Post-Stroke Visual Midline Shift Syndrome

by

Ohwod Binhilabi

A thesis

presented to the University Of Waterloo

in fulfilment of the

thesis requirement for the degree of

Master of Science

in

Vision Science

Waterloo, Ontario, Canada, 2018

AUTHOR'S DECLARATION

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

Abstract

Introduction

The definition of an individual's visual midline is the point which the individual perceives as being straight-ahead or "in front of their nose". One of the perceptual consequences of a stroke for some individuals is a shift in their perceived midline. It can be shifted vertically or laterally so that a target will be perceived as straight-ahead when, for example, it is presented in front of the left eye.

Little is understood of the epidemiology or prognosis of VMSS. The assessment is also not well standardised. It is currently assessed manually with a hand-held 'wand' to determine the individual's subjective midline position. There is no commonly accepted size and distance of the target, speed of the movement, or control of the background.

The goals of the first study were to standardize the parameters of a device using healthy participants with no history of stroke and no significant eye or systemic disorders that might influence the position of the midline. This also provided normal data against which the midline of patients can be compared. The goal of the second study was to use the device to determine the percentage of stroke survivors who experience VMSS, and whether there are associations between the perceived midline and the type and side of the stroke and other measures such as handedness, neglect, open-looped pointing and the subjective straight-ahead position. A comparison group of people without stroke, but who may have other ocular or systemic disease were included.

Methods

For the first study, twenty-four healthy control participants in two age groups (20-35 and ≥65 years) without stroke were recruited. In the first session, the perceived horizontal midline was measured with the midline shift gauge for 3 target sizes and 2 speeds at a 50 cms

distance. In the second session, the perceived vertical and horizontal midline was measured for 3 distances with a target size and speed determined from session 1.

For the second study, a history was taken including ocular, medical history, medications, handedness and stroke history. Testing included ocular dominance, confrontation fields, cognitive impairment testing with the MoCA test, a measure of the subjective straight-ahead position, visual open loop testing, neglect testing with the Bell cancellation and line bisection tests. VMSS was measured in two ways, the usual way with a hand-held "wand" and then with the VMSS gauge.

Results

In the first study, session 1, repeated measures ANOVA for the means and standard deviations showed no main effect of speed, target size or target direction and no interaction ($p>0.05$) for the perceived horizontal midline position or the variability between participants ($p>0.05$) and so one speed and target size was chosen for the second session. For the second session, repeated measures ANOVA for the horizontal midline position for age and distance (2x age, 3x distance) showed no significant effect of age and no interaction ($p>0.05$), but there was an effect of distance for the variability (standard deviations). For the vertical midline, there was an effect of both age and distance. Handedness had no significant impact on the midline position (2 sample t-test, $p>0.05$) for the older age group (all younger participants were right handed). Individual analysis of the midline position showed that all participants except one had no perceived mid-line shift.

In the second study, fourteen participants were recruited (nine non-stroke participants who ranged between 23-80 years old and five post-stroke participants, age ranging between 48-78 years old). Three (60%) post-stroke participants and five (55%) of the non-stroke participants had a perceived midline shift. Perceived midline shifts were detected with the gauge when there was no midline shift detected with the clinical wand procedure and vice versa. In some cases, a different midline shift was found at different distances from the participant. There was no obvious association between the direction of the midline shift and factors such as handedness, ocular dominance, subjective straight-ahead, open-loop pointing or intra-ocular visual acuity difference.

Conclusion

The first study shows that the measurement of midline in control participants is tolerant of differences of target size, speed and direction, but differences of age and distance were found. Normal data are presented which can be used to quantify the midline shift in future cross-sectional and longitudinal studies of post-stroke participants. The second study shows that there is no association between the variables measured, so no clear predictor of midline shift was observed. The comparison group who had other ocular and systematic morbidities also showed midline shifts. Therefore, visual midline shift is not specific to stroke or only resulting from stroke. The variability in results at different distances from the patient indicate that midline shifts should be measured at several distances in the clinical assessment of VMSS. The results also suggest that visual midline shift should be considered as a risk factor for falls in both stroke and non-stroke populations.

Acknowledgments

Supervisors:

- Dr. Susan Leat
- Dr. Tammy Labreche

Committee:

- Dr. Kristine Dalton
- Dr. Denies Hileeto

Sponsors:

- Royal Embassy of Saudi Arabia Cultural Bureau.
- Network for Aging Research (NAR) at the University of Waterloo Emerging Scholar Mentorship Grant
- Canadian Optometric Education Trust Fund (COETF)

Family and friends:

Special thanks to my younger brother Sultan.

Table of Contents

List of Figures

List of Tables

Chapter 1- Introduction

1.1 Epidemiology of stroke

1.1.1 Definitions, etiology and types of stroke

An acquired brain injury (ABI) such as cerebral vascular accident or stroke can be defined as a neurological deficit caused by a vascular change to the central nervous system injury which can occur as a result of a hemorrhage or partial or complete blockage of blood vessels (Gresham, Stason, & Duncan, 1997; Sacco et al., 2013). Cerebrovascular disease is the sixth most common global cause of chronic disease (Akbarkhodjaeva & Tursunov, 2017; Ezejimofor et al., 2016).

There are two types of stroke; ischemic stroke, and hemorrhagic stroke. Transient ischemic attack (TIA) is a small ischemic stroke with temporary symptoms and should be considered as a warning sign of a major ischemic stroke and so should be taken seriously. It is more common in patients with carotid artery stenosis over 75% (Goldstein et al., 2001). TIA causes symptoms of stroke for less than 24 hours. The symptoms are caused by tiny clots (emboli or plaques) that break up and dissolve quickly in an artery but do not permanently prevent the blood supply to the brain (Connolly et al., 2012). Ischemic strokes are the most common type of stroke causing between 60% to 80% of all major strokes (Benamer & Grosset, 2009; Gresham et al., 1997; Miller et al., 2010). They are as a result of a blood clot in the brain which causes a deficiency of oxygen supply to the brain tissues (Connolly et al., 2012). Hemorrhagic strokes are between 12 to 20% of all major strokes, and often lead to death (Gresham et al., 1997). The majority of individuals (about 64%) have hemorrhagic strokes secondary to hypertension (Benamer & Grosset, 2009). Hemorrhage strokes can be either intracerebral which happens in between 8 to 16% of all strokes or subarachnoid 4 to 8% of all strokes (Gresham et al., 1997).

The specific area and side of brain damaged can be responsible for specific impacts (Connolly et al., 2012; Hillis, 2007; Siong et al., 2014). Left sided stroke presents in most of the individuals, affecting 56.1% of all strokes (Siong et al., 2014). Right sided stroke presents in 38.3% of individuals and about 5.6% of the cases have both sides involved (Siong et al., 2014). The area of the brain affected can cause different types of impairments and disabilities (Ciuffreda et al., 2007; Gresham et al., 1997; Hillis, 2007; Siong et al., 2014). Lesions in the right hemisphere of the brain cause left body sensory disorders such as hearing, vision, and somatosensory disorders (Gresham et al., 1997) and motor deficits on the left side. A lesion in the left hemisphere may cause impairments in language such as aphasia (Hillis, 2007). Damage in the temporal lobe can result in language comprehension or logical thinking deficits, while damage in the occipital lobe might affect visual functions (Hillis, 2007; Siong et al., 2014).

1.1.2 Overall Prevalence

In 2010, around 17 million individuals experienced a stroke worldwide (393.4 per 100,000 population) (Akbarkhodjaeva & Tursunov, 2017; Ezejimofor et al., 2016). In Canada, 405,000 individuals experienced stroke in 2013 (Krueger et al., 2015) and around 400,000 Canadians are living with post-stroke disabilities in 2017 (Heart and Stroke Foundation of Canada, 2017). Every year, more than 62,000 individuals experienced a stroke in 2018 (Heart and Stroke Foundation of Canada, 2017). In the United States, 550,000 – 795,000 people experience a stroke each year between 1997- 2014 (Benjamin et al., 2018; Fang, Coca Perraillon, Ghosh, Cutler, & Rosen, 2014; Gresham et al., 1997). More recently it has been reported that 42.4 million individuals were living with a stroke in the United States in 2015 (Benjamin et al., 2018). The prevalence of stroke in Arab countries was between 42 and 68 per 100,000 population (Benamer & Grosset, 2009). Over the last four decades, the prevalence of stroke has increased in low-income countries by around 14%, in upper-middle income countries by 12%, and in lower middle-income countries by 5.4% (Ezejimofor et al., 2016; Johnson, Onuma, Owolabi, & Sachdev, 2016). Between 1990 -2010, individuals in developing countries are experiencing an increase in the prevalence of stroke, with an increase greater than 65% (Benamer & Grosset, 2009).

1.1.3 Stroke mortality

Stroke is a major cause of disability and death in the world (Sacco et al., 2013). Stroke was the second most frequent global cause of death with 5.9 to 6.2 million stroke deaths between 2009 – 2011 (Akbarkhodjaeva & Tursunov, 2017; Benamer & Grosset, 2009; Ezejimofor et al., 2016; Johnson et al., 2016). However, it was the third cause of disability after cancer, heart disease, and diabetes in 1988 and more recently in 2017 (Akbarkhodjaeva & Tursunov, 2017; Foulkes, Wolf, Price, Mohr, & Hier, 1988; Goldstein et al., 2001; Johnson et al., 2016). In 2015, stroke was the cause of 6.3 million deaths worldwide (Benjamin et al., 2018). One of every nineteen deaths was accounted for by stroke in the United States in 2015 (Benjamin et al., 2018) and stroke is the forth main cause of death in the United States (Fang et al., 2014). South Asians are at higher risk accounting for 40% of global stroke deaths (Akbarkhodjaeva & Tursunov, 2017). 87.3% of strokes are ischemic and 12.7% are hemorrhagic between 1988 to 2008 (Fang et al., 2014). Interestingly, deaths due to stroke in the United States decreased by 35.8% between 2000 to 2010 (Miller et al., 2010; Winstein et al., 2016). In Canada, the rate of mortality after ischemic stroke is 9% and 25% after hemorrhagic stroke. However, the rate of disability following an ischemic stroke is higher than a hemorrhagic stroke, 62% and 32% respectively (Krueger et al., 2015).

1.1.4 Prevalence of survival- living with the effects of stroke

In Canada, the number of stroke survivors has increased, from 261,000 to 315,000 between 1995 to 2015 (Krueger et al., 2015). Thirty six percent of survivors live with the effects of stroke up to 5 years after the stroke and more than 40% of survivors require assistance in Canada (Krueger et al., 2015). About 1.04% of the total population in Quebec and 1.26% individuals in Ontario live with the effects of the stroke (Krueger et al., 2015). Most of the stroke survivors are adults with 87.6% being community-dwelling adults, 12.3% living in residences for the elderly, and 0.1% being children under 12 years old (Krueger et al., 2015). In the United States, 70% of stroke survivors receive rehabilitation services through either hospital-based inpatient, nursing, or home rehabilitation care outpatient facilities (Gresham et al., 1997). Approximately 10% of individuals are admitted into a long-term care facility (Foulkes et al., 1988; Goldstein et al., 2001; Miller et al., 2010). Only a few individuals who experience a stroke recover completely (Foulkes et al., 1988; Goldstein et al., 2001; Miller et al., 2010).

Lower and higher income countries have an effect on stroke survival percentage worldwide. For instance, individuals from Latin America and Caribbean have the highest percentage of stoke survivors with an average of 21 per 1000 based on thirty-one different studies (Ezejimofor et al., 2016). However, the prevalence of stroke survival in Sub-Saharan Africa is much lower at 3.5 per 1000 (based on twelve different studies). This lower rate of survival might be due to lower health care investment, poverty, or co-morbidities (Benamer & Grosset, 2009; Ezejimofor et al., 2016). Enhancement in medicine increases the rate of survival from stroke (Winstein et al., 2016). However, as the survival rate increases, the number of those living with multiple impairments following strokes also increases (Rowe et al., 2008).

1.1.5 *Risk factors*

There are many factors that affect an individual risk of stroke and they can be separated into two groups; non-modifiable and modifiable risk factors (Goldstein et al., 2001). Non-modifiable risk factors include age and gender and the modifiable risk factors include cardiac disease, hypertension, diabetes, and lifestyle (Akbarkhodjaeva & Tursunov, 2017; Benamer & Grosset, 2009; Goldstein et al., 2001). Health conditions have a significant impact on the prevalence of stroke (Teh et al., 2018).

The prevalence of stroke increases with age. (Foulkes et al., 1988; Goldstein et al., 2001; Miller et al., 2010; Ontario Brain Injury Association, 2012). The risk dramatically doubles every decade over fifty-five years old (Gresham et al., 1997). It is more likely for those over the age of 85 to have a stroke than individuals between 65-74 (Foulkes et al., 1988; Goldstein et al., 2001; Miller et al., 2010). Individuals over 65 years old include two thirds of all strokes (Akbarkhodjaeva & Tursunov, 2017; Goldstein et al., 2001; Ontario Brain Injury Association, 2012).

Males are more at risk of experiencing a stroke than females with rates of 10.2% and 7.7% for men and women respectively between 2005-2008 in the US (Benamer & Grosset, 2009; Gresham et al., 1997; Krueger et al., 2015). However, in Canada in 2013, overall more females experienced a stroke than males (214,000 among females and 191,000 individuals among males) and this difference was also present in 2018 (Krueger et al., 2015). There is a difference between the sexes was found for individuals between 35-44 years old and over 85 years old, but not in the ages in between (Heart and Stroke Foundation of Canada, 2017; Goldstein et al., 2001; Gresham et al., 1997). This difference exists in the US as well (Benjamin et al., 2018). Strokes lead to death in more females than males with 59% being female stroke fatality and 41% male fatality in 2018 (Heart and Stroke Foundation of Canada, 2017; Benjamin et al., 2018; Connolly et al., 2012; Goldstein et al., 2001). The reason might be because of the long-term effect of birth control pills and pregnancy (Connolly et al., 2012; Goldstein et al., 2001).

Stroke is about 4x higher in individuals with hypertension and heart disease, 2x higher in individuals with diabetes and 8x higher in individuals with dementia (Teh et al., 2018). In developing countries, hypertension is thought to be a main cause of stroke because of poor management or because it is undiagnosed especially among younger adults (Ezejimofor et al., 2016). Adults younger than 55 years old with type 2 diabetes are at higher risk (Connolly et al., 2012). Stroke presents in 11.6 % to 69% of individuals with diabetes (Benamer & Grosset, 2009). Another health factor that might be associated with strokes is migraines. 15% of individuals with migraines younger than 45 years old experience a stroke (Benamer & Grosset, 2009). Heart disease is a main risk factor resulting in a high prevalence of stroke. About 70% of the individuals with heart disease who use anti-clotting medications in addition to having other factors such as blockage of the blood vessels in brain and high blood pressure may have a stroke (Connolly et al., 2012). Atrial fibrillation is the most common type of heart disease that can lead to stroke with about two thirds of these individuals experiencing a stroke (Fang et al., 2014; Goldstein et al., 2001; Gresham et al., 1997). This is followed by carotid artery stenosis with over 50% of individuals experiencing a stroke (Goldstein et al., 2001).

