Effects of early glaucoma on vection responses. Presented at the Association for Research in Vision and Ophthalmology, Denver, CO, 2015. *(Awarded as a Hot Topic)*

Tarita-Nistor, L., González, E.G., Brin, T.A., Mandelcorn, M.S., Scherlen, A.C., & Steinbach, M.J. Fixation Stability as a Function of Viewing Distance in Patients with AMD. *Presented at the Association for Research in Vision and Ophthalmology*, Denver, CO, 2015.

Brin, T.A., Kisilevsky, E., Trope, G.E., Tarita-Nistor, L., González, E.G., & Steinbach, M.J. Vection responses in early stage glaucoma. *Presented at the Toronto Western Research Institute Summer Student Research Day*, Toronto, Canada, August 2014.

Kisilevsky, E., Brin, T.A., Trope, G.E., González, E.G., Tarita-Nistor, L., & Steinbach, M.J. A combined structure and function index to explain vection response in glaucoma. *Presented at the Toronto Western Research Institute Summer Student Research Day*, Toronto, Canada, August 2014.

Brin, T.A., Tarita-Nistor, L., González, E.G., Hadavi, S., Markowitz, S.N., Steinbach, M.J. Vection in patients with glaucoma. *Poster presented at the Toronto Western Research Institute Research Day*, Toronto, Canada, May 2014.