The Role of Visual Fixations in Vision and Motion Sensitivity

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Abstract

Motion sensitivity is a commonly reported symptom in people with chronic dizziness and is described as a lingering symptom that persists after recovery from an acute vestibular disorder. Adults with motion sensitivity typically report discomfort instigated by environments with rich visual information. There are no effective diagnostic tools or treatments for motion sensitivity and people report being frustrated due to a failure in symptom resolution. Little has been reported in the literature regarding the aetiology of motion sensitivity, making the treatment of motion sensitivity challenging. The reporting of symptoms primarily in environments with rich visual information necessitates an increased understanding of the visual system's contribution to motion sensitivity. Thus, the overall aim of this thesis was to investigate the visual system's role in motion sensitivity and identify underlying factors that could guide the development of an intervention.

A narrative review of the literature was undertaken to understand the visual system's role in postural control. Information from the visual system is necessary to estimate movements of self and objects in relation to the environment. This information is essential for spatial orientation and postural control while navigating in an environment. Spatial orientation within the environment requires the integration of visual and vestibular information. The vestibular system contributes to visual stability by generating reflexive eye movements during head movements (the vestibulo-ocular reflex). The vestibulo-ocular reflex compensates for the head movement by moving the eyes in the opposite direction and is essential for gaze stabilisation during head movements. The moment the eyes are focused on a single location, the stabilisation of gaze occurs via visual fixation. Visual fixation consists of three small eye movements. These are microsaccades, ocular drifts and ocular tremors. These small eye movements

during visual fixation are essential for visual processing, to acquire information about the scene and to prevent visual fading. Visual fixations plays a significant role in maintaining a stable image by interacting with the environment and the vestibular system. The importance of visual fixations has been highlighted in the literature; however, there is a lack of evidence regarding visual fixations in adults with motion sensitivity. An observational exploratory study was undertaken to investigate visual fixations in adults with motion sensitivity.

The observational exploratory study exposed people to six conditions with increasing levels of visual complexity to investigate the characteristics of visual fixations and postural parameters. Healthy adult participants were compared to adults with motion sensitivity. This study demonstrated the presence of fixational instability and an increase in head and postural sway in adults with motion sensitivity, particularly in conditions with complex and moving backgrounds. This study identified two parameters that could differentiate adults with motion sensitivity from healthy adults.

The findings from the narrative review and the observational exploratory study suggested visual fixations are a key factor for people with motion sensitivity and that they may be ameliorable by an intervention. Study findings were mapped onto the Medical Research Council's framework for intervention development. The iterative cycles led to the development of a treatment theory. The treatment theory outlined the physiological basis for fixational instability which posits that the presence of an increased number of microsaccades predisposes an individual to motion sensitivity. Microsaccades increase the transient motion signals rendering an image unstable on the retina, leading to fixational instability. Future work will explore the theory by testing and developing an intervention. The current work has identified parameters that can be used to diagnose motion sensitivity. This will allow a feasible and valid diagnostic tool to be developed for use in clinical settings.

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Operational definitions

Fixational instability	Inability to maintain gaze on a target; characterised by increased number of refixations.
Focus of expansion	A point in the optic flow from which all visual motion originates. Focus of expansion lies in the direction of forward motion.
Fusional vergence	Movement of both eyes that enables fusion of monocular images producing binocular vision.
Gaze stabilisation	Maintenance of fixation on a target during head movement. Gaze stabilisation is achieved by vestibulo-ocular reflex.
Lamellar flow	Optic flow which remains parallel to the line of motion and sweeps past the observer.
Microsaccades	Largest and fastest small eye movement during visual fixation.
Microsaccadic suppression	Suppression of neural firing associated with occurrence of microsaccades.
Ocular drifts	Smooth and slow small eye movement during visual fixation. Also known as slow control.
Ocular tremors	Aperiodic, wave-like motion of the eye during visual fixation.
Optic flow	Pattern of motion of the external world over the retina.
Optokinetic reflex/response	A combination of slow-phase and fast-phase eye movements where the eyes momentarily follow a moving object, then rapidly reset to the initial position.
Optokinetic stimulation	Rotatory stimulation utilising moving visual targets along the x or y axes.
Radial flow	Optic flow which expands radially outwards and is projected onto the centre of the retina with a focus of expansion aligned with the direction of movement.
Reference signal	Information from proprioceptive feedback from the extraocular muscles, the somatosensory system, vestibular afferents, and cognition.
Retinal signal	Information from the visual system.
Retinal slip	Movement of the visual image on the surface of the retina.
Saccadic intrusions	Involuntary saccades that interrupt a visual fixation.
Temporal attention	Involves directing attention to a specific instant of time.
Vection	Illusion of self-motion.

Visual dependence	Described as having increased reliance on visual system for postural control.
Visual fading	Loss of vision due to neural adaptation during constant or uniform visual stimulation.
Visual fixation	Maintaining gaze on a single location. Also known as fixational eye movements. Visual fixation comprises of microsaccades, ocular drifts and ocular tremors.
Visual illusion	Perception of a false movement of a static image.

Abbreviations

3D	3-dimensional
AMTI	Advanced Mechanical Technology Inc.
ANOVA	Analysis of variance
AUC	Area under the curve
AUTEC	Auckland University of Technology Ethics Committee
AVOR	Angular vestibulo-ocular reflex
COM	Centre of mass
COP	Centre of pressure
DHI	Dizziness Handicap Inventory
EMC	Eisdell Moore Centre
EOG	Electrooculogram
ETG	Eye-tracking glasses
FPS	Frames per second
HAD	Hospital Anxiety and Depression Scale
HDEC	Health and Disability Ethics Committee
MRC	Medical Research Council
MV	Mean velocity
NZDBC	New Zealand Dizziness and Balance Centre
OFR	Ocular following reflex
OKR	Optokinetic reflex
OKS	Optokinetic stimulation
OPNs	Omni-directional pause neurons
PPPD	Persistent postural perceptual dizziness
RMS	Root mean square
ROC	Receiver operating curve
SCQ	Situational Characteristic Questionnaire
SMI ETG	SensoMotoric Instruments eye-tracking glasses
TVOR	Translational vestibulo-ocular reflex
VOR	Vestibulo-ocular reflex
VSR	Vestibulo-spinal reflex

Attestation of Authorship

I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person (except where explicitly defined in the acknowledgements), nor material which to a substantial extent has been submitted for the award of any other degree or diploma of a university or other institution of higher learning.

Signature: Date: 17.05.2021

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Contribution to Co-Authored Manuscripts

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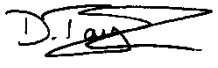
Denise Taylor	

Chapter 1: Introduction

Motion sensitivity is chronic functional dizziness characterised by nausea, dizziness, and imbalance in complex visual surroundings (Bronstein et al., 2014; Chin, 2018; Guerraz et al., 2001). These symptoms lead to difficulty moving and maintaining stability in environments with rich visual input, such as supermarkets and shopping malls. Motion sensitivity forms one of the diagnostic criteria of persistent postural perceptual dizziness (PPPD) and is different from true rotational vertigo, which is characterised by a sensation of the environment spinning. Historically, motion sensitivity has been associated with various names such as visual vertigo (Bronstein, 1995a), visual-vestibular mismatch (Longridge & Mallinson, 2000) and visual motion hypersensitivity (Winkler & Ciuffreda, 2009).

Bronstein first described motion sensitivity following a vestibular disorder, noticing that dizziness and imbalance persisted even after recovery from an acute vestibular disorder (Bronstein, 1995a, 1995b). Epidemiological research reports that vestibular disorders affect 25.2% of those who experience moderate to severe dizziness over a lifetime (Neuhauser et al., 2008). Despite the availability of data for vestibular disorders, epidemiological data for the incidence and prevalence of motion sensitivity after a vestibular disorder is scarce. This can be attributed to a limited ability to measure the severity of symptoms and a lack of adequate diagnostic tools, rendering diagnosis of motion sensitivity challenging. The lack of a definitive diagnostic test means symptoms frequently remain unexplained, leading to frustration and high anxiety levels among adults with motion sensitivity (Sezier et al., 2019; Zur et al., 2015). These chronic symptoms affect an individual's daily life, interfering with their personal, social, and work-related quality of life, thus reducing health-related outcomes (Dieterich & Staab,

2017; Holmes & Padgham, 2011; Lonardi, 2007; Mendel et al., 1997; Ödman & Maire, 2008; Staab, 2012; Ten Voorde et al., 2012; Tinetti et al., 2000; Turner & Kelly, 2000).

A recent qualitative study explored the perspective of adults suffering from this chronic symptom (Sezier et al., 2019). The authors emphasised a lack of medical diagnosis as a factor in higher anxiety levels among these individuals. The absence of a medical diagnosis and inability to explain their symptoms to others, lead to loss of self-validation and increased frustration and agitation in people living with chronic symptoms. A lack of self-validation affected people's trust in health professionals and had a huge impact on their therapeutic relationships. This had a significant detrimental effect on their personal relationships and life roles. It was suggested that having a diagnosis, even speculative, might help reduce anxiety and frustration in this population.

The lack of a clear understanding of the aetiology has made the treatment of motion sensitivity difficult. In the literature there is a scarcity of efficacious treatments for adults with motion sensitivity. Vestibular rehabilitation and optokinetic stimulation (the use of moving targets in visual field) are the two most commonly used approaches reported in the literature (Moaty et al., 2017; Pavlou et al., 2004) (Figure 1.1). These studies reported some improvement in the symptoms, but no significant improvements were seen in anxiety and phobia in motion sensitivity. Additionally, no long-term improvements were observed after using these treatments. Similar results, for improvement in the symptoms, were reported from an experimental study using immersive virtual reality with vestibular rehabilitation to treat motion sensitivity (Pavlou et al., 2012).

Given that the aetiology of motion sensitivity is not well understood, it is uncertain how the above-mentioned treatments would improve symptoms (Figure 1.1). The lack of any

significant improvements in the symptoms can be attributed to the fact that the current treatment methods use habituation and desensitisation to symptom-provoking stimuli rather than treating an underlying biological component.

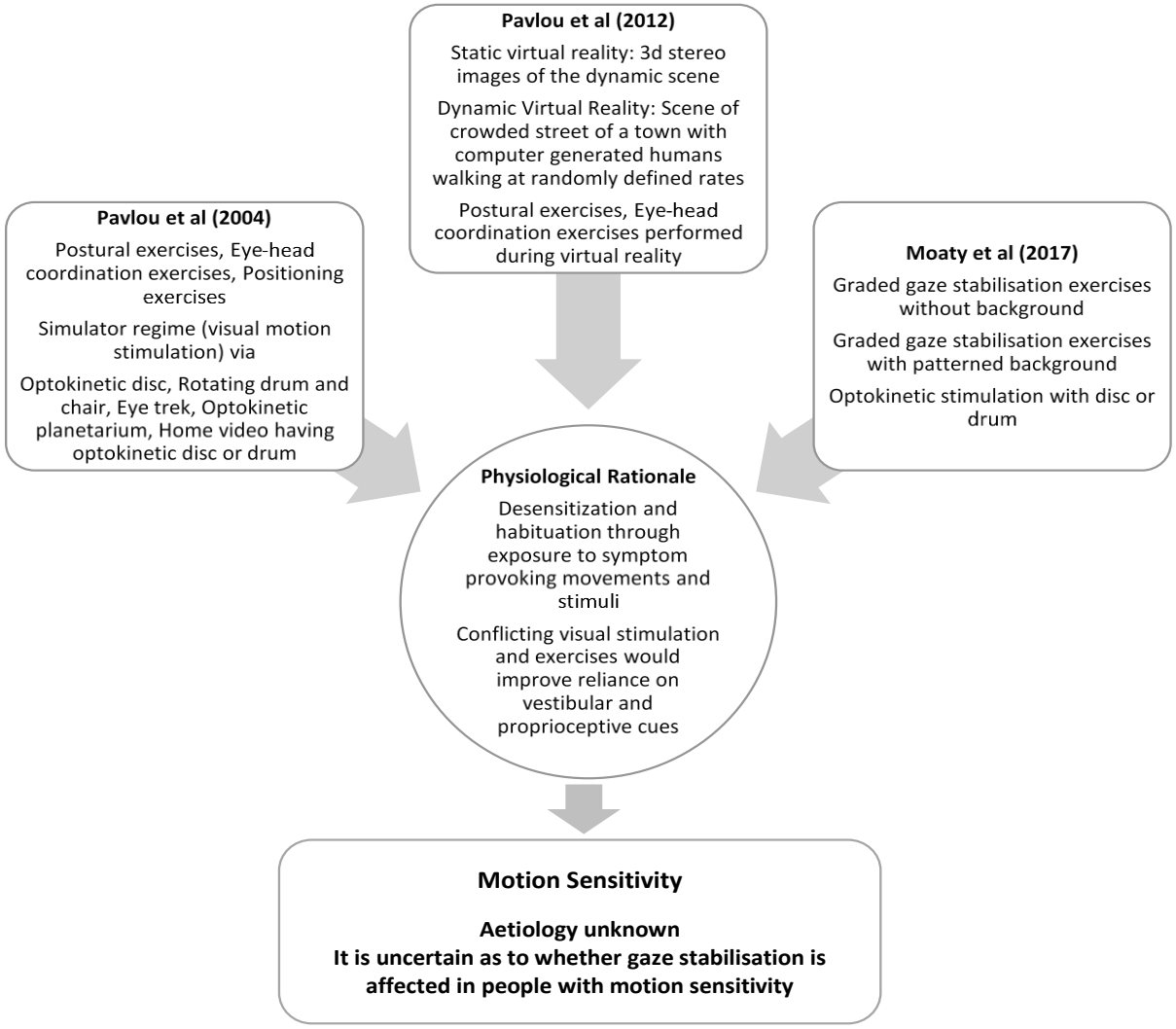


Figure 1.1 Current treatments for motion sensitivity

Experimental studies have demonstrated increased displacement of centre of pressure depicting increased postural sway in adults with motion sensitivity exposed to complex visual surroundings (Guerraz et al., 2001; Pavlou et al., 2006; Van Ombergen et al., 2016). Additionally, adults with motion sensitivity exhibited difficulty ignoring peripheral visual stimuli and the background motion behind a target when asked to maintain gaze on a fixed target (Zur et al., 2014).

Gaze stabilisation during head movements is achieved by the vestibulo-ocular reflex (VOR) which generates eye movements that compensate for head movements. This helps in maintaining visual and postural stability by coordination of head and body position in space (Angelaki et al., 1995). Additional to the VOR, visual fixations have a vital role in maintaining visual and postural stability (Martinez-Conde, 2006; Martinez-Conde & Macknik, 2008; Martinez-Conde et al., 2004; Otero-Millan et al., 2014). A large body of evidence describes visual fixation's role in suppressing destabilising oculomotor and postural responses as one of the crucial factors in maintaining a steady image and perceiving a stable world (Garzorz & MacNeilage, 2017; Murakami, 2004; Murakami et al., 2006; Pola et al., 1995; Wyatt et al., 1995). Experimental studies have demonstrated that an inability to visually hold the gaze on a target (fixational instability) can predispose a person to developing motion sensitivity (Murakami, 2004). However, there is a dearth of literature investigating visual fixations in adults with motion sensitivity. To date, only one study has investigated visual fixations in people experiencing symptoms of motion sensitivity after a vestibular disorder (Winkler & Ciuffreda, 2009).

The occurrence of symptoms in environments with rich visual input and the lack of specific treatments, necessitates exploring the visual system's role in motion sensitivity and identifying factors that could inform the development of an intervention to treat motion sensitivity symptoms effectively.

1.1 Aims and objectives of the research

The overarching aim of this research was to explore the visual system's role in motion sensitivity and identify elements that could guide the development of an intervention for people with motion sensitivity. The objectives were:

1. To understand the interactions between vision, postural control, and motion sensitivity to:
    a. Understand the visual system's interactions with the environment and the vestibular system.
    b. Identify possible factors within the visual system that could contribute to motion sensitivity.
2. To conduct an observational exploratory study to investigate:
    a. The characteristics of visual fixations in adults with motion sensitivity.
    b. Postural parameters in adults with motion sensitivity.
3. To identify and posit a theory that could inform development of an intervention informed by the results of the narrative review and the observational exploratory study.

1.2 Structure of the thesis

The flow of the thesis development and structure is outlined in Figure 1.2.

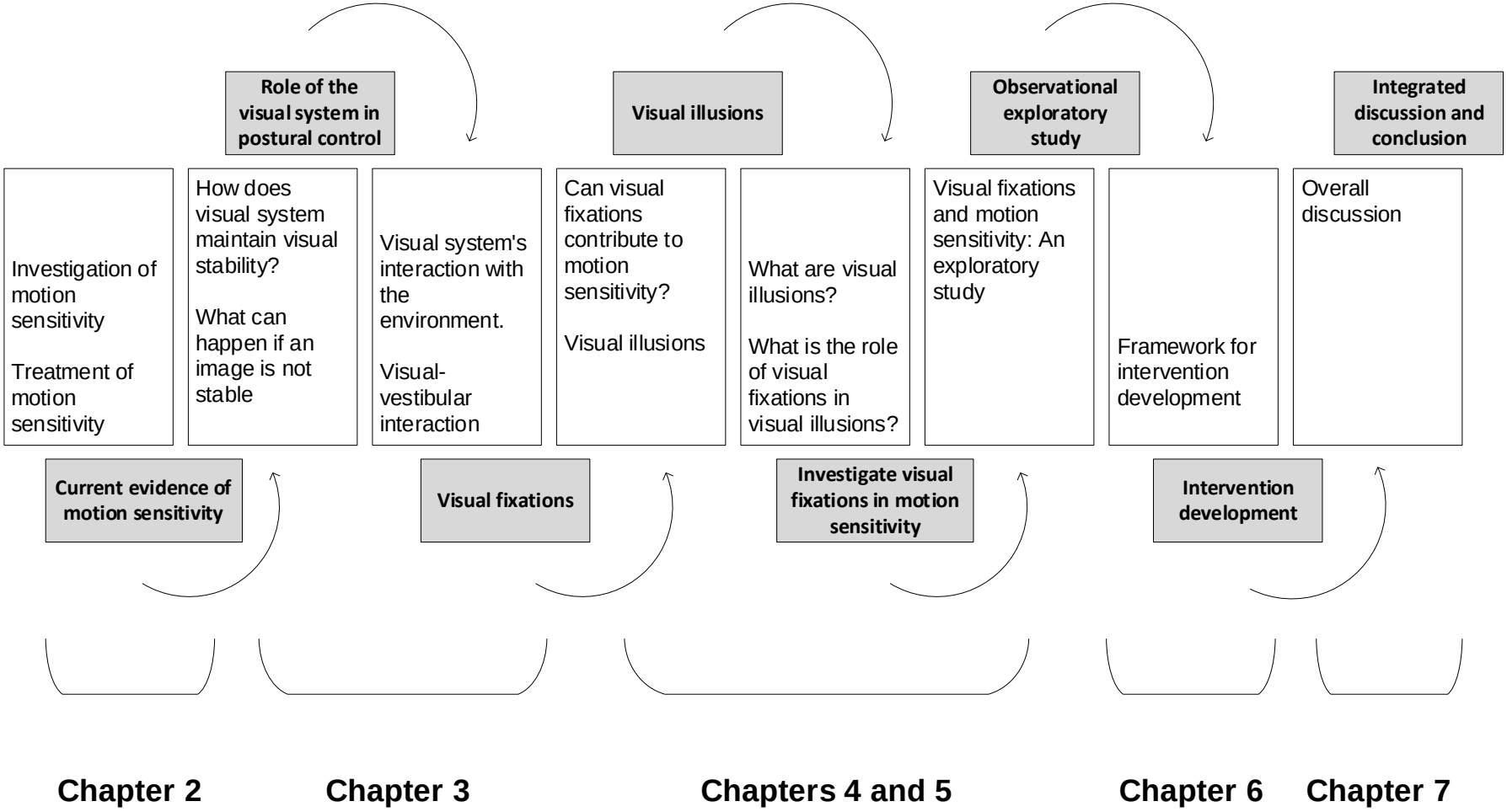


Figure 1.2 Thesis development and structure

Chapter 2 - Evidence for the assessment and treatment of motion sensitivity

This chapter describes and critically appraises the research to date, which has focussed on investigating and treating motion sensitivity. The chapter is divided into two sections. The first section describes the one study investigating visual fixations in adults with motion sensitivity. The second section elaborates on the studies undertaking treatment of motion sensitivity.

Chapter 3 – Narrative review

This chapter describes the visual system's role in postural control by outlining the key processes underlying the visual-vestibular interaction to maintain visual and postural stability. A manuscript has been submitted to the journal *Frontiers in Human Neuroscience* and is currently under review.

Chapter 4 – Protocol for an exploratory study

The narrative review led to the identification of visual fixations as a critical factor to be investigated in motion sensitivity. An observational exploratory study was designed to investigate the characteristics of visual fixations and postural parameters in adults with motion sensitivity and in healthy adults. The chapter contains the literature review exploring visual fixations and a published manuscript of the study protocol in the journal *JMIR Research Protocols*.

Chapter 5 – Visual fixations and motion sensitivity: An exploratory study

This chapter presents the results and discussion of the study. The manuscript submitted to the journal *Gait and Posture* is currently under review.

Chapter 6 – Intervention development

This chapter describes the process of intervention development by utilising a framework and findings from the narrative review and the observational exploratory study. The

chapter describes the development phase to conceptualise a theory which will underpin the development of an intervention to treat adults with motion sensitivity.

Chapter 7 – Integrated discussion and conclusion

The last chapter comprises an overview of research findings with implications for clinical practice and future research, and the strengths and limitations of the research.

Chapter 2: Evidence for the assessment and treatment of motion sensitivity

2.1 Prologue

This chapter presents the literature review of the current evidence for the assessment and treatment of motion sensitivity. The critique of this literature will be used to demonstrate why further investigation is needed to understand the role of the visual system in motion sensitivity. We will also propose an explanation for why treatments to address the symptoms of motion sensitivity have shown little long-term improvement.

2.2 Methods

The literature review was conducted systematically. Two separate searches were undertaken:

1. A search for the literature regarding the assessment of visual fixations in motion sensitivity.
2. A search for current treatments for motion sensitivity.

This section describes the separate inclusion and exclusion criteria for both searches.

2.2.1 Inclusion and exclusion criteria for the assessment of visual fixations in motion sensitivity

Studies were included if they met all the following criteria: assessment of visual fixations in motion sensitivity, history of a vestibular disorder, aged 18 years or above and appeared in peer reviewed English-language journals.

Studies were excluded if they were reviews, books, commentaries, conference papers or letters.

2.2.2 Information sources

A search (October 2017 updated in November 2020) of the following databases was undertaken: CINAHL, MEDLINE, Scopus, EBSCO health databases and Web of

Science. No limit was placed on publication date. The search strategy included the following key search terms: motion sensitivity, visual vertigo, visual motion hypersensitivity, visually induced dizziness, visual-vestibular mismatch, vestibular disorder/s, vestibular dysfunction, vestibular deficit, visual fixation/s, visual refixation/s, fixational eye movement/s.

2.2.3 Inclusion and exclusion criteria for treatments for motion sensitivity

Studies were included if they met the following criteria: involved treatment of adults with motion sensitivity after a vestibular disorder, aged 18 years or above, confirmed presence of motion sensitivity by the Situational Characteristic Questionnaire or Visual Vertigo Analogue Scale and appeared in peer reviewed English- language journals.

Studies were excluded; if the participants had motion sensitivity after a traumatic brain injury, concussion, migraine or any other neurological disorder, if reviews, books, commentaries, conference papers or letters.

2.2.4 Information sources

A search (October 2017 updated November 2020) of the following databases was undertaken: CINAHL, MEDLINE, Scopus, EBSCO health databases and Web of Science. No limit was placed on publication date. The search strategy included the following key search terms: motion sensitivity, visual vertigo, visual motion hypersensitivity, visually induced dizziness, visual-vestibular mismatch, treatment, rehabilitation, intervention, therapy, management, effectiveness, effect/s, vestibular disorder/s, vestibular dysfunction, vestibular deficit.

2.3 Results

One study was found for the assessment of visual fixations in motion sensitivity (Winkler & Ciuffreda, 2009). The second search resulted in three studies investigating treatments for motion sensitivity (Pavlou et al., 2012; Pavlou et al., 2004).

2.3.1 Assessment of study quality of the included studies for treatment of motion sensitivity

The quality of the studies was critically appraised using the modified Downs and Black checklist for the assessment of the methodological quality of randomised and non-randomised trials (Downs & Black, 1998). The checklist rates the study on five domains: Reporting, External Validity, Internal Validity-bias, Internal Validity-confounding, and Power.

All three studies utilised the Situational Characteristic Questionnaire to identify adults with motion sensitivity and only one study included a long-term follow up (16-36 months) (Pavlou et al., 2004). All three studies scored <14 on the modified Downs and Black checklist, signifying poor quality (Hooper et al., 2008). Two of the studies scored poorly on the external validity domain, limiting generalisability and transferability of findings (Pavlou et al., 2012; Pavlou et al., 2004).Two of the studies were randomised controlled trials but scored poorly on the internal validity- bias domain, signifying a high risk of bias (Pavlou et al., 2012; Pavlou et al., 2004). There was a lack of information regarding blinding the outcome assessor and blinding the participants to the intervention. One of the studies lacked information regarding the hypothesis of the study and scored poorly on the reporting domain (Moaty et al., 2017). All three studies scored poorly on the internal validity- confounding domain, as none of the studies adjusted for possible confounders, for example carry-over effects of medications which could have led to an improvement in the symptoms. One of the studies had varied duration of treatment among participants, increasing the risk of confounders (Moaty et al., 2017). Further, all studies scored poorly on the power domain as none of the studies provided sample size determination to detect a clinically important effect, reducing the power of the studies (Moaty et al., 2017; Pavlou et al., 2012; Pavlou et al., 2004).

The completed Downs and Black checklists can be found in Appendices A, B and C for the three intervention studies assessed. The characteristics of each study are described in Table 2.1. Due to the small number of studies, a systematic review was not carried out. The remainder of this chapter describes the limited current evidence for assessment and treatment of motion sensitivity.

2.4 Discussion

2.4.1 Study investigating visual fixations in adults with motion sensitivity

Motion sensitivity is a debilitating condition with a lack of evidence of successful treatment outcomes. This can partly be attributed to limited knowledge of the aetiology of the disorder (Zur et al., 2015). Experimental studies have identified that adults with motion sensitivity are visually dependent (Bronstein et al., 2020; Bronstein, 1995b, 2005; Guerraz et al., 2001), however, there is a dearth of literature exploring the role of the visual system that could help explain the mechanism and provide a deeper understanding of motion sensitivity. To date, only one study has investigated the role of the visual system in people with motion sensitivity (Winkler & Ciuffreda, 2009).

The study investigated visual fixations and binocular abnormalities in three groups of participants: those with vestibular dysfunction with motion sensitivity; those with vestibular dysfunction without motion sensitivity; and healthy adults (Winkler & Ciuffreda, 2009). The authors reported that people with motion sensitivity exhibited poorer fixation, impaired fusional vergence and higher scores on the Dizziness Handicap Inventory. The results identified that people with motion sensitivity demonstrated fixational instability characterised by an increased number of refixations while attempting to maintain fixation in a visually stimulating environment, compared to people with vestibular dysfunction without motion sensitivity, and healthy controls.

This was the first study to investigate visual fixations and identify the presence of fixational instability in adults with motion sensitivity. The authors, however, did not elaborate on the possible mechanism that could explain the results and provided a generalised explanation of findings, reiterating the existing theory of visual dependence. The increased number of refixations was attributed to attentional deficits, but the study did not utilise any outcome measure to identify attentional deficits. Despite investigating visual fixations in adults with motion sensitivity, the authors did not explain the role of the visual system in motion sensitivity after a vestibular disorder nor the contribution of visual fixations to motion sensitivity.

The authors did not measure any postural parameters which might have enhanced understanding of the relationship between visual parameters and postural control. Therefore, the current evidence is insufficient to explain the role of the visual system in motion sensitivity.

2.4.2 Current treatment methods for motion sensitivity

The previous section outlined the limited knowledge of the mechanisms of motion sensitivity. Understanding the underlying mechanisms causing the symptoms could form a basis for planning an effective treatment (O'Cathain et al., 2019; Turner et al., 2019; Zur et al., 2015). The current treatment methods outlined in the literature use vestibular rehabilitation exercises with optokinetic stimulation (Moaty et al., 2017; Pavlou et al., 2004). Additionally, immersive virtual reality has been used to provide optokinetic stimulation using real-life scenarios (Pavlou et al., 2012).

Three intervention studies were identified that focussed on the treatment of motion sensitivity (Moaty et al., 2017; Pavlou et al., 2012; Pavlou et al., 2004). However, the lack of evidence of a long-term improvement in symptoms necessitates further investigation of these studies. The three studies were critically appraised to understand

the physiological rationale behind the interventions and identify gaps in the literature. The following sections will first describe the physiological rationale behind the treatment methods, and then outline a critical appraisal of the three intervention studies.

2.4.3 Physiological rationale for current treatment methods

As outlined in Chapter 1, the most common interventions used to treat motion sensitivity are vestibular rehabilitation and optokinetic stimulation.

Vestibular rehabilitation therapy consists of progressive eye, head, and body movements and is based on the phenomenon of vestibular compensation. Vestibular compensation consists of reorganising the central nervous system to improve functional recovery and is based on adaptation and habituation mechanisms (Deveze et al., 2014; Lacour & Bernard-Demanze, 2015; Lacour et al., 2016; Tee & Chee, 2005). One of the main principles of vestibular rehabilitation is improving gaze stability by utilising gaze stabilisation exercises. The exercises are prescribed to improve the gain of the vestibulo-ocular reflex (VOR), improve visual acuity during head movement, and reduce dizziness and vertigo.

Adaptation consists of two approaches: sensory substitution and behavioural substitution (Deveze et al., 2014; Han et al., 2011; Lacour et al., 2016). Neither restore the lost function; instead, they replace it by a new operating mode using either sensory cues or a new behavioural strategy. Sensory substitution acts by undertaking sensory re-weighting of more reliable and accurate sensory cues (visual and somatosensory) after a vestibular disorder and selects a new framework for postural control and orientation. This is achieved in practice by manipulating either visual cues (eyes open, eyes closed) or somatosensory cues (standing on foam, moving surfaces) or both (Lacour & Bernard-Demanze, 2015; Lacour et al., 2016; Tee & Chee, 2005). Behavioural substitution is based on the central nervous system's propensity to reorganise functionally to

compensate for the lost vestibular functions. The most common illustration of behavioural substitution is the generation of covert saccades (saccades made prior to head movement) to compensate for the dynamic function of the VOR (Deveze et al., 2014; Lacour & Bernard-Demanze, 2015).

The second mechanism, habituation, is described as a reduction in the magnitude of the response to repetitive sensory stimulation and is induced by repetitive exposures to provoking stimuli, promoting desensitisation (Deveze et al., 2014; Han et al., 2011; Lacour & Bernard-Demanze, 2015; Lacour et al., 2016). Habituation aims to train the person to not respond to a stimulus by reducing the amplitude of excitatory post-synaptic potentials (Lacour & Bernard-Demanze, 2015; Tee & Chee, 2005). Habituation exercises consist of repetitions of movements that induce symptoms, thus reducing the amplitude of response (Norre & De Weerdt, 1980; Norré & Beckers, 1988; Whitney & Sparto, 2011).

Optokinetic stimulation comprises rotatory stimulation utilising moving visual targets along the x or y axes, using equipment such as an optokinetic drum, rotating chair or moving room. The optokinetic stimulation can be provided in various directions at varying speeds, and ranges from a whole-body to only a visual field rotation (Pavlou, 2010). Optokinetic stimulation is also based on the mechanism of habituation and desensitization and uses graded exposure to symptom-provoking stimuli to decrease the over-reliance on visual input for postural control (Moaty et al., 2017; Pavlou et al., 2004). Long-term exposure to provoking stimuli reduces dizziness by inducing structural changes in the sensory cells, resulting in decreased synaptic connections between the sensory neuron, interneurons, and motor neurons (Pavlou et al., 2011; Tee & Chee, 2005). Studies utilising optokinetic stimulation have proposed that optokinetic stimulation, when used in combination with vestibular therapy, decreases the over-reliance on visual input for postural control by inducing plastic adaptive changes which

reduce visual dependency (Pavlou et al., 2004; Pavlou et al., 2011). The reduction of visual dependency then promotes more accurate sensory re-weighting, thus improving postural stability (Pavlou, 2010; Pavlou et al., 2004). However, there is a lack of evidence concerning the plastic changes induced by optokinetic stimulation.

To treat people with motion sensitivity, all three studies utilised vestibular rehabilitation in conjunction with either optokinetic stimulation or virtual reality. The vestibular exercises varied across the studies but were usually a combination of gaze stability and postural exercises. This section discusses the limitations of the three studies, providing further insight into the applicability and efficacy of the treatment methods for adults with motion sensitivity.

Table 2.1 Characteristics of studies

Paper	Design & sample size	Treatment	Training sessions	Outcome Measures	Results
Pavlou et al. (2004)	RCT N=20 (each group)	Simulator regime + customised exercises (Group S) Customised exercises (Group C) Postural exercises Eye-head coordination exercises, Positioning exercises	1-hour sessions Twice weekly for 8 weeks Both groups received home exercise programme	Dynamic posturography	12.2% improvement (Group C); 20.4% improvement (Group S); significant effect of time
				BBS	Significant effect of time; no significant differences between groups
				Time constants of decay of vestibular sensation and slow velocity phase nystagmus	No significant main effects
				VSS	27.4% improvement (Group C); 52.4% improvement (Group S)
				SCQ	Significant effect of time for Group S. 32% greater improvement in Group S
				HADS	Global HADS-Anxiety: 32% greater improvement in Group S Global HADS-Depression: significant effect of time no significant differences between groups for both HADS-A and HADS- D
				STAI	Significant effect of time; no significant differences between groups
				CMSSQ	No significant improvements and differences between groups

Paper	Design+ Sample size	Treatment	Training sessions	Outcome Measures	Results
Pavlou et al. (2012)	RCT N=5 (Group D) N= 11(Group S); n=5 from group S transferred to group D after 2 months (Group D1)	Dynamic virtual reality (group D) Static virtual reality (Group S) + Exercises during VR+ Home exercise programme	45-minute therapy twice weekly for four weeks	SCQ	Significant between-group difference (59.2% improvement in Group D)
				BDI	No significant between-group differences
				BAI	No significant between-group differences
				Fear Questionnaire	No significant between-group differences;
				DGI	No significant between-group differences; No significant change in score from baseline
				VRCESS	Significant differences between group D and Group S (59% improvement in group D)
Moaty et al. (2017)	Retrospective N=65	Graded gaze stabilisation exercises without background Graded gaze stabilisation exercises with patterned background Optokinetic stimulation	Started with gaze stabilisation 2-3 times/day; once patients tolerated 20 times/day, proceeded to next (with background) Followed by home DVD of OKS	SCQ	75% patients showed statistically significant improvement
				NQ	63% patients showed statistically significant improvement
				DHI	68% patients showed no significant improvement
				HADS	45% and 48% patients showed no significant improvement (HAD-A and HAD-D respectively
				Vestibular office tests (oculomotor function, VOR, VSR, Gait and static balance)	Not reported

Note. BAI – Beck's Anxiety Inventory; BBS- Berg Balance Scale; BDI – Beck's Depression Inventory; CMSSQ - Childhood Short-form Motion Sickness Questionnaire; DGI - Dynamic Gait Index; HADS - Hospital Anxiety and Depression Scale; NQ - Nijmegen Questionnaire; RCT - randomised controlled trial; SCQ - Situational Characteristic Questionnaire; STAI - Speilberger State Trait Anxiety Inventory; VOR- Vestibulo-ocular reflex; VR - virtual reality; VRCESS - Virtual Reality Exercise Symptom Score; VSR - vestibulospinal reflex; VSS - Vertigo Symptom Scale.

2.4.4 Critique of current research

Pavlou and colleagues (2004) reported that they did not have a control group as the treatment method was already proven to be effective. It should be noted that the efficacy of the treatment has been evidenced in people with a vestibular disorder, but little is known about its effect on people with motion sensitivity. Motion sensitivity usually develops as a sequela of a vestibular disorder. However, the lack of an adequate diagnostic tool to identify motion sensitivity means there is limited data on the proportion of people who subsequently develop motion sensitivity. The study utilised vestibular exercises, which have a rationale of improving gaze stability by improving the gain of the VOR. However, there is a lack of evidence regarding a problem with the VOR in adults with motion sensitivity. In addition, the authors did not measure the VOR before and after treatment, which might have provided a better insight and understanding of the effect of treatment. Thus, the rationale for treatment is not clear nor well justified for people with motion sensitivity.

The results reported that pooling the scores of all participants from each group showed an overall improvement of 20.4% in Group S (simulator regime and customised exercises) and 12.2% in Group C (customised exercises) in the global composite score using Computerised Dynamic Posturography after the treatment, but no improvements were seen in the individual condition scores, including the condition providing moving surround stimulation. The authors' theory behind the treatment was based on visual desensitisation by exposing participants to symptom-provoking stimuli. One of the main symptom-provoking stimuli for adults with motion sensitivity is moving visual surroundings but the results did not demonstrate any improvement in that domain of posturography. The authors hypothesised that the treatment would improve sensory re-re-weighting by reducing visual dependence; however, the study results did not support the hypothesis.

One of the significant issues with the study is the difficulty in ascertaining where the effect came from and what led to the improvements noticed on the Situational Characteristic Questionnaire (SCQ). The authors used five different types of equipment with varied settings for optokinetic stimulation (Figure 1.1). All the participants in the simulator group (Group S) were exposed to all five pieces of equipment in each treatment session. Therefore, it is difficult to identify how the intervention elements interacted with each other and the recipient. Likewise, it is not clear which aspects of the treatment were more effective and why. The authors reported that they could not identify which equipment was beneficial, and with what specificity, leading to limited knowledge regarding the basis of improvement after utilising the treatment.