One in five strokes result from an atrial fibrillation and these strokes cause more disability (Christiansen et al., 2013). Changes in cerebral vessels usually create changes in the retinal vessels. Retinal occlusions that might resulted in stroke includes: Central Retinal Vein Occlusion (CRVO) and Central Retinal Artery Occlusion (CRAO). The central retinal vein and artery occlusions refer to ruptured veins or blocked arteries. The prevalence of

CRVO and CRAO increase with age and individuals with CRVO or CRAO in addition to atrial fibrillation have an increased risk of stroke (Christiansen et al., 2013). 33% individuals have stroke following CRAO, 23% of individuals have strokes following CRVO (Christiansen et al., 2013). Individuals aging between 60-69 are at higher risk of having stroke after having CRVO (49.6%) (Liou & Lin, 2009).

Smoking is an additional risk factor, doubling the numbers of strokes relative to non-smokers, and being associated with stroke in 1.6 to 44% of individuals (Benamer & Grosset, 2009; Connolly et al., 2012; Goldstein et al., 2001). Lifestyle factors such as obesity presents in 18% of stroke patients, physical inactivity in 25%, and drug and alcohol abuse in 5% and are important risk factors for stroke (Connolly et al., 2012; Gresham et al., 1997). However, alcohol consumption in itself and depression were not associated with stroke (Teh et al., 2018).

1.2 General impacts of stroke

Stroke is the most common cause of medical acquired brain injury (ABI) (Kapoor et al., 2001; Ontario Brain Injury Association, 2012). Although the Ontario Brain Injury Association reports (Ontario Brain Injury Association, 2012) were based on self-report by the participants rather than clinical measures of impairment, these reports give useful information about the impacts. Regarding daily impacts following ABI, 95% reported memory issues, 76% depression, 62% balance difficulties, 26% impairments in vision and 20% hearing deficits (Ontario Brain Injury Association, 2012). Fifty million stroke survivors in the world survive with some deficits (Miller et al., 2010). The general impacts of stroke can be categorized as cognitive and communication impairments, sensory impairments (including vision deficits), motor impairments, and emotional and behavioral difficulties. (Ciuffreda et al., 2007; Mercier et al, 2001; Miller et al., 2010).

1.2.1 Cognitive impacts and communication

The cognitive impact can be affected by the severity of other factors related to each post-stroke patient such as depression, frustration, medical status, and the rate of the recovery (Miller et al., 2010). Aphasia, dysarthria, apraxia and memory loss are functional disorders post- stroke. Aphasia is a common communication deficit which refers to an impairment of production and comprehension of language (Miller et al., 2010). Broca's aphasia (expressive), Wernicke's aphasia (receptive), and global aphasia are the three types of aphasia. Expressive aphasia, due to the left frontal hemisphere of the brain being affected, is characterized by non-fluent speech, language impairment and difficulty or lack of responding verbally (Hillis, 2007). Receptive aphasia occurs when individuals have the left temporal brain affected. They have difficulties understanding but are able to speak although, sometimes not correctly matching answers to the questions (Hillis, 2007). Global aphasia is when individuals have wider-spread brain damage which causes difficulty in responding and speaking (Hillis, 2007). Dysarthria and apraxia are both muscle weakness disorders that can affect speech production. Dysarthria is an impaired articulation and phonation of speech and leads to a breathy voice and slow speech rate. Apraxia is an impaired muscle movement and this can impact the ability to produce sounds which can lead to excessive pausing (Miller et al., 2010).

Furthermore, deficits in short or long-term memory is a cognitive disorder which about one third individuals of individuals experience within 3-12 months post-stroke (Winstein et al., 2016) and some of them present with executive functioning such as anosognosia. Anosognosia is a condition which leads to unawareness of self-disorder or disinhibition and behavioral problems (Miller et al., 2010). Vascular dementia is another frequent consequence of stroke. The presence of stroke doubles the likelihood of dementia

(Ivan et al., 2004). Vascular dementia presents in 51% of post-stroke individuals compared to people without a major stroke (4% Ivan et al., 2004).

1.2.2 *Sensory impairments*

Hearing deficit is not an uncommon impact of stroke which presents in about 21% of post-stroke individuals (Winstein et al., 2016). However, it has been suggested that many of the hearing loss cases might be as a result of undiagnosed previous age-related hearing loss, rather than from the stroke (Winstein et al., 2016). In about 86% of individuals with hearing impairments after stroke, the presence of hearing loss before stroke was not documented (Edwards et al., 2006; Winstein et al., 2016). Vision impairments are discussed below.

Somatosensory deficits which is denoting the sensation such as barognosis (judging the weight of objects) and stereognosis (judging the shape of objects without using vision) are noticeably common disorders post-stroke and present in about 53% individuals (Gresham et al., 1997; Winstein et al., 2016). For barognosis and stereognosis tests, post-stroke individuals took twice as much time as control individuals (Hsu et al., 2017).

1.2.3 *Motor impairments*

Hemiplegia is a neurological deficit following stroke and presents in about 60 to 80% of stroke survivors in addition to joint contracture (Gresham et al., 1997; Winstein et al., 2016) which leads to partial or total dependence in 25 to 50% of stroke survivors (Gresham et al., 1997). Right hemiparesis presents in 44% of individuals with stroke and left hemiparesis in 37% of all stroke patients (Gresham et al., 1997). Motor impairments such as hemiparesis/hemiplegia may result in postural control and balance deficits (Miller et al., 2010). Some people post stroke may experience paresis of either an arm or leg.

Motor impairments post-stroke can result in reduced ability to do daily activities and engage in the community (participation) (Miller et al., 2010). Decreased ability to reach objects and decreased walking speed, are examples of postural control changes post-stroke which cause movement limitations and lead to loss of functional activities (Miller et al., 2010). Movement time for transfer and to reach an object might be longer for stroke individuals than individuals without stroke (Hsu et al., 2017).

Balance impairments are a result of both sensory and motor disorders and can lead to an increase in the incidence of falls (Winstein et al., 2016). Post-stroke patients may report at least one fall within six months (Winstein et al., 2016) as compared to 0.6 annually in the healthy older population (Rubenstein, 2006). The inability to use the hemiparetic side to prevent a fall, in addition to the balance problems, is the likely cause of this increase in falls (Miller et al., 2010). Individuals after stroke are at about twice as likely to have a hip fracture from a fall as people without stroke (Winstein et al., 2016).

1.2.4 *Emotional and behavioural difficulties*

Emotional impairments include depression. (Gresham et al., 1997; Winstein et al., 2016). The reported rate of depression post-stroke is about 25% to 80% of individuals which makes it the most common complaint globally among stroke survivors (Miller et al., 2010; Winstein et al., 2016). It is associated with increased mortality and decreased functional recovery and social activity (Miller et al., 2010; Winstein et al., 2016). Behavioural impacts of stroke depend on the severity of the stroke and include changes such as disinhibition (saying inappropriate things to others), impulsivity (acting without thinking), and aggression (Wolfe, 2000).

1.3 Impacts on visual functions

Visual impairment is another common concern in individuals following a stroke (Kapoor et al., 2001; Rowe et al., 2008). In one study, more than half of the individuals around the world reported vision disorders after stroke (Rowe et al., 2008), while another study reported that various visual impairments following stroke present in 10-70% of individuals (Siong et al., 2014). About 25% of individuals survive from stroke with minor visual impairments while 40% survive with moderate to severe impairments according to the National Stroke Association, cited by Miller et al (2010). The various visual deficits that have been reported are low visual acuity, eye movement deficits and/or strabismus, visual field defects, or perceptual changes (Rowe et al., 2008). About 54.8% of the post-stroke individuals have a combination of two or more of these visual impairments (Rowe et al., 2008).

1.3.1 Visual acuity

The definition of mild low vision is when the visual acuity is less than 6/18 and for the moderate low vision is when the visual acuity is less than 6/60 (Siong et al., 2014). The definition of low vision in North America is often taken to be VA <6.12 (Leat, Legge, & Bullimore, 1999; Maberley et al., 2006). Best corrected visual acuity post-stroke was less than 6/18 for both near and distance vision in 13% of individuals (Rowe et al., 2008). About 34.7% of the 13% who have low vision had the visual impairment because of other common causes such as such as cataract (14.2%), glaucoma (7.9%), or age-related macular degeneration (4.4%), rather than stroke (Rowe et al., 2008; Siong et al., 2014).

1.3.2 Ocular motility

Eye movement disorder is a disability of both eyes to point to the same object of interest at the same time or to move together to follow or fixate an object of interest (Rowe, 2011). Stroke individuals might experience various eye movement impairments. Ocular motility defects are present in 68.4% of individuals with stroke (Houston, 2010; Rowe et al., 2008). Disrupted binocularity presents in 54% of post-stroke individuals and might cause double vision and reading issues which make the person's vision jump objects or miss their place while reading (Siong et al., 2014). Diplopia presents in about 15.2% of post-stroke individuals (Siong et al., 2014) and 22% had strabismus (Rowe et al., 2008) l. Depth perception might be affected as a result of stroke and individuals may be completely unable to locate objects in depth. For instance, when walking upstairs or downstairs, they may misjudge the edges of the stairs. This can cause more falls (Hillis, 2007; Rowe et al., 2008). Regarding eye movements, about 11.5% of post-stroke individuals were identified with at least one eye having an ocular motility deficit and about 53.1% having jerky movements (Siong et al., 2014). 56% had oculomotor tracking deficits including saccadic and pursuit anomalies. Saccades are the ability of the eyes to shift their fixation onto objects rapidly and the speed and accuracy is decreased after stroke. Pursuits are the ability of both eyes to track a target and after stroke this ability decreased as well (Wolter & Preda, 2006). Moreover, 12 % of stroke individuals experience nystagmus, which is when the eyes constantly move involuntarily (Rowe et al., 2008).

1.3.3 Visual field defects

Visual field defects are very common after stroke and around half of post-stroke individuals experience some form (Rowe et al., 2008). Most of the post-stroke individuals (26.5%) have monocular visual field defects, 11.5% experiencing binocular visual field defects (Siong et al., 2014). Around twenty percent of people with field defects following stroke have right side visual field defects and 22.6% have left side visual field defects (Siong et al., 2014). 29.4% of individuals with stroke have complete homonymous hemianopia. The remainder experience other types of visual field impairment such as partial homonymous hemianopia or superior or inferior quadrantanopia (Rowe et al., 2008). People with visual field loss are at a higher risk of falls (Rowe et al., 2008).

1.3.4 Perceptual changes

1.3.4.1 Visual neglect

Visual field defects can be a part of the changes in general and may occur in addition to visual attention changes such as unilateral spatial inattention or visual neglect (Kapoor et al., 2001; Rowe et al., 2008; Suchoff & Ciuffreda, 2004). Visual neglect is a neurological disorder change after a unilateral brain lesion and results in visual attention loss on one side of visual space and it is the most common perceptual change post-stroke (Chokron & Imbert, 1995; Heilman, Bowers, & Watson, 1983; Keane, Turner, Sherrington, & Beard, 2006; Rowe et al., 2008; Suchoff & Ciuffreda, 2004). Visual neglect is also called hemi-spatial neglect, which is the failure to perceive objects on the contralesional side that is caused by the decrease of attention or awareness for sensation or action on the left side of the space (Keane et al., 2006; Suchoff & Ciuffreda, 2004). The prevalence of visual neglect among post-stroke patients has a very wide estimate, depending on the varied methods to determine its presence (Suchoff & Ciuffreda, 2004). Visual neglect usually presents in about 50%-80% of stroke individuals (Keane et al., 2006; F. Rowe et al., 2008; Suchoff & Ciuffreda, 2004). Usually visual neglect results from right hemisphere stroke following right partial lobe damage of the brain and results in left neglect (Keane et al., 2006; F. Rowe et al., 2008; Suchoff & Ciuffreda, 2004). This area of the brain controls cognitive functioning for both personal and peri-personal spaces (body and within arm's length) and extra-personal space (outside arm's length) (Suchoff & Ciuffreda, 2004). Individuals with visual neglect might miss the food on half of their plates or miss half of their faces while grooming or shaving as a result of unawareness on that side. Since it is typically as a result of right parietal damage, usually it is left neglect (Suchoff & Ciuffreda, 2004).

There are various explanations of neglect in terms of the patient's reactions and functions. When there is a lesion in the brain for motor control of the left leg which happens after a right parietal lobe defect, there might be different responses from the patient (Suchoff & Ciuffreda, 2004). The first one is when the patient is asked to move his/her leg on the side of the defective pathway, and they answer that they cannot. In this case there is a basic neurological disorder and they are aware of the defect. However, in a second case, the patient is asked to move her/his leg, and they answer that they did when in fact they did not. In this second situation, there is a basic neurological disorder as well but they are unaware of it and so there is neglect in the presence of the basic neurological disorder (Suchoff & Ciuffreda, 2004). There is one other situation which is when the patient has no lesion in the motor pathway, is asked to move her/his leg and answers that they did while there is no movement. In this case, neglect is present, but there is no motor defect related to the neglect (Suchoff & Ciuffreda, 2004).

Post-stroke individuals can have both visual neglect and visual field loss (F. Rowe et al., 2008). There are various situations related to behaviors with visual neglect and visual field defect (Suchoff & Ciuffreda, 2004). Those with solely a visual field deficit are aware of the defect. On the other hand, the absence is visual neglect or in-attention behaviors such as rejecting objects on the affected space without noticing (Rossetti et al., 1998). The situation when a patient cannot see in one side of their visual field can be due to one of two situations: visual neglect or visual field defect (hemianopia). The differences between these two situations can be seen in Table 1. Firstly, there is a difference in the pathway that is affected. In hemianopia it is usually the primary visual pathway leading to the occipital lobe. In visual neglect it is the secondary feedforward dorsal visual pathway through the parietal lobe that is disrupted. A visual field defect is a sensory dysfunction whereas visual inattention is a perceptual dysfunction. For instance, if there is visual neglect, the patient will have a sense of an object being present but without fully perceiving it (Figure 1.1). One major difference between a visual field defect and visual neglect is the difficulty of rehabilitation in the case of visual neglect. This is because the patient is unaware of it. However, in the case of a visual field defect, the patient is aware of the loss, and so is more able to compensate (Suchoff & Ciuffreda, 2004).

There are different types of neglect which are relative to the person's space. These are egocentric neglect and allocentric neglect (Gallagher, Wilkinson, & Sakel, 2013). Individuals with egocentric neglect ignore objects coming from the contralesional side of the person's space or body, whereas individuals with allocentric neglect ignore the contralesional side of each object (Gallagher et al., 2013).

Visual neglect can occur in different personal spaces. Personal space refers to neglect of body parts, peri-personal space is within arm's length, and extra-personal space neglect is beyond arm's length (Gallagher et al., 2013; Ting et al., 2011).

Visual neglect can be assessed by different methods such as Behavioural Inattention Test (BIT) which contains six visual neglect tests; star/bell cancellation, letter cancellation, line crossing, line bisection, free drawing and shape copying tasks (Gallagher et al., 2013). In the first task, patients are required to cross out the presented target symbols. In the line bisection, patients are required to make a cross in the middle of a horizontal line (Gallagher et al., 2013). If a patient does have a visual neglect, the side of the visual neglect will be missing for the cancelation tasks and for the line bisection, the line that the patient draws would not cross the original line in the centre. For the last two tasks, patients are required to draw a simple figure such as a clock face or a flower and people with visual neglect are more likely to miss the side of the shape on their contralesional side (Gallagher et al., 2013).

Table 1.1 Differences between visual field defect and visual neglect (Suchoff & Ciuffreda, 2004).

Visual field defect	Visual neglect
Primary visual pathway damage	Dorsal visual pathway damage
Sensory dysfunction	Perceptual dysfunction
Patient is aware	Patient is unaware

1.3.4.2 Extinction

Extinction is a phenomenon in which the person will detect something in the affected hemifield when a stimulus is presented alone, but not when presented simultaneously with a stimulus in the other hemifield (Suchoff & Ciuffreda, 2004; Vossel et al., 2011). Extinction can be measured by asking the individual to be simultaneously aware about stimuli being presented to both the affected side and the normal side of the visual extra personal space (Suchoff & Ciuffreda, 2004). Usually the person would be unaware of the stimulus on the contralesional side when another stimulus is presented simultaneously on the other side (Suchoff & Ciuffreda, 2004).

Extinction is different from neglect as neglect is the absence of the attention to a stimulus in one side of the contralesional space of visual field but both are related and extinction is sometimes considered as a resolving form of visual neglect (Vossel et al., 2011).

1.3.4.3 Visual Midline Shift Syndrome (VMSS)

1.3.4.3.1 Definition and pathophysiological theories

The definition of the individuals' visual midline is the point which the individual perceives as being straight-ahead or "in front of their nose". After a stroke, some individuals experience a shift in their midline which develops after a few weeks. It can be shifted laterally or vertically so that a target will be perceived as straight-ahead when, for example, presented in front of the left eye rather than the centre of the nose (Padula et al., 2009; Rossetti et al., 1998). The prevalence of the visual midline shift following stroke has been not fully determined (Padula et al., 2009; Rossetti et al., 1998). There is much uncertainty regarding midline shifts, but the existing literature agrees that the altered individual's perceived midline can be a consequence of stroke that affects a specific area of the visual pathway (Houston, 2010; Kapoor et al., 2001).

An altered midline point is also called an abnormal egocentric localization (Padula et al., 2009). Authors in the (neuro) psychological field typically refer to it as an alteration in the subjective straight-ahead.

Visual Midline Shift Syndrome (VMSS) is a condition in which there is a perceived midline shift resulting from stroke which is associated with a body lean towards one side or the other. One theory regarding VMSS is that a stroke may affect a specific area of the visual pathway which is the right partial lobe of the brain (Houston, 2010). The visual pathway has two main types of fibres: one is for detailed information carried by the parvocellular retinal ganglion cells which are related to slow processing. The second type is carried by the magnocellular retinal ganglion cells, conducts shape information, relates to fast processing and is related to visual attention. The primary visual pathway is known as the retinocalcarine pathway. Here information from the retina travels along the optic nerve, through the optic chiasm and then through the lateral geniculate nucleus passing to the primary visual cortex at the occipital lobe. After this stage, information from the magnocellular cells synapse and run dorsally to the posterior parietal cortex and information from the parvocellular cells travel ventrally to the inferotemporal cortex. Damage in the right inferior or posterior lobes may result in visual neglect otherwise known as visual unilateral spatial inattention of the individual's left space (Gallagher et al., 2013). Neglect of one hemisphere results in a readjustment of the visual midline or 'subjective straight-ahead position. This may be explained as visual midline shift or abnormal egocentric localization as some researchers have named it. Therefore, according to this theory, an altered visual midline occurs as a result of visual neglect.

Padula et al. (2009) discussed the pathophysiological changes causing VMSS as resulting from a lack of information provided to the retinotectal pathway following other dysfunctions post stroke. The retinotectal pathway travels from the retina through the superior colliculus to the pulvinar nucleus in the midbrain (Padula et al., 2009). It is largely represented by information from magnocellular cells. Moreover, information that travels though this pathway combines with information from different systems such as the vestibular, proprioceptive, and kinesthetic which is responsible for the individual's awareness of self-space. Disruption of information being received from half of the body due to hemiparesis/plegia causes the brain to attempt to re-create a balance which creates a midline shift that can be defined as the VMSS. According to Padula, initially, there is a postural lean or imbalance that develops to one side. The direction of the lean seems to start off towards the contralesional side (same side as the side of body that is affected), but after a few weeks the lean can change to the other side (ipsilesional), which may be associated with the development of the shift in the perceived midline. This is not true for Pusher's syndrome which is a rare clinical disorder leading the patient to lean/"push" themselves towards the contralesional side (the hemiparetic side of the body) creating loss of posture and an imbalance. It is called Pusher's syndrome because if a therapist tries to correct their lean, they will resist this correction, pushing against the therapist (Karnath et al., 2003).

1.3.4.3.2 Assessment

There are several methods for measuring the midline shift following stroke found most often in the psychological and neuropsychological literature. A shift in midline is referred to as an altered subjective straight-ahead position. It is traditionally assessed by asking the patient to point to a position that they feel is straight-ahead while being blind folded (Chokron & Imbert, 1995; Heilman et al., 1983; Houston, 2010; Keane et al., 2006). Others started completing this task with eyes open. Houston attempted to clarify the differences by describing them in terms of the head centred reference frame. These frames are identified as a visual eye-head egocentric midline, a proprioceptive hand-head egocentric midline, and visual open loop pointing (Houston, 2010). The visual eye-head frame is measured by having the subject respond when they perceive a slowly moving target from the right and left side, as centered (Rossetti et al., 1998). This is the form of measurement of visual midline shift considered clinically. The proprioceptive hand-head frame which is essentially the subjective straight-ahead measure. The visual open loop procedure is when the patient is asked to point a target while their hand is hidden under a shelf. An alternative method is to ask the subject to look into a stereoscope and draw a line simultaneously with each hand until the pencil points touch (Houston, 2010; Rossetti et al., 1998).

A method mentioned by Kapoor is to measure the visual midline using a laser pointer target moving slowly in front of the participant while the participant looks through googles. The participant views through a mirror in front of their eyes but does not see the laser pointer. They respond with a hand-held clicker when this laser light is aligned with their midline. The participants were instructed to either look straight and not following the target or the true midline position was first demonstrated to the participant prior to the test (Kapoor et al., 2001).

Kuhn et al explained another method to measure the visual midline shift by using a small red spot presented in a perimeter in different quadrants right, left, up and down and asking the subject to verbally adjust the position of the red spot until it aligned centered to the subjective straight-ahead position/visual midline (Kuhn, Heywood, & Kerkhoff, 2010).

Clinically, Padula recommends that the assessment of the visual midline is undertaken manually. This is done using a "wand" or a hand-held target moved laterally and vertically in front of the affected space of the individual to find the subjective midline point. Padula used a 3 cm wand at a 45 cm distance, and a speed of 5.1 degrees per second for the wand movement. He did not specify the target size (Padula et al., 2009).

Currently, there is no validated clinical method of measuring the mid-line. There is no validated speed of the movement, control of the background, or the size and distance of the target.

1.3.4.3.3 Treatment

Yoked prisms have been demonstrated to be beneficial to treat the perception of the midline shift and correct the lean or postural imbalance (Padula et al., 2009). Much uncertainty regarding this management exists which extends to the underlying mechanism of action. Although yoked prisms have been suggested as a treatment for this misalignment, no clear guidelines exist regarding the duration of wear or amount of prism (Bansal, Han, & Ciuffreda, 2014; Facchin, Beschin, & Daini, 2015; Kapoor et al., 2001). Some have recommended the prescription of prisms in the glasses i.e. extended wear (Bansal et al., 2014) while others recommended prism adaptation (Facchin et al., 2015) as a vision therapy.

Rossetti et al (1998) described a treatment for VMSS with yoked prisms, described as prism adaptation. But some authors argued about its outcomes in terms of the long- and short-term effectiveness. Prism adaptation helped to correct the subjective straight-ahead position which in turn was shown to minimize signs of neglect. The effect of prism adaptation depends on the period of time that patient wear the prismatic glasses and they should do reaching tasks while they wear them (Chokron & Imbert, 1995; Keane et al., 2006; Rossetti et al., 1998). This method of adaptation has been reported to give a successful correction of the perceived midline but there is disagreement regarding how long the effect lasts, reported between a few hours, weeks, months to years depending on the amount of the prism applied, duration each day, and the period of time the prisms have been used (Farnè et al., 2002; Keane et al., 2006; Luaute et al., 2006; Rossetti et al., 1998; Serino et al., 2009). Visual neglect was decreased and VMSS was aligned after the prism adaptation experiment (Keane et al., 2006). The prism adaptation experiment compared individuals with normal vision and individuals with VMSS in order to find the differences in the adaptation between each group. The perceived midline of both the control group and those with neglect and abnormal subjective straight-ahead was shifted to the left after adaptation with a prism base left. However, for those with a subjective straight-ahead already shifted to the right, this resulted in their subjective straight-ahead being more correct (Houston, 2010; Rossetti et al., 1998). The control group quickly adjusted their midline while those with neglect maintained this new position for hours.

Alternatively, prescribed yoked prisms have been suggested as a treatment for VMSS, although, no duration of time for treating the VMSS is currently suggested (Bansal et al.,

2014) and (Facchin et al., 2015). Both ways of using prisms have changed the vision midline, balance, and reading activities (Bansal et al., 2014; Facchin et al., 2015).

It can be seen that there is very little and insufficient evidence regarding our understanding of this condition as well as the accurate assessments and treatment modalities for VMSS (Bansal et al., 2014; Facchin et al., 2015).

Chapter 2- Purpose and Research Questions

The definition of an individual's visual midline is the point which the individual perceives as being straight-ahead or "in front of their nose". After a stroke, some individuals experience a shift in their midline. It can be shifted laterally or vertically so that a target will be perceived as straight-ahead when, for example, presented in front of the left eye rather than the centre of the nose (Padula et al., 2009; Rossetti et al., 1998).

There has been little research published for this condition of visual midline shift so there are many questions to be answered in terms of the definition, causes, and treatments. There are some case reports and research studies about the visual consequences of VMSS but there are few high-quality research studies yet. There is very little and insufficient evidence about prevalence, prognosis, associations, accurate assessments and treatment modalities regarding VMSS.

The midline shift gauge has received a safety report for use with humans. A scale in cms is hidden from the participants and there is an automated moving target under motor control. The position of the target can be read off the scale. The target can be changed and the speed is variable. A table with head and chin rest is used to align participants with the center of the scale and there is a buzzer that allows the participant to indicate when the movable target is positioned at their perceived midline. When the buzzer is pressed the target stops moving and its position can be read off the scale by the experimenter.

This thesis is separated into two different studies or experiments each with a different purpose. The first study will standardize the parameters of the VMSS gauge such as the size, distance, and speed in healthy participants with unimpaired vision and no history of stroke. This will result in the development of an accurate assessment tool with specific parameters.

This study will also provide normal data against which the midline of post-stroke patients can be compared.

The research questions of the first study are:

1) What are the parameters of an assessment instrument that can reliably measure the midline shift?
2) What is the normal range of the position of the perceived midline in healthy adults?

The second study will use the device to help determine the percent of stroke survivors who experience VMSS, and to study whether it always follows stroke (prevalence), and which parts are of the brain are typically affected when it occurs. The second study is a cross-sectional study and the purpose is to gain a better understand of VMSS. The research questions of the second study are:

1) What is the prevalence of visual midline shift among individuals who have experienced a stroke?

2) Is there a consistent side of the brain that is damaged or certain type of stroke that results in this condition?

3) Are there associations between the perceived visual midline, handedness, neglect, open-looped pointing and the subjective straight-ahead position?

4) Are there any differences in the visual midline shift for post-stroke and a comparison group of non-stroke individuals who have similar general and ocular health except for the stroke experience?

Validation of a Visual Midline Shift Gauge

Ohwod Binhilabi
Susan Leat
Tammy Labreche

In preparation for submission to Ophthalmic and Physiological Optics

Key words: visual midline shift syndrome, VMSS, stroke, cerebral vascular accident, cerebral vascular incident

Authors' Contributions (please check relevant boxes for each author):

Author	Concept/Design	Data Collection	Data Analysis	Article Writing	Article Editing
Ohwod Binhilabi	√	√	√	√	√
Tammy Labreche	√				√
Susan Leat	√		√		√

The candidate certifies that:

- The above statement correctly reflects the nature and extent of the candidate's contributions to this work, and the nature of the contribution of each of the co-authors; and
- The candidate wrote all or majority of the text.

Please insert this form directly after the title page of your thesis.

Chapter 3- Validation of a Visual Midline Shift Gauge

3.1 Introduction

Cerebrovascular disease is the sixth most common global cause of chronic disability (Ezejimofor et al., 2016, Akbarkhodjaeva & Tursunov, 2017). According to the Heart and Stroke Foundation, 2017 (Heart and Stroke Foundation of Canada, 2018), the number of the cerebrovascular accidents (CVAs or stroke) in Canada has increased and this is also the case in the UK (Rothwell et al., 2004) US (Fang et al., 2014; Gresham et al., 1997), developing countries (Benamer & Grosset, 2009) and worldwide (Akbarkhodjaeva & Tursunov, 2017; Ezejimofor et al., 2016). The incidence of stroke increased by 74% from 1981 to 2004 in the UK for people older than 75 years old (Rothwell et al., 2004). Between 550,000 to 795,000 people experience a stroke each year in the United States (Fang et al., 2014; Gresham et al., 1997), and around 400,000 Canadians are living with post-stroke disabilities (Heart and Stroke Foundation of Canada, 2018). In the United States, 70% of stroke survivors receive rehabilitation services through either hospital-based inpatient, nursing, or home rehabilitation care outpatient facilities (Gresham et al., 1997). Approximately 10% of individuals are admitted to a long-term care facility after a stroke and only a few recover completely (Heart and Stroke Foundation of Canada, *2018*; Foulkes et al., 1988; Goldstein et al., 2001; Miller et al., 2010). Additionally, it is estimated that all stroke survivors have some degree of visual disorder, 60% having minor visual impairment and 40% surviving with moderate to severe impairments (Heart and Stroke Foundation of Canada, *2018*; Goldstein et al., 2001; Miller et al., 2010).