The other issue identified is that the study did not account for confounding factors that could affect the study results. The participants were asked to reduce/stop their medication before the trial. It is likely that the medicines had some effect which may have resulted in the improvement of symptoms as reported by the study results.

The authors reported a significant effect of time on the SCQ score, with a statistically significant improvement in the group receiving optokinetic stimulation (Group S). However, the long-term follow-up conducted after between 16 and 36 months revealed that 29/30 patients were still experiencing symptoms. The follow-up consisted of a phone interview in which the participants had to rate six questions on a five-point scale rather than being tested on previously used outcome measures. In addition, the authors did not provide the details and psychometric properties of the five-point scale used.

There was a statistically significant improvement in Hospital Anxiety (HAD-A) score and Depression scale score (HAD- D), but these improvements were not clinically significant. The minimal clinically important difference for HAD is 1.7 (Lemay et al., 2019) and the study results do not depict this difference. The minimal detectable change

reported in the literature for HADS-A is 3.80 and for HADS-D is 3.99 (Wang et al., 2009). The improvements in HADS-A and HADS-D were reported as percentage improvements, and the data provided does not reflect these minimal detectable changes.

The study reported statistically significant improvements in a majority of outcome measures in both groups with a greater improvement in the group receiving optokinetic stimulation. Since the improvements were seen in both groups, it suggests that attending the exercise sessions and meeting the therapist might have provided a sense of confidence and reassurance which led to the improvements reported by the study.

The second study by Pavlou and colleagues (2012) utilised immersive virtual reality in addition to vestibular exercises to treat adults with motion sensitivity. The study was also based on the physiological rationale of desensitisation and habituation to symptom-provoking stimuli. It used a static and dynamic virtual reality image of real-life scenarios to promote desensitisation and habituation. All the participants carried out vestibular exercises while viewing either the static or the dynamic virtual reality image. The dynamic image consisted of scene of a crowded town with computer-generated human walking the street (Figure 1.1). The static image was identical but with no movement. The authors again reported significant improvements in the SCQ score. There is a lack of evidence regarding the minimal detectable change and minimal clinically important difference for SCQ scores; therefore, the results from this study and the previous study cannot be used to identify whether there was a clinically significant improvement in the SCQ score.

The results demonstrate no statistical or clinical improvements for other outcome measures consisting of the Beck's Anxiety and Depression Scale and the Fear Questionnaire. It should be noted that anxiety and phobia are two of the symptoms most commonly reported by adults with motion sensitivity. Experimental studies have

reported higher levels of anxiety associated with motion sensitivity (Zur et al., 2015). Considering there was a statistically significant improvement in the SCQ score, but no significant improvements in phobia and anxiety, it is not clear whether the treatment was able to address the symptoms effectively or whether the improvement as reported by the SCQ score was due to a placebo effect of meeting the therapist and undergoing some form of exercise during the sessions. Studies have reported that adults suffering from chronic conditions and lacking a definitive diagnosis may have a poor therapeutic relationship with their practitioner (Sezier et al., 2019). Attending regular exercise sessions with the therapist might have instilled satisfaction and reassurance leading to improvement in the SCQ score. The authors hypothesised that the basis for the improvement in symptoms was habituation and improved sensory re-weighting induced by virtual reality, but the results reported no change in the baseline score of Dynamic Gait Index (DGI), signifying no improvement after treatment. Linking it back to the study hypothesis, it is unclear why there was no improvement in the DGI if the treatment led to better sensory re-weighting.

The study by Moaty and colleagues utilised customised vestibular exercises with optokinetic stimulation to treat adults with motion sensitivity (Moaty et al., 2017). It reported similar results to the previous studies, with improvements noted on the SCQ but no significant improvement in measures of anxiety and depression (Dizziness Handicap Inventory and Nijmegen Questionnaire). The authors reported that more than 45% of patients showed no improvement on anxiety and depression questionnaires. One of the study's major limitations was that it was a non-randomised, single group trial and the study did not account for differences in exposure to treatment (mean of 6.8± 5 months). Additional clinical psychology was provided for 27% of the participants, which could have improved SCQ scores. Such discrepancies place the study low on the quality checklist, with the efficacy and generalisability of findings being questionable.

Current treatment methods reported in the literature focus on desensitisation and habituation to stimuli through progressive exposure to symptom-provoking movements and situations rather than treating any underlying problem that could contribute to the generation of symptoms. The lack of treatment of an underlying factor could explain the absence of any long-term improvements and lack of significant improvements in anxiety and phobia in adults with motion sensitivity. Additionally, current treatments are based on therapy proven to be effective for adults with vestibular disorders and not necessarily motion sensitivity. This can be attributed to the scarcity in the literature of any description of an underlying biological basis for motion sensitivity that could be targeted to treat the symptoms effectively.

One of the major concerns regarding the treatment of motion sensitivity is the lack of appropriate diagnostic tools to identify and quantify the severity of symptoms. The most common questionnaires used to measure this symptom are the SCQ and the Visual Vertigo Analogue scale. However, these questionnaires fail to identify and quantify the underlying problem and there is limited data in the literature regarding the minimal detectable change that could be used to test the improvement in motion sensitivity symptoms.

The treatments described in the three papers utilised gaze and postural stability exercises to improve motion sensitivity. However, whether gaze stability is affected in adults with motion sensitivity is unknown. The experimental study investigating the visual system in motion sensitivity (Section 2.4.1) identified the presence of fixational instability in people with motion sensitivity. Gaze stability is concerned with the VOR (gaze stabilisation during head movements) whereas fixational instability is an inability to maintain gaze on a target, irrespective of whether head is moving or is stationary. Thus, the rationale behind the treatment, and its applicability, are not justified. In addition, the most common theory of motion sensitivity described in the literature is

visual dependence. Current treatments fail to provide evidence regarding an improvement in visual dependence leading to improved symptoms. These treatments do not have a convincing rationale; neither do they give the results expected of efficacious treatments of adults with motion sensitivity nor improve their health-related outcomes.

2.5 Summary

The chapter elaborated on the existing evidence regarding the investigation and treatment of motion sensitivity. The only study found in the literature investigating the visual system was unable to identify and elaborate on a factor within the visual system that could explain the development of motion sensitivity. The authors failed to provide a definitive physiological rationale for the findings. The chapter further highlighted the lack of efficacious and specific treatments for adults with motion sensitivity. The insufficient evidence regarding the aetiology and treatment of motion sensitivity necessitates further investigation, leading to the first objective for the research reported in this thesis: to understand the interactions between vision, postural control, and motion sensitivity.

Chapter 3: Narrative review

3.1 Prologue

This chapter is a narrative review of the literature describing the role of the visual system in postural control and its interaction with the environment and the vestibular system at a functional and a neuronal level. This manuscript is currently under review with a peer-reviewed journal. This chapter addresses the following research objective:

- To understand the visual system's role in postural control to:
    a. Understand the visual system's interactions with the environment and the vestibular system
    b. Identify possible factors within the visual system that could contribute to motion sensitivity.

The submitted manuscript is presented here as it is with no modification in content but a few formatting modifications to fit with the thesis structure and facilitate reading.

Start of the manuscript

Title: The visual system and its interaction for postural control – A narrative review

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Abstract

The visual system is heavily involved in postural control as it provides spatial information in the environment. The visual system is the primary source of sensory information that perceives environmental stimuli and interacts with other sensory systems to generate visual and postural responses to maintain postural stability. Although the three sensory systems – the visual system, the vestibular system, and the somatosensory system – work concurrently to maintain postural control, the visual and vestibular system interaction is vital to maintain visual and postural stability. The visual system influences postural control as it plays a key role in differentiating self-motion from external motion. The visual system's main afferent information consists of optic flow and retinal slip, and these lead to the generation of visual and postural responses. Visual fixations generated by the visual system interact with the afferent information and the vestibular system to maintain visual and postural stability. This review synthesises these roles of the visual system and their interaction with the environment and the vestibular system in maintaining postural stability.

3.2 Introduction

Vision plays a central role in maintaining postural stability as we move around in the world, by providing information and generating a clear image of the environment (Hunter & Hoffman, 2001; Wade & Jones, 1997; Wallach, 1987). Such information is essential for interpreting spatial orientation and maintaining postural control. The maintenance of postural control requires interpretation of self-motion, external motion, or a combination of both (Guerraz & Bronstein, 2008; Júnior & Barela, 2004; Redfern et al., 2001; Rogers et al., 2017).

Self-motion and the motion of an object in the environment whilst a person is stationary cause similar visual stimulation. Movement of an object within an environment is

perceived as motion, but self-movements are not always perceived as motion (Fushiki et al., 2005; Melcher, 2011; Redfern et al., 2001). For example, a head turn causes the movement of a scene relative to the retina, similar to that caused by an object's movement within an environment. Yet, we perceive the environment as stationary when turning the head (Ivanenko & Gurfinkel, 2018; Melcher, 2011; Wallach, 1987). This is because proprioceptive input provides information that the head is moving on a stationary body (Bense et al., 2005; Guerraz & Bronstein, 2008; Ivanenko & Gurfinkel, 2018; Roy & Cullen, 2002; Samuel et al., 2015; Strupp et al., 2003). The ability of the nervous system to utilise the sensory information that is more reliable over absent or conflicting sensory information is known as sensory re-weighting (Assländer & Peterka, 2014; Peterka, 2002).

Postural control requires continuous regulation of information from three systems – the visual, the vestibular, and the somatosensory systems (Ivanenko & Gurfinkel, 2018; Massion, 1994; Samuel et al., 2015). The somatosensory system receives information from the whole body whereas the visual and vestibular system only receive information from the eye and head, respectively. This review will focus on the integration of information from the visual and vestibular systems for postural control. The current review will amalgamate the fundamental concepts required to understand the visual system's role and its interaction with the environment and the vestibular system in maintaining postural stability.

3.3 Overview of the visual system

The visual system consists of the central visual system (fovea) and the peripheral visual system. The central visual system recognises objects and object motion, whereas the peripheral vision is sensitive to moving scenes and dominates the awareness of self-motion and postural control (Berencsi et al., 2005; Dichgans & Brandt, 1978; Guerraz & Bronstein, 2008; Nougier et al., 1997; Warren & Kurtz, 1992). To maintain postural

control and navigate in an environment, we need a balance between central and peripheral vision to determine the spatial orientation of self and objects in an environment. As we move, the relationship between self and objects in the environment changes, and accurate interpretation of movement using information from the visual system helps differentiate self-motion from external motion.

The pattern of motion of the external world over the retina is known as optic flow and forms a part of the afferent information to the visual system (Koenderink, 1986; Warren et al., 2001; William, 2004). For example, when walking past a line of trees, there is a changing pattern of optic flow generated on the retina. Movement of the eyes and head lead to movement of the visual image on the surface of the retina known as retinal slip, forming another part of afferent information (Gielen et al., 2004; Glasauer et al., 2005; Strupp et al., 2003). Visual fixations (which maintain gaze at a point) are generated in response to the afferent information and have a key role in maintaining visual and postural stability (Martinez-Conde, 2006; Martinez-Conde & Macknik, 2008; Martinez-Conde et al., 2004; Otero-Millan et al., 2014). The review will focus on these three central concepts of the visual system, optic flow, retinal slip and visual fixations, and their interaction with the environment and the vestibular system.

3.4 Overview of the vestibular system

The vestibular system comprises the peripheral and central vestibular systems. The primary function of the vestibular system is postural control and gaze stabilisation (Casale et al., 2020; Dieterich & Brandt, 2015; Highstein et al., 2004; Kanegaonkar et al., 2012; Khan & Chang, 2013; Tascioglu, 2005). It mediates our position in space and perception of self-motion by providing the sensory input to adjust the position of the eye, head, and body. The peripheral vestibular receptors provide information about the motion of the head in three dimensions. The central vestibular pathways use this information to control the reflexes and perception of self-motion (Dieterich & Brandt,

2015; Raphan et al., 2001; Roy & Cullen, 2002). The vestibulo-ocular reflex (VOR) and the optokinetic reflex interact with the visual system to maintain visual and postural stability (Kandel et al., 2000; Pettorossi et al., 1996; Raphan & Cohen, 2002).

The VOR is a gaze-stabilising reflex which stabilises the retinal image by rotating the eyes in the opposite direction to head movements (Dieterich & Brandt, 2015; Paige et al., 1998; Straube, 2007). It is divided into two parts: the angular VOR (AVOR) and the translational VOR (TVOR). The AVOR, mediated by semi-circular canals, compensates for rotational movements of the head. The TVOR receives its input from the semi-circular canals and otoliths and compensates for translational movements of the head.

The optokinetic reflex responds to input from the otolith organs and regulates eye position during head rotation and tilting (Kandel et al., 2000; Mestre & Masson, 1997; Tsutsumi et al., 2007). It is a combination of slow-phase and fast-phase eye movements where the eyes momentarily follow a moving object, then rapidly reset to the initial position. The optokinetic reflex is generated in response to large field movements and the movement of objects in the peripheral visual field.

3.5 Integration

The generation of vestibular reflexes in response to visual input signifies an intimate relationship between the visual and the vestibular system. Visual-vestibular interaction enhances postural stability by interpreting the head's position and generating eye movements, accordingly, thus achieving gaze stabilisation and postural control. This following section outlines visual-vestibular interaction at a functional and neuronal level.

To enhance understanding, there are three sub-sections, as follows. 1) Optic flow and postural control: this sub-section describes how optic flow is generated, what it is used for and its role in postural control. 2) Retinal slip, VOR, and postural control: this sub-

section emphasises how the retinal slip is interpreted and its interaction with the vestibular system to maintain postural control. 3) Visual fixations and postural control: this sub-section incorporates the role visual fixations play in postural control by interaction with the optic flow and the retinal slip. Following on from this section, the visual-vestibular interaction is discussed at the neuronal level.

3.5.1 Optic flow and postural control

When a person moves in an environment, it is necessary to differentiate self-motion from external motion to maintain postural stability (Fajen & Matthis, 2013; Ramkhalawansingh et al., 2018; Redfern et al., 2001; Wertheim, 1994). This distinction is dependent on perceiving whether the motion of an image on the retina is the result of a person moving relative to an object or an object moving relative to the person.

Movement of an observer in a stationary environment is interpreted as self-motion as it generates patterns of optic flow specific to self-motion (Barela et al., 2009; Fajen & Matthis, 2013; Gibson, 1950; Lappe et al., 1999). In the presence of object motion along with self-motion, the resultant optic flow is the vector sum of the object motion and self-motion components (Fajen & Matthis, 2013; Royden & Connors, 2010; Warren et al., 2001). Therefore, to achieve differentiation between self-motion and object motion, the visual system must separate the object motion component from the self-motion component. This is achieved by comparing the visual information on self-motion and the non-visual information on self-motion (Fajen & Matthis, 2013; Guerraz & Bronstein, 2008; Royden & Connors, 2010; Rushton & Warren, 2005). Visual information is known as retinal signal and non-visual information as the reference signal. The reference signal includes proprioceptive feedback from the extraocular muscles, the somatosensory system, vestibular afferents, and cognition. When the retinal and reference signals match, the object is perceived as stationary (the person is moving relative to the object: self-motion), when they differ, object motion is perceived

(the object is moving relative to the person: object motion) (Bogadhi et al., 2013; Freeman, 2007; Guerraz & Bronstein, 2008; Wertheim, 1994; Wolsley, Sakellari, et al., 1996).

The optic flow pattern created during self-motion is not consistent throughout the visual field (DeAngelis & Angelaki, 2012; William, 2004). During self-motion, optic flow expands radially outwards and is projected on to the centre of the retina with a focus of expansion aligned with the direction of movement, known as radial flow. In the peripheral field, optic flow remains parallel to the line of motion and sweeps past the observer, known as lamellar flow (Guerraz & Bronstein, 2008; Royden & Connors, 2010; Turano et al., 2005; Warren et al., 2001). If the object is not moving parallel to the observer, the direction of optic flow deviates from the radially expanding background flow and allows the detection of object motion during self-motion. These optic flow patterns from the environment also provide spatial-temporal information required for spatial orientation and visual navigation (Angelaki & Hess, 2005; Redlick et al., 2001; Warren et al., 2001).

Optic flow and vestibular signals are the two most precise cues for inferring self-motion (Dokka et al., 2015; Fetsch et al., 2009; Fetsch et al., 2007; Gu et al., 2008; Ohmi, 1996; Telford et al., 1995; Warren et al., 2001). The vestibular system provides information about the angular and linear acceleration of head in space, providing inputs for detecting self-motion. Information from the vestibular system is important in instances when optic flow elicits an illusion of self-motion known as vection (Berthoz et al., 1975; Bertin & Berthoz, 2004; Brandt et al., 1972; Harris et al., 2000; Telford et al., 1995). The most common real-life example of vection is, when one is sitting in a stationary train, the movement of a neighbouring train causes the illusory movement of the stationary train. In such instances, a combination of information from the visual and vestibular systems is necessary to determine self-motion accurately.

3.5.2 Retinal slip, vestibulo-ocular reflex, and postural control

Retinal slip is the afferent signal used to generate visually evoked postural reactions (Guerraz & Bronstein, 2008; Lacour et al., 2018; Wertheim, 1994; Wolsley, Buckwell, et al., 1996). The objective of these postural reactions is to lessen the amplitude of optic flow changes (Barela et al., 2009; Masson et al., 1995). Retinal slip is used as feedback for compensatory sway by the central nervous system (Guerraz & Bronstein, 2008; Strupp et al., 2003; Wolsley, Buckwell, et al., 1996).

During self-motion, objects within the visual scene move on the retina generating retinal slip, which can lead to a blurry perception of the scene and the object. To avoid this, the visual and vestibular systems co-function to compensate for retinal slip by generating compensatory eye movements (Angelaki & Hess, 2005; Miles, 1998; Miles & Busettini, 1992). The eye movements comprise a vestibular-driven foveal stabilisation reflex known as the TVOR and the visual system induced ocular following reflex (OFR) (Miles, 1998; Miles & Wallman, 1993; Yang et al., 1999). The compensatory eye movements help maintain the target in a stationary position on the retina while objects at different distances in the scene move relative to one another, thus minimising retinal slip (Angelaki & Hess, 2005; Angelaki et al., 2003; Miles & Busettini, 1992). The TVOR generates eye movements with an amplitude corresponding with the viewing distance (Angelaki & McHenry, 1999; Hess & Angelaki, 2003; Schwarz & Miles, 1991). The amplitude of TVOR eye movements increases as the target gets closer to the observer, enabling quick compensation for the retinal slip induced by self-motion (Angelaki & Hess, 2005; Angelaki & McHenry, 1999). The remaining retinal slip is stabilised by the OFRs. OFRs generated in response to lamellar flow comprise conjugate vertical and horizontal eye movements. To compensate for radial flow, vergence OFRs are generated. Like the TVOR, the generation of OFRs also depends on the viewing distance. However, the TVOR dominates the compensation for the first 10

milliseconds of self-motion (Busettini et al., 1997; Ramat & Zee, 2003; Schwarz & Miles, 1991).

The complexity of retinal slip increases when the observer moves closer to an object, or the object lies at an angle to the direction of motion. To maintain the body in a stable position, retinal slip must be minimised (Gielen et al., 2004). To minimise retinal slip, the amplitude of postural sway should be equal to movement of the optic flow in a direction that decreases the overall amplitude of the optic flow, which can be destabilising for the observer (Strupp et al., 2003). To prevent destabilisation, the nervous system receives information about the retinal slip by the compensatory eye movements, the TVOR, and the OFR. The eye movements break down the optic flow into three components: translation, divergence, and rotational components. The disintegration minimises the retinal slip, providing cues to the central nervous system regarding the resultant retinal slip against which the compensatory postural sway is generated (Angelaki & Hess, 2005; Gielen et al., 2004) . Thus, both the TVOR and the OFR eliminate retinal slip, maintaining visual acuity on the fovea and enabling the nervous system to provide a compensatory sway allowing the observer to maintain an upright stance (Angelaki & Hess, 2005; Strupp et al., 2003).

The functioning of the VOR depends on three significant context variables: the head movement characteristics (known as stimulus context); fixation during head movements (known as fixational context); and the motion of visual target (known as visual context) (Paige, 1996; Paige et al., 1998). The head movement characteristics mainly involve the frequency and amplitude of motion. Both the AVOR and TVOR operate at high frequencies (King & Shanidze, 2011; Paige et al., 1998).

To maintain fixation during head movement, the VOR compensates for both translational and rotational components. Compensation is dependent on fixation

distance. Fixation on a distant target requires little eye movement but, as the object gets closer, a larger amplitude of ocular responses is generated (Paige et al., 1998; Schwarz & Miles, 1991; Telford et al., 1998).

The mode of visual-vestibular interaction is dependent on whether the visual target is stationary or moving. If a visual target is stationary, the VOR efficiently compensates for any sudden perturbations of the head in space. During activities such as locomotion achieve gaze stability by activating semi-circular canal afferents through head movements, triggering the VOR. The eye movements generated are so accurate that there is no retinal slip, maintaining high visual acuity and gaze stability (Dokka et al., 2015; Fetsch et al., 2009; Paige et al., 1998; Straube, 2007). However, when the head is turned to track a moving target, the VOR must be suppressed as it would prevent tracking. Therefore, the visuomotor system suppresses the VOR and induces a pursuit movement of the eyes to maintain fixation on the moving target (Barnes & Grealy, 1992; Dietrich & Wuehr, 2019; Dokka et al., 2015; Glasauer et al., 2005; Laurens et al., 2010; Miles & Busettini, 1992; Waterston et al., 1992).

3.5.3 Visual fixations and postural control

Visual fixations keep our eyes fixed on a target while viewing a scene. Visual fixations occur between saccades, contribute to 80% of the visual experience and are essential for visual processing (Martinez-Conde, 2006; Martinez-Conde & Macknik, 2008; Otero-Millan et al., 2014; Snodderly, 2016). Within periods of visual fixation, there are small eye movements. These small eye movements are required to overcome the neural mechanisms that lead to normalising responses in cases of constant or uniform visual stimulation (Martinez-Conde, 2006; Martinez-Conde & Macknik, 2008; Martinez-Conde et al., 2004; Murakami & Cavanagh, 2001; Otero-Millan et al., 2012, 2014; Rucci & Poletti, 2015; Snodderly, 2016). In other words, visual fixations are necessary to overcome adaptation to enhance visual processing.

While they are essential for visual processing, visual fixations also help reduce optic flow, minimise retinal slip, and suppress the optokinetic response (Glennerster et al., 2001; Hoppes et al., 2018; Murakami & Cavanagh, 2001; Pola et al., 1995; Uchiyama & Demura, 2009). Minimising optic flow and retinal slip is essential as sometimes information from the optic flow is destabilising, leading to the generation of vection or an optokinetic response (Barela et al., 2009; Brandt et al., 1972; Dichgans & Brandt, 1978; Dokka et al., 2015; Júnior & Barela, 2004). Both instances can erroneously evoke destabilising postural responses making a person feel unsteady and, in the worst case, can contribute to a fall. Interpreting information from optic flow becomes more complicated in naturalistic conditions and is significantly altered during eye and head movements and by motion of objects in the visual field (Barela et al., 2009; Fajen & Matthis, 2013; Hoppes et al., 2018). By maintaining the gaze at a single point within a scene, visual fixations increase visual stability and enhance postural control by suppressing the perception of motion within the visual field. This helps maximise the peripheral vision and provide a steady image to amplify the visual signals of self-motion (Bense et al., 2005; Dokka et al., 2015; Fetsch et al., 2009; Martinez-Conde & Macknik, 2008; Thomas et al., 2016). Sensory information from extraocular muscles then helps the implementation of postural reactions (Ivanenko & Gurfinkel, 2018; Ivanenko et al., 1999).

Large-field visual motion typically generates the optokinetic response (Mestre & Masson, 1997; Tsutsumi et al., 2010; Valmaggia & Gottlob, 2002). Such stimuli can lead to two interpretations: a normal one, in which the observer perceives themselves to be stationary in a moving environment, or an abnormal one leading to a perception of self-motion, where moving surroundings appear stationary. Naturally, the optokinetic response is suppressed by maintaining visual fixation (Bense et al., 2005; Chambers & Gresty, 1982; Pola et al., 1995; Tsutsumi et al., 2007). The suppression of the

optokinetic response is required to maintain a steady image and perceive a stable world; visual-vestibular interaction is essential for visual and postural control (Bense et al., 2005; Garzorz & MacNeilage, 2017; Roberts et al., 2013). An example of this is while driving: the driver moves rapidly past stationary and moving objects, seen in the peripheral vision, necessitating a rapid ocular response, while primary fixation is maintained on the road.

Visual fixations have a key role in maintaining postural stability as visually fixating on a target decreases postural sway (Miles & Wallman, 1993; Murphy et al., 2019; Thomas et al., 2016; Uchiyama & Demura, 2009; Wallman, 1993; Wyatt et al., 1988; Wyatt et al., 1995). Two theories have been identified for this – the inflow theory and the outflow theory (Guerraz & Bronstein, 2008; Murakami & Cavanagh, 2001; Poletti et al., 2010; Thomas et al., 2016). The inflow theory suggests that proprioceptors in the extraocular muscles provide information about the degree of eye movements, leading to an interpretation of body shifts during postural sway. The outflow theory overcomes the limitation of the inflow theory, which is reliant on feedback after an eye movement is initiated. The outflow theory suggests a feed-forward mechanism based on the copy of a motor command (efferent copy) utilised by the central nervous system to maintain visual consistency. In this theory, the magnitude of eye movements is anticipated in a feed-forward manner. Therefore, to achieve visual stabilisation of posture, two mechanisms work simultaneously, the ocular mechanism dependent on the features of optic flow, and the extra-ocular mechanism based on the copy of motor command and proprioceptive signals from extraocular muscles following eye movements (Fajen & Matthis, 2013; Guerraz & Bronstein, 2008; Royden & Connors, 2010; Rushton & Warren, 2005) (Figure 3.1).

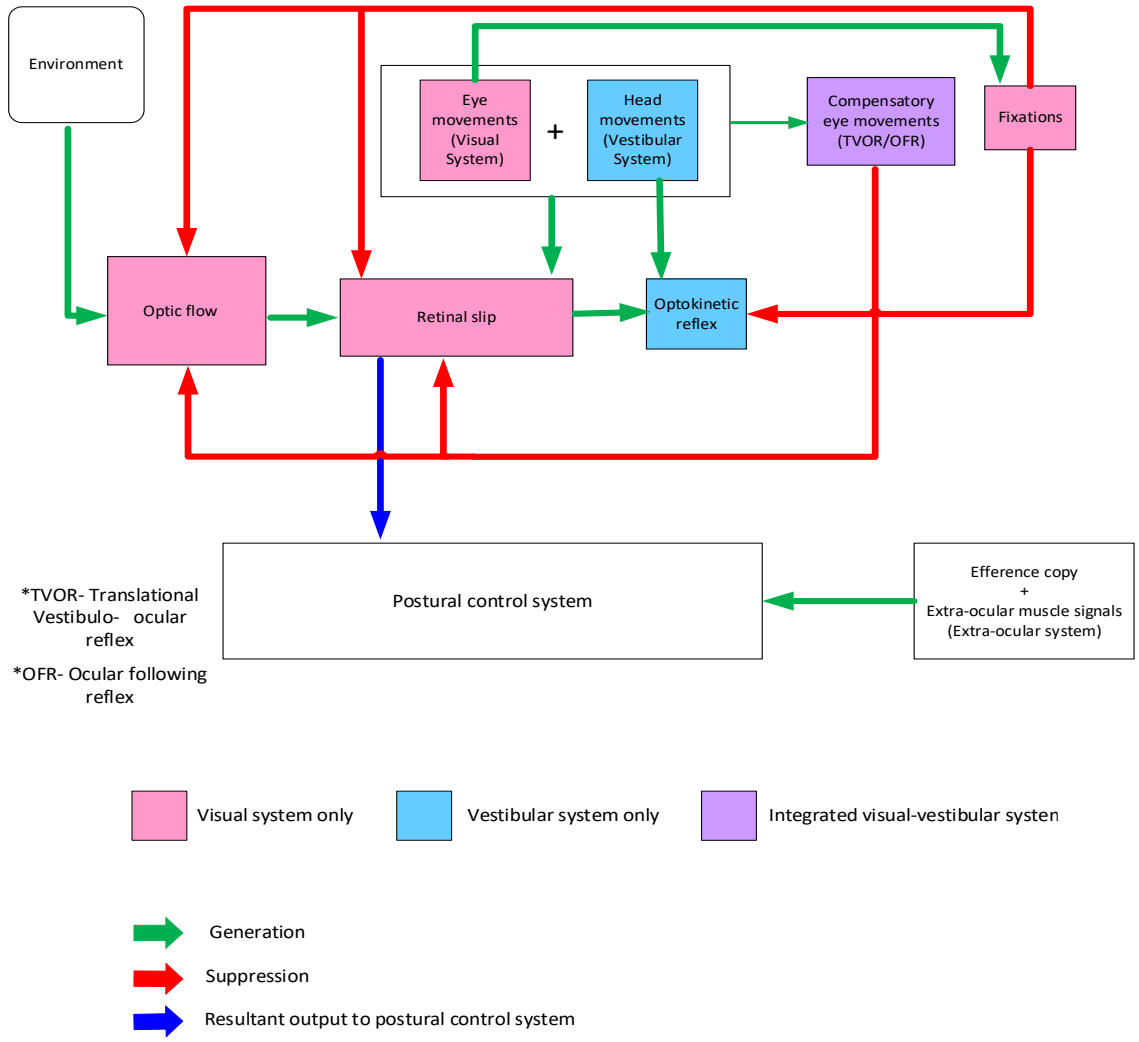


Figure 3.1 Interaction of visual and vestibular systems

3.6 Neuronal control of visual-vestibular interaction

Visual-vestibular interaction is necessary to estimate and continuously update the body position in space and to distinguish self-motion from external motion. The explanation of this interaction has been widely studied in Macau monkeys. The exact neural mechanisms for visual-vestibular integration in humans is less well understood (Roberts et al., 2017; Smith et al., 2017). Early studies have reported activation of the occipito-temporal cortex, posterior parietal cortex and subcortical structures with reduced activation within the posterior insular cortex during visual motion (Bense et al., 2006; Brandt et al., 1998; Dieterich et al., 1998; Kleinschmidt et al., 2002). Studies using

caloric vestibular stimulation identified the activation of similar regions with increased activity in the posterior insular cortex (Bense et al., 2006; Bense et al., 2005).

These findings led to the current hypothesis of reciprocal visual-vestibular interaction based on reciprocal inhibition (Brandt et al., 1998). Visual-vestibular interaction depends on the pattern of visual motion as well as the active postural and locomotor tasks. This requires a shift in the dominant sensory modality to achieve the desired functional task (Brandt et al., 1998). Functionally, during a constant visual input, there should be a decrease in the vestibular system's sensitivity to head acceleration. This is essential to avoid a mismatch between visual and vestibular inputs during involuntary head accelerations such as sitting facing in the opposite direction to that of the train in which one is travelling. Continuous vestibular inputs in such situations can be misleading, causing the perception of self-motion (Bense et al., 2005; Dokka et al., 2015). To avoid such mismatches, there is a reciprocal inhibitory interaction between the visual and vestibular systems (Brandt et al., 1998) where both systems suppress the other to produce a coherent sense of self-motion. Deactivation of the vestibular cortex prevents conflict between vestibular information on head motion from a visually induced perception of motion and vice versa. Recent studies have identified areas of cortical activation during optic flow stimulation which are consistent with the detection of self-motion (Cardin & Smith, 2010; Wall & Smith, 2008). These areas are regions within the intraparietal sulcus and cingulate sulcus visual area. The parieto-insular vestibular cortex and posterior insular cortex are also found to be activated during object motion (Frank et al., 2014).

A large number of areas have been associated with resolving perceptual conflicts (Kolling et al., 2016; Nachev et al., 2008; Roberts & Husain, 2015; Sharp et al., 2010). These include the insular cortex, the inferior frontal gyrus, and the medial frontal structures' pre-supplementary motor area. During conflicting visual-vestibular

information, there is activation of the parieto-insular vestibular cortex. Activation of this area interprets conflicting sensory input with a heavy reliance on vestibular cues during such conflict.

Additionally, the existence of visual targets in the environment requires a combination of eye and head orientation to achieve gaze stability. The visual-vestibular interaction needed to shift the gaze towards a target and then maintain fixation is regulated by omni-directional pause neurons (OPNs), located in the nucleus raphe interpositus of the paramedian pontine reticular formation (Krauzlis et al., 2017; Prsa & Galiana, 2007). These neurons fire during fixations and stop firing during saccades. The activity of the neurons has an inhibitory influence on saccades. They prevent the firing of saccade-related premotor burst neurons which are in the mesencephalic and pontomedullary reticular formations. However, a pause in their activity allows the resumption of the saccade-related burst driving the motor neurons that innervate the extraocular muscles (Krauzlis et al., 2017).

The input to the OPNs is a weighted sum of the vestibular and visual inputs (Krauzlis et al., 2017). This comprises three signals: 1. the gaze motor error, which uses a range of sensory inputs (auditory, somatosensory, and cognitive) and is the difference between the present gaze position and the final required gaze position; 2. the head velocity signal, detected via the semi-circular canals by vestibular neuron; and 3. the eye velocity signal. When the sum total of afferent signals surpasses a threshold, the OPNs are turned off, leading to a halt in activity allowing the saccadic activity, whereas when the sum is below a threshold, the OPNs turn on and induce fixation on the target (Prsa & Galiana, 2007).

Therefore, there is a continued interaction between visual and vestibular systems for postural control to maintain body and eye stability during various transitions involving head movements and constant visual motion.

3.7 Conclusion

The ability to perceive a stable world depends on the visual inputs derived from the environment. The visual information regarding the movements of self and objects in the environment is provided by optic flow. Information from the optic flow patterns helps differentiate self-motion from external motion. Concurrent information regarding self-motion is also provided by the vestibular system regarding the angular and linear acceleration of the head in space. This information is necessary in instances when information from optic flow generates a false perception of self-motion known as vection or stimulates an optokinetic response. Optic flow patterns generate retinal slip on the retina, constituting the main afferent signal to generate visually evoked postural reactions. To maintain visual and postural stability, the visual system, and the vestibular system co-function by generating the TVOR and OFR respectively to stabilise the image on the retina. The stabilisation of the retinal image eliminates retinal slip, providing information to the nervous system to maintain an upright stance by generating compensatory postural sway.

A key determinant in maintaining visual and postural stability is visual fixations, which result from the interactions with the vestibular system and the environment. Visual fixations keep the eyes fixed on a target while viewing a scene. They have a major role in suppressing the optokinetic response which can destabilise an observer. Further, they maintain visual stability during the tracking of a moving target by suppressing the VOR. Visual fixations suppress the optic flow and minimise retinal slip by maximising the peripheral vision and suppressing the generation of vection, thus enhancing postural stability.

The visual system plays a significant role in maintaining postural stability and any discrepancy in interpreting visual information leads to increased postural sway. The visual and vestibular systems interact to achieve visual stability and maintain an upright stance. The relationship between vision and vestibular function implies that visual input may influence vestibular symptoms and modify vestibular function and perception.

3.8 Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

3.9 Author's contribution

SC drafted the manuscript. DT and NS are providing PhD supervision for SC. All authors critically revised the manuscript. All authors read and approved the final manuscript.

3.10 Contribution to the field statement

Postural control requires the integration of information from three sensory systems. The current review describes the key aspects of the visual system which are essential to enhance the understanding of the visual system's contribution to postural control. Primarily, the visual and the vestibular systems interact at a functional and a neuronal level to maintain visual and postural stability. Such interaction enables an observer to perceive a stable image on the retina and provides information to the central nervous system to generate appropriate postural reactions to maintain an upright posture. The literature synthesis facilitates the understanding of the visual and vestibular interaction, emphasising the importance of these systems in differentiating self-motion from external motion as a pre-requisite for postural control. The review further elaborates on how these two systems interact and maintain visual and postural stability by suppressing the conflicting information from each system. The review highlights how the visual

system influences the function of the vestibular system and vice versa. It is important to understand this interaction as a precursor to assessment and rehabilitation for people with vestibular and visual system disorders.

End of the manuscript

3.11 Summary

The narrative review outlines the visual system's role in perceiving a stable world and maintaining an upright posture through its interactions with the vestibular system and the environment. It highlights the importance of differentiating self-motion from external motion to maintain postural stability. Information from optic flow and retinal slip generates motor responses which maintain the body in a stable position. The visual and vestibular systems generate eye movements to stabilise the gaze on targets and provide information to the central nervous system to generate postural responses. Visual fixations suppress optic flow, limiting the generation of vection and the optokinetic response. Visual fixations interact with the VOR to minimise retinal slip, thereby maintaining visual and postural stability. An inability to maintain fixation will lead to a failure to suppress vection and the optokinetic response. This means an observer may not be able to discriminate self-motion from external motion, leading to postural instability.

This narrative review highlighted visual fixations as one of the processes central to maintaining visual and postural stability. An observational exploratory study was designed to investigate visual fixations in adults with motion sensitivity.

Chapter 4: Visual fixations and motion sensitivity: protocol for an exploratory study

4.1 Prologue

The previous chapter identified visual fixation as a factor in suppressing optic flow to maintain visual and postural stability. This chapter describes related work involving visual fixations and presents a published manuscript outlining a cross-sectional observational study protocol to investigate visual fixations and postural behaviour in two groups: healthy adults and adults with motion sensitivity. This chapter addresses the following thesis objective:

- To conduct an observational exploratory study to investigate:
    a. The characteristics of visual fixations in adults with motion sensitivity
    b. Postural parameters in adults with motion sensitivity.