Within the optometric profession, there is an increased interest in neuro-optometric rehabilitation to enhance the individual's independence, function, safety, health, and optimised aging following a neurological event. After a CVA, individuals may have a wide range of visual sequelae, including impaired visual acuity, binocular vision disorders, visual field deficits, and visual perceptual difficulties (Kapoor et al., 2001; Rowe et al., 2008). Up to 70% of stroke patients report visual field defects (Miller et al., 2010). Low visual acuity post-stroke (less than 6/18 best corrected) was documented in 13% of individuals for both near and distance vision (Rowe et al., 2008). Ocular motility defects are present in 68.4% of individuals with stroke (Rowe et al., 2008). Perceptual changes include visual neglect or unilateral spatial inattention, extinction and visual midline shift.

Visual neglect is a neurological disorder which occurs after a unilateral brain lesion and can result in a visual attention loss on one side of visual space (Chokron & Imbert, 1995; Heilman et al., 1983; Keane et al., 2006; Suchoff & Ciuffreda, 2004). Visual neglect is the most common perceptual change post-stroke (Rowe et al., 2008). Extinction is a phenomenon in which the person will detect something in the affected hemifield when a stimulus is presented alone, but not when presented simultaneously with a stimulus in the other hemifield (Suchoff & Ciuffreda, 2004). Abnormal egocentric localization or visual midline shift syndrome (VMSS) (Goldstein et al., 2001; Miller et al., 2010; Padula et al., 2009) is a condition in which individual experiences a shift in their visual midline, defined as the point which the individual perceives as being straight-ahead or "in front of their nose". It can be shifted vertically or laterally so that a target will be perceived as straight-ahead when, for example, it is presented in front of the left eye rather than the centre of the nose (Padula et al., 2009; Rossetti et al., 1998). The prevalence of the visual midline shift following CVA has been not fully determined. Visual midline shift is thought to be followed by postural changes and subsequent issues with balance and safety (Heart and Stroke Foundation of Canada, *2018*; Goldstein et al., 2001; Kapoor et al., 2001; Miller et al., 2010; Padula et al., 2009).

The pathophysiology of visual midline shift is uncertain. It has been proposed that a CVA may affect a specific area of the feed-forward dorsal visual pathway within the right inferior or posterior parietal lobe of the brain (Houston, 2010) resulting in visual neglect. Neglect of one hemisphere may result in a readjustment of visual midline (Houston, 2010; Padula et al., 2009). Since visual neglect can occur in different distances from the individual (different personal spaces) (Gallagher et al., 2013; Ting et al., 2011), visual midline shift might also vary according to distance. Padula et al. (2009) proposed that as a result of hemianopia following a CVA, VMSS develops as a result of lack of information to the retinotectal pathway (Padula et al., 2009). This visual pathway travels from the retina through the superior colliculus to the pulvinar nucleus in the midbrain instead of the lateral geniculate nucleus and the primary visual cortex (Padula et al., 2009). Information that travels though this pathway combines with information from different systems such as the vestibular, proprioceptive, and kinesthetic which are responsible for the individual's awareness of self-space. Therefore, lack of information provided to that pathway causes the brain to attempt to re-create a balance which results in a postural lean away from the affected visual space disturbing posture and balance (Padula et al., 2009).

Possible treatments and rehabilitation have been suggested for patients with VMSS to correct posture and balance, improve quality of life following a stroke and possibly decrease the incidence of falls (Bansal et al., 2014; Facchin et al., 2015; Kapoor et al., 2001). Yoked prisms have been suggested, although, no clear guidelines exist regarding duration of wear or amount of prism (Bansal et al., 2014; Facchin et al., 2015).

There has been little research published regarding this condition, leaving many questions to be answered in terms of the epidemiology, pathophysiology, and evidence-based treatment modalities and this contrasts with the on-going and considerable research into visual neglect which may accompany VMSS. There is also insufficient evidence regarding accurate assessment, which is necessary for any study protocol or clinical management.

At present there is no validated clinical method of measuring the visual midline for the optometric assessment and there is discrepancy in the terminology used. Clinically, the visual midline is currently measured manually. The patient is asked to visually track a "wand" or a hand-held target moved laterally or vertically in front of the affected space of the individual to find the subjective visual midline point. Padula et al (Padula et al., 2009) presented a 30 cm sized target against a blank wall at approximately 45 cm from the patient. The speed of the target was 5.1 degrees per second. He did not explain his rationale for choosing these parameters (Padula et al., 2009). Houston (Houston, 2010) called the visual midline the visual eye-head egocentric midline and measured it in a similar way except that a laser pointer was used as a stimulus. Kapoor et al also used a laser pointer, but this was viewed through a mirror, the participant's midline was measured after demonstrating the position of the true midline and participants were asked to maintain their fixation straight-ahead i.e. not tracking the target (Kapoor et al., 2001). Kuhn et al (Kuhn et al., 2010) describe a method to measure the visual midline in which a small red spot is presented in a perimeter and a method of adjustment is used whereby the subject asks for the target to be moved until it aligns with their midline, which they called the visual subjective straight-ahead position (Kuhn et al., 2010).

Houston (Houston, 2010) described two other types of perceptual misalignment, the proprioceptive hand-head egocentric midline (which he also called the subjective straight-ahead) and visual open loop pointing (Houston, 2010). The proprioceptive hand-head egocentric was measured by asking the participant to point to the straight position while being blindfolded (Foulkes et al., 1988; Goldstein et al., 2001; Houston, 2010; Miller et al., 2010). The visual open loop position was measured when the subject is asked to point to a target without being able to visualise their hand (Houston, 2010; Rossetti et al., 1998).

The purpose of this study is to standardize the parameters of a midline shift gauge using participants with unimpaired vision and no history of stroke. The gauge was based on the measure of midline shift, as described by Padula and as has become accepted clinically. This information will be used to develop an accurate assessment tool to be used with post-stroke patients and to gather normal data against which the midline of post-CVA patients can be compared.

3.2 Methods

A Midline Gauge was created, which consists of a metal bar against a solid black background. The bar and the background are both the same black colour. A removable white sphere of three sizes, small (4 mm), medium (7 mm), and large (13 mm) is situated just behind the bar and can be moved with different speeds of either 1.15 or 2.3 degrees per second. The target moves mechanically, so as to control the speed. The participant is seated so that their eyes are level with the target (Figure 1). A headrest is used so as to control head position as well as target distance. The participant responds with a buzzer when the target is aligned with their visual midline, which causes the target to stop. The bar has a numbered scale in centimetres which is not visible to the participant.

This study received clearance through a University of Waterloo Research Ethics Committee and adheres to the principles of the Declaration of Helsinki. Twenty-four control participants were recruited, in each of two age groups. Below 65 years old there were 8 female and 4 males with age ranging between 20-35, mean =25.6, SD=3.34) and ≥65 years there were 7 females and 5 males with age ranging between 65-85, mean =75.2, SD=6.40) They were recruited from among the University of Waterloo School of Optometry and Vision Sciences graduate students, staff, faculty and their families as well as Optometry Clinics. Snowball recruiting was also used. When estimating the parameters of the midline gauge and to establish normal data, we used inclusion and exclusion criteria to include only healthy older individuals with no significant eye disorders that might influence the position of the midline so that we could assume that there was no midline shift. The younger group was included as a comparison with the older group. Inclusion criteria were; either gender, no significant previous ocular or health history, 6/7.5 visual acuity or better in each eye, no more than one-line intra-ocular difference in visual acuity and no strabismus. Participants were excluded if they had neurological disorders, such as Parkinson's, multiple sclerosis, cerebellar dysfunction, vestibular dysfunction, cerebral palsy, dizziness/vertigo, a diagnosis of dementia or cognitive impairment, previous history of stroke or any medication that would affect balance.

Participants were screened for visual acuity using two different ETDRS charts (one for each eye), visual field loss by confrontation and ocular alignment with the unilateral cover test. Ocular history, medical history and any medications the person was taking was recorded. They were also asked about their handedness (right, left or ambidextrous). The visual midline testing required attendance for two sessions.

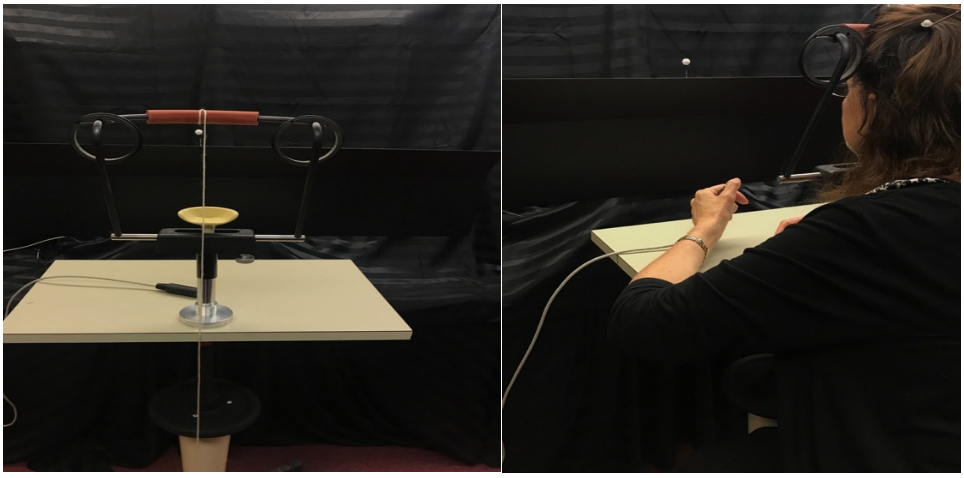

Figure 3.1 Post stoke visual midline gauge, head chin table, buzzer and numbered scale showing the target.

Session 1: The participant was seated with their head position controlled with a head and chin rest. They were positioned so as to be centred in line with the '0' midpoint on the device. The room lights were fully on. The participant was instructed to follow the target with their eyes and push the buzzer when the target was in line with the tip of their nose. The participants were allowed to visually track the target. In the first session, the horizontal midline was measured varying the target size (small, medium, and large) and speed (1.15 or 2.3 degrees per second) at a 50 cm test distance. The parameters were varied in a counter-balanced order between participants to control for fatigue and practice effects.

The target was placed in a position removed from the participant's anticipated midline on alternating sides (left or right) and moved towards the expected midline position Participants were allowed to ask the experimenter to repeat or adjust the measurement if they did not believe it was in line with their midline. The measurements were repeated five times from each direction. The results of the first session were analysed to decide on the optimum speed and size for use in the second session.

In the second session, VMSS testing was conducted with the target size and speed that were determined from the first session. The target size and speed were constant (1.3 cms diameter white sphere moving at 2.3 degrees per second. In this session, the vertical and horizontal midline was measured at different distances (0.25, 0.50, and 100 cm). Once again, the parameters were varied in a counter-balanced order and five measurements were taken from left, right, up and down starting points. The first two readings from each direction for each direction and distance were taken to develop the normal data for use in clinical settings and then three more readings were taken from each starting position.

3.3 Analysis

In session 1, mixed ANOVA was used to test the effect of age group, size and speed on the horizontal midline position and on the variability of the position (as measured by the standard deviations). Another repeated measure ANOVA for the midline position was done to determine whether any effect of the side from which the target approached. In session 2, mixed ANOVA was used to determine the effect age and distance on the horizontal and vertical midline measures.

A one-sample t-test for each individual was used to check our assumption that these normal observers do not have a significant midline shift, i.e. whether their perceived midline was significantly different from zero. Since many t-tests were undertaken (for each distance, vertical and horizontal, a Bonferroni correction was used and the usual p value of 0.05 was changed to less than $0.05/n = 0.00035$ for significance. A one sample t-test for each distance for horizontal and vertical measures for each age group collectively to determine if the average position of the midline was centred on zero. ($p<0.05$).

A two-sample t-test was used to determine if there was any difference in the midline position based on handedness. Normal data were calculated as the mean and 1.96 x SD (95% range). A p value of 0.05 was used for significance and Systat10 software and Excel Microsoft office were used to analyze the data.

3.4 Results

<u>3.4.1 Session 1</u>

For the first session, mixed ANOVA (2 age groups x 2 speeds x 3 target sizes) for the perceived position of the midline showed no main effect of age group, speed or target size, no two-way interactions ($p>0.05$) and no higher order three-way interaction (Figure 3 & 4). For the variability of the perceived position of the midline (standard deviation), mixed ANOVA (2 groups x 2 speeds x 3 target sizes) showed no main effect of age, speed or target size and no interactions ($p>0.05$).

There was no significant difference in the measured position of the midline whether the target approached from the left or the right with different target sizes and speeds (repeated ANOVA, $p>0.05$). Since there was no effect of speed or size, one speed (2.3 degrees per second) and target size (1.3 cms diameter white sphere) were chosen for the second session, and for calculating the mean and 95% range of normal.

Since there was no significant difference of speed and target size for both age groups, a one sample t-test for the average across all observers was undertaken to measure if the perceived midline differs from zero for all of the participants and this was not significant ($p=0.120$).

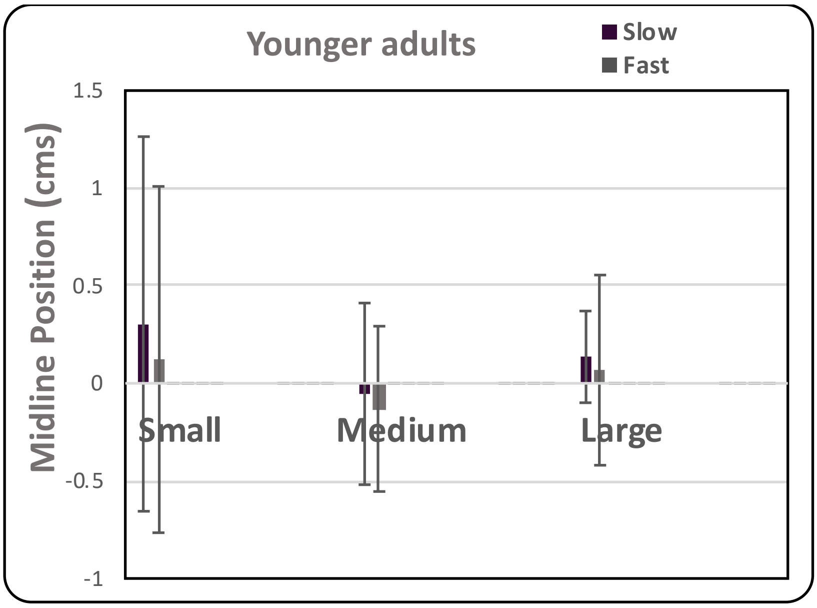

Figure 3.2A. Midline positions for 20-35-year-olds for three target sizes and two speeds at 50 cm distance.