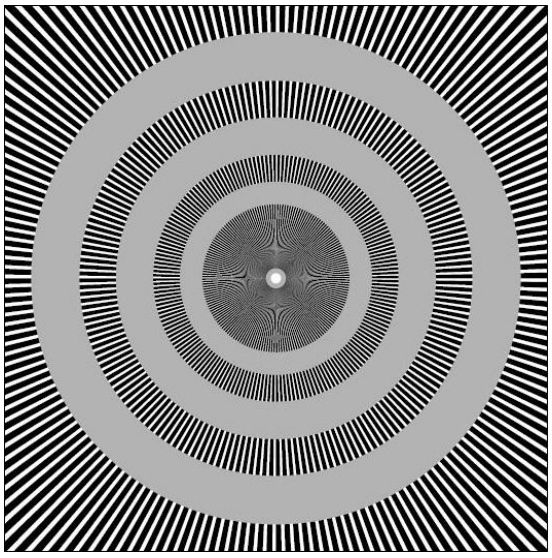
The supporting documents associated with this chapter can be found in the appendices and include: the published manuscript (Appendix D), a copy of the ethics approval letter (Appendix E), locality approval (Appendix F), participant information sheets (Appendices G and H), advertisement for recruiting healthy adults (Appendix I), advertisement for adults with motion sensitivity (Appendix J), consent form (Appendix K), screening sheet (Appendix L), Visual Vertigo Analogue Scale (Appendix M), and Dizziness Handicap Inventory (Appendix N).

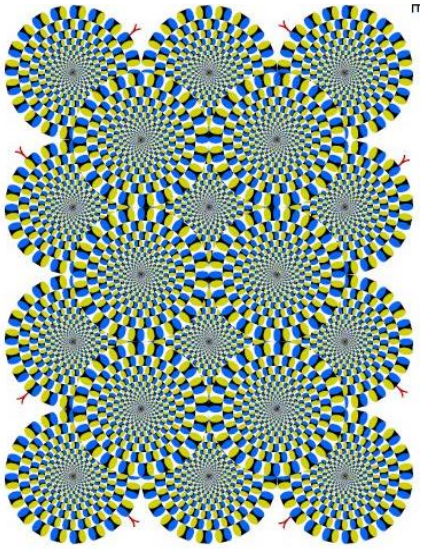
4.2 Literature review on the role of visual fixations in visual illusions

Given that visual fixations suppress optic flow in natural conditions and help prevent vection, it was essential to understand whether they contribute to the perception of a false movement of a static image known as a visual illusion. As adults with motion sensitivity complain of nausea, dizziness, and imbalance in complex visual environments, it was queried whether an inability to fixate could predispose a person to

perceive visual illusions, which can degrade postural stability. Thus, literature review was undertaken to explore the role of visual fixations in the perception of visual illusions (Fermüller et al., 1997; Hamburger, 2016).

The concept of visual illusion has been explored in research using static images such as the 'enigma' and 'rotating snakes' illusions (Fermüller et al., 1997; Hamburger, 2016; Kitaoka, 2005). The enigma illusion (Figure 4.1A) elicits an illusory movement inside rings which keep changing direction. The rotating snakes' illusion (Figure 4.1B) generates the perception of rotational illusory motion in the direction that follows the coloured patches.





A: Enigma illusion B: The rotating snakes' illusion

Figure 4.1 Visual illusions

Most observers perceive visual illusions due to the retinal slip generated by eye movements. Maintaining a stable visual fixation eliminates retinal slip, rendering the retinal image stable and thus abolishing visual illusion. (Faubert & Herbert, 1999; Fermüller et al., 2010; Fermüller et al., 1997).

Experimental studies have established a positive relationship between the strength of visual illusions and fixation instability (Murakami, 2003; Murakami et al., 2006). It was observed that the poorer the visual fixation (fixational instability), the higher the

perception of visual illusion (Beer et al., 2008; Murakami, 2003; Murakami et al., 2006). This can be attributed to an unstable fixation, leading to gaze fluctuation. As gaze fluctuates, the retinal image of a physically static figure fluctuates and these jittery movements on the retina lead to vigorous impressions of illusory motion (Beer et al., 2008; Murakami et al., 2006; Otero-Millan et al., 2012; Poletti et al., 2010). A failure to compensate for these images on the retina leads the brain to interpret retinal motion as actual motion, resulting in illusory motion perception.

The literature review on visual fixations and narrative review findings suggest that the suppression of illusory motion such as vection and visual illusions necessitates a stable visual fixation. The work led to the identification of visual fixations as a critical factor to be investigated in motion sensitivity, thus leading to the development of the following protocol for an observational exploratory study.

The published manuscript (Chaudhary et al., 2020) is presented here as it is with no modification in content but a few formatting modifications to fit with the thesis structure and facilitate reading.

Publication citation: Chaudhary, S., Saywell, N., Kumar, A., Taylor, D. (2020).

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JMIR Research Protocols, 9(7), e16805.

URL: https://www.researchprotocols.org/2020/7/e16805

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Link to original publication: http://dx.doi.org/10.2196/16805

Start of the published manuscript

4.3 Abstract

Background: Motion sensitivity after vestibular disorders is associated with symptoms of nausea, dizziness, and imbalance in busy environments. Dizziness and imbalance are reported in places such as supermarkets and shopping malls which have unstable visual backgrounds; however, the mechanism of motion sensitivity is poorly understood.

Objective: The main aim of this exploratory observational study is to investigate visual fixations and postural sway in response to increasingly complex visual environments in healthy adults and adults with motion sensitivity.

Methods: A total of 20 healthy adults and 20 adults with motion sensitivity will be recruited for this study. Visual fixations, postural sway, and body kinematics will be measured with a mobile eye-tracking device, force plate, and 3D motion capture system, respectively. Participants will be exposed to experimental tasks requiring visual fixation on letters, projected on a range of backgrounds on a large screen during quiet stance. Descriptive statistics (mean and standard deviation) will be calculated for each of the variables. One-way independent measures analyses of variance will be performed to investigate the differences between groups for all variables.

Results: Data collection was started in May 2019 and was completed by February 2020. It was approved by Health and Disability Ethics Committees, Ministry of Health, New Zealand, on November 2, 2018 (Ethics ref: 18/CEN/193). We are currently processing the data and will begin data analysis in July 2020. We expect the results to be available for publication by the end of 2020. The trial was funded by the Neurology Special Interest Group, Physiotherapy New Zealand, and the Eisdell Moore Centre in November 2018.

Conclusions: This study will provide a detailed investigation of visual fixations in response to increasingly complex visual environments. Investigating the characteristics of visual fixations in healthy adults and those with motion sensitivity will provide insight into this disabling condition and may inform the development of new intervention strategies which explicitly cater to the needs of this population.

Trial Registration: Australian New Zealand Clinical Trials Registry, ACTRN12619000254190; https://tinyurl.com/yxbn7nks

International Registered Report Identifier (IRRID): PRR1-10.2196/16805

(JMIR Res Protoc 2020;9(7):e16805) doi: 10.2196/16805

KEYWORDS

motion sensitivity; vestibular disorder; complex environments; visual fixations; postural control; posture; kinematics; inner ear; visual.

4.4 Introduction

Motion sensitivity is characterised by nausea, dizziness, and imbalance in response to motion of the visual environment (Bronstein et al., 2014). It can develop as a sequela of a vestibular disorder and is one of the diagnostic criteria for persistent postural perceptual dizziness (Bronstein et al., 2014; Chin, 2018; Popkirov et al., 2018). The symptoms are due to a misinterpretation of, or overreliance on, visual cues for orientation in space (Bronstein, 2004; Bronstein et al., 2014; Chin, 2018; Guerraz et al., 2001; Zur et al., 2015). Dizziness and imbalance are triggered in busy surroundings with visual motion or complex repetitive patterns. Consequently, people with motion sensitivity tend to avoid crowded or busy environments such as supermarkets or driving on motorways (Bronstein, 1995b). This frequently leads to an interruption of daily activities, sick leave from work and, in extreme cases, a reluctance to leave the house

(Benecke et al., 2013; Neuhauser et al., 2008). Motion sensitivity may affect people following an acute vestibular insult or people with chronic recurrent dizziness (Roberts et al., 2013).

Information from the visual system has a role in differentiating self-motion from external motion (Redfern et al., 2001). This differentiation is dependent on perceiving whether motion on the retina is due to an object moving relative to the person or the person moving relative to the object (Angelaki & Hess, 2005; Fajen & Matthis, 2013). This distinction between self-motion and external motion is achieved by a mechanism that compares the retinal signal and the reference signal. The reference signal comprises information from vision, vestibular afferents, proprioceptive feedback from the extraocular muscles, somatosensory kinesthetic proprioception, and cognition (Wertheim, 1994) (Figure 4.2).

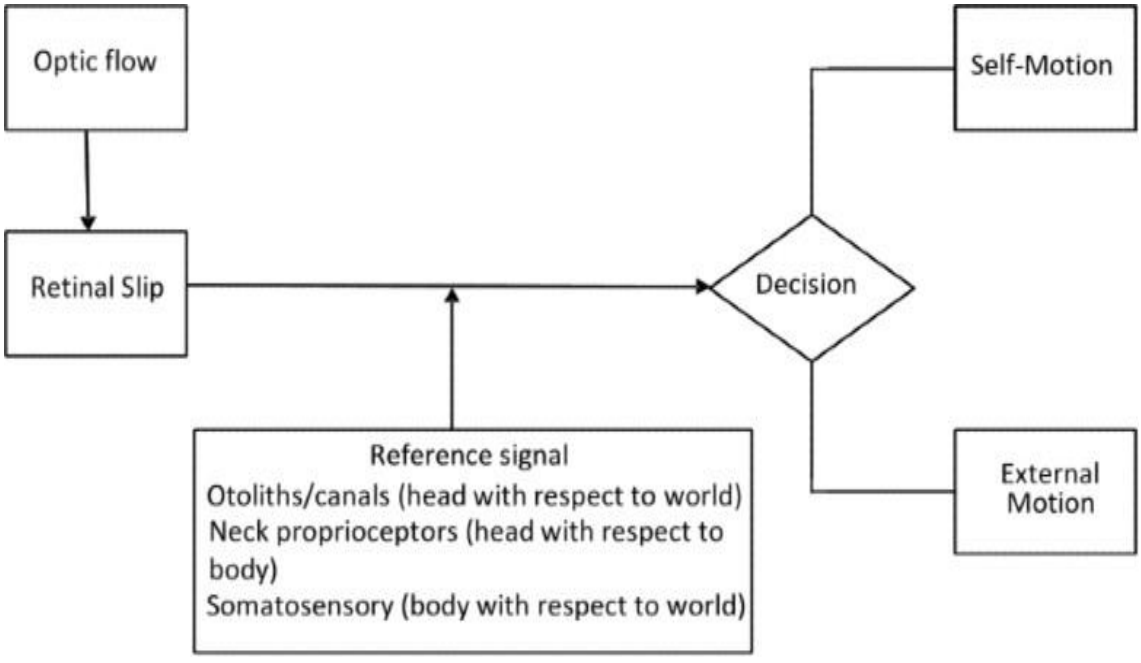

Figure 4.2 The sources of information to allow differentiation of self-motion and object motion components

Note. The various sources are shown as giving information with respect to different reference frames.

A crucial aspect of the stabilisation of posture is dependent on the visual input received from the environment. An essential component of visual input is optic flow

(Koenderink, 1986; Lee & Kalmus, 1980). Optic flow helps perception of spatiotemporal information from the environment which is then used to move around and maintain orientation in space (Angelaki & Hess, 2005; Warren et al., 2001). Optic flow generates retinal slip, defined as motion of the visual image of the environment on the surface of the retina (Guerraz & Bronstein, 2008). This information is used to adjust the amount of postural sway. The main aim of visually induced postural movements is to reduce the overall amplitude of the optic flow field by minimising retinal slip (Barela et al., 2009; Masson et al., 1995; Strupp et al., 2003).

Because optic flow plays a vital role in postural correction, perceiving inaccurate information can be destabilising. Optic flow that is a part of the background motion behind a target is not normally used as a visual input for postural control as it can stimulate an optokinetic response (which evokes a combination of a slow-phase and fast-phase eye movements where the eyes momentarily follow the moving object and then rapidly reset back to the initial position) (Wallman, 1993). This response can induce a standing subject to move in response to the direction of the motion and can be destabilising (Wallman, 1993). In normal circumstances, this optokinetic response to background motion is suppressed by visually fixating on a target (Pola et al., 1995).

Visual fixations contribute to 80% of the total visual experience (Martinez-Conde, 2006), and help to reduce optic flow, minimise retinal slip, and suppress the optokinetic response (Pola et al., 1995). When fixating on a stationary target, there is almost no retinal slip, and the vestibulo-ocular reflex keeps the gaze on target during head movements (Strupp et al., 2003). By contrast, maintaining fixation on a moving object requires suppression of the vestibulo-ocular reflex for the eyes and the head to move in the same direction (Glasauer et al., 2005; Laurens et al., 2010; Strupp et al., 2003).

Fixations contribute to a person's sense of spatial orientation. Fixations suppress visual-field motion perception by maximising the peripheral vision and rendering a stable image to enhance the visual signals of self-motion (Martinez-Conde et al., 2004). Sensations of small body movements then facilitate the execution of compensatory postural reactions (Thomas et al., 2016).

Fixational instability may predispose a person to develop motion sensitivity (Beer et al., 2008; Otero-Millan et al., 2012; Poletti et al., 2010). Studies have shown that people with motion sensitivity after vestibular disorders exhibit fixational instability and have increased perceptual and postural responses to complex visual surroundings (Lencer & Clarke, 1998; Otero-Millan et al., 2012; Van Ombergen et al., 2016; Winkler & Ciuffreda, 2009). Several studies have investigated the relationship between fixational instability and the strength of illusory motion (Beer et al., 2008; Otero-Millan et al., 2012; Poletti et al., 2010). Fixational instability can be detected by the frequency of refixations and saccades (Lencer & Clarke, 1998; Winkler & Ciuffreda, 2009). Studies have reported that a person with fixational instability would have a high frequency of saccades and refixations while attempting fixation (Lencer & Clarke, 1998; Winkler & Ciuffreda, 2009).

Any difficulty in differentiating self-motion from external motion will require adjustments to determine the correct orientation in space. A peripheral or central vestibular disorder disrupts the normal visual-vestibular interaction (Redfern & Furman, 1993), which can alter the perception of motion. It can lead to illusory motion perception, thereby degrading postural stability. Adults with motion sensitivity report a worsening of symptoms and reduced postural control in visually stimulating environments, which may be explained by fixation instability. However, to date, visual fixations have not been well investigated in people with motion sensitivity. Previous

studies have used video oculography or electrooculogram and optokinetic stimulation rotating around the naso-occipital centre to study eye movements in adults with motion sensitivity (Lencer & Clarke, 1998; Winkler & Ciuffreda, 2009). This study aims to investigate the characteristics of fixations in people with motion sensitivity and how they differ from those of healthy adults by using a mobile eye-tracking device in a more naturalistic yet controlled laboratory setting.

This research will investigate visual fixations, postural sway, and the kinematics of adults with motion sensitivity, compared with healthy adults, in complex visual environments. Centre of pressure (COP) measurement will be used to evaluate postural sway. COP parameters have been used widely to describe stability and quantify alterations in postural control (Cotton et al., 2009; Palmieri et al., 2002). The exploratory nature of this study will also allow the investigation of mean saccadic velocity and saccadic peak amplitude between groups. Several studies have identified anomalies in mean saccadic velocities in a range of health conditions (Di Stasi et al., 2013; Di Stasi et al., 2012).

This study is the first step toward recognising the components that may be essential in a rehabilitation programme addressing the challenging clinical issue of motion sensitivity and may guide the development of rehabilitation programmes for adults with motion sensitivity.

4.5 Methods

4.5.1 Aim

To conduct an observational study with 40 adults (20 in each group: healthy adults and adults with motion sensitivity). The study will determine whether complex visual environments are associated with fixational instability, altered COP displacement, and

altered centre of mass (COM) displacements of the head and body in adults with motion sensitivity compared with healthy adults.

4.5.2 Hypothesis

Complex visual environments in people with motion sensitivity compared with healthy adults will be associated with (1) increased number of visual refixations, (2) increased displacement of COP, and (3) differences in the body COM displacement and differences in the head COM displacement.

4.5.3 Trial design, setting, and participants

This is a cross-sectional exploratory single-session experimental study that will be laboratory based in Auckland University of Technology. A total of 40 adults will participate in the study (20 healthy adults and 20 adults with motion sensitivity after vestibular disorder). Healthy adults aged between 18 and 60 who are independently mobile and have no history of neurological conditions will be recruited through neurorehabilitation research team networks and community advertisements. Adults with motion sensitivity will be recruited through a specialised vestibular disorders clinic. They will be included if they have had a history of vestibular disorder (confirmed by a clinician in the vestibular disorder clinic) but have no current signs of acute vestibular deficits, are aged between 18 and 60 (Agarwal et al., 2012; Bisdorff et al., 2013), have a history of motion sensitivity symptoms as reported by the Visual Vertigo Analogue Scale (score >5) (Dannenbaum et al., 2011; Sharon & Hullar, 2014; Silva et al., 2016), and score >40 on the Dizziness Handicap Inventory (Silva et al., 2016). People with a history of previous eye surgery, or a medical condition that may influence eye movements, such as sarcoidosis, Lyme disease, diabetes mellitus, traumatic brain injury, or migraine, will be excluded from the study.

4.5.4 Recruitment

Potential participants will be provided with a participant information sheet and requested to contact the corresponding author by email or telephone. All potential participants will be made aware that participating in this study will not influence their current health care.

4.5.5 Screening

Potential participants will be screened against the study's inclusion and exclusion criteria via telephone or through a face-to-face meeting with the researcher (SC). Eligible potential participants will be asked to provide written informed consent.

4.5.6 Experimental setup

The experimental setup consists of a projector screen (Brateck Lumi), a mobile eye-tracking device (SensoMotoric Instruments), a force plate (Advanced Mechanical Technology Inc.), and a 3D motion capture system (Qualisys Motion Analysis Capture System; Qualisys Medical AB). Visual fixations will be recorded using a mobile eye tracker (SMI BeGaze; SensoMotoric Instruments). A 3D motion capture system and a force plate will be used to record kinematics and postural sway, respectively. The projector screen (135 in., 16:9 aspect ratio) will be mounted at 3.5-m distance from the force plate for projecting the visual environments (Figure 4.3).

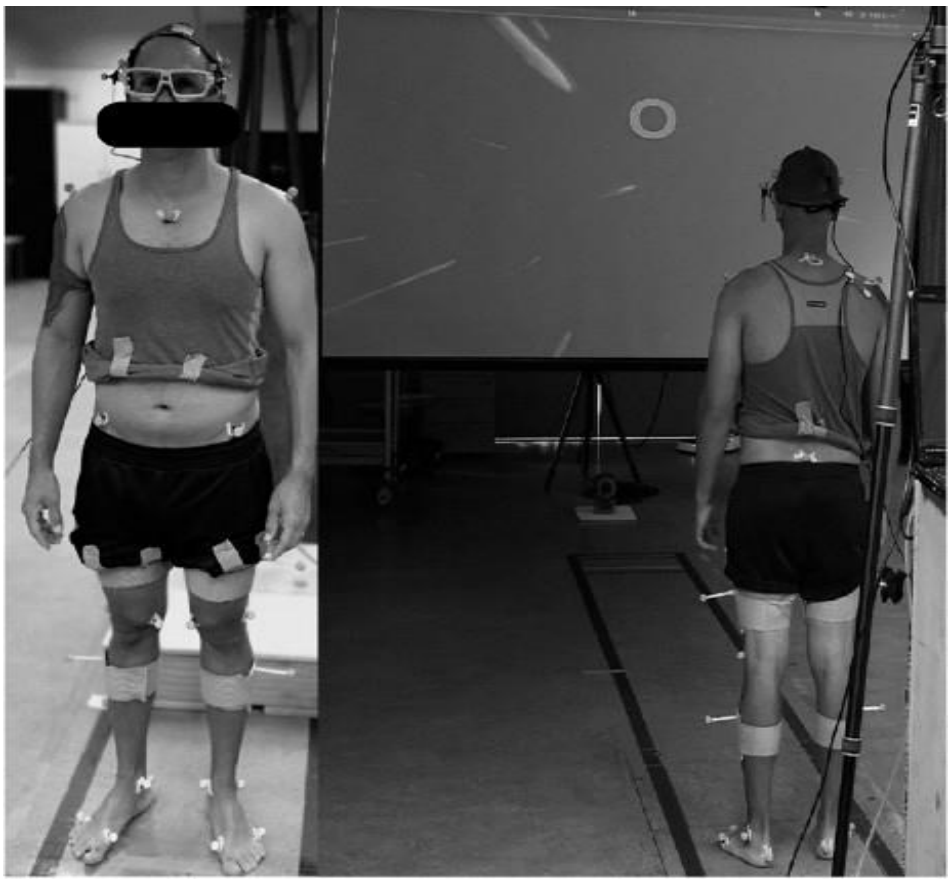

Figure 4.3 The experimental setup

4.5.7 SensoMotoric Instruments eye-tracking glasses (SMI ETG)

The SMI eye-tracking glasses (SMI ETG) are a mobile eye-tracking device with a binocular sampling rate of 120 Hz (Figure 4.4). SMI ETG uses an infrared light of wavelength around 789-880 nm to increase the contrast between the pupil and iris which is easily detected by the camera. SMI ETG is a video-based eye tracker based on the concept of pupil centre corneal reflection. The scene camera has a resolution of 1280 × 960 pixels @ 24 frames per second (FPS), 960 × 720 pixels @ 30 FPS, with a 60° horizontal and 46° vertical field of view. The gaze position accuracy is 0.5° for all distances and the gaze tracking range is 80° horizontal and 60° vertical.

The SMI software uses a frame-by-frame analysis of the gaze data. These data involve defining the location and type of gaze behaviour for each frame of data collected. Frame numbers are used to determine the duration of the eye movement. SMI uses an in-built

detector for identifying saccades, fixations, and blinks. According to the detector, a blink is identified by points where eye data are not present, a saccade represents a quick change in gaze location, and a fixation is bordered by two saccades.

Data collected by the eye-tracking glasses identify the primary event as fixation and therefore a dispersion-based algorithm is used. The algorithm identifies fixations as groups of successive points within a dispersion, or maximum separation. A blink is determined based on the whole trial data where the pupil diameter is either zero, or the horizontal and vertical gaze positions are zero, or they lie outside a calculated valid pupil range. Once fixations and blinks are identified, a saccadic event is created between the detected blinks and fixations.

Figure 4.4 SMI eye-tracking glasses with 3D reflective markers

4.5.8 Qualisys system

Qualisys is a motion capture system used to track movement. Small retro-reflective markers reflecting infrared light are attached to the participant's skin. Frame-by-frame analysis is used to track each marker from one frame to the next. Each marker's data and its 3D position trajectory can be used to calculate joint and movement trajectories. The force plates and SMI eye tracker are integrated, and time synced in the Qualisys system. The SMI program is installed on the Qualisys system. The data from the SMI

system are synchronised to Qualisys via a start command, so as to capture the SMI data together with all the other data in the Qualisys system. The force plates are connected to the Qualisys computer via an analogue board to capture analogue signals from the force plate with the motion capture data. The data from the force plates are synchronised with the motion capture data via a synchronisation signal between the Qualisys camera system and the analogue board. The sync signal from the camera system is connected to an external trigger input on the analogue board to start the capture of analogue data using hardware synchronisation.

Kinematics will be measured using an infrared motion analysis capture system, consisting of nine Oqus 3D motion analysis capture units. A set of 27 reflective markers will be placed on the participant. Markers will be attached using a double-sided tape directly onto the skin. Pelvis markers will be placed in accordance with the modified Helen Hayes model as a set of three: one marker on each anterior superior iliac spine and one on the sacrum (midpoint). For the thigh segment, markers will be placed on midthigh, medial femur epicondyle, and femur lateral epicondyle for each extremity. The shank segment includes markers on midshank, medial malleolus, and lateral malleolus. The foot segment will be created using a set of markers on the head of the fifth metatarsus, head of the first metatarsus, and posterior surface of the calcaneus. Further markers will be placed on the right and left acromion process, sternoclavicular notch, and C7 vertebra to create the thorax segment. To create the head segment, one marker will be placed on each side of the head.

3D co-ordinates of each reflective marker will be tracked using Qualisys Track Manager. Visual 3D software will be used to process the data files. After placement of markers, a static image of the participant standing in an anatomical position will be taken.

4.5.9 AMTI force plates

Postural control as the COP movement will be measured with an AMTI force platform (Advanced Mechanical Technology Inc.). The force platform measures the three force components, F_x, F_y, and F_z (where x, y, and z are the medial–lateral, anterior–posterior, and vertical directions, respectively), at the sampling frequency of 1200 Hz. The AMTI force plate is a static-force measurement system and is a computer-based system which synchronises with a computer using a serial link. The COP movement track data (in millimetres) will be collected for each participant and will be converted into mediolateral and anterior-posterior components for analysis.

Participants will stand on the force plate with arms relaxed at their sides. Participants will be asked to stand with their feet shoulder width apart. They will be instructed to maintain their gaze on the letter while maintaining a quiet stance for the duration of a task.

4.5.10 Experimental tasks

The experimental tasks have been designed to simulate eye movements in visually complex environments. Tasks will increase in the level of complexity, starting from easy visual tasks and progressing to more visually complex tasks. Letters will be projected in a random sequence on to a range of visually complex background images (Figure 4.5). The font of the letters, backgrounds, and duration of each task were finalised after piloting. There are six tasks, each lasting 70 seconds. The letters appear on the screen for 7 seconds each, at different positions on the screen. Python programming language has been used to select letters and their positions on screen. Participants will be instructed to focus on a letter as they appear on the screen. The tasks increase in difficulty in two ways: (1) the background behind the letter progresses from neutral to busy (i.e., to a complex moving background); and (2) by the appearance of either a single letter or multiple letters on screen. In the single-letter tasks (tasks 1, 2, 5,

and 6), the participants will be instructed to focus their gaze on each projected letter for the duration of the task. In the multiple letters' tasks (tasks 3 and 4), the participants will be instructed to find the letter *E* and maintain visual fixation on it for the duration of the task. The tasks will be presented from the lowest to highest difficulty of background and number of letters (as described in 4.5). The tasks will not be randomised as the more difficult tasks might provoke symptoms of dizziness which would hinder the performance of participants in the subsequent tasks.

4.5.11 Data collection

Data will be collected for all tasks in one session. The motion analysis system and force plate will be calibrated before the participant arrives in the laboratory. Upon arrival, the participant will be orientated to the laboratory setup. The Dizziness Handicap Inventory and Visual Vertigo Analogue Scale screening will be completed. After setting up the markers, experimental tasks will be explained, and the eye-tracking glasses will be fitted for comfort and calibrated. The participant will then stand on the force plate wearing the calibrated eye tracker with reflective markers (Figure 4.6). During the experimental tasks, appropriate rest intervals will be provided after each task to minimise provocation of symptoms such as dizziness and nausea.

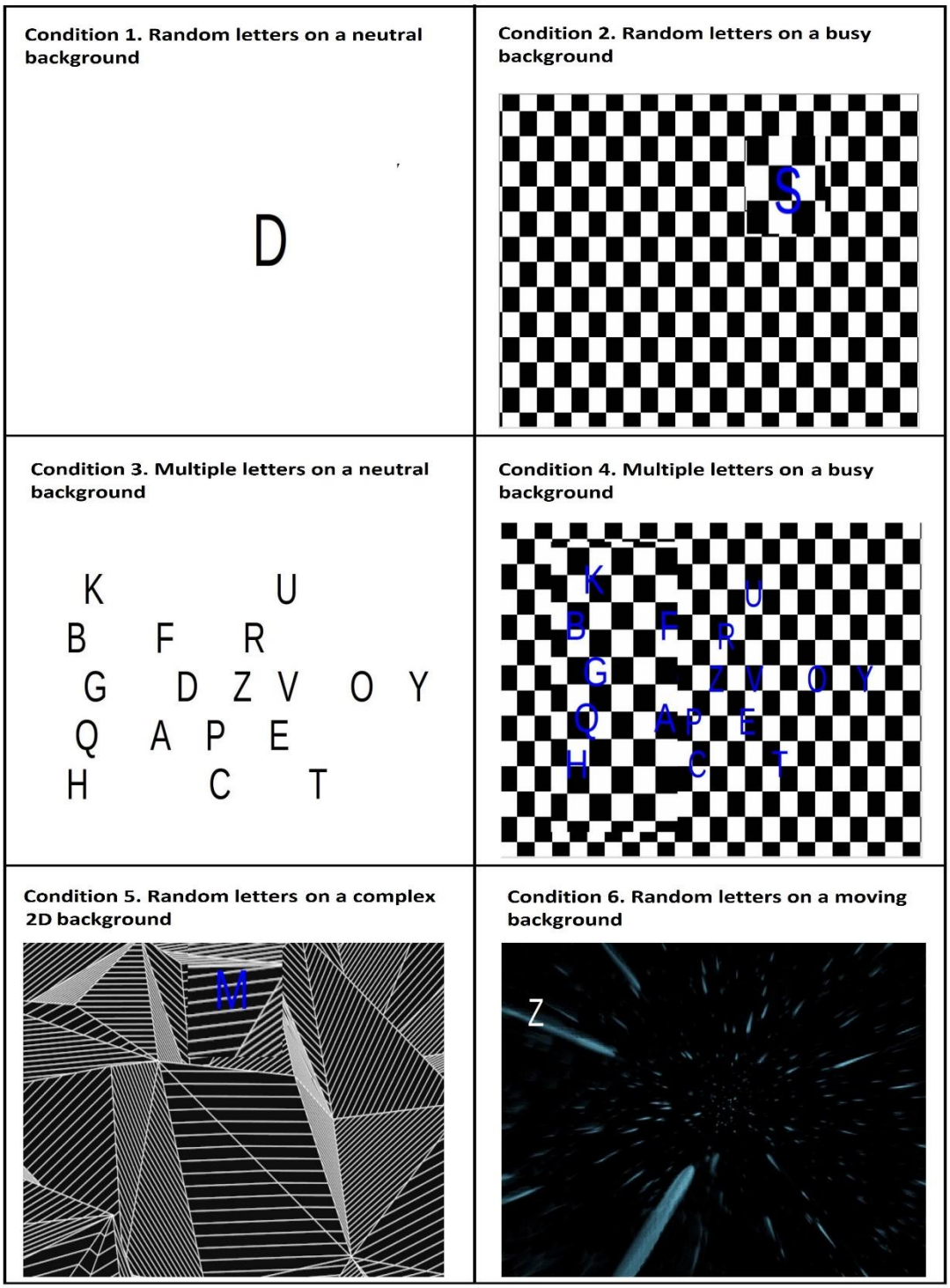

Figure 4.5 The experimental tasks

Note. Letters have been magnified for clear visibility.

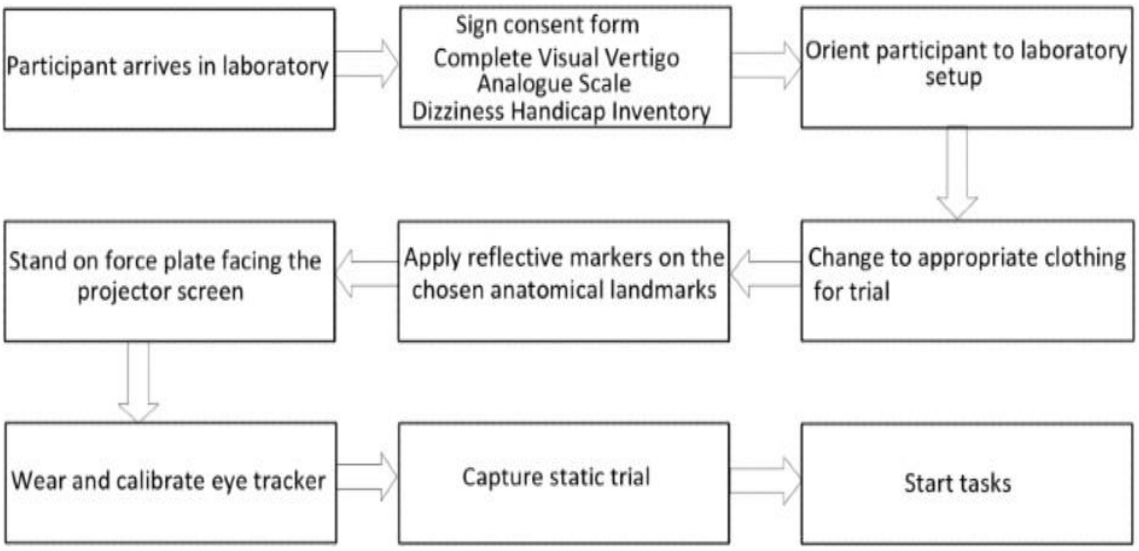

Figure 4.6 Data collection procedure

4.6 Outcome measures

The following outcome measures will be explored and analysed for this study.

4.6.1 Visual fixations

Fixation characteristics for each group will be computed using the SMI ETG software and will measure the total number of refixations, the maximum fixation duration, and the number of saccades. The software determines a fixation as a window with a minimum duration of 80 ms and a maximum dispersion of 100 pixels. Refixations are calculated if the eye crosses the maximum dispersion threshold of 100 pixels. The fixation duration will be calculated as the total time spent in fixating during a trial. The maximum fixation duration will be calculated as the longest fixation within each trial. A saccade event is computed as any event that does not meet the fixation criteria between the new and the previous fixation.

4.6.2 Postural sway: Centre of pressure

COP displacement time series obtained from the force platform will be down sampled to 100 Hz and subsequently will be processed using a low-pass filter at 5 Hz (fourth-order, zero-phase-lag, Butterworth) (Lin et al., 2008). The mean velocity, root mean

square, and maximum range of the COP displacement will be computed to evaluate postural sway (Prieto et al., 1996).

4.6.3 Kinematics

Raw data from the Qualisys motion analysis will be imported into Visual 3D, where a six-degrees-of-freedom model will be constructed. Data will be interpolated and processed using a fourth-order Butterworth low-pass filter with cut-off frequency of 12 Hz. The body COM and the COM of the head segment will be calculated using a pipeline in Visual 3D. The mean velocity, root mean square, and maximum range of the COM of the head and whole-body displacement will be calculated (Lee & Powers, 2014).

4.6.4 Safety measures

The study will be using moving background/moving images, which may induce dizziness, imbalance, or nausea in some participants. An assistant will stand close to the participant to provide assistance and prevent a fall in case of imbalance. We will monitor how a participant is feeling throughout each task, and appropriate rest intervals will be provided. The session would be stopped at any stage if required.

In the unlikely event of a physical injury, rehabilitation, and compensation for injury by accident may be available from the Accident Compensation Corporation, provided the incident details satisfy the requirements of the law and the Corporation's regulations.

4.7 Statistical analysis

4.7.1 Sample size calculation

There is a lack of experimental evidence in the population of interest to conduct a power calculation for the required sample size. It is unclear if factors such as age or gender affect visual fixations and there is minimal information on population variation. Therefore, an arbitrary sample size of 20 in each group has been selected. This has been

selected in accordance with studies performed in adults with motion sensitivity (Van Ombergen et al., 2016; Winkler & Ciuffreda, 2009). The data from this study may help inform future studies with regard to the required sample size.

4.7.2 Analysis

Descriptive statistics (mean and standard deviation) will be calculated for each of the variables. Data normality will be examined using the Kolmogorov–Smirnov statistic. One-way independent measures analyses of variance will be performed to investigate the differences between groups for all variables. Post-hoc analysis with Sidak adjustment will be used for multiple comparisons (Kahya et al., 2018). Finally, a receiver operating characteristic curve analysis will be applied to determine threshold values in gaze, COP, and COM parameters, allowing the identification of the impairment induced by motion sensitivity. The optimal cut-off point will be determined using the Youden Index. Areas under the curve, specificity, and sensitivity will also be calculated. Values of areas under the curve will be categorised as follows: excellent (0.90), good (0.80-0.90), fair (0.70-0.79), and poor (<0.70).

4.8 Confidentiality

During the screening, the researcher will make note of whether the potential participant meets the study criteria. For those who do not meet the criteria, only the reason for exclusion from the project will be recorded in a database and will not be identifiable.

4.9 Ethics approval and consent to participate

Ethics approval for this study has been obtained from the New Zealand Health and Disability Ethics Committee (HDEC) and Auckland University of Technology Ethics Committee (AUTEC). Eligible potential participants will be asked to provide written informed consent. Ethics committee approval for any protocol modifications will be sought from HDEC and AUTEC. Any changes will lead to an amendment in the

Australian New Zealand Clinical Trials Registry (HDEC reference number: 18/CEN/193; AUTEC reference number: 19/38).

4.10 Dissemination of study data

A summary of the results from the study will be offered to all participants as per the consent form. Results from the study will be published in a peer-reviewed journal and presented at national and international conferences.

4.11 Availability of data and materials

All participants will be given a numerical code upon acceptance into the project. All health information will be stored in physical and electronic records that are identified by the participant code only. Only the named investigators will have access to the forms that contain information about the participant's name and their code. These forms will be stored in a secured cabinet in coordinating investigator's office, separate from any records containing health information. The data sets used and analysed during this study are available from the corresponding author on reasonable request.

4.12 Results

Data collection was started in May 2019 and was completed by February 2020. It was approved by the Institutional Review Board on November 2, 2018 (Ethics ref: 18/CEN/193). We are currently processing the data and will begin data analysis in July 2020. We expect the results to be available for publication by the end of 2020. The trial was funded by the Neurology Special Interest Group, Physiotherapy New Zealand, and the Eisdell Moore Centre in November 2018.