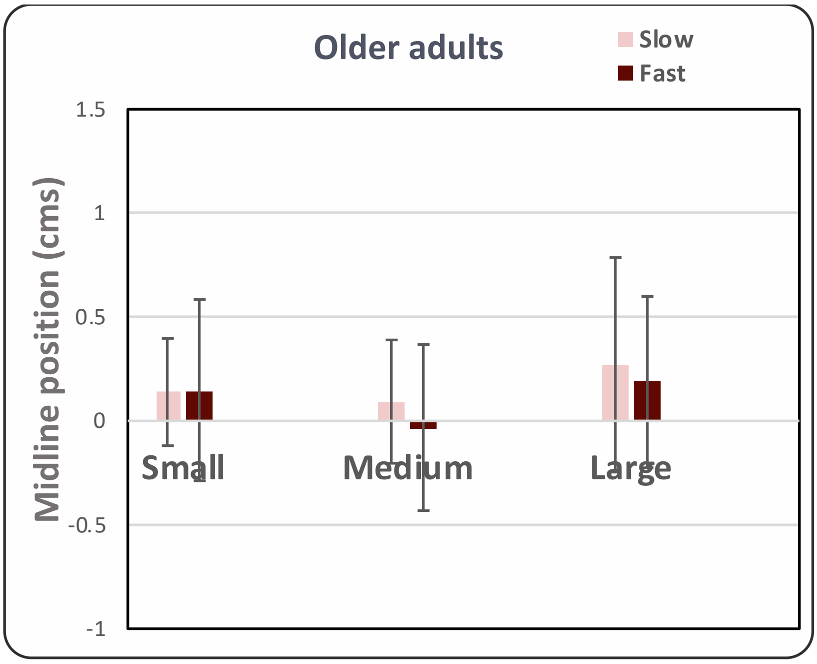

Figure 3.2B. Midline positions for the over 65+ year-old group for three target sizes and two speeds at 50 cm distance.

3.4.2 Session 2

Mixed ANOVAs for the horizontal and vertical midline position for age and distance (2x age, 3x distance) showed no significant effect of age or distance and no interaction ($p>0.05$). For the horizontal variability, there was an effect of distance ($p=0.013$) but not of age. For the vertical midline variability, there was an effect of both age ($p= 0.025$) and distance ($p=0.003$).

A one-sample t-test for all participants for their average midline position compared to zero showed that there was no significant difference from zero of the vertical midline ($p=0.933$) There was a significant difference from zero for the horizontal midline (midline = 0.14, $p=0.028$) but this did not remain significant after Bonferroni correction.

Handedness had no significant impact on the midline position for any distance (2 sample t-test, $p>0.05$) for the older age group. This could not be analysed for the younger participants as they were all right handed.

Our original assumption was that these healthy individuals would not have a significant mid-line shift. The one-sample t-test compared with zero for the position of the midline (with Bonferroni correction) showed that only one younger participant showed a statistically significant downwards vertical midline shift at the 100 cms distance. This person's midline for this position was -1.32, p=0.00003. So, our hypothesis that these healthy individuals do not have a significant midline shift was correct for the majority of individuals and measurements.

Since there was an effect of distance, normal data were calculated for each distance separately. Furthermore, since there was no effect of age for the horizontal measurements, the data were amalgamated for the two age groups (Table 1). As there was an effect of age for the vertical midline, normal data were calculated for each age separately (Table 2). Means and the 95% range of normal (1.96 x SD) are shown in Table 1 and 2.

Table 3.1 Normal data for both age groups at each distance for the horizontal midline position in centimeters and prism diopters.

	25cm	50cm	100cm
Mean(cm)	0.01	0.31	0.10
95% range	0.60 (2.4pd) to -0.57 (-2.26pd)	0.98 (1.96pd) to -0.37 (-0.74pd)	1.56 (1.56pd) to -1.35 (-1.35pd)

Table 3.2 Normal data for each age group at each distance for the vertical midline position in centimeters and prism diopters.

20-35 years old			
Distance	25cm	50cm	100cm
Mean(cm)	-0.15	-0.15	0.001
95% range	1.11(4.44pd) to -1.42(-5.68pd)	0.97(1.94pd) to -1.26 (-2.52pd)	1.10 (1.1pd) to -1.09 (-1.09pd)
Over 65+ years old			
Distance	25cm	50cm	100cm
Mean(cm)	0.04	0.16	0.15
95% range	0.63(2.52pd) to -0.55 (-2.2pd)	0.86(1.72pd) to -0.54 (1.08pd)	1.22(1.22pd) to -0.91 (0.91pd)

3.5 Discussion

The purpose of the study was to develop and test a new device to measure the perceived visual midline shift in post-stroke patients. This study investigated the effect of parameters such as size, distance and speed of movement in individuals with normal vision. This study is important, as, although other authors have described various methods for measuring the midline, there are currently no studies of the parameters of the measurement or published normal data.

Padula (2009) used one target size (30 cm) and one speed (4 cm per second) at one distance (45 cm), but he did not explain the basis of choosing these parameters to measure the

VMSS. This paper focussed on how to choose the best prism correction for VMSS (Padula et al., 2009).

A method mentioned by Kapoor (Kapoor et al., 2001) to measure the visual midline uses a laser pointer target moving slowly in front of the participant while the participant looks through a goggle and sees a reflected mirror image in front of their eyes but not the laser pointer. They used a hand-held clicker whenever this laser point is aligned with their midline. Some of the participants were instructed to look straight and not to follow the target while the true subjective straight-ahead position was demonstrated to other participants prior to the test (Kapoor et al., 2001).

Houston (Houston, 2010) explained methods for measuring the visual eye-head egocentric midline, proprioceptive hand-head egocentric midline, and visual open loop pointing (Houston, 2010). The visual eye-head midline is measured by asking the subject to respond when a slowly moving target such as a laser pointer from the right and left side is perceived at the center (Houston, 2010). The proprioceptive hand-head egocentric midline is the subjective straight-ahead position described in psychological literature and is when the subject is asked to point to a target as being straight-ahead while blind folded (Chokron & Imbert, 1995; Heilman et al., 1983; Houston, 2010; Keane et al., 2006). The visual open loop is when the subject is asked to point to a target while their hand is hidden from their sight or by asking the subject to look into a stereoscope and draw a line simultaneously with each hand until the pencil points touch (Houston, 2010; Rossetti et al., 1998).

This description indicates that there are conflicting visual midline measures and often no information given regarding the choice of parameters. For the visual eye-head egocentric midline (Houston, 2010). Houston mentioned that some experimenters ask the participant to track the target with their eyes while others ask the participant to fixate straight-ahead

(Houston, 2010). In both cases, they respond by clicking a buzzer. Houston et al. did not give a specific method to rely on. However, we used his eye head egocentric midline method. For the proprioceptive hand-head egocentric midline or the visual subjective straight-ahead (Houston, 2010), Houston did not state the target size or distance from the target, although he did state that the room should be dark. Kuhn et al's (2010) method for measuring the visual midline shift involves a red spot presented in the perimeter in different quadrants right, left, up and down and asking the subject to verbally adjust the position of the red spot until it aligns with their subjective straight-ahead position (Kuhn et al., 2010).

In this study, we assumed that the optimum target parameters would be those that gave the least variability and the closest measure of the midline to the true straight-ahead position. It was assumed in this study that people with normal vision would not have a significant midline shift. In the first session, we found no significant difference effect of target speed and size. So, the largest target and the fastest speed were chosen based on clinical considerations. The larger target was chosen because it would allow measurement of the midline with people with poor visual acuity due to concurrent eye disorders or due to the stroke itself. The faster movement was chosen as it would make the testing more efficient in a clinical setting. This speed was slower than Padula's which was 5 degrees per second, but much faster than Kapoor's which was 0.5 degrees per second. In the second session, we measured the midline position at three different distances in order to see whether the midline changes in personal space, intrapersonal-space, and external space. This is important as one underlying pathophysiological theory is that an altered midline occurs as a result of neglect which may differently affect these spaces.

The second session showed some significant differences regarding age and distance. Therefore, the normal data is presented separated according to these. The differences were related to the variability between the measurements (SD) especially for the 50 cm distance.

One limitation is that this study did not include participants aged between 35-65 years old. This was because most people who experience a stroke are usually older than 65 years and a younger group was included as a comparison, to see the effect of age. However, some individuals of less than 65 years can experience a stroke. For the horizontal data, there was no effect of age, so we have presented normal data which is relevant for all ages (35 upwards). However, for the vertical measurements, there was an effect of age, so at present we cannot present normal data for patients aged 35-65.

In this type of study, there are a large number of parameters that can be tested. We did not test the impact of speed or target size for vertical midline position, and same target as was chosen for the horizontal measurements. In clinical practice, this is justified, as one would use the same target for all measurements.

Prisms are the suggested method to control and treat midline shift syndrome (Bansal et al., 2014; Padula et al., 2009; Rossetti et al., 1998). There are two approaches. Some have recommended the prescription of prisms in the glasses i.e. extended wear (Padula et al., 2009) and others have recommended prism adaptation (Facchin et al., 2015; Rossetti et al., 1998) while undergoing therapy as a management. In either case it would be expected that there should be some relationship between the degree of midline shift and the amount of prism used and so an accurate measure of the presence and degree of midline shift is desired, as can be provided by this gauge.

3.6 Conclusion

This is the first research study to attempt to standardize the assessment of midline shift. We have shown that the measurement of the perceived midline is relatively insensitive to the target size and speed within the range that we tested. This is also the first study to provide normal data, against which post-stroke patients can be compared.

Futures studies are indicated to use the midline gauge to determine the range of midline position in people without stroke, but who might have other ocular disorders, and to determine the prevalence and natural history of midline shift in the post-stroke population.

Chapter 4 - The Visual Midline Shift and its Associations in Post-stroke Patients and Controls

4.1 Introduction

The visual midline of an individual should be perceived in front of the tip of their nose with binocular viewing. However, after an acquired brain injury, such as a stroke, sometimes an altered concept of the midline occurs together with a lean to one side, which is referred to as the visual midline shift syndrome (VMSS). The individual's midline can be shifted laterally or vertically so, for instance, it might be perceived in front of the left eye rather than the centre of the nose.

Signs of VMSS include an altered posture which may lead to altered gait and balance resulting in a prolonged rehabilitation or a plateau in recovery, an increased risk of falling, and a reduction in quality of life (Padula et al., 2009; Shiraishi et al., 2010).

Although case reports exist in the literature, there are few research studies of the prevalence, recovery and treatment of this condition, leaving many questions unanswered. These include 1) Is there a consistent brain area or side of brain that is damaged and is it linked to a particular type of stroke (hemorrhagic or ischemic) that results in this condition? 2) How frequently does it occur and does VMSS naturally recover within the post-stroke period? 3) Does the visual midline change when measured at different distances from the patient i.e. at different personal spaces (personal space, peri- personal space, and extra-personal space). 4) Are there associations between the visual perceived midline, handedness, visual neglect, visual open-looped pointing and the subjective straight-ahead position? The proposed study is a cross sectional study with a longitudinal natural history component which attempts to answer some of these questions. The information will help inform next steps regarding treatment of VMSS. This preliminary study is the first study to quantify and describe visual midline shift in the post-stroke period. Visual midline results will be compared to the normal data presented in Chapter 3 obtained for healthy participants. Participants for the control population were chosen to have no significant eye disorders, systemic conditions or medications that might influence the position of the midline and/or affect balance (see Chapter 3). However, the data obtained may not be typical of the older population who are more likely to experience a stroke or its sequelae. In other words, there are other ocular and systemic conditions which may affect the midline. To address this variation, this study includes a comparison group who had not experienced a stroke, but who may have had a range of other conditions.

4.2 Methods

This was a cross sectional study of people who have experienced a stroke within the previous 2 years. The midline shift was measured together with other visual and perceptual measures. If a visual midline shift was determined, they were invited to attend at monthly intervals following the initial visit.

Post-stroke participants were included if they were: adult (>18 years of age) first time post-stroke patients within two years post-stroke, male or female, any type of stroke, any race. Participants were excluded if they were not English or Arabic speaking or had no translator available, had a diagnosis of dementia or other cognitive impairment, receptive aphasia, were physically unable to be positioned in the device or have any other neurological disorders (Parkinson's, multiple sclerosis (MS), cerebellar dysfunction, vestibular dysfunction, cerebral palsy (CP), dizziness/vertigo, concussion or previous head injury with residual symptoms.

The inclusion/exclusion criteria for the comparison group were the same, except for not having experienced a stroke.

Participants with a previous history of only one stroke within the previous 2 years were recruited from the Waterloo Optometry and Vision Science Clinic A telephone questionnaire was used to determine initial eligibility (see Appendix A). At the first visit a general health and history of stroke questionnaire was undertaken (see Appendix B). This included age, sex, handedness, ocular, medical and complete stroke history including the impact and sequelae of the stroke. Permission was obtained to retrieve information regarding the type of stroke from their family doctor or geriatrician.

Then the following clinical tests were done in order as follows (all were undertaken with the participant's habitual spectacle correction):

- MoCA-Blind assessment. This is a cognitive assessment test modified for those with visual impairment (Nasreddine, 2012). The MoCA is scored out of a potential maximum score of 30 while the MoCA-Blind is scored out of 22, as the first two subtests are not used, because they are visually-based. We used the adjustment for educational level, for which one point is added if the highest level of education was less than twelve years (Nasreddine et al., 2005).
- Visual neglect testing. The line bisection test (the participant makes a mark in the perceived centre of a horizontal line), and the Bell's test (the participant is asked to cross out all the bells (35) among other shapes arranged in a visually distracting array). The line bisection test results were calculated by observation of whether the drawn vertical line looked centred in the horizontal line. The scores were calculated as shifted to the right (positive shift), shifted to the left (negative shift) or centred (no neglect). The Bell's test results were calculated depending on how many bells were crossed out. For example, if three or more bells were not crossed out on one side, that was scored as positive for an attentional deficits i.e. left or right neglect (Gauthier, Dehaut, & Joanette, 1989)

- Extinction. This was measured by asking the participant to look at the examiner's nose and to identify how many fingers in total the examiner was holding up on both sides of their midline simultaneously.
- Distance visual acuity. Monocular and binocular visual acuity was tested with the ETDRS letter chart. A different chart was used for each eye and binocularly. The results were determined with by-letter scoring which is based on the number of correct letters read correctly (Hazel & Elliott, 2002). The results were recorded in LogMAR.

1. Visual field assessment. Arc perimetry was used wherein the participant was asked to view a centre target on the handheld arc perimeter and was be asked to state when they are first able to detect a target brought in from their peripheral vison. The test was done monocularly for both eyes with a 13 mm white target along the 45, 90, 135, 180 meridia.

- Unilateral cover test. The participant was asked to steadily look at a small light target set at 4m distance, while the experimenter covered each eye in turn with a paddle to check for strabismus.
- Binocular pointing ocular dominance. The participant was asked to point using both index fingers held together towards a cross in the center of a scale that was located in front of the participant (Dalton, Guillon, & Naroo, 2015). The scale was 200 cms away from the participant and was marked in prism dioptres. The participant pointed with both eyes open. Then the participant was asked where their fingers were aligned when the right and left eye was covered in turn. Each of these values was recorded (Dalton et al., 2015). Pointing to the left was considered a negative score and to the right was positive. The results from pointing with each eye covered were summed and

any score > 2 or <-2 was considered right or left eye dominant respectively (Dalton et al., 2015).

- Subjective straight-ahead. The participant was asked to close his/her eyes and point straight-ahead to a 13mm white target located on a table and centred at the centre of their body. The score was measured on a scale on the table (Figure 4.1) (Chokron & Imbert, 1995; Heilman et al., 1983; Houston, 2010; Keane et al., 2006).
- Visual open loop testing. The participant was asked to point straight-ahead to a 13mm white target located on a table centred at the midline of their body. They were asked to point with their eyes open but without being able to see their arm, which was positioned under a table and covered with a black sheet. The score was measured on a hidden scale at the back of the table (Figure 4.2) (Houston, 2010; Rossetti et al., 1998).
- Clinical perceived midline testing. The visual midline was assessed manually with the standard method of moving a wand in the horizontal or vertical plane. A 13 mm target was used at 50 cm distance moved at approximately 0.5 degree per second speed (Padula et al., 2009). The participant verbally indicated when it was in the straight-ahead position at which point the experimenter stopped moving the target. The experimenter then brought the target straight towards the participants face, and estimated whether it was centered or positioned more to the left or right eye. The position of the target from the nose was estimated in cms. Two readings from each direction for both horizontal and vertical midlines were taken.
- Perceived midline assessed with the midline gauge. The method is described in Chapter 3. Briefly, the target moved mechanically at 2.3 degree per second from one side or the other towards the participant's midline. S/he was asked to press a buzzer when the 13 mm size target appeared in line with their perceived midline (straight-

ahead position). The target distance varied (25, 50, 100 cms) as well as the orientation of travel (horizontally or vertically).

Lastly, a photograph of the participant in the seated position was taken and a video of their walking balance and posture for those participants capable of walking.

For line bisection, midline shift, subjective straight-ahead, visual open loop pointing and ocular dominance, a leftwards shift was counted as negative and a rightwards shift as positive. An upwards shift was positive and downwards was negative.

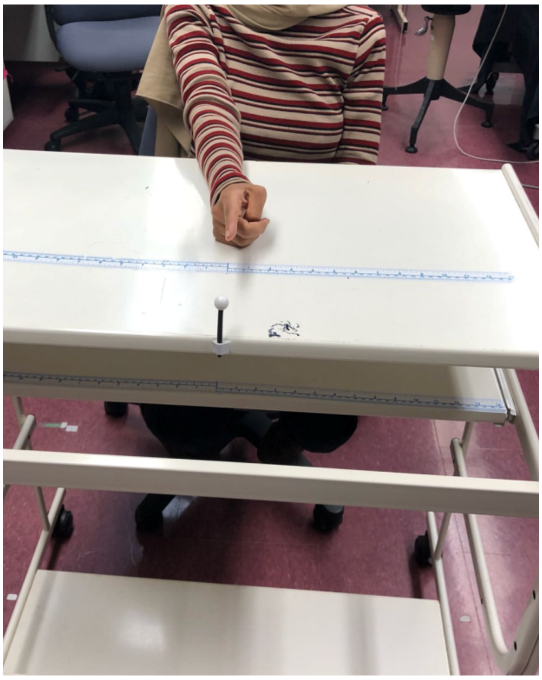

Figure 4.1 The subjective straight-ahead position test.

Figure 4.2 The visual open loop test.

4.3 Analysis

Descriptive analysis was used for this study to describe each of the measures recorded. Two–sample t-tests were used for numerical values to compare the two groups. 3x3 tables were created to consider the associations between variables.

4.4 Results

Fourteen participants were recruited into this study, nine non-stroke participants with ages that ranged between 23-80 years old and five post-stroke age ranging between 48-78 years old. A summary of the results is tabulated in Table 4.1.

For the post-stroke participants, three had ischemic and two had hemorrhagic type stroke. Three were right brain lesions and two were left brain lesions. The MoCA results for non-stroke participants ranged between 19- 22 with a mean of 20 and for the stroke participants it ranged between 12-19 with a mean of 16.8. A two-sample t-test for the MoCA scores between post-stroke and non-stroke participants shows that the non-stroke participants had a borderline higher MoCA score than the stroke participants (p=0.053).

The mean for the visual acuity for the non-stroke group was -0.033 for the right eye, -0.038 left eye, and -0.078 for both eyes while the for the stroke group these values were 0.35, 0.2, and 0.23LogMAR respectively. Two sample t-tests were done for the visual acuities between post-stroke and non-stroke groups and showed that there is a significant difference for the right eye (p= 0.009), but no significant difference between groups for the left eye or both eyes.

One person from each group had strabismus (one hypertropia from post-stroke group, and one esotropia from the non-stroke group). All the non-stroke group had a full visual field and none demonstrated extinction. In the post-stroke group, three individuals had a full field, one had right homonymous quadrantanopia and one had a partial left homonymous hemianopia. Two post-stroke participants had left extinction (one who had a left partial hemianopia and one with full visual field).

Table 4.1 A descriptive analysis of post-stroke and non-stroke participants.

Groups		Non-stroke (n=9)	Stroke (n=5)
Age		Mean = 49, Range 23-80	Mean = 65, Range 48-78
Type of stroke			3 ischemic, 2 hemorrhagic
Laterality of stroke			3 right side, 2 left side
MoCA-Blind		Mean = 20, Range 19-22	Mean = 16.8, range 12-19
LogMar	**OD**	-0.033	0.35
	OS	-0.038	0.2
	OU	-0.078	0.23
Strabismus		1 Esotropia, 8 non-strabismic	1 hypertropia, 4 non-strabismic
VF	**FULL**	9 full	3 full
	Defect	0	1 with R quadrantanopia, 1 partial left hemianopia
Ocular Dominance		4 left, 4 right, 1 equal	5 left dominant
Subjective Straight		4 left, 5 right	3 left, 2 right
Visual Open Loop		6 left, 3 right	2 left, 3 right
Midline Shift Wand	**Horizontal**	None	1 right, 2 left
	Vertical	None	1 up

Midline Shift (device)	**Within normal**	4	2
	Outside normal	5	3
Visual Neglect	**Bells**	Mean = 34.2, range = 32-35	Mean = 32.8, range= 30- 35
	Bisection	no neglect	4 centred and one towards the right
Handedness		9 right handed	3 right, 2 left handed
Extinction		None	2 left extinction (one with left partial hemianopia and one with full fields)

All of the non-stroke individuals were right handed while three post-stroke individuals were right handed and two were left handed. All of the post-stroke individuals were left dominant eye which is different from the non-stroke individuals among whom right or left eye dominance was split equally - four were left dominant, four were right dominant, and one was equi-dominant. For the subjective straight-ahead position, about equal numbers in both groups had a left or right subjective straight-ahead. For the visual open loop, more participants in the non-stroke group had a leftwards shift, while slightly more had a rightwards shift in the stroke group.

The visual midline shift with the clinical wand procedure showed that none of the non-stroke group had a horizontal shift, while 2 participants in the stroke group had a noticeable shift to the left and one to the right. For the vertical shift, only one in the stroke group had an upwards shift. With the mid-line shift gauge, 5 non-stroke individuals gave measurements of their perceived midline that were outside the normal range. Four had a horizontal shift at one distance or another, while 3 participants had a significant vertical shift. Two had both a vertical and horizontal shift. Three post-stroke participants had both a horizontal and vertical midline shift and two were within the normal range. In total, therefore, 55.5% of non-stroke participants and 60% of stroke participants had some midline shift.

In some cases, there was a difference between the midline shift with the wand and the gauge. Stroke participants 1 and 5 (Table 4.2) had a midline shift measured with the wand, but not with the gauge and a number of both stroke and non-stroke participants showed a midline shift with the gauge but not with the wand (Tables 4.2 and 4.3).

The perceived midline was sometimes different at the three distances and this occurred for both non-stroke and post-stroke participants. Among post-stroke participants, two participants showed different midline shift results at different distances (see Table 4.2). One had a midline shift in the opposite direction depending on the distance (a left shift at 50 cm but right shift at 25 cm) Among non-stroke participants, three participants had a different midline position result depending on the distance (Table 4.3).

The Bells and bisection tests showed that none of the non-stroke participants had visual attention loss. One stroke participant had a left neglect which was shown by the bisection test and scored less than 32 in the Bells test, but the errors were in various visual field positions and did not show a pattern of neglect. It is noteworthy that this participant also had hypertropia and complained about diplopia.

Table 4.2 shows the details for the stroke participants and 4.3 show the details for the non-stroke participants. It can be seen that there is no obvious pattern of association between visual midline shift, handedness, subjective straight-ahead, open loop pointing, ocular dominance, intra-ocular VA differences, visual neglect and visual field loss in either the post-stroke or the non-stroke groups.

Table 4.2. Demographics and results of post stroke participants. Blue shading represents measures that might shift the midline to the right, pink shading represents measures that might shift the midline to the left. MoCA-Blind = Montreal Cognitive Assessment, CT = Cover test, VF = Visual Field, VA = Visual Acuity.

Participants no.	**1**	**2**	**3**	**4**	**5**
Type of stroke	Ischemic	Ischemic	Ischemic	Hemorrhage	Hemorrhage
Side of brain damaged	Left	Right	Left	Right	Right
Onset	Few months	A year	Two years	A year	Two years
Handedness	Right	Right	Left	Left	Right
Age	66	78	67	48	66
MoCA-Blind	16	19	19	12	18
VA					
OD	**0.16**	**0.36**	**0.84**	**0.3**	**0.08**
OS	**-0.02**	**0.14**	**0.46**	**0.46**	**-0.04**
OU	**-0.04**	**0.16**	**0.76**	**0.26**	**0.02**
CT	no strabismus	no strabismus	hypertropia	no strabismus	no strabismus
VF	right quadrantanopia	Partial left hemianopia	full	full	full
Ocular dominance	Left	Left	Left	Left	Left
Subjective straight-ahead	-0.1	**-0.9**	**4**	**0.75**	**-2**
Visual open loop	-2.25	**2.1**	**1.5**	**0.25**	**-2.875**
Visual neglect					
Bells	32	35	30, but no pattern of neglect	32	35
Bisections	No neglect	No neglect	Left neglect	No neglect	No neglect
Visual midline wand at 50 cm					
Horizontal	**-1.175**	0.6	2.75	0.5	-2.4375
Vertical	-0.125	-0.125	**0**	**1.25**	**0**
Visual midline device 100 cm					
Horizontal shift (cms)	0.35	0.025	0.425	1.85	-0.8
Vertical shift (cms)	0.15	1.75	-1.075	-1.1	-0.25
Visual midline device 50 cm					

Horizontal shift (cms)	0.525	1.275	-0.475	2	-0.225
Vertical	0.425	-0.075	-0.975	-1.325	-0.1
Visual midline device 25 cm					
Horizontal	-0.55	2.175	1.775	1.725	0.15
Vertical	0.25	-0.35	-1.175	-1.45	0

Table 4.3. Demographics and results of non-stroke participants. Blue shading represents measures that might shift the midline to the right, pink shading represents measures that might shift the midline to the left. MoCA = Montreal Cognitive Assessment, CT = Cover test, VF = Visual Field, VA = Visual Acuity.

Participants no.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Handedness	Right	Right	Right	Right	Right	Right	Right	Right	Right
Age	56	42	47	24	48	23	61	63	80
MoCA	22	22	20	20	19	21	22	19	19
VA									
OD	-0.08	-0.08	0.1	-0.24	-0.18	-0.14	0.08	0.2	0.04
OS	0.02	-0.06	0.06	-0.24	-0.2	-0.18	0.16	0.02	0.08
OU	0	-0.1	-0.14	-0.24	-0.22	-0.2	0.16	-0.06	0.1
CT	no strabismus	no strabismus	no strabismus	no strabismus	no strabismus	no strabismus	no strabismus	no strabismus	exotropia
VF	full	full	full	Full	full	full	full	full	full
Ocular dominance	left	right	left	Left	right	right	left	equal	right
Subjective straight-ahead	-2.5	-1.75	1.75	0.5	-1	2.35	0.25	0.15	-0.6
Visual open loop	-3	-0.75	1.25	-1.25	1	-1.5	0	-1.25	-2.25
Visual neglects									
Bells	full	full	full	Full	full	full	full	full	full
Bisections	Centred	Centred	Centred	Centred	Centred	Centred	Centred	Centred	Centred
Visual midline wand 50 cm									

Horizontal	0	0	0	-0.125	-0.625	0	-0.25	-0.375	-0.25
Vertical	0	-0.225	-0.2	0	0	0	-0.25	-0.125	-0.25
Visual midline device 100 cm									
Horizontal	-0.825	-0.475	-0.05	-0.55	-1.45	-0.75	0.525	-0.05	-0.8
Vertical	-1.6	0.45	0.6	1	-0.375	-0.025	-0.025	-0.5	0.3
Visual midline device 50 cm									
Horizontal	-0.025	-1.175	-0.475	-0.05	-1.55	0.075	-0.225	0.075	0.775
Vertical	-1.275	-0.525	0.4	0.15	0.25	-2.275	0.475	-0.55	0.375
Visual midline device 25 cm									
Horizontal	-0.275	0.15	-1.15	0.375	-0.65	0.8	-0.075	-0.225	0.35
Vertical	-1.075	0.975	1.3	0.875	0.45	-2.55	-0.025	-0.75	0.2

Tables 4.4 and 4.5. 3x3 tables of the perceived midline verses different variables such as ocular dominance, handedness, subjective straight-ahead, visual open loop, visual midline with the gauge versus the wand, and the side of brain damage confirmed what was already illustrated in the previous tables.