4.13 Discussion

This is an exploratory study with the primary aim to identify whether fixational instability is associated with motion sensitivity and whether it leads to increased postural sway and altered kinematics in adults with motion sensitivity.

This study will provide a detailed investigation of visual fixations, postural sway, and kinematics in complex visual environments. The use of a mobile eye-tracking device will investigate naturalistic eye behaviour when exposed to experimental stimuli. The task hierarchy will help in understanding how the characteristics of visual fixations change when a person views a complex visual environment as opposed to neutral environments. The experimental tasks might provoke symptoms in some participants; however, we expect that all participants will be able to complete the protocol with appropriate rest intervals between tasks. Our sample size of 20 participants in each group is a foundational step in exploring whether visual fixations contribute to motion sensitivity after vestibular disorder. We anticipate the outcomes will be able to detect a difference between healthy adults and those with motion sensitivity. Results from this study will inform future trials and will be used to inform development of diagnostic and rehabilitation programmes.

We hope that this study will increase our understanding of the complex interactions of vision and balance in people with motion sensitivity. If we determine that gaze and postural control characteristics are altered, we will develop an intervention that is designed to re-align the gaze and postural control characteristics closer to those of the control population. This intervention would then be tested in a series of clinical trials to determine effectiveness.

4.14 Acknowledgments

The Neurology Special Interest Group (NSIG), Physiotherapy New Zealand, and Eisdell Moore Centre of Balance and Hearing Disorders (University of Auckland) jointly funded the following: purchase of the projector screen, software development, two research assistants to assist during data collection, administrative costs, and travel vouchers for participants. Each funding body undertook a peer review of the study

protocol. Funding from the New Zealand Dizziness and Balance Clinic (NZDBC) was used to pay tuition fees for the corresponding author.

4.15 Author's contribution

SC, DT, and NS conceptualised and designed the project and obtained the funding. AK developed the experimental tasks and contributed to protocol. SC drafted the manuscript. DT and NS are providing PhD supervision for SC. All authors critically revised the manuscript. All authors read and approved the final manuscript.

4.16 Conflicts of interest

None declared.

End of the published manuscript

4.17 Summary

This chapter describes the protocol of a study informed by the findings of the narrative review (Chapter 3:) and the literature review on visual fixations (Section 4.2). Since visual fixations have a vital role in maintaining visual and postural stability by suppressing the optic flow and perception of visual illusions, the experimental tasks were designed to understand the characteristics of visual fixations of healthy adults in environments with varied level of visual complexities and how that differs in adults with motion sensitivity. The exploratory nature of the study allowed a detailed investigation of postural parameters, including head kinematics. Since there is a lack of literature regarding the aetiology of motion sensitivity, a thorough examination of visual and postural parameters would enhance the understanding of the symptoms and inform the development of an effective intervention. The published protocol was followed precisely, with no deviations, in the research reported in this thesis. The findings of the study are discussed in detail in the next chapter.

Chapter 5: Visual fixations and motion sensitivity: an exploratory study

5.1 Prologue

This chapter comprises a submitted manuscript on the cross-sectional observational exploratory study investigating visual fixations and postural behaviour in two groups: healthy adults and adults with motion sensitivity. The manuscript is currently under review with a peer-reviewed journal. This chapter addresses the following thesis objective:

- To conduct an observational exploratory study to investigate:
    a. The characteristics of visual fixations in adults with motion sensitivity
    b. Postural parameters in adults with motion sensitivity.

The submitted manuscript is presented here as it is, with no modification in content but a few formatting modifications to fit with the thesis structure and facilitate reading.

Start of submitted manuscript

5.2 Abstract

Background: Motion sensitivity can develop as a sequela of a vestibular disorder and is characterised by symptoms of nausea, dizziness, and imbalance in rich visual environments such as supermarkets and shopping malls. To date, the mechanisms underlying motion sensitivity are poorly understood.

Research Question: What are the characteristics of visual fixations and postural sway in adults with motion sensitivity compared to healthy adults when exposed to increasingly complex visual environments?

Methods: We recruited 20 adults with motion sensitivity and 20 healthy adults to this cross-sectional exploratory study. Participants were instructed to maintain gaze on letters projected on a large screen with backgrounds of differing visual complexity. The number of visual refixations, movement of the centre of pressure, and movement of the head and body centres of mass were recorded.

Results: Adults with motion sensitivity showed a significantly higher number of visual refixations ($F= 10.592$, $p< 0.01$), and increased mean velocity of head and body centres of mass movement ($F= 14.034$, $p< 0.01$ and $F= 6.553$, $p< 0.05$ respectively) compared to healthy adults.

Significance: Adults with motion sensitivity exhibited visual fixational instability and increased postural and head sway compared to healthy adults. This was mainly observed in conditions with complex and moving backgrounds. This may account for reports from adults with motion sensitivity of worsening symptoms in busy environments. The results from the study can be used to identify components essential for developing interventions to reduce symptoms of motion sensitivity.

Keywords: Motion sensitivity, dizziness, vestibular disorder, complex environments, visual fixations, postural control, eye tracking.

5.3 Introduction

Following a vestibular disorder, some people experience ongoing symptoms of motion sensitivity (Bronstein et al., 2020; Chin, 2018). Motion sensitivity forms one of the diagnostic criteria of the persistent postural perceptual dizziness (PPPD) syndrome (Popkirov et al., 2018), and sufferers report nausea, dizziness and postural instability in environments with rich visual input such as shopping malls (Chin, 2018; Guerraz et al., 2001). This limits people's ability to navigate through public places, restricting participation in daily activities and reducing quality of life (Benecke et al., 2013).

One commonly proposed explanation for motion sensitivity is an over-reliance on visual information after a vestibular disorder (Guerraz et al., 2001; Zur et al., 2015). Studies show that adults who are visually dependent have increased postural sway in situations with disorienting visual backgrounds, with reports of difficulty in maintaining gaze on a fixed target (Guerraz et al., 2001; Van Ombergen et al., 2016).

Visual fixations, which maintain gaze at a single point, have a major role in the suppression of motion perception within the visual field (Martinez-Conde et al., 2004). Studies have identified that adults with fixational instability are susceptible to developing motion sensitivity and exhibiting increased postural responses in complex visual surroundings (Lencer & Clarke, 1998; Murakami, 2004; Van Ombergen et al., 2016; Winkler & Ciuffreda, 2009). Investigating differences in visual fixations and postural parameters in adults with motion sensitivity compared to healthy adults could inform the development of interventions to reduce the impact of this disabling symptom.

Most studies investigating visual fixations have used optokinetic stimulation settings (Lencer & Clarke, 1998; Winkler & Ciuffreda, 2009); however, this can influence the perception of self-motion and amplitude of postural responses (Pavlou, 2010). The current study investigated visual fixations and postural sway using a mobile eye-tracking device in a range of complex visual environments. The primary hypothesis was that adults with motion sensitivity, when compared to healthy adults, would have an increased number of visual refixations, and increased postural instability, in complex visual environments.

5.4 Methods

The study was a cross-sectional, single session experimental study. Data were collected in a movement analysis laboratory. Forty participants were recruited (20 healthy adults

and 20 adults with motion sensitivity) aged between 18 and 60. Healthy participants were independently mobile with no history of vestibular or neurological disorders. Adults with motion sensitivity had a history of a vestibular disorder without current acute vestibular signs, and reported motion sensitivity (scored >5 on the Visual Vertigo analogue scale (Dannenbaum et al., 2011) and scored >40 on the Dizziness Handicap Inventory (Silva et al., 2016)). Exclusion criteria were a history of eye surgery, or a medical condition that could influence eye movements such as diabetes mellitus, traumatic brain injury or migraine. A detailed study protocol has been published elsewhere (Chaudhary et al., 2020).

5.4.1 Instruments

The setup consisted of a projector screen (Brateck Lumi), SMI mobile eye tracker (SMI ETG, SensoMotoric Instruments, Germany), AMTI force plate (Advanced Mechanical Technology Inc., Watertown, MA, USA) and Qualisys 3D motion capture system (Qualisys Medical AB, Göteborg, Sweden). Twenty-seven reflective markers were attached to participants' skin using a double-sided tape. The eye-tracking glasses and force plate were integrated and time-synced with the Qualisys system.

5.4.2 Experimental conditions

The experimental task consisted of six conditions each lasting 70 seconds. In each condition target letters were projected for 7 seconds at different positions in a random sequence onto increasingly visually complex background images, with 10 repetitions of the target letter presented in each condition. Participants were instructed to look at the target letter from the time it appeared on the screen until it disappeared. The conditions increased in difficulty in two ways: 1) by the background progressing from neutral to complex; and 2) by the appearance of either a single target letter or multiple distractor letters on the screen (Figure 5.1). In single-letter conditions, participants were instructed to focus on each projected letter for the duration of the task. In multiple letter

conditions, they were instructed to find the letter *E* and keep looking at it for the duration of the task. Participants completed all six conditions.

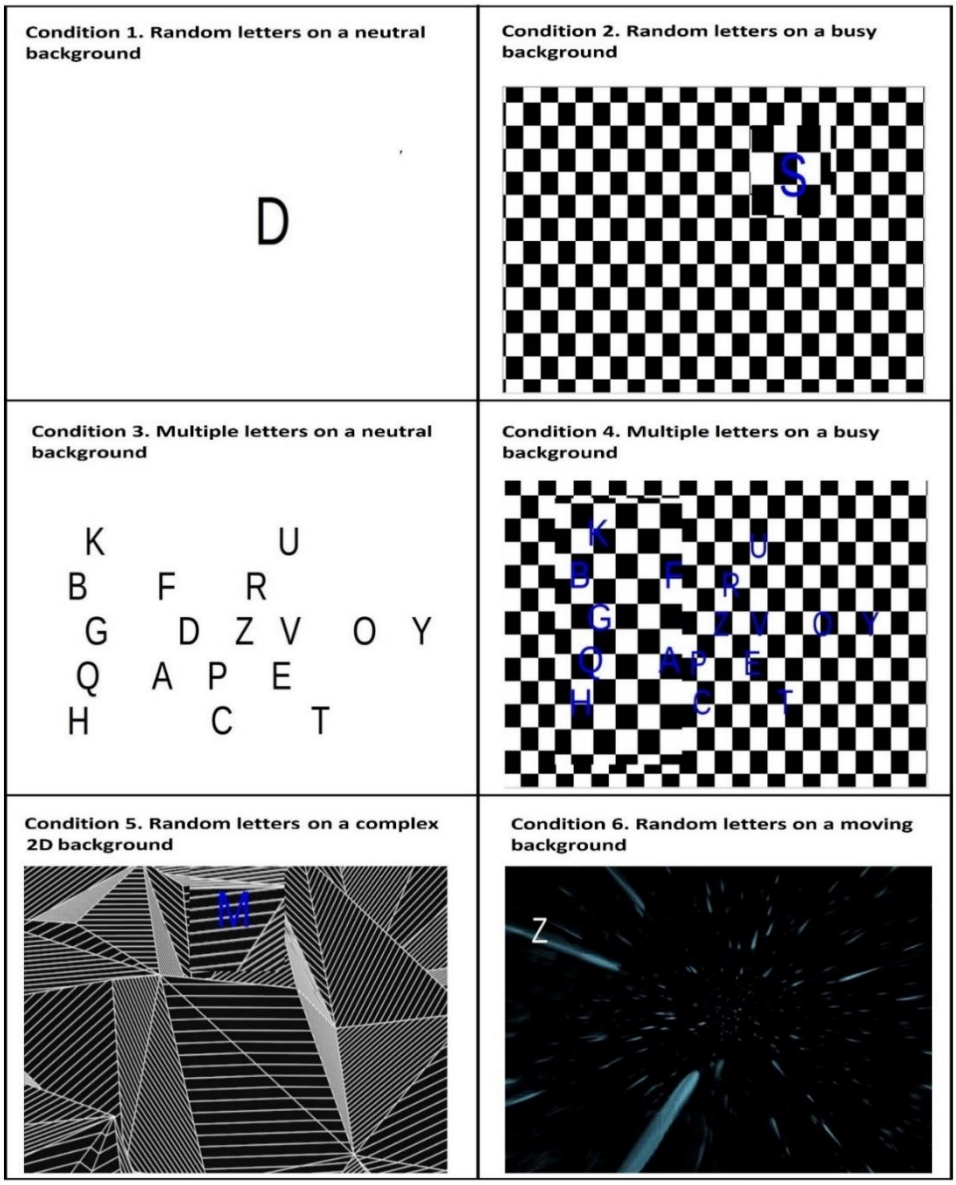

Figure 5.1 The experimental conditions

5.4.3 Data collection

Each participant stood on the force plate with feet shoulder width apart and arms relaxed at their sides. They were instructed to maintain quiet stance for the duration of the condition. The conditions were presented from the lowest to highest complexity of background. A rest interval of at least 1 minute was provided after each condition to minimise the provocation of symptoms such as dizziness and nausea.

5.4.4 Outcome measures and data processing

Visual fixations

The total number of visual refixations, the maximum fixation duration and the number of saccades were determined using a dispersion-based algorithm in the SMI ETG software. A refixation was defined if the eye movement crossed a maximum dispersion threshold of 100 pixels. The maximum fixation duration was calculated as the longest fixation within each condition. A saccade was defined as an event that did not meet the fixation criteria and occurred between the new and the previous fixation.

Postural sway: Centre of pressure (COP)

Raw COP displacement data (1200 Hz) were extracted from the Qualisys system and processed using LabVIEW software (version 9.0, National Instruments, USA). The COP signal was low-pass filtered (fourth order Butterworth, zero-phase-lag, 5 Hz cut-off frequency) (Lin et al., 2008). For the COP analysis, time series were down sampled by linear interpolation at 100 Hz (Ruhe et al., 2010). To quantify postural control, the following parameters were calculated: mean velocity, maximum range and root mean square of the COP displacement (Prieto et al., 1996).

Kinematics

Raw data from the Qualisys system were imported into Visual3D. A six-degrees-of-freedom model was constructed in Visual 3D for calculating centre of mass (COM) displacements. The COM of the body and the head segments were calculated in Visual3D. The COM signals were low-pass filtered (fourth order Butterworth, zero-phase-lag, 5 Hz cut-off frequency) (Lin et al., 2008). The mean velocity, root mean square, and maximum range of the body and head COM displacements were calculated to quantify the participants' body and head sway.

5.4.5 Statistical analysis

Data were analysed using SPSS (version 25, IBM Corp., Armonk, NY, USA). Data normality was examined using a Kolmogorov-Smirnov test. Descriptive statistics (mean and standard deviation) were calculated for each variable. Two-way mixed analyses of variance (ANOVAs), with *condition* being the within-subject factor (six levels) and *group* the between-subject factor (two levels), were performed to examine the differences between groups across conditions for all variables. Post-hoc analysis with Sidak adjustment was used for multiple comparisons (Kahya et al., 2018). A receiver operating characteristic (ROC) curve was used to determine reference cut-off values that discriminated adults with motion sensitivity from adults in the healthy group. The area under the curve (AUC) was interpreted as excellent ($0.8 < AUC \leq 0.9$), acceptable ($0.7 < AUC \leq 0.8$), or no discrimination ($AUC \leq 0.7$) (Zhou et al., 2009). The optimal threshold point was determined using the Youden Index to maximise both sensitivity and specificity indexes (Youden, 1950). ROC analyses were only applied in those visual and balance parameters that showed the highest significant differences between groups.

5.5 Results

Forty participants were recruited for the study (Table 5.1). Thirty-nine completed without adverse events or protocol deviations. One healthy participant was excluded due to an inability to complete all conditions. Despite no previous vestibular disorder or symptoms of motion sensitivity, the participant became dizzy after the third condition and elected not to continue.

Table 5.1 Characteristics of participants

Parameter	Motion sensitivity	Healthy control
Sex	Female = 16	Female= 8
	Male = 4	Male = 12
Median age (year), Range (min, max)	51 (31,60)	42 (22,63)
Visual Vertigo Analogue Scale, median, range (min, max)	37.5 (12,62)	NA
Dizziness Handicap Inventory, median, range (min, max)	50 (42, 70)	NA

Visual fixations

ANOVA between-subject main effects showed that adults with motion sensitivity had a significantly higher number of visual refixations (F-score= 10.592, p= 0.002) and lower maximum fixation duration (F-score= 9.435, p= 0.004) than healthy adults for all conditions. No significant between-group differences were found for the number of saccades (Table 5.2). A significant within-subject main effect was also observed for the number of visual refixations (F-score= 8.809, p< 0.001). Post-hoc analyses showed an increase in the number of visual refixations in condition 4 (p< 0.05) compared with single letter conditions (1, 2, 5 and 6) for the healthy group (Table 5.2). In addition, people with motion sensitivity showed fewer visual refixations in condition 1 compared to the other conditions (p< 0.05). No interaction effect was observed for any of the three visual parameters.

Table 5.2 Differences in the number of visual refixations, maximum fixation duration and number of saccades between adults with motion sensitivity and healthy adults

	Healthy		**Motion sensitivity**		*ANOVA*		
Number of visual refixations							
Condition 1	74.6	(43.1)	106.8	(34.0) *	*Group*	10.592	(0.002)
Condition 2	78.1	(47.9)	132.4	(57.0) *[1]	*Condition*	8.809	(<0.001)
Condition 3	95.5	(38.0)	139.6	(38.5) *[1]	*Group* × *Condition*	1.513	(0.188)
Condition 4	109.3	(40.8)[1,2]	140.6	(44.2) *[1]			
Condition 5	74.3	(50.2)[4]	128.8	(61.3) *			
Condition 6	73.8	(51.7)[4]	123.7	(67.8) *			
Maximum fixation duration (s)							
Condition 1	5.09	(1.85)	3.95	(1.45) *	*Group*	9.435	(0.004)
Condition 2	5.40	(1.79)	3.40	(1.98) *	*Condition*	2.000	(0.081)
Condition 3	5.19	(1.44)	3.87	(1.59) *	*Group* × *Condition*	1.472	(0.201)
Condition 4	4.67	(1.66)	3.84	(1.70)			
Condition 5	5.80	(2.31)	3.87	(1.92) *			
Condition 6	5.74	(2.02)	4.17	(2.12) *			
Number of saccades							
Condition 1	56.21	(34.62)	66.65	(30.96)	*Group*	2.570	(0.117)
Condition 2	55.68	(30.61)	70.35	(34.69)	*Condition*	39.364	(<0.001)
Condition 3	78.6	(36.6)[1,2]	95.1	(27.7)[1,2]	*Group* × *Condition*	0.330	(0.894)
Condition 4	85.1	(27.5)[1,2]	94.2	(32.7)[1,2]			
Condition 5	47.11	(24.79)[3,4]	63.30	(30.96)[3,4]			
Condition 6	41.58	(21.52)[2,3,4]	56.25	(30.32)[2,3,4]			

Two-way mixed ANOVAs were carried out being *Group* and *Condition* the between-subject and the within-subject factors, respectively. ANOVA main effects *(Group; Condition*) and interactions (*Group* × *Condition*) are presented as *F* score (*p*). Descriptive data are presented as mean (SD).

*Significantly different from the healthy control group ($p<0.05$); [1]Significantly different from condition 1 ($p<0.05$); [2]Significantly different from condition 2 ($p<0.05$); [3]Significantly different from condition 3 ($p<0.05$); [4]Significantly different from condition 4 ($p<0.05$).

Centre of pressure parameters

ANOVA did not show a significant between-group effect for any of the COP parameters. Nevertheless, post-hoc analyses revealed a significantly higher mean velocity ($p= 0.013$), maximum range ($p= 0.008$) and root mean square ($p= 0.28$) for adults with motion sensitivity for condition 5 (random letters on complex 2D background). ANOVA showed a significant within-subject main effect between conditions for mean velocity (F-score= 4.156; $p= 0.001$), maximum range (F-score= 6.848, $p< 0.001$) and root mean square (F-score= 7.630, $p< 0.001$). A significant

interaction effect was observed for the maximum range (F-score= 2.801, p= 0.018) and root mean square (F-score= 3.614, p= 0.004) (Table 5.3).

Table 5.3 Differences in the centre of pressure parameters between adults with motion sensitivity and healthy adults

	Healthy		**Motion sensitivity**		*ANOVA effects*		
Mean velocity (mm/s)							
Condition 1	7.80	(2.21)	8.82	(4.04)	*Group*	2.544	(0.119)
Condition 2	7.26	(2.97)	8.38	(3.90)	*Condition*	4.156	(0.001)
Condition 3	7.34	(2.88)	8.05	(4.52)	*Group* × *Condition*	2.402	(0.039)
Condition 4	7.56	(3.04)	9.22	(4.57)			
Condition 5	7.41	(2.32)	10.24	(4.15) *[3]			
Condition 6	7.91	(2.67)	10.78	(5.74)[3]			
Maximum range (mm)							
Condition 1	34.35	(13.86)	32.50	(9.97)	*Group*	1.949	(0.171)
Condition 2	26.00	(16.00)	25.69	(10.48)	*Condition*	6.848	(<0.001)
Condition 3	22.90	(9.98)[1]	25.13	(10.00)	*Group* × *Condition*	2.801	(0.018)
Condition 4	25.73	(12.37)	29.56	(11.90)			
Condition 5	24.09	(5.60)	36.45	(18.43) *[3]			
Condition 6	30.46	(11.02)	40.37	(24.41)[3]			
Root mean square (mm)							
Condition 1	7.00	(3.83)	5.50	(1.49)	*Group*	0.366	(0.549)
Condition 2	5.00	(2.30)	4.75	(1.86)	*Condition*	7.630	(<0.001)
Condition 3	4.57	(2.52)1	4.55	(1.48)	*Group* × *Condition*	3.614	(0.004)
Condition 4	4.90	(2.93)1	5.35	(1.75)[3]			
Condition 5	4.95	(1.36)	6.93	(3.52)*[3]			
Condition 6	6.19	(2.33)	7.86	(5.24)[2,3]			

Two-way mixed ANOVAs were carried out being *Group* and *Condition* the between-subject and the within-subject factors, respectively. ANOVA main effects *(Group; Condition*) and interactions (*Group* × *Condition*) are presented as *F* score (*p*). Descriptive data are presented as mean (SD).

*Significantly different from the healthy control group (p<0.05); [2]Significantly different from condition 2 (p<0.05); [3]Significantly different from condition 3 (p<0.05).

Body and head centre of mass parameters

ANOVA showed significant between-group main effects for mean velocity of the body COM (F-score= 6.553, p= 0.015) and head COM (F-score = 14.034, p= 0.001). Pairwise comparisons showed that people with motion sensitivity displayed significantly higher results for all COM parameters (p< 0.05) for mean velocity, maximum range and root mean square compared to the healthy adults, in conditions with a busy and moving

background (conditions 4, 5 and 6). Significant within-subject main effects were also observed for all body and head centre of mass parameters (F-score= 3.336- 8.374, $p< 0.05$). Significant interaction effects were seen for all parameters (F-score= 2.403-5.589, $p< 0.05$) (Table 5.4).

Table 5.4 Differences in the body and head centre of mass parameters between adults with motion sensitivity and healthy adults

	Healthy		**Motion sensitivity**		***ANOVA effects***		
Mean velocity of the body centre of mass (mm/s)							
Condition 1	3.26	(1.04)	3.27	(0.79)	*Group*	6.553	(0.015)
Condition 2	2.88	(1.09)	3.47	(1.10)	*Condition*	3.336	(0.007)
Condition 3	2.84	(0.86)	3.13	(0.94)	*Group × Condition*	4.291	(0.001)
Condition 4	2.92	(0.87)	3.57	(1.07) *[3]			
Condition 5	2.82	(0.62)	4.46	(2.07) *[1,2,3]			
Condition 6	2.96	(0.77)	4.67	(3.14) *[3]			
Maximum range of the body centre of mass (mm)							
Condition 1	26.35	(13.02)	24.76	(6.92)	*Group*	1.201	(0.280)
Condition 2	19.73	(8.47)[1]	20.00	(9.42)	*Condition*	6.662	(<0.001)
Condition 3	19.31	(9.01)	19.24	(7.32)	*Group × Condition*	2.403	(0.039)
Condition 4	20.87	(10.68)	23.04	(7.96)[3]			
Condition 5	19.57	(5.37)	28.67	(14.60) *[3]			
Condition 6	25.09	(8.94)	32.02	(21.92)[2,3]			
Root mean square of the body centre of mass (mm)							
Condition 1	6.51	(3.98)	4.96	(1.40)	*Group*	0.095	(0.760)
Condition 2	4.63	(2.14)	4.27	(1.83)	*Condition*	7.372	(<0.001)
Condition 3	4.23	(2.53)	4.07	(1.36)	*Group × Condition*	3.085	(0.011)
Condition 4	4.56	(2.92)	4.87	(1.66)[3]			
Condition 5	4.68	(1.54)	6.32	(3.31)[2,3]			
Condition 6	5.89	(2.34)	7.16	(4.99)[2,3]			
Mean velocity of the head centre of mass (mm/s)							
Condition1	6.23	(1.41)	6.83	(1.37)	*Group*	14.034	(0.001)
Condition 2	5.68	(1.65)	7.08	(1.64) *	*Condition*	4.144	(0.001)
Condition 3	5.84	(1.29)	6.73	(1.57)	*Group × Condition*	4.548	(0.001)
Condition 4	5.88	(1.44)	7.63	(1.90) *			
Condition 5	5.70	(0.97)	8.85	(3.33) *[1,2]			
Condition 6	6.01	(1.23)	9.28	(4.70) *			

Maximum range of the head centre of mass (mm)							
Condition 1	43.71	(14.93)	39.63	(9.67)	*Group*	3.611	(0.065)
Condition 2	36.12	(13.05)	37.75	(11.74)	*Condition*	6.930	(<0.001)
Condition 3	34.93	(10.58)	37.57	(11.66)	*Group × Condition*	4.467	(0.001)
Condition 4	37.08	(14.35)	44.20	(14.63)			
Condition 5	35.45	(7.96)	56.32	(26.59) *[1,2]			
Condition 6	44.08	(14.33)	58.51	(33.88)[1,2]			
Root mean square of the head centre of mass (mm)							
Condition 1	10.64	(4.31)	8.37	(2.00) *	*Group*	1.115	(0.298)
Condition 2	8.22	(2.69)	7.88	(2.43)	*Condition*	8.374	(<0.001)
Condition 3	7.73	(2.85)	7.94	(2.20)	*Group × Condition*	5.589	(<0.001)
Condition 4	8.22	(3.91)	9.45	(2.87)			
Condition 5	8.19	(2.11)	12.09	(5.67) *[1,2]			
Condition 6	10.06	(3.53)	12.77	(6.98)[1,2]			

Two-way mixed ANOVAs were carried out being *Group* and *Condition* the between-subject and the within-subject factors, respectively. ANOVA main effects *(Group; Condition*) and interactions (*Group × Condition*) are presented as *F* score (*p*). Descriptive data are presented as mean (SD).

*Significantly different from the healthy control group ($p<0.05$); [1]Significantly different from condition 1 ($p<0.05$); [2]Significantly different from condition 2 ($p<0.05$); [3]Significantly different from condition 3 ($p<0.05$).

ROC curve analysis

ROC curve analyses for condition 5 revealed that the most sensitive visual parameter for discriminating between groups was the number of visual refixations, with a cut-off score of 85 (AUC: 0.772; sensitivity: 80.0%; 1-specificity: 21.1%). For postural performance, COM parameters were more sensitive than COP for discriminating between groups, especially the mean velocity of the head COM (cut-off: 6.12 mm/s; AUC: 0.929; sensitivity: 95.0%; 1-specificity: 15.8%) and body COM (cut-off: 2.92; mm/s; AUC: 0.808; sensitivity: 85.0%; 1-specificity: 26.3%). Combining the number of visual refixations and mean velocity of the head COM increased the sensitivity in identifying adults with motion sensitivity (Figure 5.2).

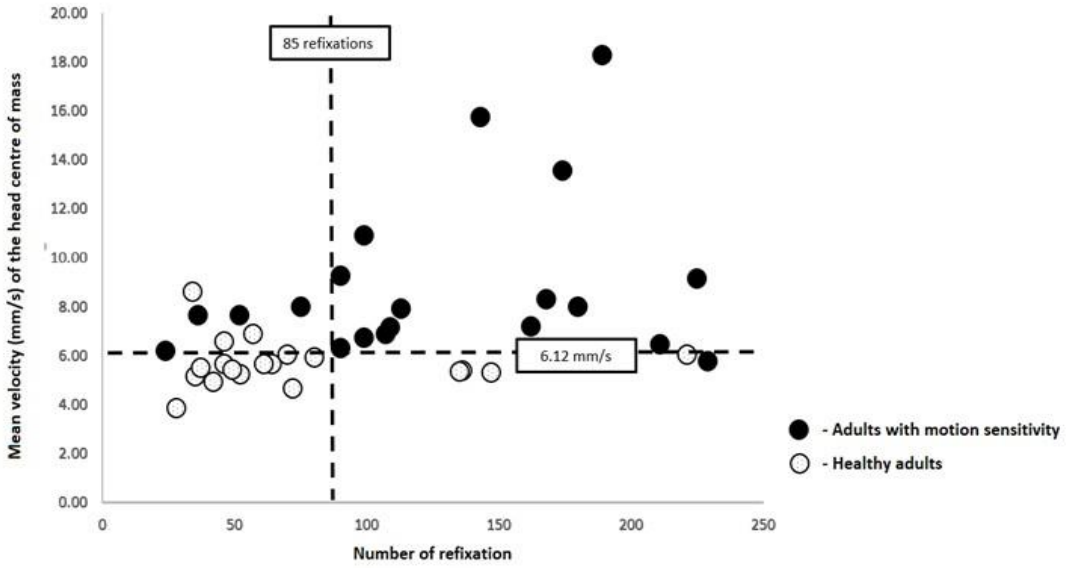

Figure 5.2 Number of visual refixations vs mean velocity of the head centre of mass plot

Note. Cut-off values: Number of refixations: 85; sensitivity 80.0%; 1-specificity: 21.1%; Mean velocity of the head COM: 6.12 mm/s; sensitivity: 95.0%; 1-specificity: 15.8%, for condition 5.

5.6 Discussion

The findings of this study confirmed our hypothesis that, compared to healthy adults, adults with motion sensitivity have an increased number of visual refixations, altered COP displacement and differences in body and head kinematics in complex visual environments.

To our knowledge, this is the first study investigating the characteristics of visual fixations, movement of the COP and of the COM of the head and body using a series of conditions with increasing levels of complexity. The number of visual refixations was significantly higher in adults with motion sensitivity for conditions with a busy and moving background compared to conditions with a neutral background. Adults with motion sensitivity showed a significant reduction in the maximum fixation duration for all conditions, indicating that they had difficulty in maintaining gaze on a single point during the task. Additionally, the duration of each fixation significantly decreased as the background increased in complexity, indicating greater fixational instability in busy visual environments. Adults in the healthy control group also showed an increase in the

number of visual refixations in conditions 3 and 4. This can be attributed to these conditions having multiple distractor letters on screen, with the task being to search for a target letter and to then maintain gaze on it. Interestingly, even in the presence of a high number of visual refixations in conditions 3 and 4, adults in the healthy control group did not show a significant decrease in the maximum fixation duration compared to conditions with a single letter (conditions 1, 2, 5 and 6). This suggests that adults in the healthy group were able to find the target letter more quickly and maintain fixation for a longer duration compared to adults with motion sensitivity.

The COP exhibited a significant interaction effect in maximum range and root mean square, indicating increased postural sway with increasing task complexity in adults with motion sensitivity. Adults with motion sensitivity also showed higher mean velocity of the COM of the head and body. Maximum range and root mean square are reported to be associated with the effectiveness of the postural control system, and the mean velocity is considered to represent the amount of regulatory activity associated with stability (Jeka et al., 2004; Maki et al., 1990; Prieto et al., 1996). These findings indicate a decline in the ability of the postural control system of adults with motion sensitivity to efficiently achieve stability in environments with increased visual complexity. Additionally, the higher COM oscillation of head indicates that adults with motion sensitivity have reduced ability to maintain head stability in space, particularly in complex visual environments.

Three possible mechanisms may explain our findings. These are fixational instability, impaired visual-vestibular interaction, and impaired sensory re-weighting. The presence of fixational instability has been previously associated with increased postural sway in complex visual environments (Laurens et al., 2010; Lencer & Clarke, 1998; Van Ombergen et al., 2016). Visual fixations have a crucial role in postural control as they minimise optic flow and retinal slip to reduce the consequent amplitude of postural

reactions (Glasauer et al., 2005; Laurens et al., 2010; Strupp et al., 2003). An inability to suppress optic flow can lead to an increased postural sway (Angelaki & Hess, 2005; Gielen et al., 2004). The results of our study revealed the presence of fixational instability in complex environments in adults with motion sensitivity leading to increased postural sway. Furthermore, postural sway was significantly higher in conditions with moving backgrounds, suggesting there may be an inability to suppress optic flow and minimise retinal slip generated due to the movement of a visual image on the retina.

The second possible mechanism is an impaired visual-vestibular interaction in adults with motion sensitivity. For the current study, adults with motion sensitivity were only recruited if they had recovered from a vestibular disorder and had no vertigo at the time of testing. Nevertheless, the findings suggest an impaired compensation of the vestibular system in visually complex environments. There was a significant increase in head sway during conditions with a moving background. It may be that the vestibular system was less able to provide accurate angular and linear acceleration information from head and body movements. The consequent unstable retinal image may then have disrupted the perception of self-motion by interrupting a normal interaction between the visual and the vestibular system (Dieterich & Brandt, 2015).

A third possible mechanism may be an inability to effectively re-weight the use of sensory inputs. The ability to counteract a disorienting visual stimulus depends on the presence of alternative reliable sensory inputs and central re-weighting of those inputs to favour the more accurate ones (Peterka, 2002). To achieve postural stability in the presence of destabilising visual inputs, such as those displayed to participants in this study, the postural control system should rely on vestibular and proprioceptive information more than visual information. Adults with motion sensitivity seemed less able to re-weight and switch from visual to a more accurate source of information for

postural control due to an over-reliance on visual input (Bronstein et al., 2020; Guerraz et al., 2001). This is reflected in our findings of an increase in postural and head sway in adults with motion sensitivity in conditions with busy and moving backgrounds. This study positioned participants on a fixed surface so proprioception through the lower limbs provided accurate information to maintain postural control (Jeka et al., 2004; Peterka, 2002). Studies have reported that patients with acute vestibular disorders are sensitive to visual motion but, as compensation progresses, there is a shift to using proprioception to inform postural control (Bles et al., 1983). The findings of our study suggest that this may not occur in adults with motion sensitivity, who appear to have an over-reliance on the visual system preventing accurate re-weighting of information. This accords with reports of poor postural control in busy environments in everyday life being experienced by people with motion sensitivity.

The ROC analyses were performed to find potential thresholds of visual and postural parameters that could be used to discriminate between adults with motion sensitivity and healthy adults. Based on the ROC plot, when performing visual fixation tasks against complex backgrounds (such as in condition 5) more than 85 refixations combined with a head COM mean velocity higher than 6.12 mm/s is indicative of fixational instability and impaired postural control suggesting the presence of motion sensitivity. These values could be used to clinically differentiate those with motion sensitivity and to facilitate the monitoring of natural recovery and the effects of rehabilitation.

Our study had some limitations. First, the conditions were not presented in a random order, but from simplest to most complex, to avoid the provocation of any debilitating symptoms. This could have led to a possible habituation to the surroundings and a gradual adaptation of the postural behaviour as the conditions became increasingly difficult. Second, the use of a mobile eye tracker utilising a dispersion-based algorithm

limited our ability to accurately identify saccades and could explain why there were no between-group differences in the number of saccades. However, for this study, the use of a dispersion-based algorithm was appropriate as our aim was to investigate visual refixations.

5.7 Conclusion

Adults with motion sensitivity exhibited fixational instability and increased postural and head sway with increased visual complexity. Our results highlight the clinical implications of this study, enabling the recognition of thresholds of visual and postural parameters that could help identify adults susceptible to developing motion sensitivity. The findings of this study could be used as a starting point for the development of a rehabilitation programme aimed at reducing fixational instability, which may improve postural control in adults with motion sensitivity. The thresholds could also be used as a tool to assess and track the progress of such a programme.

5.8 Ethics

Ethics approval for the study was obtained from the New Zealand Health and Disability Ethics Committee (HDEC reference number: 18/CEN/193) and Auckland University of Technology Ethics Committee (AUTEC reference number: 19/38). Trial Registration: Australian New Zealand Clinical Trials Registry (ACTRN12619000254190).

5.9 Funding

The Neurology Special Interest Group (NSIG) of Physiotherapy New Zealand and the Eisdell Moore Centre of Balance and Hearing Disorders (University of Auckland) jointly funded the following: purchase of the projector screen, software development, two research assistants to assist during data collection, administrative costs, and travel vouchers for participants. Each funding body undertook a peer review of the study

protocol. Funding from the New Zealand Dizziness and Balance Centre (NZDBC) was used to pay tuition fees for the corresponding author.

5.10 Credit author statement

Shikha Chaudhary: Conceptualisation, Data curation, Formal analysis, Investigation, Methodology, Funding acquisition, Writing, Visualisation. **David Barbado**: Formal Analysis, Data Curation, Review and Editing. **Nicola Saywell** and **Denise Taylor**: Conceptualisation, Methodology, Funding acquisition, Review and Editing.

5.11 Declaration of competing interests

None declared.

End of submitted manuscript

5.12 Summary

This exploratory study investigated visual fixations and postural parameters in adults with motion sensitivity in environments with increasing levels of visual complexity. The results of the study provided a deeper understanding of visual fixations and postural parameters in motion sensitivity and how the visual environment influences these parameters. Additional graphical analysis of the results can be found in Appendices O, P, Q and R. The study results provided a physiological basis for the symptoms by identifying the presence of fixational instability in adults with motion sensitivity. To date, studies have provided the theory of visual dependency in motion sensitivity but have failed to identify the factor within the visual system that could predispose a person to develop these symptoms. The detailed investigation of visual and postural parameters identified two factors that could differentiate healthy adults from adults with motion sensitivity. After understanding the role of visual fixations in postural control and the identification of fixational instability in motion sensitivity, we can suggest that

improving visual fixations may improve the symptoms of motion sensitivity. The next phase of this doctoral research is the conception of an intervention based on the findings of the narrative review and the observational exploratory study.

Chapter 6: Intervention development

6.1 Prologue

This chapter draws on a framework to guide development of an intervention informed by results of this doctoral research. This chapter addresses the following thesis objective:

- To identify and posit a theory that could inform development of an intervention informed by the results of the narrative review and observational exploratory study.

6.2 Background

The findings of the narrative review and the observational exploratory study suggested visual fixations as a factor that could be targeted to treat motion sensitivity. Consequently, the next phase of the doctoral research undertook the conception of an intervention. The intervention development process followed the Medical Research Council's (MRC) recommendations for the development of complex interventions (Watson, 2000).

The lack of understanding of the aetiology, diagnostic tools, interventions, and complexity related to motion sensitivity makes the development of the intervention complex. The MRC framework has been designed to guide an informed and iterative approach to intervention development by identifying the underlying physiology.

There are various approaches reported in the literature for intervention development (O'Cathain et al., 2019). Regardless of the approach undertaken, it is essential to use a framework encompassing fundamental principles and action points to develop an effective intervention (O'Cathain et al., 2019). The fundamental principles are: dynamic, iterative, and open to change, and looking forward to future execution. These principles

are revisited regularly as the intervention evolves (O'Cathain et al., 2019; Turner et al., 2019). Adopting fundamental principles and action points enhances intervention development, as learning from one action influences plans for other actions. This helps understand the interaction between various components within an intervention and with the recipients (Bleijenberg et al., 2018; O'Cathain et al., 2019). Further, working through action points helps identify the barriers and facilitators to implementation of the intervention.

6.3 Framework for intervention development

Studies have reported that 85% of research waste is attributed to poor methods used in developing interventions that are not feasible (Ioannidis, 2016; Ioannidis et al., 2014). Interventions intended to improve health outcomes need careful and detailed development to be effective and must be easily adopted in the real world. Using a framework strengthens the development by undertaking a methodical approach, reduces the research waste, enhances the design, increases value, and minimises the risk of participants being exposed to ineffective interventions (Bleijenberg et al., 2018; Croot et al., 2019; O'Cathain et al., 2019). Further, developing interventions involving laboratory-based research, a framework helps identify essential components to address vital questions for implementation into the real world. The current work utilised the revised version of the Medical Research Council's framework for intervention development (Bleijenberg et al., 2018), which is discussed in detail in the upcoming sections.

6.4 Development phase of the intervention

The revised version of the MRC framework (Figure 6.1) consists of six essential elements to be implemented in the development phase before undertaking definitive randomised controlled trials for long-term implementation (Bleijenberg et al., 2018;

Craig et al., 2008; Watson, 2000). The elements are: identifying the problem, identify existing theories, articulate a developing theory, determine the needs of recipients, examine the practice context, and model processes and outcomes (Figure 6.2).

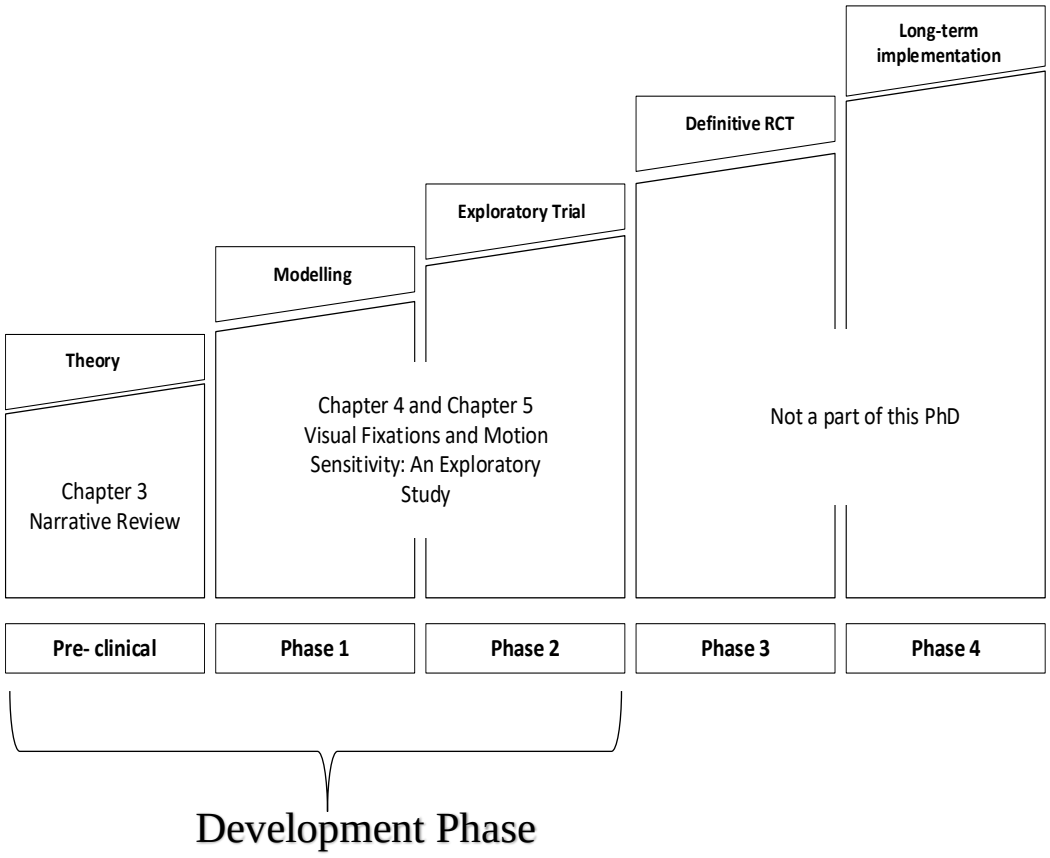

Figure 6.1 Phases of MRC framework mapped onto phases of this doctoral research

Note. Adapted from MRC (Watson, 2000).

As indicated in Figure 6.1, the narrative review (Chapter 3) outlined the theoretical rationale and evidence underpinning visual fixations as a key aspect in the preclinical phase of the MRC framework. The exploratory study (Chapters 4 and 5) form phase 1 and phase 2 of the framework, encompassing modelling and an exploratory trial of visual fixations to understand the underlying mechanisms and influence on visual and postural stability. The doctoral thesis has finished one iterative cycle that identified visual fixations as a determinant to be used in intervention development for adults with motion sensitivity. Results from the preclinical phase, phase 1 and phase 2 were used to begin the next iterative cycle, the conception of a theory for intervention.

6.5 Elements of the development phase

The elements of the development phase utilised for the initiation of the second iterative cycle are illustrated in Figure 6.2. The elements pertaining to the current thesis (yellow) are described in detail in the upcoming sections. The elements in green will be undertaken as part of a planned post-doctoral programme.

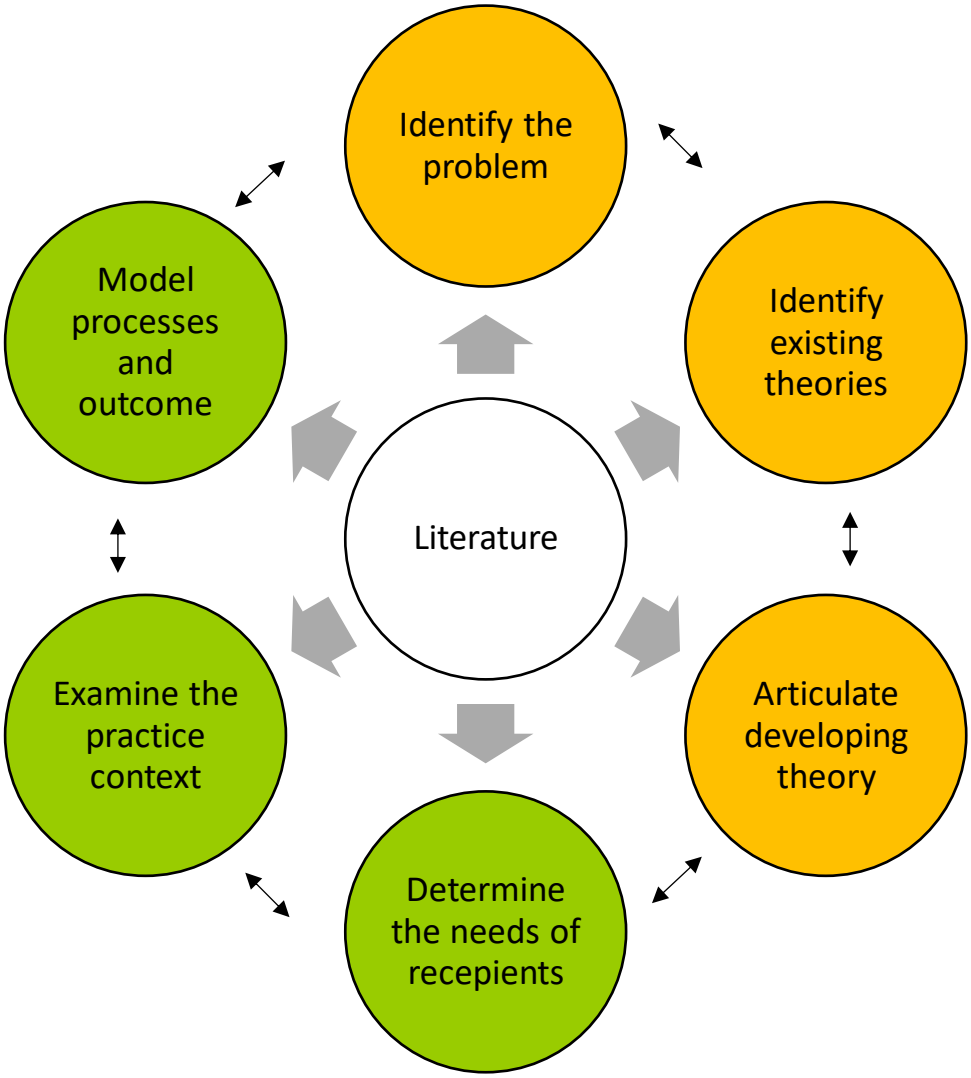

Figure 6.2 Elements of the development phase

Note. Modified from Bleijenberg et al. (2018). Yellow elements form the part of this thesis. Green elements will be undertaken as future work.

6.5.1 Identify the problem

As discussed in Chapter 1, motion sensitivity is debilitating for patients affecting many activities of daily living. The lack of a definitive diagnosis increases anxiety symptoms, further impacting health-related outcomes (Longridge et al., 2002; Zur et al., 2015) .

The inability to obtain a definitive diagnosis frequently instills distrust of a medical practitioner and can lead to suspicion of professional incompetence. This affects therapeutic relationships between patients and health professionals (Sezier et al., 2019). The absence of adequate diagnostic tools and the inability to classify the severity of symptoms has made the treatment of motion sensitivity difficult. To reduce the impact of motion sensitivity on an individual's life, there is a need to develop an effective treatment. To address a disorder lacking appropriate diagnostic tools makes this intervention development complex.

Findings from the narrative review indicated visual fixations are an essential factor in maintaining visual and postural stability. Following on from the findings of narrative review and related work (Chapter 3), the observational exploratory study (Chapters 4 and 5) investigated visual fixations in adults with motion sensitivity and identified the presence of fixational instability in adults with motion sensitivity. As discussed in the previous chapters, the presence of fixational instability leads an individual to have difficulty stabilising the retinal image, increasing the perception of visual illusions and, therefore, causing poor postural control as reported by adults with motion sensitivity.

The inability to stabilise a retinal image in the presence of fixational instability can be attributed to the fact that even when we fixate, there are small eye movements that occur (Martinez-Conde et al., 2004; Otero-Millan et al., 2014; Snodderly, 2016). These are microsaccades, ocular drifts and ocular tremors. These small eye movements generate retinal slip that needs to be suppressed to maintain visual stability. The inability to suppress the retinal slip caused by these small movements increases random noise in the visual system, making an image appear shaky and increasing the perception of visual illusions (Beer et al., 2008; Murakami, 2004).

Maintaining a stable image is a prerequisite for obtaining visual stability, which then enhances postural stability. Hence it can be inferred that fixational instability in adults with motion sensitivity is a problem that needs to be treated. The current research suggests fixational instability as a potential target for interventions to improve motion sensitivity, highlighting the novel contribution of this work, as there is a lack of literature regarding effective treatments for adults with motion sensitivity.

6.5.2 Identify existing theories

As illustrated in Chapter 1 and discussed in Chapter 2, the current evidence for the treatment of motion sensitivity is of poor quality and fails to identify a physiological rationale specific to the symptoms of motion sensitivity. Figure 6.3 illustrates the physiological rationale utilised by the authors and contrasts it with the evidence from the literature and findings presented in this thesis. This thesis provides elements that could be used to conceptualise a theory for designing an intervention and treating adults with motion sensitivity. The MRC framework was applied to the findings of this thesis to articulate a new theory for intervention development.

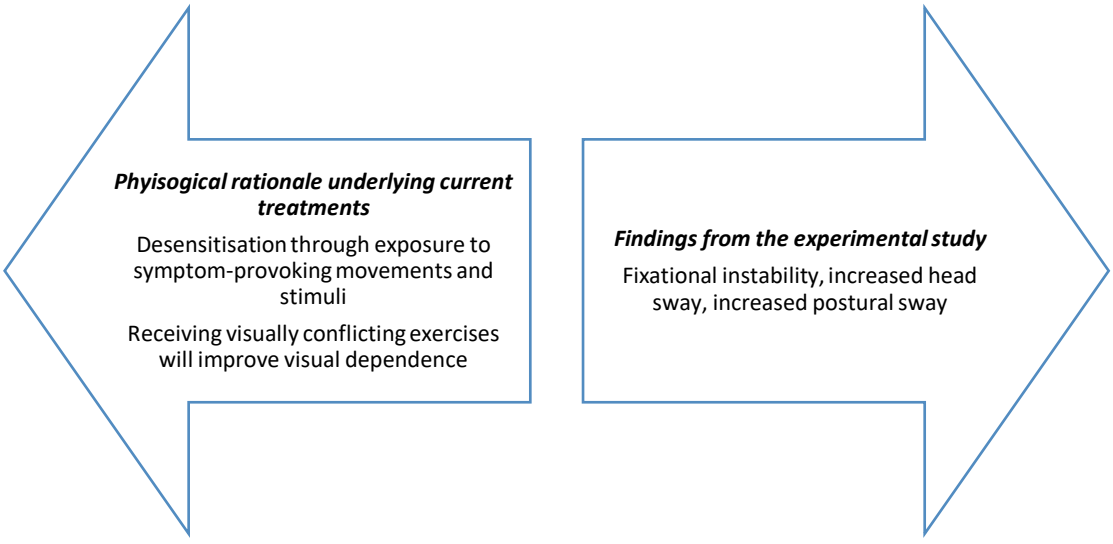

Figure 6.3 Existing theories vs findings from the experimental study

6.5.3 Articulate developing theory

This doctoral research identified fixational instability as a specific factor that can be targeted to improve symptoms and treat adults with motion sensitivity. Using the results of the studies completed as part of this doctoral research combined with evidence from the literature, we propose a new theory to explain motion sensitivity. The proposed new theory can be used as a starting point from which to develop an intervention. It is based on the small eye movements generated during visual fixation, primarily microsaccades. As outlined in section 6.5.1, the small eye movements that occur during visual fixation are microsaccades, ocular drifts, and ocular tremors (Martinez-Conde et al., 2004; Otero-Millan et al., 2014; Snodderly, 2016). These small eye movements stabilise the image on the retina and are essential for visual processing.

Microsaccades are the largest and fastest of the small eye movements, occurring at a rate of 2 to 3 per second during a sustained visual fixation and are essential for preventing visual fading (Martinez-Conde, 2006; Martinez-Conde & Macknik, 2017; Martinez-Conde et al., 2002, 2004; Martinez-Conde et al., 2013). Visual fading is described as a loss of vision due to neural adaptation during constant or uniform visual stimulation (Collewijn & Kowler, 2008). When maintaining fixation on a target, images in the periphery of vision tend to fade away due to the absence of retinal motion. Microsaccades refresh the retinal motion by carrying the retinal image across several dozen to several hundred photoreceptors leading to an increase in the neural activity and generating a transient visual motion effect that overcomes neural adaptation (Martinez-Conde & Macknik, 2017; Martinez-Conde et al., 2004; Martinez-Conde et al., 2013). Such ability makes microsaccades capable of acquiring increased information from a scene, but the ability to generate strong and transient visual motion effect triggers stronger illusory motion (Fermüller et al., 1997; Murakami et al., 2006; Otero-Millan et al., 2012). Small eye movements, or microsaccades within a visual fixation are

necessary, as insufficient eye motion can lead to visual fading. However, excessive motion can make vision unstable, predisposing an individual to perceive visual illusions and leading to diminished postural control.

Studies have identified that participants could be trained to suppress the occurrence of microsaccades and reduce them from 2 to 3 per second to approximately one every 2 seconds (Fiorentini & Ercoles, 1966; Martinez-Conde et al., 2013; Steinman et al., 1967; Steinman et al., 1973). The suppression of microsaccades has been shown during the performance of high acuity tasks such as shooting a rifle, threading a needle, and reading (Martinez-Conde et al., 2013; Steinman et al., 1967; Winterson & Collewun, 1976). It was demonstrated that such tasks suppress microsaccades to achieve a stable fixation and maintain the stability of an image on the retina.

Recent experimental studies have investigated microsaccades and ocular drift dynamics to understand visual stability during a visual fixation (Alexander et al., 2018; Martinez-Conde et al., 2002; Martinez-Conde et al., 2013). Studies have demonstrated that during the reduction of microsaccades, ocular drifts contribute to eye position and stability (Kowler & Steinman, 1979; Martinez-Conde, 2006; Martinez-Conde et al., 2002; Martinez-Conde et al., 2013; Steinman et al., 1967). Ocular drifts are a velocity-compensating system that reduces retinal image motion and keeps the target image stabilised on the retina (Collewijn & Kowler, 2008; Epelboim & Kowler, 1993; Martinez-Conde & Macknik, 2017; Sansbury et al., 1973).

Maintaining stability of the retinal image by actively reducing microsaccades is known as microsaccadic suppression. It is the suppression of the neural firing associated with the occurrence of microsaccades (Hafed & Krauzlis, 2010; Rolfs et al., 2008; Rolfs & Ohl, 2011). The suppression of such signals leads to a reduction in the blurry input caused by rapid shifts in the retinal image. Experimental studies have identified that the

presentation of a visual stimulus during a task directs voluntary temporal attention to the stimulus and decreases the microsaccadic rate, resulting in early microsaccadic suppression in anticipation of the attended stimulus (Betta & Turatto, 2006; Denison et al., 2019). This phenomenon has recently been investigated in participants with Attention Deficit Hyperactivity Disorder (ADHD) as an index of temporal attention (Dankner et al., 2017; Fried et al., 2014). The authors hypothesised that microsaccadic suppression starts earlier, when the stimulus is anticipated, providing insight into the ability of the mechanism directing temporal anticipation. It was found that subjects with ADHD had an increased rate of microsaccades compared to healthy controls, signifying an inability to allocate attention while anticipating visual stimuli (Dankner et al., 2017; Fried et al., 2014).

A strong link has been identified between microsaccades and attention (both spatial and temporal) (Laubrock et al., 2010; Pastukhov et al., 2013). Studies have demonstrated that higher attentional load is associated with lower microsaccadic rate (Pastukhov et al., 2013). The proposed pathway for microsaccadic modulation involves the superior colliculus, the activity of which can be manipulated by shifts of attention (Denison et al., 2019; Hafed et al., 2009; Hafed & Krauzlis, 2010; Rolfs & Ohl, 2011). Figure 6.4 illustrates a model showing likely neural pathways for microsaccadic activity.

Recently a microsaccades-to-saccade continuum has been proposed, suggesting that both saccades and microsaccades have a common oculomotor origin (Otero-Millan et al., 2008; Otero-Millan et al., 2011; Rolfs, 2009; Rolfs et al., 2007). Experimental studies have found that OPNs in the brainstem, which act a gate to saccades, are paused during microsaccades, further indicating a common oculomotor origin (Brien et al., 2010; Martinez-Conde et al., 2013). This led to the identification of saccadic intrusions (involuntary saccades that interrupt a visual fixation) as a factor affecting the stability of visual fixation (Gowen et al., 2007; McCamy et al., 2013; Otero-Millan et al., 2018;

Otero-Millan et al., 2011). Fixational instability can be explained by the presence of these saccadic intrusions interrupting a precise fixation, increasing the number of visual refixations in adults with motion sensitivity, as seen in the exploratory study's results.

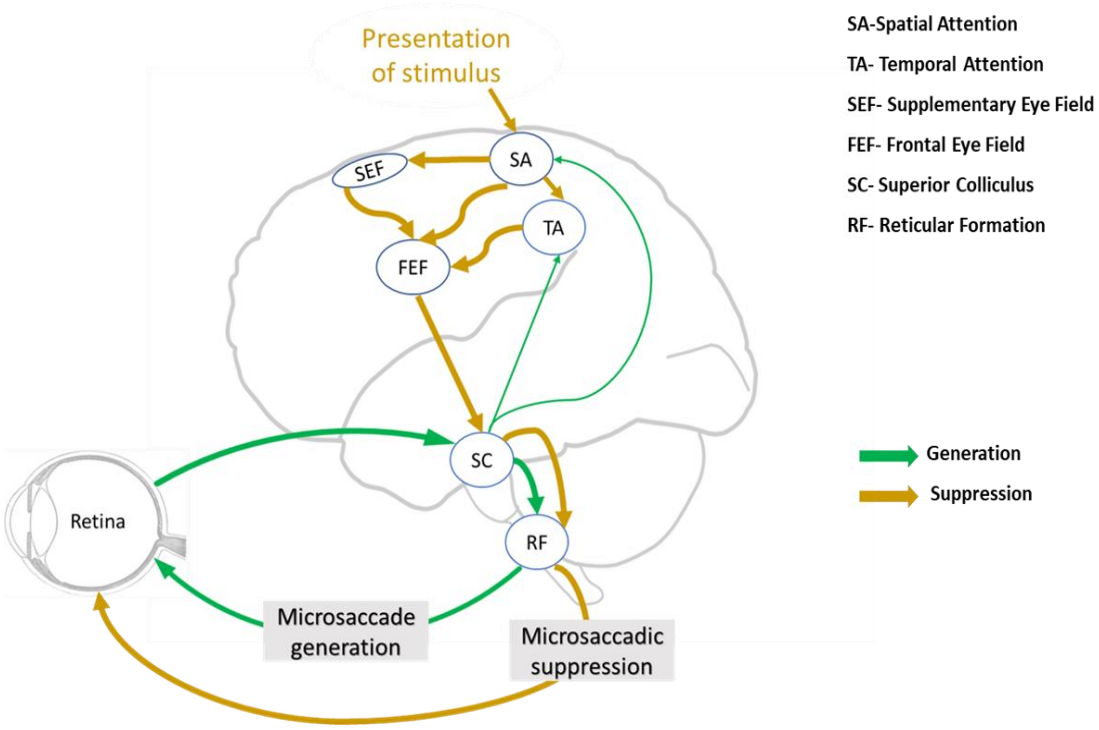

Figure 6.4 Neural pathway for microsaccadic activity

Note. Microsaccadic generation – Shift in activity of SC rostral pole increases activity in RF burst neurons, triggering microsaccades. Microsaccadic suppression – SC activity is altered by spatial and temporal attention suppressing microsaccades.

Supporting this, studies have demonstrated an increase in the generation of microsaccades in environments with complex visual information (Martinez-Conde & Macknik, 2017; McCamy et al., 2014; Otero-Millan et al., 2013). Increased microsaccades help the visual system acquire richer information (McCamy et al., 2014; Otero-Millan et al., 2013; Otero-Millan et al., 2008). This helps explain why symptoms reported by adults with motion sensitivity are induced by environments like supermarkets, shopping malls, and crowds. These environments increase the generation of microsaccades, leading to increased retinal motion, rendering visual fixations unstable. This was clearly demonstrated in the exploratory study.

The theory of making visual fixations stable by suppressing the generation of microsaccades can be used to treat adults with motion sensitivity. If an individual is trained to reduce the generation of microsaccades, it may lead to fewer microsaccades generated in complex visual environments, rendering visual fixation stable, thus improving visual and postural stability.

The scientific evidence involving the suppression of microsaccades to improve fixation stability provides a promising theory underpinning the intervention development. After understanding microsaccadic physiology and how it relates to symptoms experienced by adults with motion sensitivity, developing an intervention focussed on improving the stability of visual fixation by training the suppression of microsaccades could improve symptoms of motion sensitivity.

6.5.4 Determine the needs of recipients and examine the practice context

The second iterative cycle involving the preclinical phase and phase 1 of the MRC framework has identified microsaccades as a modifiable determinant that could influence the stability of visual fixation. The next phase would involve both interviews and focus groups to determine the needs and perceptions of the recipients and the providers. This would involve working closely with adults with motion sensitivity and the interdisciplinary team to develop an intervention. Involving interdisciplinary team would determine existing practice and identify facilitators and barriers to the proposed intervention. Examining current practice would guide the implementation of the proposed intervention.

6.5.5 Model processes and outcome

After understanding the current practice and needs of adults with motion sensitivity, the next phase would be to undertake the modelling of the intervention prototype. This would involve measuring microsaccades' susceptibility to change and the association of

such change with improving the outcome of fixational instability. This would include creation of a prototype and presentation to a multidisciplinary team, including stakeholders and adults with motion sensitivity, for feedback.

The phases of determining the needs, examining the practice context, the modelling phase and further phases of the framework do not form part of this doctoral thesis; they are part of a planned post-doctoral programme.

6.6 Summary

This chapter outlined the process of intervention development utilising the MRC framework by applying the findings from the narrative review and the observational exploratory study. It further described the scientific underpinnings of the new theory to guide the development of an intervention. The scientific evidence regarding microsaccades provides a solid foundation for the development of an effective intervention to treat adults with motion sensitivity.

Chapter 7: Integrated discussion and conclusion

7.1 Prologue

This doctoral research explored the visual system's role in motion sensitivity. The thesis comprises a narrative review of the literature, and a cross-sectional observational exploratory study investigating the characteristics of visual fixations and postural parameters in adults with motion sensitivity. The research reported in this thesis has utilised a framework to begin the development of an intervention for people with motion sensitivity.

This chapter revisits the research aims and objectives, presents an overview of research findings, implications for clinical practice and future research, and the research's strengths and weaknesses.

7.2 Revisiting the aims and objectives of the doctoral research

The overarching aim was to explore the visual system's role in motion sensitivity and identify elements that could guide the development of an intervention for people with motion sensitivity. The objectives were:

1. To understand the interactions between vision, postural control, and motion sensitivity to:
    a. Understand the visual system's interactions with the environment and the vestibular system.
    b. Identify possible factors within the visual system that could contribute to motion sensitivity.
2. To conduct an observational exploratory study to investigate:
    a. The characteristics of visual fixations in adults with motion sensitivity.
    b. Postural parameters in adults with motion sensitivity.

3. To identify and posit a theory that could inform development of an intervention informed by the results of the narrative review and observational exploratory study.

The following work was undertaken to achieve these objectives.

A critical review of the literature involving the assessment and treatment of motion sensitivity was carried out (Chapter 2). This included a study exploring the role of the visual system and studies undertaking treatment of motion sensitivity. The critical appraisal led to identification of the gap in the literature and guided the first objective of the thesis. A narrative review of the literature (Chapter 3) was carried out to understand the visual system's role in motion sensitivity by exploring and identifying the visual system's interactions with the environment and the vestibular system. The narrative review and literature review on visual fixations (Chapter 4) determined visual fixations to be a key factor that could contribute to motion sensitivity. After identifying visual fixations as a key factor, an observational exploratory study titled "Visual Fixations and Motion Sensitivity: An Exploratory Study" (Chapters 4 and 5) was conducted to investigate the characteristics of visual fixations and postural parameters in adults with motion sensitivity. The MRC framework for intervention development was utilised to conceptualise an intervention informed by findings of the narrative review and results of the observational exploratory study (Chapter 6).

7.3 Overview of the thesis findings

Motion sensitivity is a disabling chronic disorder characterised by dizziness, nausea, and imbalance induced by complex visual environments such as shopping malls and supermarkets. Epidemiological data on motion sensitivity is scarce due to the unavailability of standardised diagnostic tools. Two interventions have been trialled to date to treat motion sensitivity (Moaty et al., 2017; Pavlou et al., 2012; Pavlou et al., 2004). The lack of a strong theoretical rationale underpinning the interventions may, at

least in part, explain their limited efficacy. As a result, there is no specific treatment to treat motion sensitivity. Patients with motion sensitivity are often anxious and frustrated due to the lack of a definitive diagnosis and effective treatment (Sezier et al., 2019; Zur et al., 2015). This thesis has highlighted the inability of current treatments to improve outcomes for adults with motion sensitivity emphasising the need for specific diagnostic tools and interventions to treat this debilitating condition.

This comprehensive body of work adds to the understanding of motion sensitivity by identifying sensitive parameters useful for diagnosis. Additionally, this work has generated a specific theory which will be used to develop an intervention to reduce the symptoms associated with motion sensitivity.

The narrative review highlighted visual fixations vital in maintaining visual and postural stability by the interactions of the visual system with the vestibular system and the environment. Visual fixations help stabilise images on the retina during head movements and motion in the environment by suppressing the generation of vection and the optokinetic response. Further, they help suppress optic flow and retinal slip, reducing the amplitude of postural reactions and maintaining postural stability. The inability to maintain visual fixation (fixational instability) increases the perception of visual illusions leading to reduced visual stability and diminished postural control.

The presence of fixational instability was identified in adults with motion sensitivity, as demonstrated by the observational exploratory study results. The study investigated the characteristics of visual fixations and postural parameters in adults with motion sensitivity when they are exposed to conditions with increasing levels of visual complexities. The research protocol was designed to examine visual fixations, head and body COM parameters and COP parameters in adults with motion sensitivity. The detailed investigation of the parameters provided a comprehensive picture of how

complex visual environments affect adults with motion sensitivity. The study results provided a detailed insight into motion sensitivity by increasing the understanding of the symptoms. The exploratory study led to the identification of sensitive parameters to differentiate adults with motion sensitivity from healthy adults. The study results demonstrated presence of fixational instability and increased postural and head sway in adults with motion sensitivity. The use of head markers to quantify head COM identified the presence of head sway in tasks with complex and moving backgrounds. This has not been reported in previous studies. Further, the study highlighted the potential inability to effectively re-weight the information from the three sensory systems as adults with motion sensitivity rely more on the visual system than the proprioceptive or vestibular system. The results provided a possible explanation of symptoms induced by environments with rich visual information. The combined findings of the narrative review and the observational exploratory study established visual fixations as a contributing factor in the development of symptoms of motion sensitivity.

The framework utilised to develop an intervention for adults with motion sensitivity articulated a specific scientific theory informed by the literature and the results presented in this thesis. The theory of fixational instability describes the possible link between microsaccade generation and the symptoms of motion sensitivity. Environments with rich visual inputs increase the generation of microsaccades which increase the neural activity and enhance retinal image motion (Figure 7.1). This retinal image motion renders the image unstable on the retina, impacting visual stability. This leads the brain to register these retinal motions as actual motion, triggering illusory motion perception impacting postural stability. The theory of fixational instability identified microsaccadic suppression as a factor that may improve the stability of visual fixation. This theory promises a measurable factor to be used in an intervention to treat

adults with motion sensitivity. The modelling processes consisting of prototyping the intervention will provide further insight on microsaccades' susceptibility to change and training an individual to sup press microsaccades.

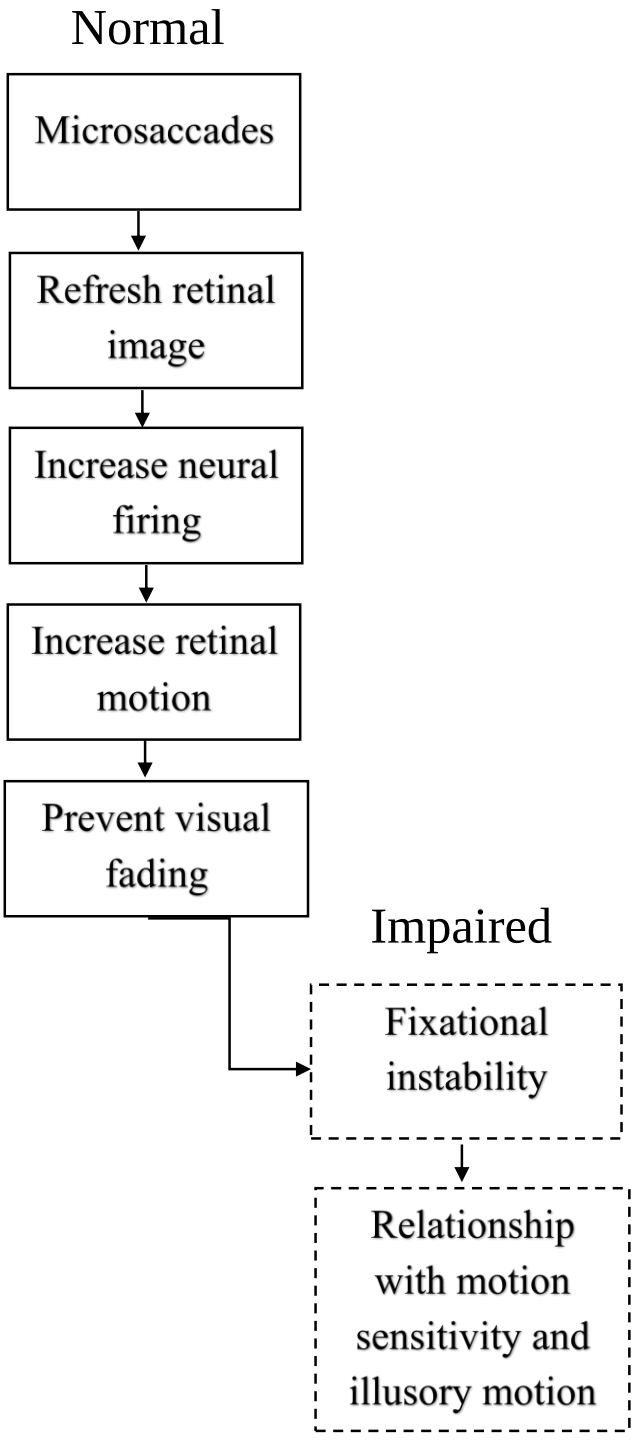

Figure 7.1 Proposed theory for fixational instability

7.4 Implications for clinical practice

Although the work presented in this thesis does not have immediate clinical implications, it does provide novel knowledge regarding motion sensitivity. The identified parameters can be developed into a tool that would be an important step in the diagnostic pathway for people with motion sensitivity. Additionally, the work provides a promising theory to inform the development of an intervention. Future work could concentrate on translating the findings of the thesis into clinical practice.

7.5 Implications for future research

This thesis has proposed a theory of microsaccadic suppression to improve the stability of visual fixations which we hypothesize will reduce the symptoms of people who experience motion sensitivity. However, more research is needed to confirm whether it is possible to enhance the stability of visual fixation by suppressing microsaccades and, if it is possible, whether it reduces the symptoms of motion sensitivity.

Assuming a reduction in symptoms using this approach, we could develop a clinically feasible device to measure visual fixations. This research used a high-cost eye tracker to investigate visual fixations which is likely to be unavailable in most settings. The lack of clinical studies investigating visual fixations can be attributed to the equipment required for capturing visual fixations. Future research is recommended to develop a feasible clinical tool to measure visual fixations. One possibility we are investigating is the use of electro-oculography (EOG). EOG can measure the potential difference across the eye resulting from eye movements and is low cost and easy to use. A custom EOG system could be adapted to pick up visual fixations and tested through a simulated excitation-function generator to test the function and safety of the device. The output of the EOG system can be transmitted wirelessly to a PC and software such as MATLAB could be used for signal processing through a customised algorithm to identify and

analyse visual fixations. Key considerations in the development of a new device are its reliability, validity, and responsiveness. The device should be tested in a variety of environments to evaluate the consistency of the EOG system.

We did not perform any post-hoc power analysis as this approach is considered flawed. The flaw is that the post-hoc "observed power" can be directly inferred from the p-value and a power analysis does not add any additional value (Hoenig & Heisey, 2001). We have reported effect sizes along with their confidence intervals. Future researchers interested in confirming our finding with a more robust study design such as an RCT can utilise this information to choose a sample size appropriate to their design.

7.6 Strengths

This research investigated the visual system's contribution to motion sensitivity. It provided a detailed investigation of the characteristics of visual fixations and postural parameters by using tasks with increasing levels of complexity, thereby enhancing the understanding of the changes in visual and postural behaviour. This is the first study to investigate head stability in adults with motion sensitivity. The head contains two systems that play a vital role in postural control, the visual and the vestibular system. Head stabilisation is crucial for optimal processing of information from these systems to maintain postural stability. The study's exploratory nature allowed the interrogation of the data and the identification of parameters that could diagnose motion sensitivity. The findings have contributed to an increased understanding of motion sensitivity and have provided future research directions that could be undertaken to develop a diagnostic tool and an intervention for adults with motion sensitivity.