Table 4.4 3x3 tables of Visual midline vs other variables for post-stroke participants

Visual midline vs. Ocular dominance

Visual midline	**Ocular dominance**		
	Right	Left	None
Right	0	2	0
Left	0	1	0
None	0	2	0

Visual midline vs. Handedness

Visual midline	**Handedness**		
	Right	Left	None
Right	1	2	0
Left	0	0	0
None	2	0	0

Visual midline vs. Subjective straight-ahead

Visual midline	**Subjective straight-ahead**		
	Right	Left	None
Right	1	0	2
Left	0	0	0
None	0	1	1

Visual midline vs. Visual open loop

Visual midline	**Visual open loop**		
	Right	Left	None
Right	2	0	1
Left	0	0	0
None	0	2	0

Visual midline gauge vs. Visual midline Wand

Visual midline gauge	**Visual midline Wand**		
	Right	Left	None
Right	1	0	2
Left	0	0	0
None	0	2	0

Visual midline vs. Side of brain

Visual midline	**Side of brain**		
	Right	Left	None
Right	2	1	0
Left	0	0	0
None	1	1	0

Table 4.5. 3x3 tables of VMSS vs other variables for non-stroke participants**.**

Visual midline vs. Ocular dominance

Visual midline	**Ocular dominance**		
	Right	Left	None
Right	1	0	0
Left	2	1	0
None	1	3	1

Visual midline vs. Handedness

VMSS	**Handedness**		
	Right	Left	None
Right	1	0	0
Left	3	0	0
None	5	0	0

Visual midline vs Subjective straight-ahead

Visual midline	**Subjective Straight-ahead**		
	Right	Left	None
Right	1	0	0
Left	1	1	1
None	0	1	4

Visual midline vs. Visual open loop

Visual midline	**Visual open loop**		
	Right	Left	None
Right	0	0	1
Left	0	0	3
None	0	2	3

Visual midline gauge vs. Visual midline Wand

Visual midline gauge	**Visual midline Wand**		
	Right	Left	None
Right	0	0	1
Left	0	0	3
None	0	0	5

4.5 Discussion

The purpose of this study was to use the standardized midline gauge to help determine the prevalence of visual midline shift among stroke survivors, which side of the brain are typically affected when it occurs and if other associations exist.

For stroke group, 3/5 participants (60%) had a shifted perceived midline, but it was found that almost as many of the non-stroke participants 5/9 (55.5%) had a shift. This preliminary result is an important finding, as there are no studies which have measured the perceived midline for a non-stroke group with other visual or systemic morbidities. This indicates that visual midline shift is not a specific test for stroke or a condition that is specific to stroke. Additionally, we do not know the degree of midline shift that would be clinically relevant. It is possible that the shifts that we have documented, while outside the normal range, are not large enough to affect a person's balance and create symptoms. The other main finding of this preliminary study is that there are no clear associations between midline shift or other factors such as subjective straight-ahead, open loop pointing, ocular dominance etc. in either the stroke or non-stroke groups. Neither is there any obvious association between the midline measured with the clinical wand method or the gauge. However, at present there are no normal published data for the wand results by which we can decide on whether there is a shift or not. We noticed that a displacement of 1cm or more was noticeable, and this is the amount we have used to signify a shift in Tables 4.2 and 4.3. Note that a normal distance between the two eyes (PD = pupillary distance) for an adult is about 6.2 cms (half PD is 3 cms) so 1 cm can be considered as "in front of" one eye rather than the other. This is also true for the subjective straight-ahead and open loop pointing. We are not aware of any normal data or criterion in the literature with which to judge whether there is a significant shift. As with the shift measured with the gauge, there is no data on what degree of shift is clinically relevant.

Different distances can affect the visual neglect depending on the personal spaces. The perceived midline might be affected by different personal spaces as well that is the reason why we choose different distances for measuring the perceived midline.

4.5.1 Limitations

The main limitation of this study is the small sample size. It is difficult to be certain of the prevalence and associations of midline shift with this number and so any findings are preliminary and suggestive only.

4.6 Conclusion

From our preliminary results, the perceived midline varied between post-stroke and non-stroke individuals depending on the presence of the strabismus and visual field deficits. There was no association between the handedness, or the presence of stroke.

These are preliminary results only. We cannot state with certainty any association between the perceived midline and the presence of the strabismus which this might reflect as well on the results for the subjective straight-ahead position and the visual open loop for post-stroke group but not for non-stroke group.

Chapter 5 - Discussion

The purpose of the first study was to develop and test a new device to measure the perceived visual midline shift in post-stroke patients. This study investigated the effect of parameters such as size, distance and speed of movement in individuals with normal vision. This study is important, as, although other authors have described various methods for measuring the midline, there are currently no validated studies of the parameters of the measurement or published normal data.

Houston explained methods for measuring the visual eye-head egocentric midline, proprioceptive hand-head egocentric midline, and visual open loop pointing (Houston, 2010). He proposed that all should be considered when evaluating a patient's midline. Of these the visual eye-head egocentric midline was a similar measurement to what we have defined as the perceived midline using different target than the midline gauge evaluated in this study. However, no information was given regarding the choice of parameters. (Houston, 2010). The visual midline is measured in a variety of ways. Houston mentioned that some experimenters ask the participant to track the target with their eyes while others ask the participant to fixate straight-ahead. In both cases, by tracking the target or fixating straight-ahead, they respond by clicking a buzzer (Houston, 2010). For the visual subjective straight-ahead or the hand-head egocentric midline, Houston did not state the target size or distance from the target, although he did state that the room should be dark. Houston described two procedures for visual open loop pointing. One was by asking the participant to point with a centred laser pointer target while having their hands hidden under a shelf and the other involves drawing two lines with each hand while looking through a stereoscope (Houston, 2010).

Kuhn et al's method for measuring the visual midline shift involves a stationery red spot which was positioned at different locations (Kuhn et al., 2010). Subjects are asked to adjust the position of the spot until it is at their perceived midline. This is a different approach, and gives the participant more time and the opportunity to change their response. In the current study we noted that the judgement of the midline is a difficult judgement to make, and some participants ask the experimenter to move the target again once they have pressed the buzzer and it has stopped. Additionally, in any method which uses a moving target, the response time or anticipation of the participant may be a factor. Kuhn et al's method eliminates this. On the other hand, the accuracy of Kuhn et al's technique would depend on the closeness of the different spot positions, which is not reported, whereas in our test there was a continuous scale (Kuhn et al., 2010).

Kapoor et al (Kapoor et al., 2001) created a portable device to measure the perceived midline shift after brain injury. The target was moved by hand by the clinician and the target speed was about 0.5 degree per second which is very slow compared to the current study in which the final speed was 2.3 degrees per second. The participant was allowed to look at a mirror but were not allowed to follow the laser pointer light which is different from the current study. Asking a person to look straight-ahead may give them an additional clue as to where their midline might be.

Padula et al., (2009) did suggest some standard parameters, (target size of 30 cm and speed of 5.1 degrees per second at a distance of 45 cm, but he did not explain the basis of choosing these parameters. Padula's speed was more than twice as fast as the speed chosen in the current study. It should be noted however, that there was no impact of size and speed in the current study.

There were many different midline target sizes and speeds presented in various studies. Some studies such as Padula used very large. Padula used a wand of 30 cm length but did not state the target size (width). Some studies used a much smaller target size than in the present study such as Kuhn's and Kapoor's who used a laser pointer. We did not find an effect of size. Moreover, the speed was very slow in Kapoor's study (0.5 degrees per second) and in Padula's study the speed was faster than in the current study (5.1 degrees per second).

So, it is possible that these parameters can vary and are not critical. Despite this, there is a value of the gauge, which can allow more accurate measurement of the midline, including a quantifiable result. The presentation of normal data in the current study, allows a more objective determination of whether a person does have a midline shift or not, and its extent. The value of the gauge is that the numerical result allows tracking of changes of the visual midline over time in an individual. A clinical estimate without any scale for measurement would not allow this to be done accurately.

The purpose of the second study was to use the standardized device to help determine the extent of stroke survivors who experience visual midline shift, whether it always follows stroke (prevalence), and which parts are of the brain are typically affected when it occurs. The second study explains the association of the perceived midline shift with the handedness, strabismus, visual neglect, subjective straight-ahead, visual open loop and the type of stroke and the side of brain damaged for post-stroke individuals. We have demonstrated midline shifts that are outside the normal range, but we do not know if they are clinically relevant i.e. cause a balance impairment or symptoms. At present, there is no reference published data for this. This is an area for future study.

The preliminary results showed no association between these variables; however, the comparison group with other ocular and systematic morbidities also showed midline shifts outside the normal range. Therefore, midline shift is not specific to stroke and it might be an important risk factor for falls in non-stroke patients and should be considered in them or in studies of the visual risk factors for falls. No studies of visual risk factors for falls have measured this parameter as well as no studies of visual midline shift to our knowledge been included those who have not experienced a stroke.

If visual midline shifts are in some way associated with neglect, different personal spaces might affect the results of the perceived midline and the second study showed that this was indeed the case. Other studies used only one distance to test the visual midline such as Padula's study and clinically visual midline is measured only at one distance which is usually at 50 cm. This is the first study to investigate the visual midline position at different distances with regards to personal space. If visual midline shift is a type of visual neglect, then it may be expected to vary according to personal space and this should be measured in the clinical assessment of VMSS. From these preliminary results, there was a difference when measured at 25, 50 or 100 cms from the participant.

Moreover, there was discrepancy between the two methods for measuring the visual midline (hand held "wand" and new gauge). A visual midline shift was seen in non-stroke individuals with the gauge but this was missed with the wand. In stroke patients it went both ways. Some showed a midline shift with the wand and not the gauge and others showed it with the gauge and not the wand. These differences need further investigation.

5.1 Limitations

One limitation of Experiment 1 is that this study did not include participants aged between 35-65 years old. This was because most people who experience a stroke are older than 65 years and a younger group was included as a comparison to see the effect of age. However, some individuals of less than 65 years can experience a stroke. For the horizontal data, there was no effect of age, so we have presented normal data which is relevant for all ages (35 upwards). However, for the vertical measurements, there was an effect of age, so at present we cannot present normal data for patients aged 35-65.

In this type of study, there are a large number of parameters that can be tested. We did not test the impact of speed or target size for vertical midline position, and we used the same target as was chosen for the horizontal measurements. In clinical practice, this is justified, as one would use the same target for all measurements.

One limitation of Experiment 2 is that the sample size is too small to rely on especially for the post-stroke group because of the limited time as well as limited criteria for the post-stroke individuals who experienced their first stroke within two years.

Chapter 6 - Conclusion

Following an acquired brain injury (ABI) due to stroke there are frequently visual concerns such as visual acuity loss, binocular and motility disorders, field loss and perceptual disorders such as neglect and visual midline shift syndrome (VMSS). This will be first research to standardize the assessment of midlife shift and to focus on quantifying visual midline shift immediately after a stroke.

The data of the first study shows that the measurement of midline in control participants is tolerant of differences of target size, speed and direction, but there are differences of age and distance. Normal data is presented to detect and quantify the midline shift for the second study which was a cross-sectional study with a longitudinal component of post-stroke participants.

The results of the second preliminary study showed that 60% of post-stroke participants have a visual midline shift and 55.5% of non-stroke participants also have a perceived midline. These percentages indicate that there is little association between the visual midline shift and stroke, and other factors should be considered. It also indicates that a midline shift measured in a person with stroke might be pre-existing. Different distances regarding different personal spaces can affect the perceived midline for post-stroke as well as non-stroke individuals and therefore it is important to measure the perceived midline at different distances.

Appendix A

A telephone questionnaire to determine initial eligibility of post-stroke and non-stroke participants

Hello, May I talk to ….. my name is Ohwod Binhilabi. I am a researcher working at the School of Optometry and Vision Science at the University of Waterloo. I sent a letter a week ago and I am following up with you if you are interested in taking part in my study?

If yes, I would like to ask you few questions in the beginning:
Taken from Initial questionnaire, have you been diagnosed of any of the following:
Neurological other disorders ☐ Vestibular Dysfunctions ☐ MS ☐ Receptive Aphasia ☐
Cerebellar dysfunction ☐ Parkinson’s disease ☐ Previous history of another stroke ☐
Vertigo ☐ Meniere’s disease ☐ Concussion or head injury with residual symptoms ☐

- If answered any yes of the above: Unfortunately, you are not a suitable participant for our study. Thank you very much for your time.

- If answered no to all of the above, do you have any further questions?

If so, explain study further.

Appendix B

A general health and history of stroke questionnaire

Post-Stroke Visual Midline Shift Syndrome

Study ID No ________________ **Date** ___________________
Birth date ____year _____month **Sex M** ☐ **F** ☐

General health:
Do you have a diagnosis of any of the following?
Current Medical Conditions: Hypertension ☐ Hypotension ☐ Heart disease ☐ High cholesterol ☐ Other circulatory disorders ☐ Cancer ☐ Depression ☐ Respiratory disorders (e.g. COPD, asthma, pneumonia) ☐ Thyroid ☐ Hearing problems

____

____

Diabetes ☐ complications from diabetes, including feet ________________________________
Arthritis ☐ type? ________which joints are affected and how much? ______________________________
☐ Other (describe) ______________________________
Medications
____

Do you have a list of your medication? Yes ☐ No ☐
Ocular History: Glaucoma ☐ cataract ☐ cataract surgery ☐ diabetic changes ☐ macular degeneration ☐ retinal vein or artery occlusion ☐ other retinal problems ☐

____

____

Are these you must recent glasses? Yes ☐ No ☐
Spectacles: Distance ☐ Reading ☐ Bifocals ☐ PALs ☐
Stroke History ☐ What is the date ____Year ____Day ____Month
What is the side of brain affected? Right ☐ Left ☐
Type of stroke (vascular (bleed)/ischaemic (blockage)): ______________________________
Which side of body affected? ______________________________
Is there any paralysis (Hemiplegia)? Yes ☐ No ☐
Can you move it a bit or not? Yes ☐ No ☐
Arms: Right ☐ Left ☐
Legs: Right ☐ Left ☐
Any double vision? Yes ☐ No ☐
Is it worse in different directions of gaze (when you look to one side)? Yes ☐ No ☐
Explain __________________________
Aphasia or language impairments? ☐ Expressive or Receptive aphasia? ______________________________

Do you have difficulty saying the words or difficulty on thinking of the words? ______________________________

Did the stroke cause any other symptoms or changes? ______________________________
How much have these resolved since the stroke:
Aphasia ___________________________
Physical ____________________________
Vision _______________________________
Other _________________________________
Total days in hospital after stroke ________________________
Falls before stroke? Yes ☐ No ☐ Number in 3 months before stroke _____
Falls since stroke? Yes ☐ No ☐ Number since stroke _____
Problems with balance since stroke? Yes ☐ No ☐
Have you been missing food on one half of your plate? Yes ☐ No ☐
Have you been missing one half of make-up or grooming? Yes ☐ No ☐
Bumping into objects on one side or not seeing people if they are on one side? Yes ☐ No ☐
Difficulty reading? Yes ☐ No ☐
What is difficult? ________________________
What was your dominant hand before stroke? Right ☐ Left ☐ ambidextrous ☐
What is your preferred hand since the stroke? Right ☐ Left ☐ ambidextrous ☐
Mobility Aids: Cane ☐ Walker ☐ Assistance ☐

Permission to contact GP? Yes ☐ No ☐
GPs Name ___________________________
GPs Address ___________________________
MoCA completed? ☐ ___________________________

Bibliography

Akbarkhodjaeva, Z. A., & Tursunov, J. (2017). Prevalence of stroke in the world. *Journal of Stroke and Cerebrovascular Diseases,* 4(26), 913-914.