7.7 Limitations

This was the first study to investigate visual parameters in adults with motion sensitivity. It has not yet been replicated, limiting the ability to generalise the findings

across the population. Although adults with motion sensitivity were recruited from a specialised vestibular clinic, the lack of a complete vestibular assessment immediately before the study limits our understanding of the status of the vestibular system at the time of the study. However, restrictions on time and resources needed for complete vestibular assessment were prohibitive. A further issue that limits our findings' generalisability is the nature of the symptoms and difficulty in diagnosis. Although the study utilised a specific questionnaire to include adults with motion sensitivity, the lack of reported psychometric properties of the questionnaire limited our diagnostic ability regarding the presence of motion sensitivity. This can be attributed to the lack of research in this population leading to researchers being dependent on the subjective quantification of symptoms.

There were some technical limitations to our set up that should be highlighted. Although the projector screen had a widescreen aspect ratio of 16:9 and was the largest screen we could purchase (3m x1.68m; WxH) it did not provide a full-field visual stimulation. It is possible that the presence of other objects in the laboratory provided a sense of steadiness to adults with motion sensitivity as peripheral vision dominates postural control. This could have affected their postural behaviour. However, the results suggest this did not have a major impact. We had considered the use of virtual reality goggles to provide visual stimulation but that would have limited our ability to measure eye movements.

The study utilised multiple statistical measures that pose some risks to results. P-value adjustments for multiple comparisons are advised to safeguard against the risk of rejecting a true null hypothesis (Rothman, 1990). But these adjustments increase the risk of not rejecting the null when it is indeed false. These two risks must be balanced against each other. In this exploratory work we decided to not apply any adjustment for

the multiple comparisons to minimise the risk of not rejecting the null when it is false (Kenneth, 1990).

7.8 Conclusion

The findings of the research presented in this thesis identified a possible physiological rationale for motion sensitivity. The research has provided evidence for visual fixations as a contributing factor in motion sensitivity. The investigation of visual fixations and postural parameters revealed nuances related to motion sensitivity and identified increased head sway in complex visual environments in adults with motion sensitivity. The work led to the identification of parameters not previously reported that could be developed into a clinical diagnostic tool. Utilising the MRC framework, we identified a specific theory from which to develop an intervention to treat motion sensitivity. The methodological approach taken by utilising the MRC framework for intervention development will continue to be developed and tested in future trials.

7.9 Impact of COVID-19 pandemic

The pandemic negatively affected the work completed for this thesis. A n= 1 case series was planned to test the theory for intervention development, but the lockdowns rendered this impossible in the timeframe.

Publications and Conference Presentations

- **Chaudhary, S.**, Saywell, N., Kumar, A., & Taylor, D. (2020). Visual fixations and motion sensitivity: Protocol for an exploratory study. *JMIR Research Protocols, 9*(7), e16805. https://doi.org/10.2196/16805. PMID: 32716003; PMCID: PMC7418000.
- **Chaudhary, S.**, Barbado, D., Saywell, N., & Taylor, D. *Visual fixations and motion sensitivity: An exploratory study.* Manuscript submitted for publication 2021.
- **Chaudhary, S.**, Saywell, N., & Taylor, D. *The visual system and its interactions for postural control: A narrative review.* Manuscript submitted for publication 2021.
- **Chaudhary, S.**, Saywell, N., & Taylor, D. (2020). *Visual fixations and motion sensitivity: An exploratory study* [Poster presentation]. The Eisdell Moore Centre \Symposium, Auckland, New Zealand.
- **Chaudhary, S.**, Saywell, N., & Taylor, D. (2019). *Visual fixations and motion sensitivity: An exploratory study* [Podium presentation]. New Zealand Society for Balance Dizziness and Vertigo (NZSBDV) and New Zealand Society of Otolaryngology, Head and Neck Surgery (NZSOHNS) Combined Clinical and Scientific Meeting. Dunedin, New Zealand.
- **Chaudhary, S., Saywell, N.,** Taylor, D., & Signal N. (2018). *Role of optic flow and eye movements in motion sensitivity* [Podium presentation]. Physiotherapy New Zealand Conference, Auckland, New Zealand.
- **Chaudhary, S., Saywell, N.,** Taylor, D., & Signal, N. (2017). *Role of optic flow and eye movements in motion sensitivity* [Podium presentation]. New Zealand Society for Balance Dizziness and Vertigo (NZSBDV) meeting, Auckland, New Zealand.

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Appendices

Appendix A: Modified Downs and Black checklist for Pavlou et al. (2004)

Simulator based rehabilitation in refractory dizziness.

Item	Criteria	Possible Answers
Reporting		
1	*Is the hypothesis/aim/objective of the study clearly described?*	Yes = 1
2	*Are the main outcomes to be measured clearly described in the Introduction orMethods section?* If the main outcomes are first mentioned in the Results section, the question should be answered no.	Yes = 1
3	*Are the characteristics of the patients included in the study clearly described?* In cohort studies and trials, inclusion and/or exclusion criteria should be given.In case-control studies, a case-definition and the source for controls should be given.	Yes = 1
4	*Are the interventions of interest clearly described?* Treatments and placebo(where relevant) that are to be compared should be clearly described.	Yes = 1
5	*Are the distributions of principal confounders in each group of subjects to becompared clearly described?* A list of principal confounders is provided.	No = 0
6	*Are the main findings of the study clearly described?* Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions. (Thisquestion does not cover statistical tests which are considered below).	Yes = 1
7	*Does the study provide estimates of the random variability in the data for themain outcomes?* In non-normally distributed data the interquartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported. If the distribution of the data is not described, it must be assumed that the estimatesused were appropriate and the question should be answered yes.	Yes = 1
8	*Have all important adverse events that may be a consequence of the intervention been reported?* This should be answered yes if the study demonstrates that there was a comprehensive attempt to measure adverseevents. (A list of possible adverse events is provided).	No = 0
9	*Have the characteristics of patients lost to follow-up been described?* This should be answered yes where there were no losses to follow-up or where losses to follow-up were so small that findings would be unaffected by theirinclusion. This should be answered no where a study does not report the number of patients lost to follow-up.	No = 0
10	*Have actual probability values been reported (e.g. 0.035 rather than <0.05)for the main outcomes except where the probability value is less than 0.001?*	No = 0

Item	Criteria	Possible Answers
External validity		
11	*Were the subjects asked to participate in the study representative of the entire population from which they were recruited?* The study must identify the sourcepopulation for patients and describe how the patients were selected. Patients would be representative if they comprised the entire source population, an unselected sample of consecutive patients, or a random sample. Random sampling is only feasible where a list of all members of the relevant populationexists. Where a study does not report the proportion of the source population from which the patients are derived, the question should be answered as unableto determine.	Unable to determine = 0
12	*Were those subjects who were prepared to participate representative of the entire population from which they were recruited?* The proportion of those asked who agreed should be stated. Validation that the sample was representative would include demonstrating that the distribution of the mainconfounding factors was the same in the study sample and the source population.	No = 0
13	*Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?* For the question to be answered yes the study should demonstrate that the interventionwas representative of that in use in the source population. The question shouldbe answered no if, for example, the intervention was undertaken in a specialistcentre unrepresentative of the hospitals most of the source population would attend.	No = 0
Internal validity - bias		
14	*Was an attempt made to blind study subjects to the intervention they have received?* For studies where the patients would have no way of knowing whichintervention they received, this should be answered yes.	No = 0
15	*Was an attempt made to blind those measuring the main outcomes of theintervention?*	Unable to determine = 0
16	*If any of the results of the study were based on "data dredging", was this madeclear?* Any analyses that had not been planned at the outset of the study shouldbe clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.	Yes = 1
17	*In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between theintervention and outcome the same for cases and controls?* Where follow-up was the same for all study patients the answer should be yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.	Unable to determine = 0
18	*Were the statistical tests used to assess the main outcomes appropriate?* The statistical techniques used must be appropriate to the data. For example nonparametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias,the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.	Yes = 1
19	*Was compliance with the intervention/s reliable?* Where there was non-compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the effect of any misclassification was likely to bias any association to the null, the questionshould be answered yes.	Yes = 1
20	*Were the main outcome measures used accurate (valid and reliable)?* For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates theoutcome measures are accurate, the question should be answered as yes.	Yes = 1

Item	Criteria	Possible Answers
Internal validity - confounding (selection bias)		
21	*Were the patients in different intervention groups (trials and cohort studies) orwere the cases and controls (case-control studies) recruited from the same population?* For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information	Yes = 1
	concerning the source of patients included in the study.	
22	*Were study subjects in different intervention groups (trials and cohort studies)or were the cases and controls (case-control studies) recruited over the same period of time?* For a study which does not specify the time period over whichpatients were recruited, the question should be answered as unable to determine.	Unable to determine = 0
23	*Were study subjects randomized to intervention groups?* Studies which state that subjects were randomized should be answered yes except where method ofrandomization would not ensure random allocation. For example alternate allocation would score no because it is predictable.	Yes = 1
24	*Was the randomized intervention assignment concealed from both patients andhealth care staff until recruitment was complete and irrevocable?* All non- randomized studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.	Yes = 1
25	*Was there adequate adjustment for confounding in the analyses from which themain findings were drawn?* This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In non-randomized studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.	No = 0
26	*Were losses of patients to follow-up taken into account?* If the numbers of patients lost to follow-up are not reported, the question should be answered asunable to determine. If the proportion lost to follow-up was too small to affectthe main findings, the question should be answered yes.	Unable to determine = 0
Power		
27*	*Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?* Sample sizes have been calculated to detect a difference of x% and y%.	No = 0

*Item has been modified.

Appendix B: Modified Downs and Black checklist for Pavlou et al. (2012)

The effect of virtual reality on visual vertigo symptoms in patients with peripheral vestibular dysfunction: A pilot study

Item	Criteria	Possible Answers
Reporting		
1	*Is the hypothesis/aim/objective of the study clearly described?*	No = 0
2	*Are the main outcomes to be measured clearly described in the Introduction orMethods section?* If the main outcomes are first mentioned in the Results section, the question should be answered no.	Yes = 1
3	*Are the characteristics of the patients included in the study clearly described?* In cohort studies and trials, inclusion and/or exclusion criteria should be given.In case-control studies, a case-definition and the source for controls should be given.	Yes = 1
4	*Are the interventions of interest clearly described?* Treatments and placebo(where relevant) that are to be compared should be clearly described.	Yes = 1
5	*Are the distributions of principal confounders in each group of subjects to becompared clearly described?* A list of principal confounders is provided.	No = 0
6	*Are the main findings of the study clearly described?* Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions. (Thisquestion does not cover statistical tests which are considered below).	Yes = 1
7	*Does the study provide estimates of the random variability in the data for themain outcomes?* In non-normally distributed data the interquartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported. If the distribution of the data is not described, it must be assumed that the estimatesused were appropriate and the question should be answered yes.	Yes = 1
8	*Have all important adverse events that may be a consequence of the intervention been reported?* This should be answered yes if the study demonstrates that there was a comprehensive attempt to measure adverseevents. (A list of possible adverse events is provided).	No = 0
9	*Have the characteristics of patients lost to follow-up been described?* This should be answered yes where there were no losses to follow-up or where losses to follow-up were so small that findings would be unaffected by theirinclusion. This should be answered no where a study does not report the number of patients lost to follow-up.	No = 0
10	*Have actual probability values been reported (e.g. 0.035 rather than <0.05)for the main outcomes except where the probability value is less than 0.001?*	Yes = 1

Item	Criteria	Possible Answers
External validity		
11	*Were the subjects asked to participate in the study representative of the entire population from which they were recruited?* The study must identify the sourcepopulation for patients and describe how the patients were selected. Patients would be representative if they comprised the entire source population, an unselected sample of consecutive patients, or a random sample. Random sampling is only feasible where a list of all members of the relevant populationexists. Where a study does not report the proportion of the source population from which the patients are derived, the question should be answered as unableto determine.	Yes = 1
12	*Were those subjects who were prepared to participate representative of the entire population from which they were recruited?* The proportion of those asked who agreed should be stated. Validation that the sample was representative would include demonstrating that the distribution of the mainconfounding factors was the same in the study sample and the source population.	No = 0
13	*Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?* For the question to be answered yes the study should demonstrate that the interventionwas representative of that in use in the source population. The question shouldbe answered no if, for example, the intervention was undertaken in a specialistcentre unrepresentative of the hospitals most of the source population would attend.	No = 0
Internal validity - bias		
14	*Was an attempt made to blind study subjects to the intervention they have received?* For studies where the patients would have no way of knowing whichintervention they received, this should be answered yes.	No = 0
15	*Was an attempt made to blind those measuring the main outcomes of theintervention?*	No = 0
16	*If any of the results of the study were based on "data dredging", was this madeclear?* Any analyses that had not been planned at the outset of the study shouldbe clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.	Unable to determine = 0
17	*In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between theintervention and outcome the same for cases and controls?* Where follow-up was the same for all study patients the answer should be yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.	No = 0
18	*Were the statistical tests used to assess the main outcomes appropriate?* The statistical techniques used must be appropriate to the data. For example nonparametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias,the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.	Yes = 1
19	*Was compliance with the intervention/s reliable?* Where there was non-compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the effect of any misclassification was likely to bias any association to the null, the questionshould be answered yes.	Yes = 1
20	*Were the main outcome measures used accurate (valid and reliable)?* For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates theoutcome measures are accurate, the question should be answered as yes.	Yes = 1

Item	Criteria	Possible Answers
Internal validity - confounding (selection bias)		
21	*Were the patients in different intervention groups (trials and cohort studies) orwere the cases and controls (case-control studies) recruited from the same population?* For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information	Yes = 1
	concerning the source of patients included in the study.	
22	*Were study subjects in different intervention groups (trials and cohort studies)or were the cases and controls (case-control studies) recruited over the same period of time?* For a study which does not specify the time period over whichpatients were recruited, the question should be answered as unable to determine.	Yes = 1
23	*Were study subjects randomized to intervention groups?* Studies which state that subjects were randomized should be answered yes except where method ofrandomization would not ensure random allocation. For example alternate allocation would score no because it is predictable.	Yes = 1
24	*Was the randomized intervention assignment concealed from both patients andhealth care staff until recruitment was complete and irrevocable?* All non- randomized studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.	No = 0
25	*Was there adequate adjustment for confounding in the analyses from which themain findings were drawn?* This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In non-randomized studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.	No = 0
26	*Were losses of patients to follow-up taken into account?* If the numbers of patients lost to follow-up are not reported, the question should be answered asunable to determine. If the proportion lost to follow-up was too small to affectthe main findings, the question should be answered yes.	Unable to determine = 0
Power		
27*	*Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?* Sample sizes have been calculated to detect a difference of x% and y%.	No = 0

*Item has been modified.

Appendix C: Modified Downs and Black checklist for Moaty et al. (2017)

The role of customized vestibular rehabilitation with visual desensitization in the management of visual vertigo syndrome

Item	Criteria	Possible Answers
Reporting		
1	*Is the hypothesis/aim/objective of the study clearly described?*	No = 0
2	*Are the main outcomes to be measured clearly described in the Introduction orMethods section?* If the main outcomes are first mentioned in the Results section, the question should be answered no.	Yes = 1
3	*Are the characteristics of the patients included in the study clearly described?* In cohort studies and trials, inclusion and/or exclusion criteria should be given.In case-control studies, a case-definition and the source for controls should be given.	Yes = 1
4	*Are the interventions of interest clearly described?* Treatments and placebo(where relevant) that are to be compared should be clearly described.	Yes = 1
5	*Are the distributions of principal confounders in each group of subjects to becompared clearly described?* A list of principal confounders is provided.	No = 0
6	*Are the main findings of the study clearly described?* Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions. (Thisquestion does not cover statistical tests which are considered below).	Yes = 1
7	*Does the study provide estimates of the random variability in the data for themain outcomes?* In non-normally distributed data the interquartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported. If the distribution of the data is not described, it must be assumed that the estimatesused were appropriate and the question should be answered yes.	Yes = 1
8	*Have all important adverse events that may be a consequence of the intervention been reported?* This should be answered yes if the study demonstrates that there was a comprehensive attempt to measure adverseevents. (A list of possible adverse events is provided).	No = 0
9	*Have the characteristics of patients lost to follow-up been described?* This should be answered yes where there were no losses to follow-up or where losses to follow-up were so small that findings would be unaffected by theirinclusion. This should be answered no where a study does not report the number of patients lost to follow-up.	No = 0
10	*Have actual probability values been reported (e.g. 0.035 rather than <0.05)for the main outcomes except where the probability value is less than 0.001?*	Yes = 1

Item	Criteria	Possible Answers
External validity		
11	*Were the subjects asked to participate in the study representative of the entire population from which they were recruited?* The study must identify the sourcepopulation for patients and describe how the patients were selected. Patients would be representative if they comprised the entire source population, an unselected sample of consecutive patients, or a random sample. Random sampling is only feasible where a list of all members of the relevant populationexists. Where a study does not report the proportion of the source population from which the patients are derived, the question should be answered as unableto determine.	Yes = 1
12	*Were those subjects who were prepared to participate representative of the entire population from which they were recruited?* The proportion of those asked who agreed should be stated. Validation that the sample was representative would include demonstrating that the distribution of the mainconfounding factors was the same in the study sample and the source population.	Yes = 1
13	*Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?* For the question to be answered yes the study should demonstrate that the interventionwas representative of that in use in the source population. The question shouldbe answered no if, for example, the intervention was undertaken in a specialistcentre unrepresentative of the hospitals most of the source population would attend.	Yes = 1
Internal validity - bias		
14	*Was an attempt made to blind study subjects to the intervention they have received?* For studies where the patients would have no way of knowing whichintervention they received, this should be answered yes.	No = 0
15	*Was an attempt made to blind those measuring the main outcomes of theintervention?*	No = 0
16	*If any of the results of the study were based on "data dredging", was this madeclear?* Any analyses that had not been planned at the outset of the study shouldbe clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.	Unable to determine = 0
17	*In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between theintervention and outcome the same for cases and controls?* Where follow-up was the same for all study patients the answer should be yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.	No = 0
18	*Were the statistical tests used to assess the main outcomes appropriate?* The statistical techniques used must be appropriate to the data. For example nonparametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias,the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.	Yes = 1
19	*Was compliance with the intervention/s reliable?* Where there was non-compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the effect of any misclassification was likely to bias any association to the null, the questionshould be answered yes.	Unable to determine = 0
20	*Were the main outcome measures used accurate (valid and reliable)?* For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates theoutcome measures are accurate, the question should be answered as yes.	Yes = 1

Item	Criteria	Possible Answers
Internal validity - confounding (selection bias)		
21	*Were the patients in different intervention groups (trials and cohort studies) orwere the cases and controls (case-control studies) recruited from the same population?* For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information concerning the source of patients included in the study.	No = 0
22	*Were study subjects in different intervention groups (trials and cohort studies)or were the cases and controls (case-control studies) recruited over the same period of time?* For a study which does not specify the time period over whichpatients were recruited, the question should be answered as unable to determine.	Yes = 1
23	*Were study subjects randomized to intervention groups?* Studies which state that subjects were randomized should be answered yes except where method ofrandomization would not ensure random allocation. For example alternate allocation would score no because it is predictable.	No = 0
24	*Was the randomized intervention assignment concealed from both patients andhealth care staff until recruitment was complete and irrevocable?* All non- randomized studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.	No = 0
25	*Was there adequate adjustment for confounding in the analyses from which themain findings were drawn?* This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In non-randomized studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.	No = 0
26	*Were losses of patients to follow-up taken into account?* If the numbers of patients lost to follow-up are not reported, the question should be answered asunable to determine. If the proportion lost to follow-up was too small to affectthe main findings, the question should be answered yes.	No = 0
Power		
27*	*Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?* Sample sizes have been calculated to detect a difference of x% and y%.	No = 0

*Item has been modified.

Appendix D: Published manuscript

Protocol

Visual Fixations and Motion Sensitivity: Protocol for an Exploratory Study

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Abstract

Background: Motion sensitivity after vestibular disorders is associated with symptoms of nausea, dizziness, and imbalance in busy environments. Dizziness and imbalance are reported in places such as supermarkets and shopping malls which have unstable visual backgrounds; however, the mechanism of motion sensitivity is poorly understood.

Objective: The main aim of this exploratory observational study is to investigate visual fixations and postural sway in response to increasingly complex visual environments in healthy adults and adults with motion sensitivity.

Methods: A total of 20 healthy adults and 20 adults with motion sensitivity will be recruited for this study. Visual fixations, postural sway, and body kinematics will be measured with a mobile eye tracker device, force plate, and 3D motion capture system, respectively. Participants will be exposed to experimental tasks requiring visual fixation on letters, projected on a range of backgrounds on a large screen during quiet stance. Descriptive statistics (mean and standard deviation) will be calculated for each of the variables. One-way independent-measures analyses of variance will be performed to investigate the differences between groups for all variables.

Results: Data collection was started in May 2019 and was completed by February 2020. It was approved by Health and Disability Ethics Committees, Ministry of Health, New Zealand on November 2, 2018 (Ethics ref: 18/CEN/193). We are currently processing the data and will begin data analysis in July 2020. We expect the results to be available for publication by the end of 2020. The trial was funded by the Neurology Special Interest Group, Physiotherapy New Zealand, and the Eisdell Moore Centre in November 2018.

Conclusions: This study will provide a detailed investigation of visual fixations in response to increasingly complex visual environments. Investigating characteristics of visual fixations in healthy adults and those with motion sensitivity will provide insight into this disabling condition and may inform the development of new intervention strategies which explicitly cater to the needs of this population.

Trial Registration: Australian New Zealand Clinical Trials Registry, ACTRN12619000254190; https://tinyurl.com/yxbn7nks

International Registered Report Identifier (IRRID): PRR1-10.2196/16805

(JMIR Res Protoc 2020;9(7):e16805) doi: 10.2196/16805

KEYWORDS

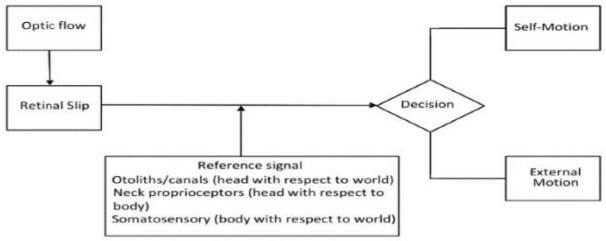
motion sensitivity; vestibular disorder; complex environments; visual fixations; postural control; posture; kinematics; inner ear; visual

Introduction

Motion sensitivity is characterized by nausea, dizziness, and imbalance in response to motion of the visual environment [1]. It can develop as a sequela of a vestibular disorder and is one of the diagnostic criteria for persistent postural perceptual dizziness [1-3]. The symptoms are due to a misinterpretation of, or overreliance on, visual cues for orientation in space [1,3-6]. Dizziness and imbalance are triggered in busy surroundings with visual motion or complex repetitive patterns. Consequently, people with motion sensitivity tend to avoid crowded or busy environments such as supermarkets or driving on motorways [7]. This frequently leads to an interruption of daily activities, sick leave from work, and in extreme cases a reluctance to leaving the house [8,9]. Motion sensitivity may affect people following an acute vestibular insult or people with chronic recurrent dizziness [10].

Information from the visual system has a role in differentiating self-motion from external motion [11]. This differentiation is dependent on perceiving whether motion on the retina is due to an object moving relative to the person or the person moving relative to the object [12,13]. This distinction between self-motion and external motion is achieved by a mechanism that compares the retinal signal and the reference signal. The reference signal comprises information from vision, vestibular afferents, proprioceptive feedback from the extraocular muscles, somatosensory kinaesthetic proprioception, and cognition [14] (Figure 1).

Figure 1. The sources of information to allow differentiation of self-motion and object motion components. The various sources are shown as giving information with respect to different reference frames.



A crucial aspect of the stabilization of posture is dependent on the visual input received from the environment. An essential component of visual input is optic flow [15,16]. Optic flow helps perception of spatiotemporal information from the environment which is then used to move around and maintain orientation in space [12,17]. Optic flow generates retinal slip, defined as motion of the visual image of the environment on the surface of the retina [18]. This information is used to adjust the amount of postural sway. The main aim of visually induced postural movements is to reduce the overall amplitude of the optic flow field by minimizing retinal slip [19-21].

Because optic flow plays a vital role in postural correction, perceiving inaccurate information can be destabilizing. Optic flow that is a part of the background motion behind a target is not normally used as a visual input for postural control as it can stimulate an optokinetic response (which evokes a combination of a slow-phase and fast-phase eye movements where the eyes momentarily follow the moving object and then rapidly reset back to the initial position) [22]. This response can induce a standing subject to move in response to the direction of the motion and can be destabilizing [22]. In normal circumstances, this optokinetic response to background motion is suppressed by visually fixating on a target [23].

Visual fixations contribute to 80% of the total visual experience [24], and help to reduce optic flow, minimize retinal slip, and suppress the optokinetic response [23]. When fixating on a stationary target, there is almost no retinal slip, and the vestibulo-ocular reflex keeps the gaze on target during head movements [21]. By contrast, maintaining fixation on a moving object requires suppression of the vestibulo-ocular reflex for the eyes and the head to move in the same direction [21,25,26].

Fixations contribute to a person's sense of spatial orientation. Fixations suppress visual field motion perception by maximizing the peripheral vision and rendering a stable image to enhance the visual signals of self-motion [27]. Sensations of small body movements then facilitate the execution of compensatory postural reactions [28].

Fixational instability may predispose a person to develop motion sensitivity [29-31]. Studies have shown that people with motion sensitivity after vestibular disorders exhibit fixational instability and have increased perceptual and postural responses to complex visual surroundings [31-34]. Several studies have investigated the relationship between fixational instability and the strength of illusionary motion [29-31]. Fixational instability can be detected by frequency of refixations and saccades [32,34]. Studies have reported that a person with fixational instability would have a high frequency of saccades and refixations while attempting fixation [32,34].

Any difficulty in differentiating self-motion from external motion will require adjustments to determine the correct orientation in space. A peripheral or central vestibular disorder disrupts the normal visual–vestibular interaction [35], which can alter the perception of motion. It can lead to illusionary motion perception, thereby degrading postural stability. Adults with motion sensitivity report worsening of symptoms and reduced postural control in visually stimulating environments which may be explained by fixation instability. However, to date, visual fixations have not been well investigated in people

with motion sensitivity. Previous studies have used video oculography or electrooculogram and optokinetic stimulation rotating around the naso-occipital center to study eye movements in adults with motion sensitivity [32-34]. This study aims to investigate the characteristics of fixations in people with motion sensitivity and how they differ from those of healthy adults by using a mobile eye tracker device in a more naturalistic yet controlled laboratory setting.

This research will investigate visual fixations, postural sway, and kinematics of adults with motion sensitivity, compared with healthy adults, in complex visual environments. Center of pressure (COP) measurement will be used to evaluate postural sway. COP parameters have been used widely to describe stability and quantify alterations in postural control [36,37]. The exploratory nature of this study will also allow the investigation of mean saccadic velocity and saccadic peak amplitude between groups. Several studies have identified anomalies in mean saccadic velocities in a range of health conditions [38,39].

This study is the first step toward recognizing the components that may be essential in a rehabilitation programme addressing the challenging clinical issue of motion sensitivity and may guide the development of rehabilitation programs for adults with motion sensitivity.

Methods

Aim

To conduct an observational study with 40 adults (20 in each group; healthy adults and adults with motion sensitivity). The study will determine whether complex visual environments are associated with fixational instability, altered COP displacement, and altered center of mass (COM) displacements of the head and body in adults with motion sensitivity compared with healthy adults.

Hypothesis

Complex visual environments in people with motion sensitivity compared with healthy adults will be associated with (1) increased number of visual refixations, (2) increased displacement of COP, and (3) differences in the body COM displacement and differences in the head COM displacement.

Trial Design, Setting, and Participants

This is a cross-sectional exploratory single-session experimental study that will be laboratory based in Auckland University of Technology. A total of 40 adults will participate in the study (20 healthy adults and 20 adults with motion sensitivity after vestibular disorder). Healthy adults aged between 18 and 60 who are independently mobile and have no history of neurological conditions will be recruited through neurorehabilitation research team networks and community advertisements. Adults with motion sensitivity will be recruited through a specialized vestibular disorders clinic. They will be included if they have had a history of vestibular disorder (confirmed by a clinician in the vestibular disorder clinic) but have no current signs of acute vestibular deficits, are aged between 18 and 60 [40,41], have a history of motion sensitivity symptoms as reported by the Visual Vertigo Analogue Scale (score >5) [42-44], and score >40 on the Dizziness Handicap Inventory [44]. People with a history of previous eye surgery, or a medical condition that may influence eye movements such as sarcoidosis, Lyme disease, diabetes mellitus, traumatic brain injury, and migraine will be excluded from the study.

Recruitment

Potential participants will be provided with a Participant Information Sheet and be requested to contact the corresponding author by email or telephone. All potential participants will be made aware that participating in this study will not influence their current health care.

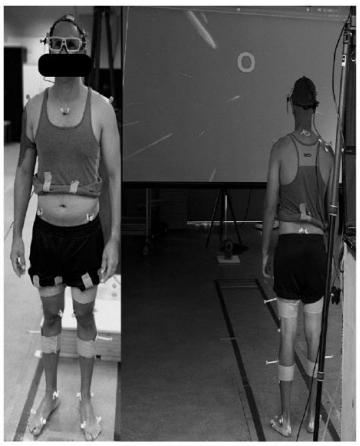
Screening

Potential participants will be screened against the study's inclusion and exclusion criteria via telephone or through a face-to-face meeting with the researcher (SC). Eligible potential participants will be asked to provide written informed consent.

Experimental Setup

The experimental setup consists of a projector screen (Brateck Lumi), a mobile eye tracker device (SensoMotoric Instruments), a force plate (Advanced Mechanical Technology Inc.), and a 3D motion capture system (Qualisys Motion Analysis Capture System; Qualisys Medical AB). Visual fixations will be recorded using a mobile eye tracker (SMI BeGaze; SensoMotoric Instruments). A 3D motion capture system and a force plate will be used to record kinematics and postural sway, respectively. The projector screen (135 in., 16:9 aspect ratio) will be mounted at 3.5-m distance from the force plate for projecting the visual environments (Figure 2).

Figure 2. The experimental setup.



Sensor Motoric Instruments Eye Tracking Glasses (SMI ETG)

The SMI Eye Tracking Glasses (SMI ETG) are a mobile eye-tracking device with a binocular sampling rate of 120 Hz (Figure 3). SMI uses infrared light of wavelength around 789-880 nm to increase the contrast between the pupil and iris which is easily detected by the camera. SMI is a video-based eye tracker based on the concept of pupil center corneal reflection. The scene camera has a resolution of 1280 × 960 pixels @ 24FPS, 960 × 720 pixels @ 30 FPS with a 60° horizontal and 46° vertical field of view. The gaze position accuracy is 0.5° for all distances and the gaze tracking range is 80° horizontal and 60° vertical.

The SMI software uses a frame-by-frame analysis of the gaze data. These data involve defining the location and type of gaze behavior for each frame of data collected. Frame numbers are used to determine the duration of the eye movement. SMI uses an in-built detector for identifying saccades, fixations, and blinks. According to the detector, a blink is identified by points where eye data are not present, a saccade represents a quick change in gaze location, and a fixation is bordered by 2 saccades.

Data collected by the eye-tracking glasses identify the primary event as fixation and therefore a dispersion-based algorithm is used. The algorithm identifies fixations as groups of successive points within a dispersion, or maximum separation. A blink is determined based on the whole trial data where the pupil diameter is either zero, or the horizontal and vertical gaze positions are zero, or they lie outside a calculated valid pupil range. Once fixations and blinks are identified, a saccadic event is created between the detected blinks and fixations.

Figure 3. SMI Eye Tracking Glasses with 3D reflective markers.

Qualisys System

Qualisys is a motion capture system used to track movement. Small retro-reflective markers reflecting infrared light are attached to the participant's skin. Frame-by-frame analysis is used to track each marker from one frame to the next. Each marker data and their 3D position trajectory can be used to calculate joint and movement trajectories. The force plates and SMI eye tracker are integrated and time synced in the Qualisys system. The SMI program is installed on the Qualisys system. The data from the SMI system are synchronized to Qualisys via a start command, so as to capture its data together with all the other data in the Qualisys system. The force plates are connected to the Qualisys computer via an analog board to capture analog signals from the force plate with the motion capture data. The data from the force plates are synchronized with the motion capture data via a synchronization signal between the Qualisys camera system and the analog board. The sync signal from the camera system is connected to an external trigger input on the analog board to start the capture of analog data using hardware synchronization.

Kinematics will be measured using an infrared motion analysis capture system, consisting of 9 Oqus 3D Motion analysis capture units. A set of 27 reflective markers will be placed on the participant. Markers will be attached using a double-sided tape

directly onto the skin. Pelvis markers will be placed in accordance with the modified Helen Hayes model as a set of 3: 1 marker on each anterior superior iliac spine and 1 on sacrum (midpoint). For the thigh segment, markers will be placed on midthigh, medial femur epicondyle, and femur lateral epicondyle for each extremity. The shank segment includes markers on midshank, medial malleolus, and lateral malleolus. The foot segment will be created using a set of markers on the head of the fifth metatarsus, head of the first metatarsus, and posterior surface of the calcaneus. Further, markers will be placed on the right and left acromion process, sternoclavicular notch, and C7 vertebra to create the thorax segment. To create the head segment, 1 marker will be placed on each side of the head.

3D co-ordinates of each reflective marker will be tracked using Qualisys Track Manager. Visual 3D software will be used to process the data files. After placement of markers, a static image of the participant standing in an anatomical position will be taken.

AMTI Force Plates

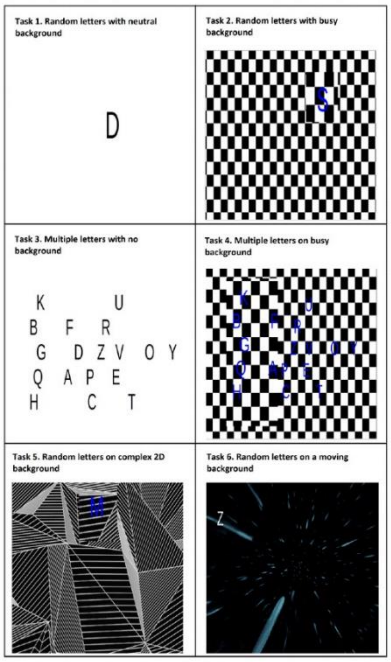
Postural control as the COP movement will be measured with an AMTI force platform (Advanced Mechanical Technology Inc.). The force platform measures the 3 force components, F_x, F_y, and F_z (where x, y, and z are the medial–lateral, anterior–posterior, and vertical directions, respectively), at the sampling frequency of 1200 Hz. The AMTI force plate is a static-force measurement system and is a computer-based system which synchronizes with a computer using a serial link. The COP movement track data (in millimeter) will be collected for each participant and will be converted into mediolateral and anterior–posterior components for analysis.

Participants will stand on the force plate with arms relaxed at their sides. Participants will be asked to stand with their feet shoulder width apart. They will be instructed to maintain their gaze on the letter while maintaining a quiet stance for the duration of a task.

Experimental Tasks

The experimental tasks have been designed to simulate eye movements in visually complex environments. Tasks will increase in the level of complexity, starting from easy visual tasks progressing to more visually complex tasks. Letters will be projected in a random sequence on to a range of visually complex background images (Figure 4). The font of the letters, backgrounds, and duration of each task were finalized after piloting. There are 6 tasks, each lasting 70 seconds. The letters appear on the screen for 7 seconds each, at different positions on the screen. Python programming language has been used to select letters and their positions on screen. Participants will be instructed to focus on a letter as they appear on the screen. The tasks increase in difficulty in two ways: (1) the background behind the letter progresses from neutral to busy (ie, to a complex moving background), and (2) by the appearance of either a single letter or multiple letters on screen. In the single-letter tasks (tasks 1, 2, 5, and 6), the participants will be instructed to focus their gaze on each projected letter for the duration of the task. In the multiple letters' tasks (tasks 3 and 4), the participant will be instructed to find letter *E* and maintain visual fixation on it for the duration of the task. The tasks will be presented from the lowest to highest difficulty of background and number of letters (as described in Figure 4). The tasks will not be randomized as the more difficult tasks might provoke symptoms of dizziness which would hinder the performance of participants in the subsequent tasks.

Figure 4. The experimental tasks. *Letters have been magnified for clear visibility.



Data Collection

Data will be collected for all tasks in 1 session. The motion analysis system and force plate will be calibrated before the participant arrives in the laboratory. Upon arrival, the participant will be orientated to the laboratory setup. The Dizziness Handicap Inventory and Visual Vertigo Analogue Scale screening will be completed. After setting up the markers, experimental tasks will be explained, and the eye tracker glasses will be fitted for comfort and calibrated. The participant will then stand on the force plate wearing the calibrated eye tracker with reflective markers (Figure 5). During the experimental tasks, appropriate rest intervals will be provided after each task to minimize provocation of symptoms such as dizziness and nausea.

Figure 5. Data collection procedure.

Outcome Measures

The following outcome measures will be explored and analyzed for this study.

Visual Fixations

Fixation characteristics for each group will be computed using the SMI ETG software and will measure the total number of refixations, the maximum fixation duration, and the number of saccades. The software determines a fixation as a window with a minimum duration of 80 ms and a maximum dispersion of 100 pixels. Refixations are calculated if the eye crosses the maximum dispersion threshold of 100 pixels. The fixation duration will be calculated as the total time spent in fixating during a trial. The maximum fixation duration will be calculated

as the longest fixation within each trial. A saccade event is computed as any event that does not meet the fixation criteria between the new and the previous fixation.

Postural Sway: Center of Pressure

COP displacement times series obtained from the force platform will be down sampled to 100 Hz and subsequently will be processed using a low-pass filter at 5 Hz (fourth-order, zero-phase-lag, Butterworth) [45]. The mean velocity, root mean square, and maximum range of the COP displacement will be computed to evaluate postural sway [46].

Kinematics

Raw data from the Qualisys motion analysis will be imported into Visual 3D, where a 6 degree-of-freedom model will be constructed. Data will be interpolated and processed using a fourth-order Butterworth low-pass filter with cutoff frequency of 12 Hz. The body COM and the COM of the head segment will be calculated using a pipeline in Visual 3D. The mean velocity, root mean square, and maximum range of the COM of the head and whole-body displacement will be calculated [47].

Safety Measures

The study will be using moving background/moving images, which may induce dizziness, imbalance, or nausea in some participants. An assistant will stand close to the participant to provide assistance and prevent a fall in case of imbalance. We will monitor how a participant is feeling throughout each task, and appropriate rest intervals will be provided. The session would be stopped at any stage if required.

In the unlikely event of a physical injury, rehabilitation and compensation for injury by accident may be available from the Accident Compensation Corporation, provided the incident details satisfy the requirements of the law and the Corporation's regulations.

Statistical Analysis

Sample Size Calculation

There is a lack of experimental evidence in the population of interest to conduct a power calculation for the required sample size. It is unclear if factors such as age or gender affect visual fixations and there is minimal information on population variation. Therefore, an arbitrary sample size of 20 in each group has been selected. This has been selected in accordance with studies performed in adults with motion sensitivity [33,34]. The data from this study may help inform future studies for the required sample size.

Analysis

Descriptive statistics (mean and standard deviation) will be calculated for each of the variables. Data normality will be examined using the Kolmogorov–Smirnov statistic. One-way independent-measures analyses of variance will be performed to investigate the differences between groups for all variables. Post-hoc analysis with Šidák adjustment will be used for multiple comparisons [48]. Finally, a receiver operating characteristic curve analysis will be applied to determine threshold values in gaze, COP, and COM parameters, allowing identification of the impairment induced by motion sensitivity. The optimal cutoff point will be determined using the Youden Index. Areas under the curve, specificity, and sensitivity will also be calculated. Values of areas under the curve will be categorized as follows: excellent (≥0.90), good (0.80-0.90), fair (0.70-0.79), and poor (<0.70).

Confidentiality

During the screening, the researcher will make note of whether the potential participant meets the study criteria. For those who do not meet the criteria, only the reason for exclusion from the project will be recorded in a database and will not be identifiable.

Ethics Approval and Consent to Participate

Ethical approval for this study has been obtained from the New Zealand Health and Disability Ethics Committee (HDEC) and Auckland University of Technology Ethics Committee (AUTEC). Eligible potential participants will be asked to provide written informed consent. Ethics committee approval for any protocol modifications will be sought from HDEC and AUTEC. Any changes will lead to an amendment in the Australian New Zealand Clinical Trials Registry (HDEC reference number: 18/CEN/193; AUTEC reference number: 19/38).

Dissemination of Study Data

A summary of the results from the study will be offered to all participants as per the consent form. Results from the study will be published in a peer-reviewed journal and presented at national and international conferences.

Availability of Data and Materials

All participants will be given a numerical code upon acceptance into the project. All health information will be stored in physical and electronic records that are identified by the participant code only. Only the named investigators will have access to the forms that contain information about the participant's name and their code. These forms will be stored in a secured cabinet in co-ordinating investigator's office, separate from any records containing health information.

The data sets used and analyzed during this study are available from the corresponding author on reasonable request.

Results

Data collection was started in May 2019 and was completed by February 2020. It was approved by the Institutional Review Board on November 2, 2018 (Ethics ref: 18/CEN/193). We are currently processing the data and will begin data analysis in July 2020. We expect the results to be available for publication by the end of 2020. The trial was funded by the Neurology Special Interest Group, Physiotherapy New Zealand, and the Eisdell Moore Centre in November 2018.

Discussion

This is an exploratory study with the primary aim to identify whether fixational instability is associated with motion

sensitivity and whether it leads to increased postural sway and altered kinematics in adults with motion sensitivity.

This study will provide a detailed investigation of visual fixations, postural sway, and kinematics in complex visual environments. The use of a mobile eye tracker device will investigate naturalistic eye behavior when exposed to experimental stimuli. The task hierarchy will help in understanding how characteristics of visual fixations change when a person views a complex visual environment as opposed to neutral environments. The experimental tasks might provoke symptoms in some participants; however, we expect that all participants will be able to complete the protocol with appropriate rest intervals between tasks. Our sample size of 20 participants in each group is a foundational step in exploring whether visual fixations contribute to motion sensitivity after vestibular disorder. We anticipate the outcomes will be able to detect a difference between healthy adults and those with motion sensitivity. Results from this study will inform future trials and will be used to inform development of diagnostic and rehabilitation programs.

We hope that this study will increase our understanding of the complex interactions of vision and balance in people with motion sensitivity. If we determine that gaze and postural control characteristics are altered, we will develop an intervention that is designed to re-align the gaze and postural control characteristics closer to those of the control population. This intervention would then be tested in a series of clinical trials to determine effectiveness.

Acknowledgments

The Neurology Special Interest Group (NSIG), Physiotherapy New Zealand, and Eisdell Moore Centre of Balance and Hearing disorders (University of Auckland) jointly funded the following: purchase of the projector screen, software development, 2 research assistants to assist during data collection, administrative costs, and travel vouchers for participants. Each funding body undertook a peer-review of the study protocol. Funding from the New Zealand Dizziness and Balance Clinic (NZDBC) was used to pay tuition fees for the corresponding author.

Authors' Contributions

SC, DT, and NS conceptualized and designed the project and obtained the funding. AK developed the experimental tasks and contributed to protocol. SC drafted the manuscript. DT and NS are providing PhD supervision for SC. All authors critically revised the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

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Appendix E: Ethical approval letter

Health and Disability Ethics Committees

Ministry of Health 133 Molesworth Street
PO Box 5013
Wellington
6011

0800 4 ETHICS
hdecs@moh.govt.nz

02 November 2018

Ms Shikha Chaudhary HRRI
AUT University- North Shore Campus 90 Akoranga Drive
Northcote 0627

Dear Ms Chaudhary

Re:	**Ethics ref:**	**18/CEN/193**
	Study title:	What are the characteristics of visual fixation in people with motion sensitivity after vestibular insult compared to healthy adults when subjected to different visual environments?

I am pleased to advise that this application has been *approved* by the Central Health and Disability Ethics Committee. This decision was made through the HDEC-Expedited Review pathway.

The Committee would like to see a slightly better introduction to the study in the Participant Information Sheet such as for healthy volunteers; "you have been sent this information sheet because you have indicated your interest in the study as a healthy volunteer."

Conditions of HDEC approval

HDEC approval for this study is subject to the following conditions being met prior to the commencement of the study in New Zealand. It is your responsibility, and that of the study's sponsor, to ensure that these conditions are met. No further review by the Central Health and Disability Ethics Committee is required.

Standard conditions:

1. Before the study commences at *any* locality in New Zealand, all relevant regulatory approvals must be obtained.
2. Before the study commences at *any* locality in New Zealand, it must be registered in a clinical trials registry. This should be a WHO-approved registry (such as the Australia New Zealand Clinical Trials Registry, www.anzctr.org.au) or https://clinicaltrials.gov/.
3. Before the study commences at *each given* locality in New Zealand, it must be authorised by that locality in Online Forms. Locality authorisation confirms that the locality is suitable for the safe and effective conduct of the study, and that local research governance issues have been addressed.

Non-standard conditions:

4. Please include version number and dates to the footer of the Participant Information Sheet.

Non-standard conditions must be completed before commencing your study, however, they do not need to be submitted to or reviewed by HDEC.

If you would like an acknowledgement of completion of your non-standard conditions you may submit a post approval form amendment through Online Forms. Please clearly identify in the amendment form that the changes relate to non-standard conditions and ensure that supporting documents (if requested) are tracked/highlighted with changes.

For information on non-standard conditions please see section 128 and 129 of the *Standard Operating Procedures for Health and Disability Ethics Committees* (available on www.ethics.health.govt.nz)

After HDEC review

Please refer to the *Standard Operating Procedures for Health and Disability Ethics Committees* (available on www.ethics.health.govt.nz) for HDEC requirements relating to amendments and other post-approval processes.

Your next progress report is due by 01 November 2019.

Participant access to ACC

The Central Health and Disability Ethics Committee is satisfied that your study is not a clinical trial that is to be conducted principally for the benefit of the manufacturer or distributor of the medicine or item being trialled. Participants injured as a result of treatment received as part of your study may therefore be eligible for publicly-funded compensation through the Accident Compensation Corporation (ACC).

Please don't hesitate to contact the HDEC secretariat for further information. We wish you all the best for your study.

Yours sincerely,

Mrs Helen Walker Chairperson
Central Health and Disability Ethics Committee

Appendix F: Locality approval letter

Auckland University of Technology Ethics Committee (AUTEC)

Auckland University of Technology
D-88, Private Bag 92006, Auckland 1142, NZ
T: +64 9 921 9999 ext. 8316
E: ethics@aut.ac.nz
www.aut.ac.nz/researchethics

28 February 2020

Denise Taylor
Faculty of Health and Environmental Sciences

Dear Denise

Ethics Application: **19/38 What are the characteristics of visual fixation in people with motion sensitivity after vestibular insult compared to healthy adults when subjected to different visual environments**

At their meeting of 10 February 2020, the Auckland University of Technology Ethics Committee (AUTEC) received the report on your ethics application. AUTEC noted your report and asked us to thank you.

On behalf of AUTEC, we congratulate the researchers on the project and look forward to reading more about it in future reports.

When communicating with us about this application, we ask that you use the application number and study title to enable us to provide you with prompt service. Should you have any further enquiries regarding this matter, you are welcome to contact me by email at ethics@aut.ac.nz or by telephone on 921 9999 at extension 6038.

(This is a computer-generated letter for which no signature is required)
The AUTEC Secretariat
Auckland University of Technology Ethics Committee
Cc: shikha.chaudhary27@gmail.com; nsaywell@aut.ac.nz

Appendix G: Participant information sheet for healthy participants

Participant Information Sheet

Study title:	**What are the characteristics of visual fixation in people with motion sensitivity after vestibular insult compared to healthy adults when subjected to different visual environments?**		
Locality:	**AUT campus, Akoranga Drive**	Ethics committee ref.: 18/CEN/193	
Lead investigator:	**Shikha Chaudhary**	Contact phone number:	099219999 ext.: 5527

Kia ora and Hello!

My name is Shikha and I am a PhD student at AUT. You are invited to take part in a study to assess the eye movements of people who experience nausea and dizziness in busy environments such as shopping malls, supermarkets etc. This research will help in understanding the eye behavior and enable health professionals to develop rehabilitation programme to improve these symptoms of nausea and dizziness. You have been sent this information sheet because you have indicated your interest in the study as a healthy volunteer.

Whether or not you take part is your choice. If you don't want to take part, you don't have to give a reason, and it won't affect the care you receive. If you do want to take part now, but change your mind later, you can pull out of the study at any time.

This Participant Information Sheet will help you decide if you would like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether you will participate in this study. Before you decide, you may want to talk about the study with other people, such as family, whanau, friends, or healthcare providers. Feel free to do this.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

This document is eight pages long, including the Consent Form. Please make sure you have read and understood all the pages.

What is the purpose of the study?

Dizziness is associated with decline in quality of life and increased functional disability. Dizziness and imbalance occurring in a dynamic visual environment indicates the presence of motion sensitivity and is associated with symptoms like nausea, dizziness and imbalance when exposed to busy visual surrounds such as crowded places, supermarkets and shopping malls. Motion sensitivity frequently occurs after recovering from an inner ear disorder.

The human eyes work to produce binocular vision by picking up reflections of light from objects in the environment. Our eyes work in a coordinated manner with head and body to move through the environment and maintain balance. There are three eye movements: saccades; quick eye movements from one point to another; visual fixation; which maintain vision at a single object, and smooth pursuits; which are used to track a moving entity in the environment. Visual fixation is most important contributor in providing visual stability. Inability to maintain fixation can predispose a person to develop motion sensitivity. Studying eye movements provides us information like where people looking in day-day life scenes, how these differ while viewing a stationary scene or a moving scene. This research will explore visual fixation and postural sway occurring in response to complex visual scenes, in healthy adults and people with motion sensitivity after a vestibular disorder. Participants will stand on a force plate wearing a mobile eye tracker device with retroreflective markers attached to forehead. They will be asked to maintain focus on letters projected on a screen. The background image behind the letters will be changed from neutral, to a complex patterned and finally a moving background. Eye movement, head position and body sway will be recorded. We will repeat the protocol in a virtual reality environment to allow comparison between a laboratory environment. Understanding the relationship of these eye movements will be the first step in developing a rehabilitation program catering to needs of these people.

This work has potential to reduce disability and improve quality of life in this population by maximising rehabilitation programmes.

This study is the first step towards recognising the components that are essential in a rehab programme addressing the challenging clinical issue of motion sensitivity. The outcomes of this study will be presented to rehabilitation health professionals and researchers at conferences and published in rehabilitation and neuroscience journals.

What will my participation in the study involve?

You are being invited to participate in this study as you are aged between 18- 60 years, can walk independently and have had no eye surgery in the past.

You may be eligible for this study if you meet the following entry criteria:

- No history neurological conditions that could interfere with eye movements.
- No History of any previous eye surgery
- No Medical condition which may influence the eye movements results such as sarcoidosis, Lyme disease, diabetes mellitus etc.
- Do not have any evidence and/or physical examination evidence of cerebellar lesion or cerebellar stroke
- Do not have history of epilepsy, head injury or concussion in the last six months
- Do not have a skull fracture or other known skull defects

If you are eligible to participate, and would like to participate in the study, you will be given a consent form to read and sign. We will then inform your GP about your enrolment in the study.

What will happen in this research?

The study involves 1 session lasting about 1.5 hours. You will be required to wear eye tracking glasses with a reflective marker attached to your head to record your head movements and standing on a force plate to record your balance. You will be asked to look at letters projected on a screen. There are 6 tasks in the session and with each new task the background behind the letters will get more complex. You are required to maintain focus on letters that are projected in front of you.

What are the possible benefits and risks of this study?

There is a small chance that the procedures being used in this study may make some people dizzy/ nauseous. We will minimise this chance by making sure you are fully informed about what to expect prior to any procedure. We will monitor how you are feeling throughout each procedure and you are able to stop the session at any stage.

How will these discomforts and risks be alleviated?

An assistant will be standing near to you to make sure you don't fall and can assist you in case needed. Appropriate rest intervals will be provided. Basic utilities such as water, tissues will be provided. We will monitor how you are

feeling throughout each session and you are able to stop the session at any stage.

What are the benefits?

There are no direct benefits to you. However, by taking part in this study you are acting, as co-researcher and your contribution will help to develop rehabilitation device for people with motion sensitivity. You will also have the experience of participating in a modern research laboratory project.

Who pays for the study?

The cost to you is your time. This would be a total of 1.5 hours excluding your travel time. Travel vouchers will be provided for visit to compensate for your time and to assist with travel costs incurred for traveling to and from the laboratory.

What if something goes wrong?

In the unlikely event of a physical injury because of your participation in this study, rehabilitation and compensation for injury by accident may be available from the Accident Compensation Corporation, providing the incident details satisfy the requirements of the law and the Corporation's regulations.

What are my rights?

- Your participation in this research is voluntary (it is your choice) and whether you choose to participate will neither advantage nor disadvantage you. You can withdraw from the study at any time. If you choose to withdraw from the study, then you will be offered the choice between having any data that is identifiable as belonging to you removed or allowing it to continue to be used. However, once the findings have been produced, removal of your data may not be possible.

- To consider your participation in the study, you are provided with an opportunity to take time and discuss it with your family/whanau.

-You have the right to privacy and confidentiality. Your privacy will be maintained throughout the research process, as you will always be identified by a code number. Researchers will only have access to coded data, which will prevent them from knowing your identity. The collected data and the consent forms will be stored in separate locked cabinets in Researchers office. When results are reported, no names or any material that could identify you will be published or presented. After ten years, this data will be destroyed.

-You have the right to access information collected about you during the study.

What happens after the study or if I change my mind?

Following the study, further research and development will be done on eye movements before being able to design rehabilitation program. If you are interested in receiving information about other rehabilitation services in your area the researcher can advise you.

-You can withdraw from the study at any time. If you choose to withdraw from the study, then you will be offered the choice between having any data that is identifiable as belonging to you removed or allowing it to continue to be used. However, once the findings have been produced, removal of your data may not be possible.

-The collected data and the consent forms will be stored in separate locked cabinets for ten years. This will ensure that no association can be made between the results and the consent forms. Only members of the research team directly involved in data collection and analysis will have access to raw data. After ten years, all original data collection sheets and questionnaires will be shredded. The files in the external hard drive will be deleted.

-You are given an opportunity on the consent form to indicate if you would like to receive a feedback on your results. If you answer “yes” to this, a copy of your results and a short summary of the overall findings will be sent to you on completion of the study. This will be sent to the contact details that you provide on the consent form.

Who do I contact for more information or if I have concerns?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Doctoral Student	Shikha Chaudhary Health and Rehabilitation Research Institute AUT University Private Bag 92006 Auckland 1142 02108524639 Shikha.chaudhary27@gmail.com
Project Supervisor	Prof. Denise Taylor Health and Rehabilitation Research Institute AUT University Private Bag 92006 Auckland 1142 Ph. 09 921 9999 Denise.taylor@aut.ac.nz

For Maori Health support please contact :
He Kamaka Walora
Waitemata District Health Board
09 486 8324 ext 3553
Auckland District Health Board
09 307 4949 ext 29400

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Prof. Denise Taylor, HRRI
09 921 9680
Denise.taylor@aut.ac.nz

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone : 0800 555 050
Fax : 0800 2 SUPPORT (0800 2787 7678)
Email : advocacy@hdc.org.nz

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 ETHICS
Email: hdecs@moh.govt.nz

Appendix H: Participant information sheet for participants with motion sensitivity

Participant Information Sheet

Study title:	**What are the characteristics of visual fixation in people with motion sensitivity after vestibular insult compared to healthy adults when subjected to different visual environments?**		
Locality:	**AUT campus, Akoranga Drive**	Ethics committee ref.: 18/CEN/193	
Lead investigator:	**Shikha Chaudhary**	Contact phone number:	099219999 ext.: 5527

Kia ora and Hello!

My name is Shikha and I am a PhD student at AUT. You are invited to take part in a study to assess the eye movements of people having a feeling of nausea and dizziness in busy environments such as shopping malls, supermarkets etc. This research would help in understanding the eye behavior of such people and will enable health professionals to develop rehabilitation programme to improve these symptoms of nausea and dizziness. You have been sent this information sheet because you have indicated your interest in the study as a participant with motion sensitivity.

Whether or not you take part is your choice. If you don't want to take part, you don't have to give a reason, and it won't affect the care you receive. If you do want to take part now, but change your mind later, you can pull out of the study at any time.

This Participant Information Sheet will help you decide if you would like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether you will participate in this study. Before you decide, you may want to talk about the study with other people, such as family, whanau, friends, or healthcare providers. Feel free to do this.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

This document is eight pages long, including the Consent Form. Please make sure you have read and understood all the pages.

What is the purpose of the study?

Dizziness is associated with decline in quality of life and increased functional disability. Dizziness and imbalance occurring in a dynamic visual environment indicates the presence of motion sensitivity and is associated with symptoms like nausea, dizziness and imbalance when exposed to busy visual surrounds such as crowded places, supermarkets and shopping malls. Motion sensitivity frequently occurs after recovering from an inner ear disorder.

The human eyes work to produce binocular vision by picking up reflections of light from objects in the environment. Our eyes work in a coordinated manner with head and body to move through the environment and maintain balance. There are three eye movements: saccades; quick eye movements from one point to another; visual fixation; which maintain vision at a single object, and smooth pursuits; which are used to track a moving entity in the environment. 'visual fixation' is most important contributor in providing visual stability. Inability to maintain fixation can predispose a person to develop motion sensitivity. Studying eye movements provides us information like where people looking in day-day life scenes, how these differ while viewing a stationary scene or a moving scene. This research will explore visual fixation and postural sway occurring in response to complex visual scenes, in healthy adults and people with motion sensitivity after a vestibular disorder. Participants will stand on a force plate wearing a mobile eye tracker device with retroreflective markers attached to forehead. They will be asked to maintain focus on letters projected on a screen. The background image behind the letters will be changed from neutral, to a complex patterned and finally a moving background. Eye movement, head position and body sway will be recorded. We will repeat the protocol in a virtual reality environment to allow comparison between a laboratory environment. Understanding the relationship of these eye movements will be the first step in developing a rehabilitation program catering to needs of these people.

This work has potential to reduce disability and improve quality of life in this population by maximising rehabilitation programmes.

This study is the first step towards recognising the components that are essential in a rehab programme addressing the challenging clinical issue of motion sensitivity. The outcomes of this study will be presented to rehabilitation health professionals and researchers at conferences and published in rehabilitation and neuroscience journals.

What will my participation in the study involve?

You are being invited to participate in this study as you are aged between 18- 60 years, have had vestibular disorder (recovered), have symptoms of nausea, dizziness and imbalance while viewing crowded places, have difficulty in visiting supermarkets, shopping malls etc. and can walk independently.

You may be eligible for this study if you meet the following entry criteria:

- No history neurological conditions that could interfere with eye movements.
- No History of any previous eye surgery
- No Medical condition which may influence the eye movements results such as sarcoidosis, Lyme disease, diabetes mellitus etc.
- Do not have any evidence and/or physical examination evidence of cerebellar lesion or cerebellar stroke
- Do not have history of epilepsy, head injury or concussion in the last six months
- Do not have a skull fracture or other known skull defects

If you are eligible to participate, and would like to participate in the study, you will be given a consent form to read and sign. We will then inform your GP about your enrolment in the study.

What will happen in this research?

The study involves 1 session lasting about 1.5 hours. You will be required to wear eye tracking glasses with a reflective marker attached to your head to record your head movements and standing on a force plate to record your balance. You will be asked to look at letters projected on a screen. There are 6 tasks in the session and with each new task the background behind the letters will get more complex. You are required to maintain focus on letters that are projected in front of you.

What are the possible benefits and risks of this study?

There is a small chance that the procedures being used in this study may make some people dizzy/ nauseous. We will minimise this chance by making sure you are fully informed about what to expect prior to any procedure. We will monitor how you are feeling throughout each procedure and you are able to stop the session at any stage.

How will these discomforts and risks be alleviated?

An assistant will be standing near to you to make sure you don't fall and can assist you in case needed. Appropriate rest intervals will be provided. Basic utilities such as water, tissues will be provided. We will monitor how you are feeling throughout each session and you are able to stop the session at any stage.

What are the benefits?

There are no direct benefits to you. However, by taking part in this study you are acting, as co-researcher and your contribution will help to develop rehabilitation device for people with motion sensitivity. You will also have the experience of participating in a modern research laboratory project.

Who pays for the study?

The cost to you is your time. This would be a total of 1.5 hours excluding your travel time. Travel vouchers will be provided for visit to compensate for your time and to assist with travel costs incurred for traveling to and from the laboratory.

What if something goes wrong?

In the unlikely event of a physical injury because of your participation in this study, rehabilitation and compensation for injury by accident may be available from the Accident Compensation Corporation, providing the incident details satisfy the requirements of the law and the Corporation's regulations.

What are my rights?

- Your participation in this research is voluntary (it is your choice) and whether you choose to participate will neither advantage nor disadvantage you. You can withdraw from the study at any time. If you choose to withdraw from the study, then you will be offered the choice between having any data that is identifiable as belonging to you removed or allowing it to continue to be used. However, once the findings have been produced, removal of your data may not be possible.

- To consider your participation in the study, you are provided with an opportunity to take time and discuss it with your family/whanau.

-You have the right to privacy and confidentiality. Your privacy will be maintained throughout the research process, as you will always be identified by a code number. Researchers will only have access to coded data, which will prevent them from knowing your identity. The collected data and the consent forms will be stored in separate locked cabinets in Researchers office. When results are

reported, no names or any material that could identify you will be published or presented. After ten years, this data will be destroyed.

-You have the right to access information collected about you during the study.

What happens after the study or if I change my mind?

Following the study, further research and development will be done on eye movements before being able to design rehabilitation program. If you are interested in receiving information about other rehabilitation services in your area the researcher can advise you.

-You can withdraw from the study at any time. If you choose to withdraw from the study, then you will be offered the choice between having any data that is identifiable as belonging to you removed or allowing it to continue to be used. However, once the findings have been produced, removal of your data may not be possible.

-The collected data and the consent forms will be stored in separate locked cabinets for ten years. This will ensure that no association can be made between the results and the consent forms. Only members of the research team directly involved in data collection and analysis will have access to raw data. After ten years, all original data collection sheets and questionnaires will be shredded. The files in the external hard drive will be deleted.

-You are given an opportunity on the consent form to indicate if you would like to receive a feedback on your results. If you answer “yes” to this, a copy of your results and a short summary of the overall findings will be sent to you on completion of the study. This will be sent to the contact details that you provide on the consent form.

Who do I contact for more information or if I have concerns?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Doctoral Student	Shikha Chaudhary Health and Rehabilitation Research Institute AUT University Private Bag 92006 Auckland 1142 02108524639 Shikha.chaudhary27@gmail.com
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Appendix I: Advertisement for recruiting healthy adults.

VOLUNTEERS REQUIRED FOR A RESEARCH PROJECT

AUT
UNIVERSITY
TE WĀNANGA ARONUI O TAMAKI MAKAU RAU

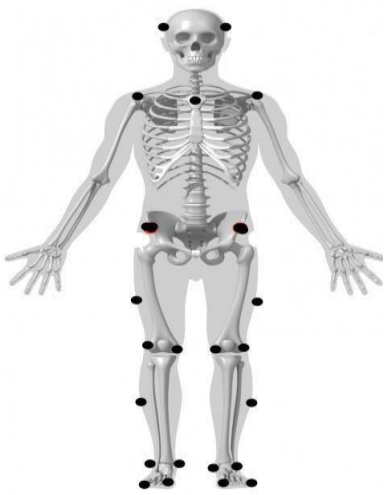
"Do eye movements trigger dizziness?"

We are looking for **healthy people aged 18- 60 years** to participate in a study aiming to investigate eye movements. This research would help us to develop rehabilitation programmes to improve these symptoms of nausea and dizziness.

To participate you must have:

- No history of eye surgeries
- No history of head injury, epilepsy or migraine

This research will explore eye movements and balance in response to complex visual scenes. Participants will stand on a force plate that measures how much you sway, wearing a mobile eye tracker device (see picture below), that measures eye movement and with retroreflective markers put on to your head, shoulders, hips, knees, and feet, that measures how you move during the experiment (See picture below).



This study is the first step towards understanding the components that are essential in a rehabilitation programme to address the challenging clinical issue of motion sensitivity. It has the potential to reduce disability and improve quality of life for people with motion sensitivity.
The experiment will take about 1.5 hours of your time at the **AUT University Campus (Akoranga Drive, Northcote)**. A $20 voucher will be provided to contribute to travel expenses.

If you are interested in taking part in this study, or would like further information, please contact Shikha Chaudhary (shikha.chaudhary@aut.ac.nz) Phone- 099219999 ext:5527.

Appendix J: Advertisement for recruiting adults with motion sensitivity.

VOLUNTEERS REQUIRED FOR A RESEARCH PROJECT

AUT UNIVERSITY
TE WĀNANGA ARONUI O TAMAKI MAKAU RAU

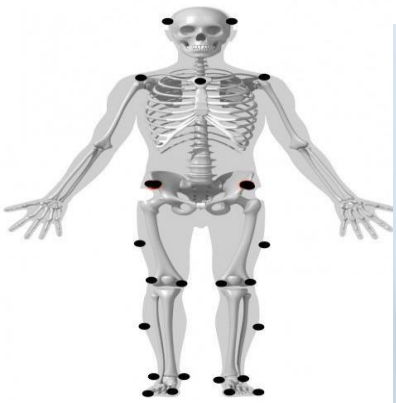
"Do eye movements trigger dizziness?"

We are looking for people with motion sensitivity (feeling dizzy or nauseous in busy places like supermarkets, or shopping malls), who have had an inner ear disorder and are aged between 18-60 years to participate in a study aiming to investigate eye movements. This research would help us to develop rehabilitation programmes to improve these symptoms of nausea and dizziness.

To participate you must have/had:

- No eye surgery
- A recovered vestibular disorder (No vertigo/spinning sensation within the last 3 months)
- No history of head injury, epilepsy or migraine.

This research will explore eye movements and balance in response to complex visual scenes. Participants will stand on a force plate that measures how much you sway, wearing a mobile eye tracker device (see picture below), that measures eye movement and with retroreflective markers put on to your head, shoulders, hips, knees and feet, that measures how you move during the experiment (See picture below)



This study is the first step towards understanding the components that are essential in a rehabilitation programme to address the challenging clinical issue of motion sensitivity. It has the potential to reduce disability and improve quality of life for people with motion sensitivity.

The experiment will take about 1.5 hours of your time at the **AUT University Campus (Akoranga Drive, Northcote)**. A $20 voucher will be provided to contribute to travel expenses.

If you are interested in taking part in this study, or would like further information, please contact

Shikha Chaudhary (shikha.chaudhary@aut.ac.nz)

Phone-099219999 ext- 5527

Appendix K: Consent form

Consent Form

Please tick to indicate you consent to the following

I have read or have had read to me in my first language, and I understand the Participant Information Sheet.	Yes ☐	No ☐
I have been given sufficient time to consider whether to participate in this study.	Yes ☐	No ☐
I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.	Yes ☐	No ☐
I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.	Yes ☐	No ☐
I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.	Yes ☐	No ☐
I consent to the research staff collecting and processing my information, including information about my health.	Yes ☐	No ☐
If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.	Yes ☐	No ☐
I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study.	Yes ☐	No ☐
I agree to an approved auditor appointed by the New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.	Yes ☐	No ☐

I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.	Yes ☐	No ☐
I understand the compensation provisions in case of injury during the study.	Yes ☐	No ☐
I know who to contact if I have any questions about the study in general.	Yes ☐	No ☐
I understand my responsibilities as a study participant.	Yes ☐	
I wish to receive a summary of the results from the study.	Yes ☐	No ☐

Declaration by participant:

I hereby consent to take part in this study.

Participant's name: _____

Signature: _____ Date: _____

Declaration by member of research team:

I have given a verbal explanation of the research project to the participant and have answered the participant's questions about it.

I believe that the participant understands the study and has given informed consent to participate.

Researcher's name: _____

Signature: _____ Date: _____

Appendix L: Screening sheet

Screening Checklist for participating in the study of visual fixation in people with motion sensitivity after vestibular insult compared to healthy adults when subjected to moving visual environments.

Participant ID:_____

Volunteer D.O.B.:_____ Date:_____

	Yes/ No
Have you ever been diagnosed with any neurological conditions?	
Any previous history of eye surgery?	
Do you have any known eye movement disorders?	
Have you ever had a skull fracture?	
Do you have any known skull defects?	
Do you suffer from migraine?	
Have you suffered a head injury or concussion?	

The participant will be excluded from the study if they state yes for any of the above.

Checklist completed by: _____

Signature: _____

Date: _____

Appendix M: Visual Vertigo Analogue Scale

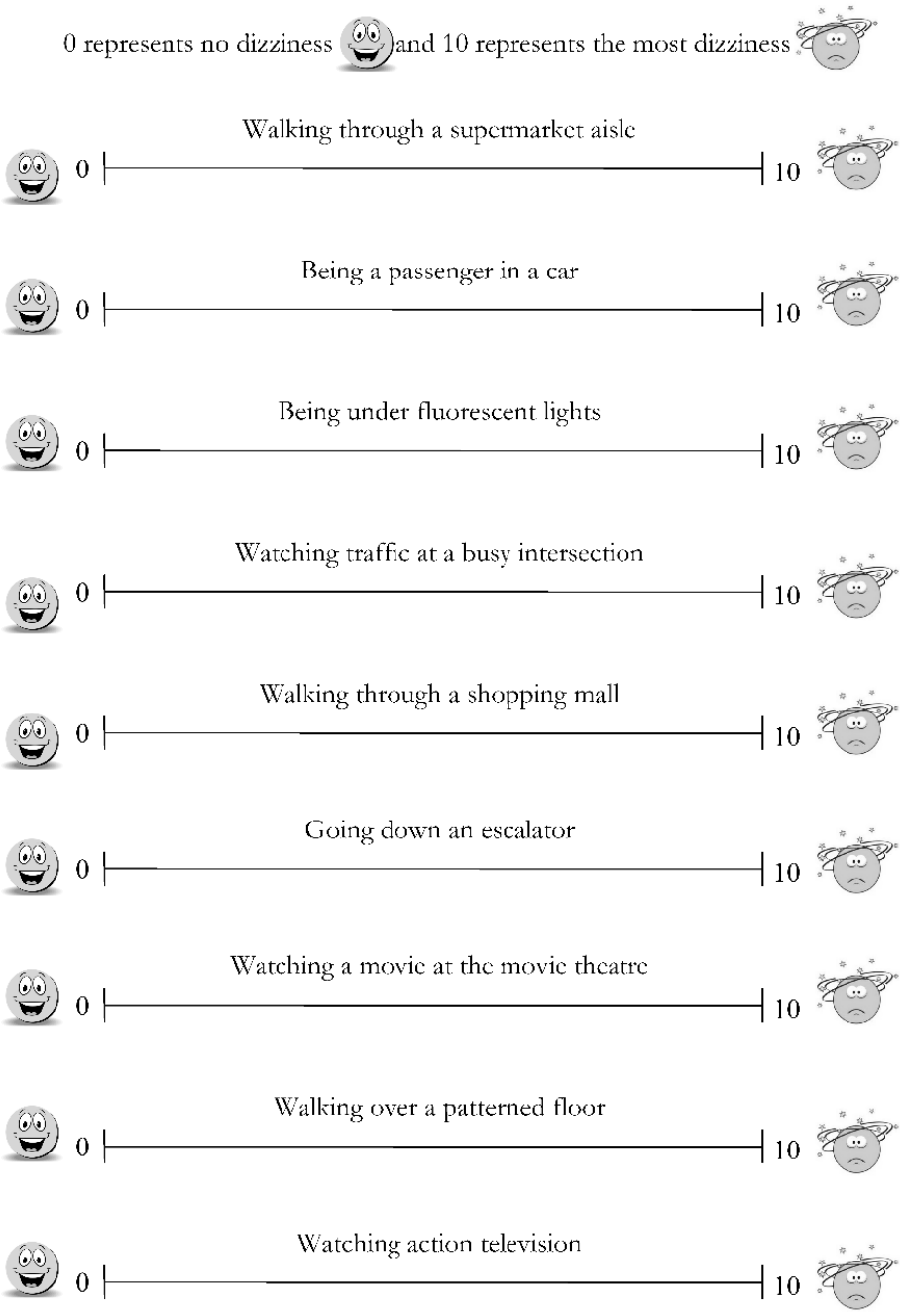
Hôpital juif de réadaptation
Jewish Rehabilitation Hospital

Visual Vertigo Analogue Scale

(Adapted from Longridge et al., 2002)

Indicate the amount of dizziness you experience in the following situations by marking off the scales below.

0 represents no dizziness and 10 represents the most dizziness



from: J. Vestib Res. 2011;21(3):153-9.

Appendix N: Dizziness Handicap Inventory

DIZZINESS HANDICAP INVENTORY

Name: _____ **Date:** _____

Part I

Instructions: The purpose of this scale is to identify difficulties that you may be experiencing because of your dizziness or unsteadiness. Please indicate answer by circling "yes or "no" or "sometimes" for each question. Answer each question as it pertains to your dizziness or unsteadiness problem only.

P1. Does looking up increase your problem?	Yes	No	Sometimes
E2. Because of your problem, do you feel frustrated?	Yes	No	Sometimes
F3. Because of your problem, do you restrict your travel for business or recreation?	Yes	No	Sometimes
P4. Does walking down the aisle of a supermarket increase your problem?	Yes	No	Sometimes
F5. Because of your problem, do you have difficulty getting into or out of bed?	Yes	No	Sometimes
F6. Does your problem significantly restrict your participation in social activities such As going out to dinner, going to the movies, dancing, or to parties?	Yes	No	Sometimes
F7. Because of your problem, do you have difficulty reading?	Yes	No	Sometimes
P8. Does performing more ambitious activities like sports, dancing, household chores Such as sweeping or putting away dishes increase your problem?	Yes	No	Sometimes
E9. Because of your problem, are you afraid to leave your home without having someone accompany you?	Yes	No	Sometimes
E10. Because of your problem, have you been embarrassed in front of others	Yes	No	Sometimes
P11. Do quick movements of your head increase your problem?	Yes	No	Sometimes
F12. Because of your problem, do you avoid heights?	Yes	No	Sometimes
P13. Does turning over in bed increase your problem?	Yes	No	Sometimes
F14. Because of your problem, is it difficult for you to do strenuous housework or yard work?	Yes	No	Sometimes
E15. Because of your problem, are you afraid people might think you are intoxicated?	Yes	No	Sometimes
F16. Because of your problem, is it difficult for you to go for a walk by yourself?	Yes	No	Sometimes
P17. Does walking down a sidewalk increase your problem?	Yes	No	Sometimes
E18. Because of your problem, is it difficult for you to concentrate?	Yes	No	Sometimes

F19. Because of your problem, is it difficult for you walk around the house in the dark?	Yes	No	Sometimes
E20. Because of your problem, are you afraid to stay home alone?	Yes	No	Sometimes
E21. Because of your problem, do you feel handicapped?	Yes	No	Sometimes
E22. Has your problem placed stress on your relationships with members of your family or friends?	Yes	No	Sometimes
E23. Because of your problem, are you depressed?	Yes	No	Sometimes
F24. Does your problem interfere with your job or household responsibilities?	Yes	No	Sometimes
P25. Does bending over increase your problem?	Yes	No	Sometimes

Part II
Instructions: Put a check in the box that best describes you.