Bansal, S., Han, E., & Ciuffreda, K. J. (2014). Use of yoked prisms in patients with acquired brain injury: A retrospective analysis. *Brain Injury, 2*8(11), 1441-1446.

Benamer, H. T., & Grosset, D. (2009). Stroke in Arab countries: A systematic literature review. *Journal of the Neurological Sciences, 28*4(1-2), 18-23.

Benjamin, E. J., Virani, S. S., Callaway, C. W., Chamberlain, A. M., Chang, A. R., Cheng, S., . . . Deo, R. (2018). Forecasting the future of cardiovascular disease in the United States: A policy statement from the American Heart Association. *Circulation, 13*7(12), e67-e492.

Chokron, S., & Imbert, M. (1995). Variations of the egocentric reference among normal subjects and a patient with unilateral neglect. *Neuropsychologia, 3*3(6), 703-711.

Christiansen, C. B., Lip, G. Y., Lamberts, M., Gislason, G., Torp-Pedersen, C., & Olesen, J. (2013). Retinal vein and artery occlusions: A risk factor for stroke in atrial fibrillation. *Journal of Thrombosis and Haemostasis, 1*1(8), 1485-1492.

Ciuffreda, K. J., Kapoor, N., Rutner, D., Suchoff, I. B., Han, M., & Craig, S. (2007). Occurrence of oculomotor dysfunctions in acquired brain injury: A retrospective analysis. *Optometry-Journal of the American Optometric Association, 7*8(4), 155-161.

Connolly, E. S., Jr, Rabinstein, A. A., Carhuapoma, J. R., Derdeyn, C. P., Dion, J., Higashida, R. T., . . . Council on Clinical Cardiology. (2012). Guidelines for the management of aneurysmal subarachnoid hemorrhage: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke, 4*3(6), 1711-1737.

Dalton, K., Guillon, M., & Naroo, S. A. (2015). Ocular dominance and handedness in golf putting. *Optometry and Vision Science, 92*(10), 968-975.

Different strokes recovery triumphs and challenges at any age. (2017). (Stroke report). Heart and Stroke Foundation of Canada. Retrieved from http://www.heartandstroke.ca/-/media/pdf-files/canada/stroke-report/strokereport2017en.ashx?la=en&hash=67F86E4C3338D5A7FE7862EA5D0DD57CA8539847

Edwards, D. F., Hahn, M. G., Baum, C. M., Perlmutter, M. S., Sheedy, C., & Dromerick, A. W. (2006). Screening patients with stroke for rehabilitation needs: Validation of the post-stroke rehabilitation guidelines. *Neurorehabilitation and Neural Repair, 20*(1), 42-48.

Ezejimofor, M. C., Chen, Y. F., Kandala, N. B., Ezejimofor, B. C., Ezeabasili, A. C., Stranges, S., & Uthman, O. A. (2016). Stroke survivors in low- and middle-income countries: A meta-analysis of prevalence and secular trends. *Journal of the Neurological Sciences, 364*, 68-76.

Facchin, A., Beschin, N., & Daini, R. (2015). Not prism prescription, but prism adaptation rehabilitates spatial neglect; a reply to Bansal, Han and Ciuffreda. *Brain Injury, 29*(4), 533-534.

Fang, M. C., Coca Perraillon, M., Ghosh, K., Cutler, D. M., & Rosen, A. B. (2014). Trends in stroke rates, risk, and outcomes in the United States, 1988 to 2008. *The American Journal of Medicine, 127*(7), 608-615.

Farnè, A., Rossetti, Y., Toniolo, S., & Làdavas, E. (2002). Ameliorating neglect with prism adaptation: Visuo-manual and visuo-verbal measures. *Neuropsychologia, 40*(7), 718-729.

Foulkes, M. A., Wolf, P. A., Price, T. R., Mohr, J. P., & Hier, D. B. (1988). The stroke data bank: Design, methods, and baseline characteristics. *Stroke, 19*(5), 547-554.

Gallagher, M., Wilkinson, D., & Sakel, M. (2013). Hemispatial neglect: Clinical features, assessment and treatment. *British Journal of Neuroscience Nursing,* 9(6), 273-277.

Gauthier, L., Dehaut, F., & Joanette, Y. (1989). The bells test: A quantitative and qualitative test for visual neglect. *International Journal of Clinical Neuropsychology,*

Goldstein, L. B., Adams, R., Becker, K., Furberg, C. D., Gorelick, P. B., Hademenos, G., . . . del Zoppo, G. J. (2001). Primary prevention of ischemic stroke: A statement for healthcare professionals from the Stroke Council of the American Heart Association. *Circulation, 10*3(1), 163-182.

Gresham, G. E., Stason, W. B., & Duncan, P. W. (1997). *Post-stroke rehabilitatio*n Diane Publishing.

Hazel, C. A., & Elliott, D. B. (2002). The dependency of logMAR visual acuity measurements on chart design and scoring rule. *Optometry and Vision Science, 7*9(12), 788-792.

Heilman, K. M., Bowers, D., & Watson, R. T. (1983). Performance on hemispatial pointing task by patients with neglect syndrome. *Neurology, 3*3(5), 661-661.

Hillis, A. E. (2007). Aphasia: Progress in the last quarter of a century. *Neurology, 6*9(2), 200-213.

Houston, K. E. (2010). Measuring visual midline shift syndrome & disorders of spatial localization: A literature review & report of a new clinical protocol. *Journal of Behavioral Optometry, 2*1(4)

Hsu, H., Ke, C., Kuan, T., Yang, H., Tsai, C., & Kuo, L. (2017). Impacts of sensation, perception, and motor abilities of the ipsilesional upper limb on hand functions in unilateral stroke: Quantifications from biomechanical and functional perspectives. *Pm&r, 10*(2), 146-153.

Ivan, C. S., Seshadri, S., Beiser, A., Au, R., Kase, C. S., Kelly-Hayes, M., & Wolf, P. A. (2004). Dementia after stroke: The Framingham study. *Stroke, 35*(6), 1264-1268.

Johnson, W., Onuma, O., Owolabi, M., & Sachdev, S. (2016). Stroke: A global response is needed. *Bulletin of the World Health Organization, 94*(9), 634-634A.

Kapoor, N., Ciuffreda, K., Harris, G., Suchoff, I., Kim, J., Huang, M., & Bae, P. (2001). A new portable clinical device for measuring egocentric localization. *Journal of Behavioral Optometry, 12*(5), 115-119.

Karnath HO, Ferber S, Dichgans J. (2003). The neural representation of postural control in humans. Proceedings of the National Academy of Science, U S A. 2000;97(25):13931–36. [PMID: 11087818]. Erratum in: Proceedings of the National Academy of Science, U S A. 2001;98(2):777

Keane, S., Turner, C., Sherrington, C., & Beard, J. R. (2006). Use of Fresnel prism glasses to treat stroke patients with hemispatial neglect. *Archives of Physical Medicine and Rehabilitation, 87*(12), 1668-1672.

Krueger, H., Koot, J., Hall, R. E., O'Callaghan, C., Bayley, M., & Corbett, D. (2015). Prevalence of individuals experiencing the effects of stroke in Canada: Trends and projections. *Stroke, 46*(8), 2226-2231.

Kuhn, C., Heywood, C., & Kerkhoff, G. (2010). Oblique spatial shifts of subjective visual straight ahead orientation in quadrantic visual field defects. *Neuropsychologia, 48*(11), 3205-3210.

Leat, S. J., Legge, G. E., & Bullimore, M. (1999). What is low vision. *Optometry and Vision Science, 76*, 198-211.

Liou, S., & Lin, H. (2009). Retinal vein occlusion and the risk of stroke development: A five-year follow-up study. *American Journal of Ophthalmology, 147*(2), 283-290. e2.

Luaute, J., Michel, C., Rode, G., Pisella, L., Jacquin-Courtois, S., Costes, N., . . . Rossetti, Y. (2006). Functional anatomy of the therapeutic effects of prism adaptation on left neglect. *Neurology, 6*6(12), 1859-1867.

Maberley, D., Hollands, H., Chuo, J., Tam, G., Konkal, J., Roesch, M., . . . Bassett, K. (2006). The prevalence of low vision and blindness in Canada. *Eye, 2*0(3), 341.

Mercier, L., Audet, T., Hébert, R., Rochette, A., & Dubois, M. (2001). Impact of motor, cognitive, and perceptual disorders on ability to perform activities of daily living after stroke. *Stroke, 3*2(11), 2602-2608.

Miller, E. L., Murray, L., Richards, L., Zorowitz, R. D., Bakas, T., Clark, P., . . . American Heart Association Council on Cardiovascular Nursing and the Stroke Council. (2010). Comprehensive overview of nursing and interdisciplinary rehabilitation care of the stroke patient: A scientific statement from the American Heart Association. *Stroke, 4*1(10), 2402-2448.

Nasreddine, Z. (2012). *Montreal Cognitive Assessment (MoCA): Administration and Scoring Instructions.* http://www.mocatest.org/pdf_fi les/instructions/MoCA-Instructions-English_2010.pdf.

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., . . . Chertkow, H. (2005). The Montreal cognitive assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society, 5*3(4), 695-699.

Ontario Brain Injury Association. (2012). The OBIA impact report 2012: A statistical snapshot of acquired brain injury and its effects on survivors and caregivers. *St. Catharines, ON: Ontario Brain Injury Association,* Padula, W. V., Nelson, C. A., Padula, W. V., Benabib, R., Yilmaz, T., & Krevisky, S. (2009). Modifying postural adaptation following a CVA through prismatic shift of visuo-spatial egocenter. *Brain Injury, 2*3(6), 566-576.

Rossetti, Y., Rode, G., Pisella, L., Farné, A., Li, L., Boisson, D., & Perenin, M. (1998). Prism adaptation to a rightward optical deviation rehabilitates left hemispatial neglect. *Nature, 39*5(6698), 166.

Rothwell, P., Coull, A., Giles, M., Howard, S., Silver, L., Bull, L., . . . Sackley, C. (2004). Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire, UK from 1981 to 2004 (Oxford vascular study). *The Lancet, 36*3(9425), 1925-1933.

Rowe, F. J. (2011). The importance of accurate visual assessment after stroke. *Expert Review of Ophthalmology,* 6(2), 133-136.

Rowe, F., Brand, D., Jackson, C. A., Price, A., Walker, L., Harrison, S., . . . Dodridge, C. (2008). Visual impairment following stroke: Do stroke patients require vision assessment*? Age and Ageing, 3*8(2), 188-193.

Rubenstein, L. Z. (2006). Falls in older people: Epidemiology, risk factors and strategies for prevention. *Age and Ageing, 3*5(suppl_2), ii37-ii41.

Sacco, R. L., Kasner, S. E., Broderick, J. P., Caplan, L. R., Connors, J. J., Culebras, A., . . . Council on Nutrition, Physical Activity and Metabolism. (2013). An updated definition of stroke for the 21st century: A statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke, 4*4(7), 2064-2089.

Serino, A., Barbiani, M., Rinaldesi, M. L., & Ladavas, E. (2009). Effectiveness of prism adaptation in neglect rehabilitation: A controlled trial study. *Stroke, 40*(4), 1392-1398.

Shiraishi, H., Muraki, T., Itou, A., Sampei, Y., & Hirayama, K. (2010). Prism intervention helped sustainability of effects and ADL performances in chronic hemispatial neglect: A follow-up study. *Neurorehabilitation, 27*(2), 165-172.

Siong, K. H., Woo, G. C., Chan, D. Y., Chung, K. Y. K., Li, L. S. W., Cheung, H. K. Y., . . . Cheong, A. M. Y. (2014). Prevalence of visual problems among stroke survivors in Hong Kong Chinese. *Clinical and Experimental Optometry, 97*(5), 433-441.

Suchoff, I. B., & Ciuffreda, K. J. (2004). A primer for the optometric management of unilateral spatial inattention. *Optometry-Journal of the American Optometric Association, 75*(5), 305-318.

Teh, W. L., Abdin, E., Vaingankar, J. A., Seow, E., Sagayadevan, V., Shafie, S., . . . Subramaniam, M. (2018). Prevalence of stroke, risk factors, disability and care need in older adults in Singapore: Results from the WiSE study. *BMJ Open, 8*(3), e020285-2017-020285.

Ting, D. S., Pollock, A., Dutton, G. N., Doubal, F. N., Ting, D. S., Thompson, M., & Dhillon, B. (2011). Visual neglect following stroke: Current concepts and future focus. *Survey of Ophthalmology, 56*(2), 114-134.

Vossel, S., Eschenbeck, P., Weiss, P. H., Weidner, R., Saliger, J., Karbe, H., & Fink, G. R. (2011). Visual extinction in relation to visuospatial neglect after right-hemispheric stroke: Quantitative assessment and statistical lesion-symptom mapping. *Journal of Neurology, Neurosurgery, and Psychiatry, 82*(8), 862-868.

Winstein, C. J., Stein, J., Arena, R., Bates, B., Cherney, L. R., Cramer, S. C., . . . American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Quality of Care and Outcomes Research. (2016). Guidelines for adult stroke rehabilitation and recovery: A guideline for healthcare professionals from the American Heart Association/American stroke association. *Stroke, 47*(6), e98-e169.

Wolfe, C. D. (2000). The impact of stroke. *British Medical Bulletin, 56*(2), 275-286.

Wolter, M., & Preda, S. (2006). Visual deficits following stroke: Maximizing participation in rehabilitation. *Topics in Stroke Rehabilitation, 13*(3), 12-21.