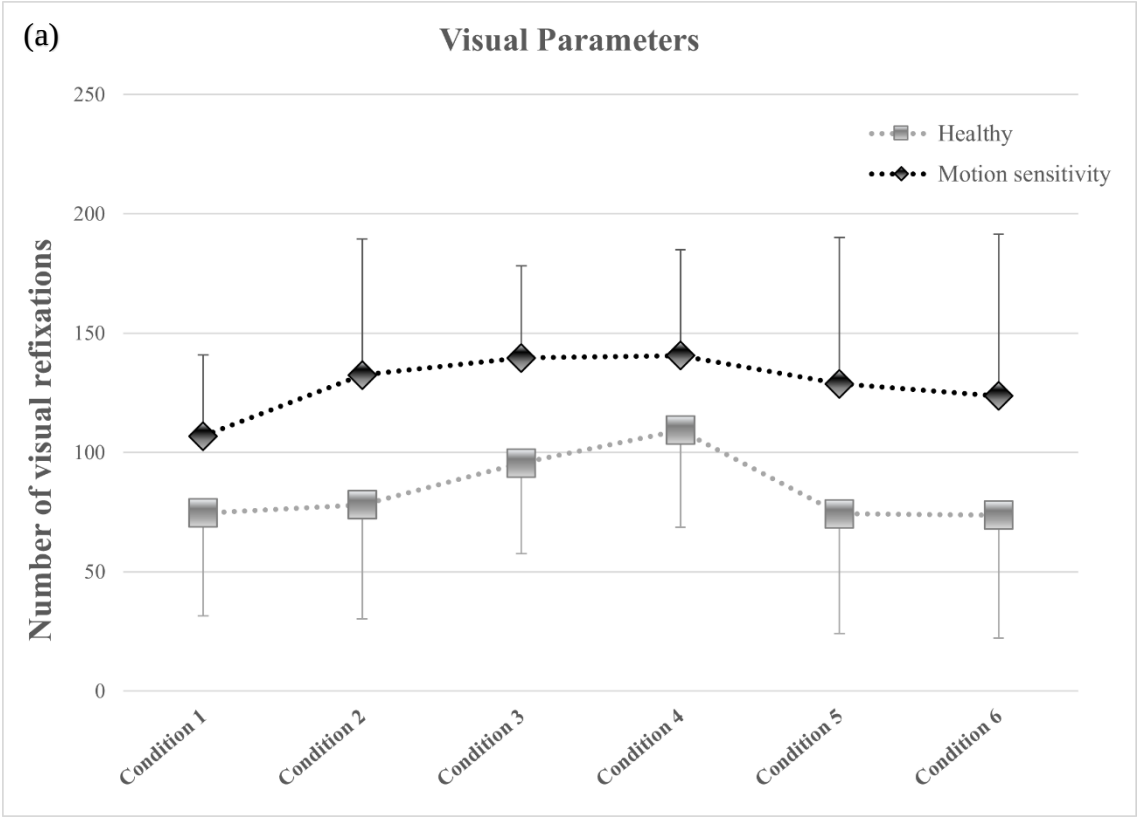
☐	**Negligible symptoms (0)**
☐	**Bothersome symptoms (1)**
☐	**Performs usual work duties but symptoms interfere with outside activities (2)**
☐	**Symptoms disrupt performance of both usual work duties and outside activities (3)**
☐	**Currently on medical leave or had to change jobs because of symptoms (4)**
☐	**Unable to work for over one year or established permanent disability with compensation payments (5)**

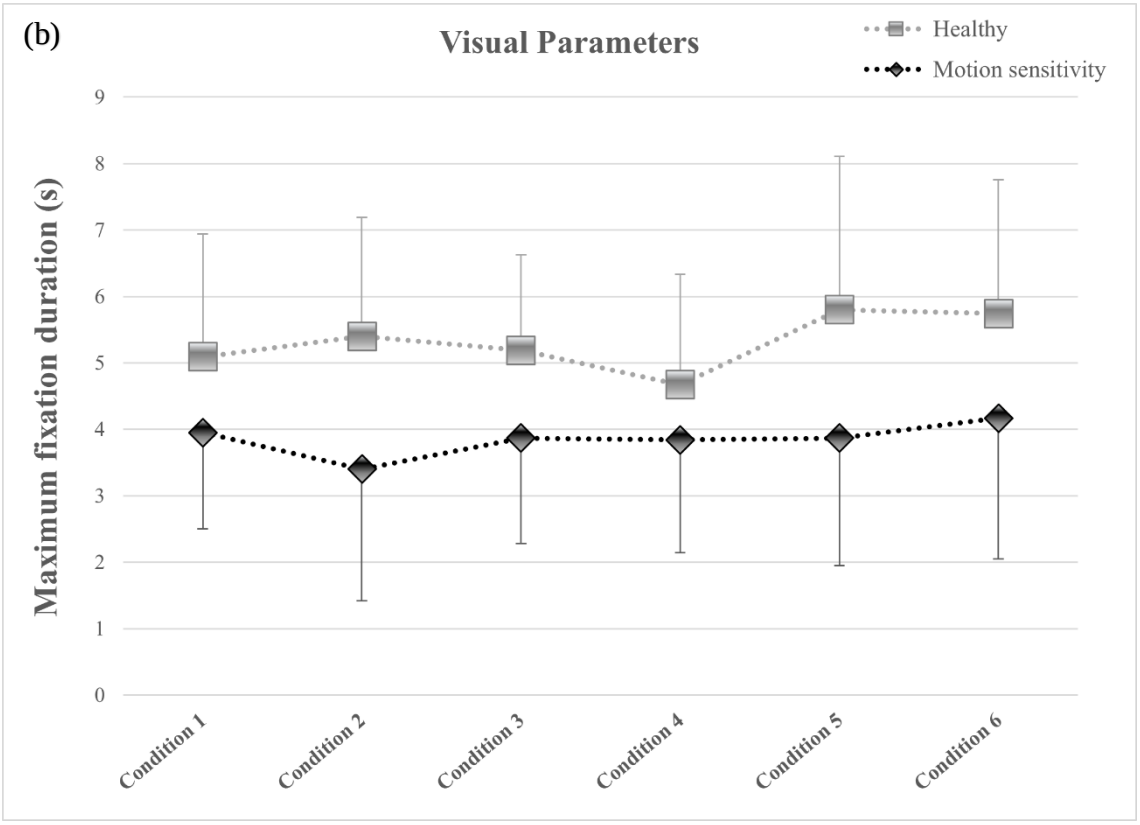
STOP HERE

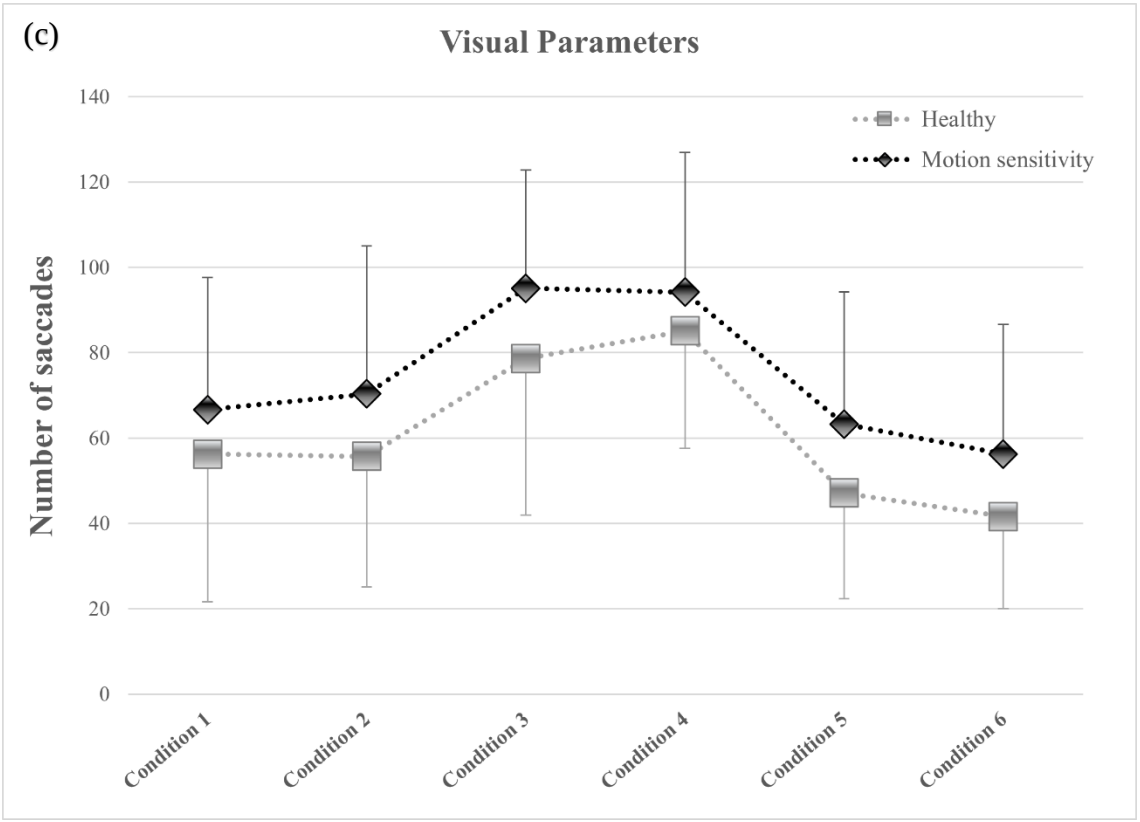
	Yes		Sometimes		No	
P(7)	_____x4=____	+	_____x2=_____	+	_____x0=____	**Physical Items**_____ **(28)**
E(9)	_____x4=____	+	_____x2=_____	+	_____x0=____	**Emotional Items**_____ **(36)**
F(9)	_____x4=____	+	_____x2=_____	+	_____x0=____	**Functional Items**_____ **(36)**

TOTAL_____
(max 100 pts)

Appendix O: Graph illustrating means and standard deviations of visual parameters across groups

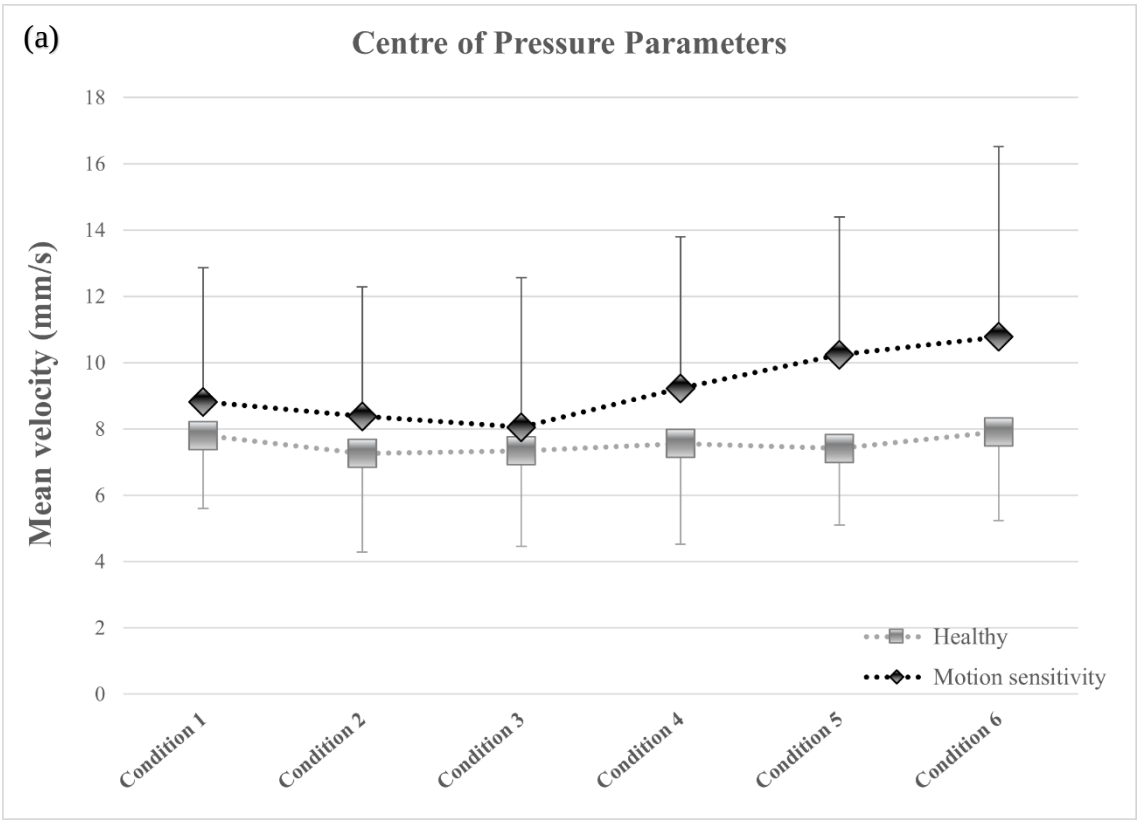


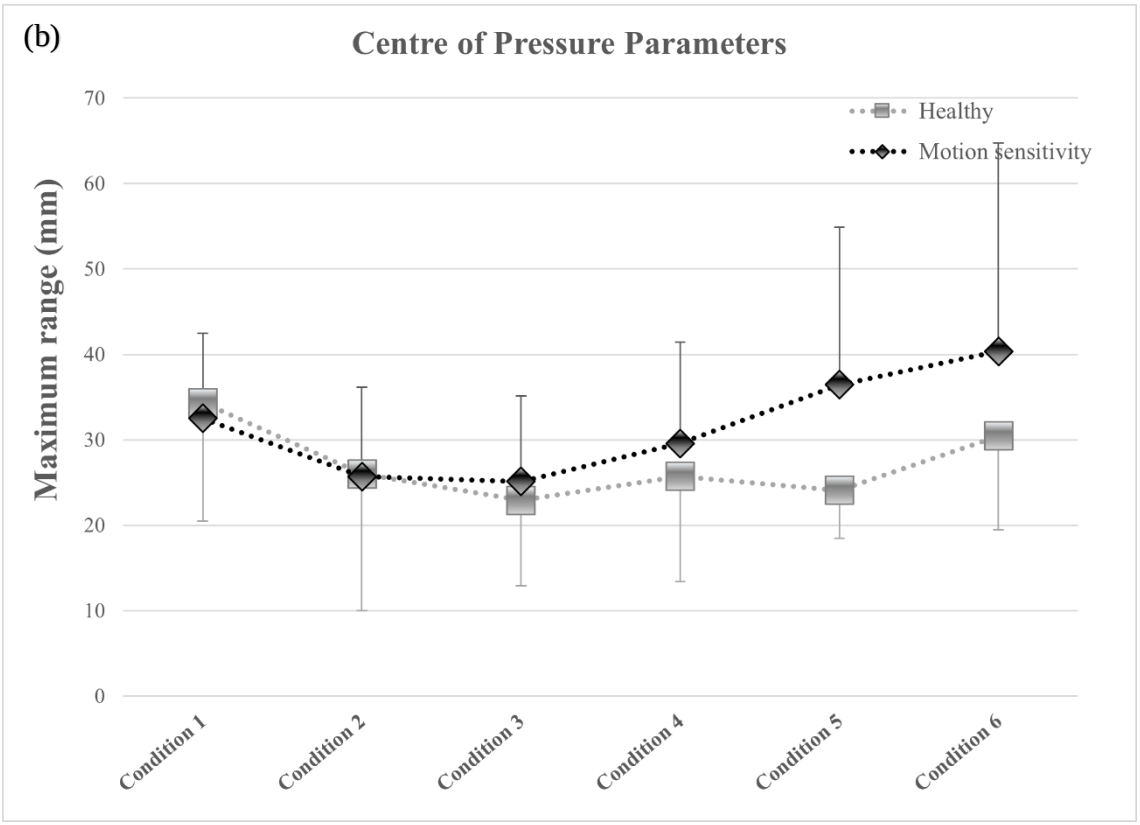


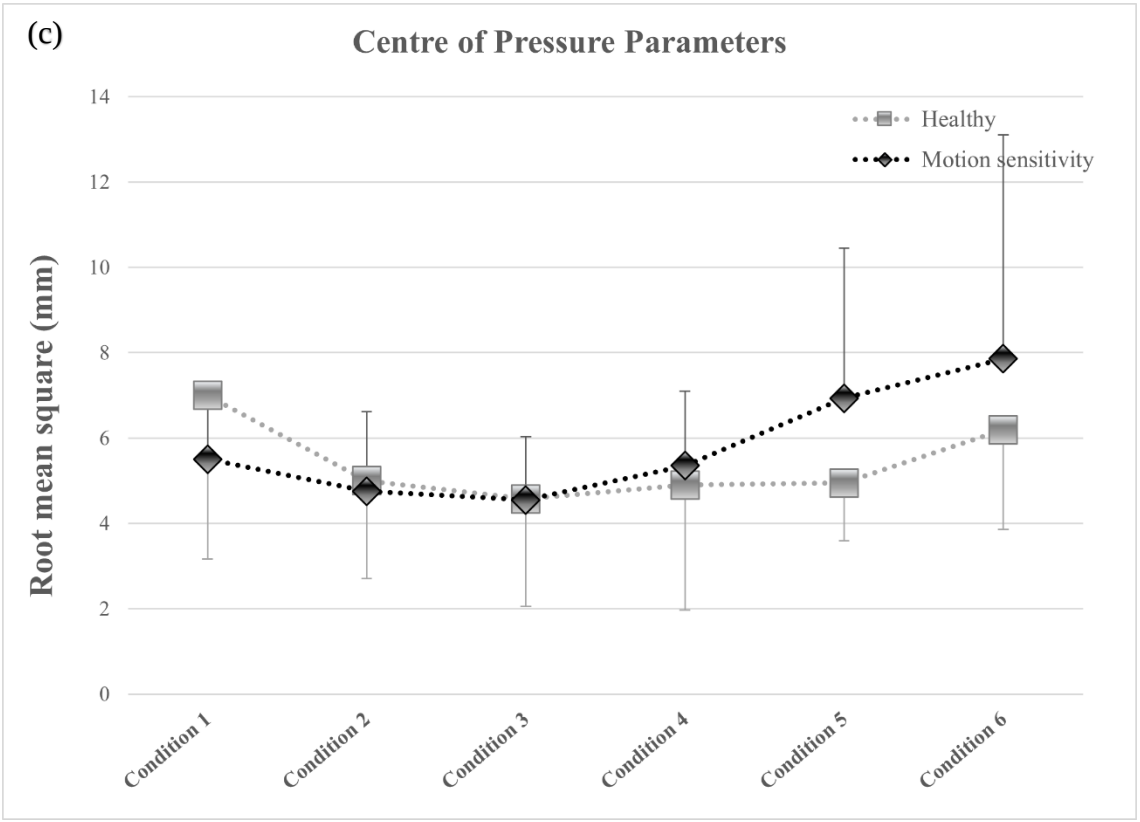


(a) Number of visual refixations; (b) Maximum fixation duration; (c) Number of saccades

Appendix P: Graphs illustrating means and standard deviations of centre of pressure parameters across groups

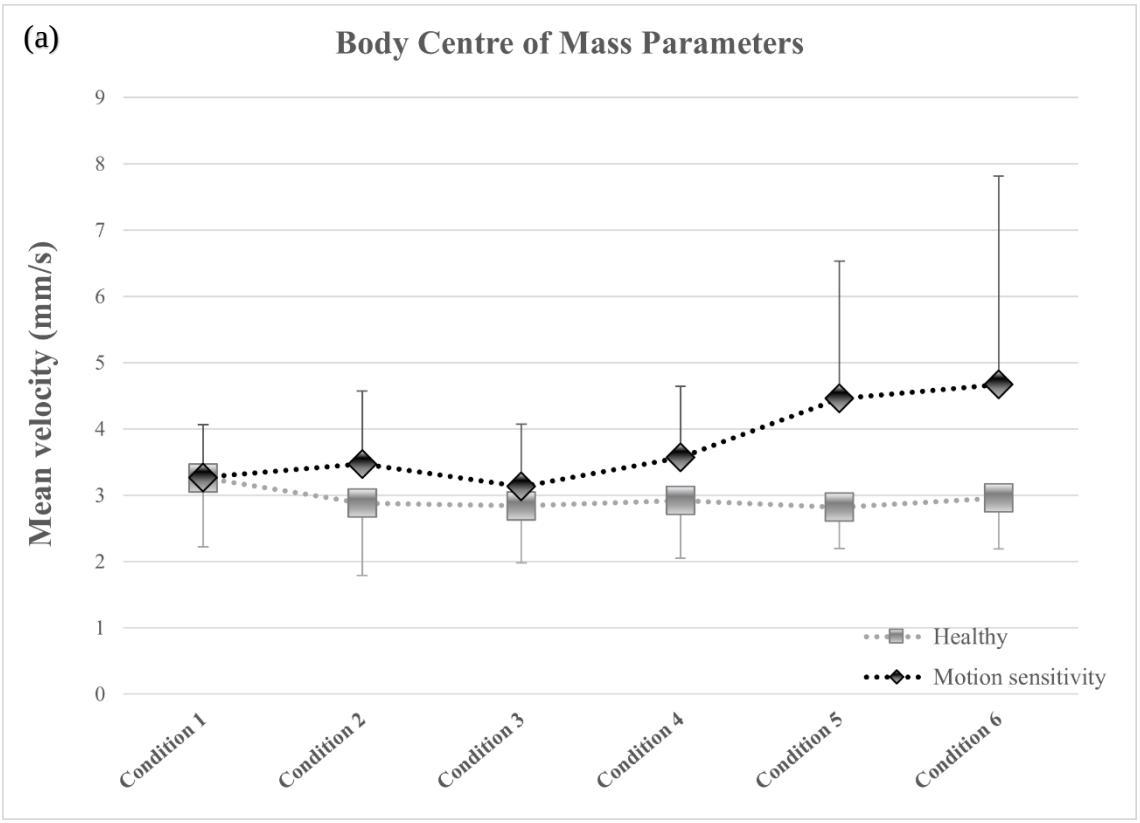


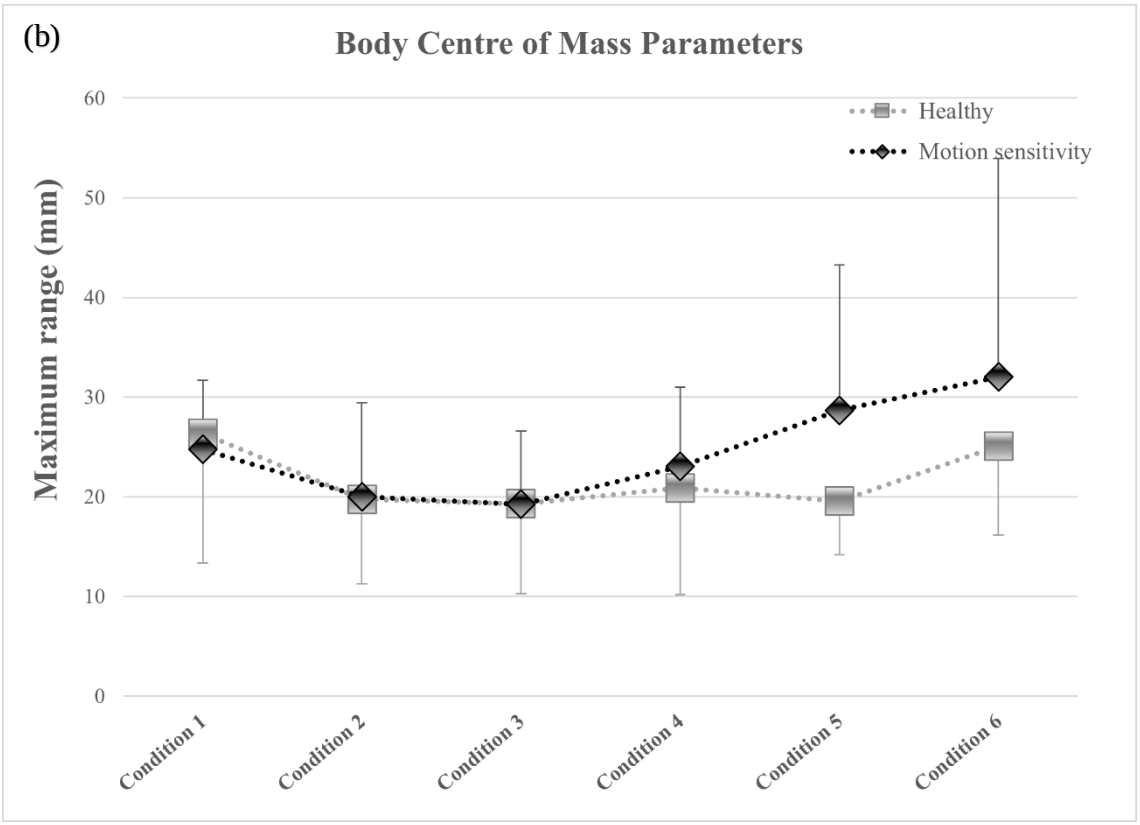


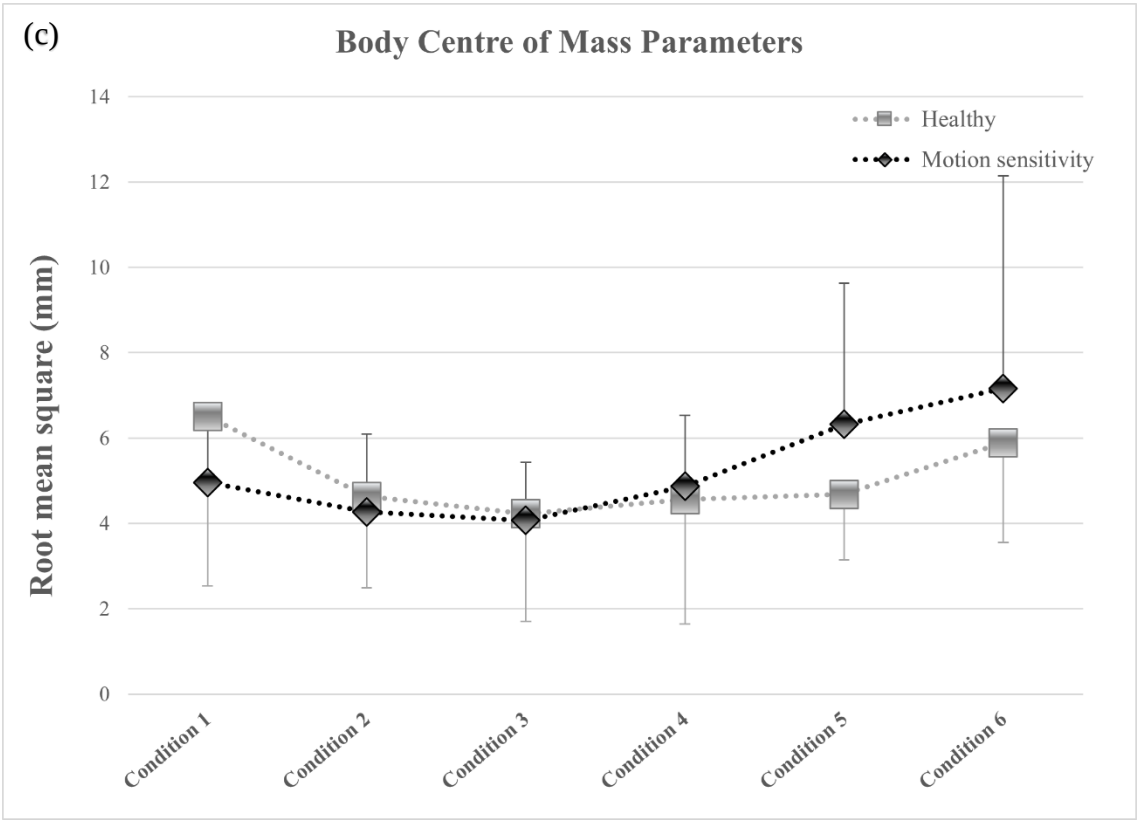


(a) Mean velocity; (b) Maximum range; (c) Root mean square

Appendix Q: Graphs illustrating means and standard deviations of body centre of mass parameters across groups

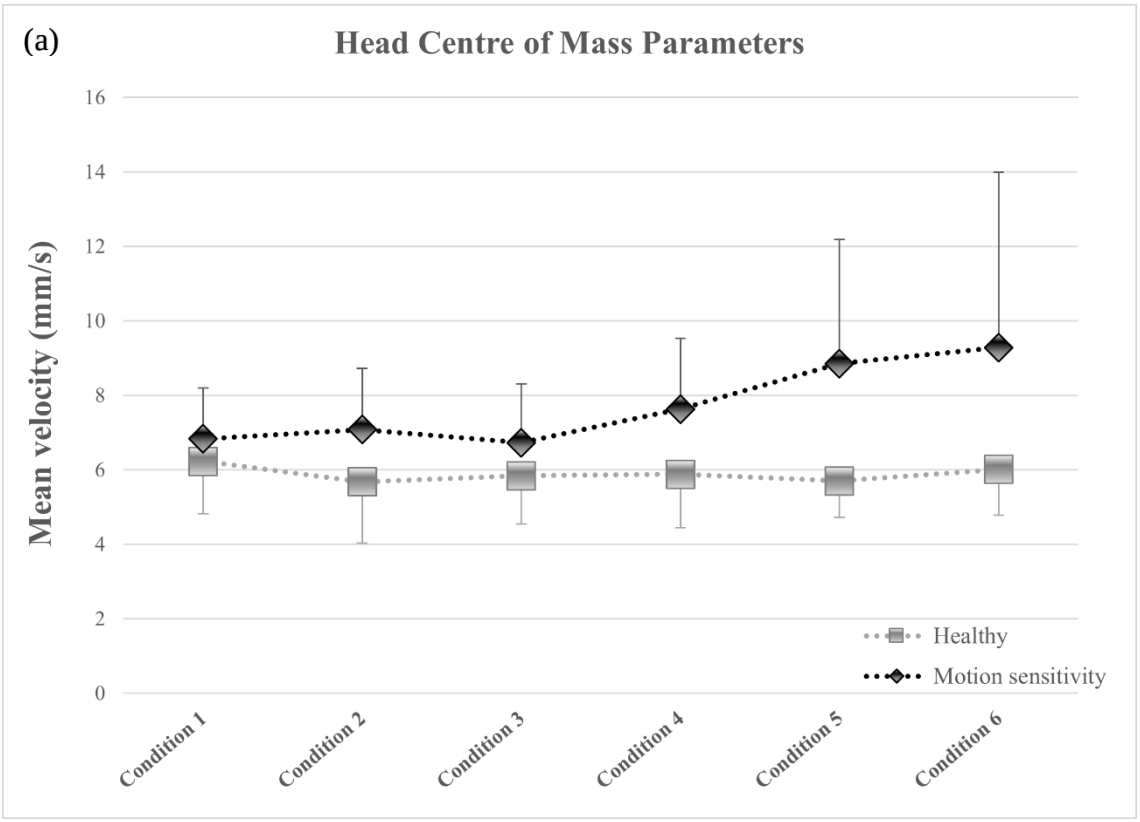


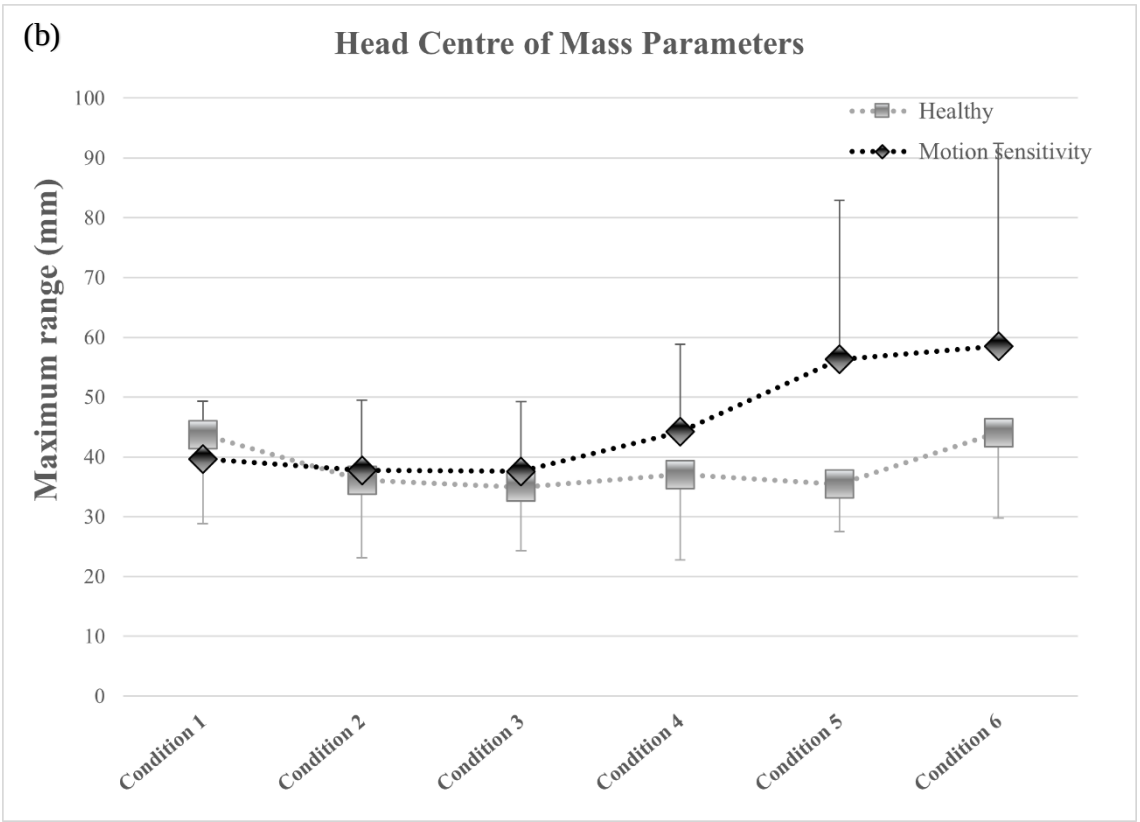


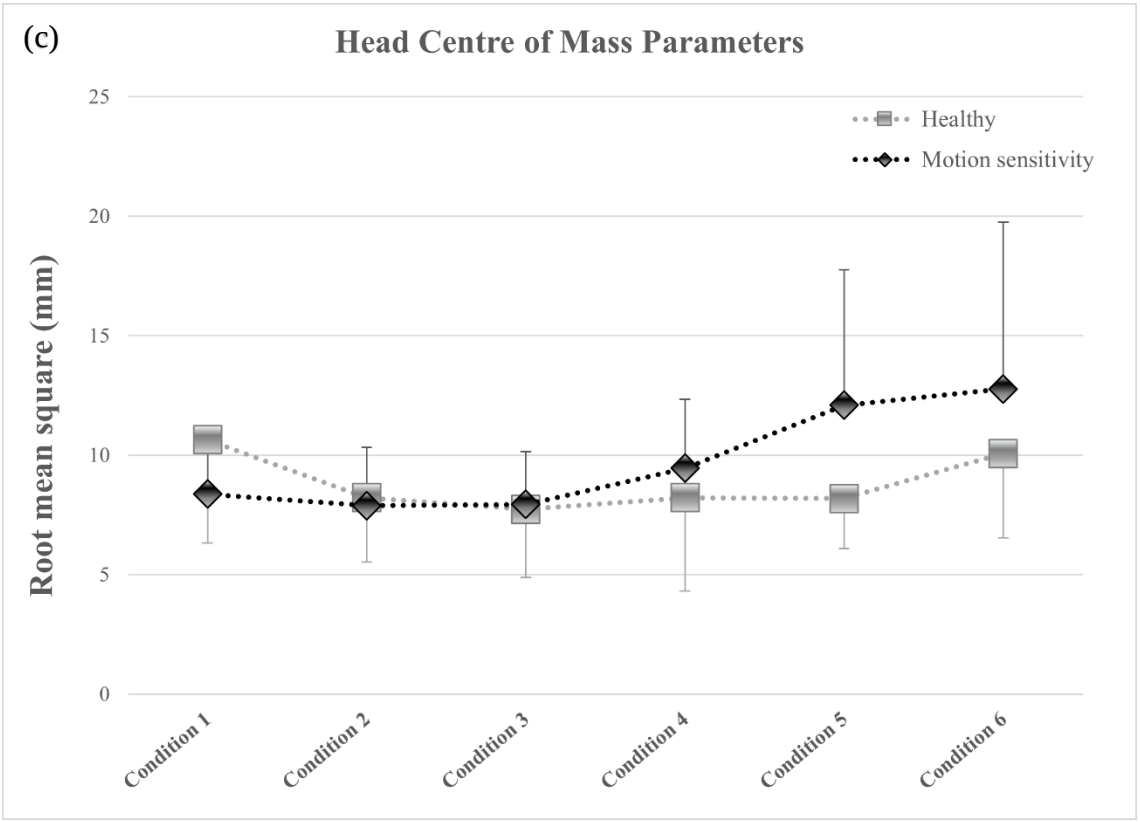


(a) Mean velocity; (b) Maximum range; (c) Root mean square

Appendix R: Graphs illustrating head centre of mass parameters across groups







(a) Mean velocity; (b) Maximum range; (c) Root mean square