The presence of visuospatial neglect impairs the ability of post-stroke individuals to safely negotiate moving obstacles while walking

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STATEMENT OF AUTHORSHIP

I, Gayatri Aravind, certify that I am the primary author of this thesis. I claim full responsibility for the content and style of the text included herein.

STATEMENT OF ORIGINALITY

This thesis contains no material that has been published elsewhere, except where specific references are made. The studies presented in chapters 3,4,5,6 are original material and represent contributions to knowledge in the fields of locomotion, stroke, and virtual reality. In this work, I have used a novel, virtual reality setup to assess obstacle avoidance abilities in persons with visuospatial neglect after a stroke, a topic that has not been studied despite its relevance to the safety and independence during community ambulation. The studies contribute new knowledge that furthers our understanding of how the perceptual-attentional deficits resulting from visuospatial neglect interfere with the detection of moving obstacles and the modulation of walking strategies in response to these moving obstacles. Also, for the first time, the deleterious effects of dual-tasking on locomotor obstacle avoidance performance in persons with visuospatial neglect were demonstrated. The results of this PhD thesis provide more insights in the factors leading to poor community ambulation in stroke survivors with visuospatial neglect in comparison to those without visuospatial neglect.

All data presented in this thesis were collected at the Feil & Oberfeld Research Centre of the Jewish Rehabilitation Hospital; Site of the Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal (CRIR), affiliated to McGill University. The different studies have been approved by the Ethics Board of CRIR.

DEDICATIONS

This thesis is dedicated to my family. To my amma and appa, for providing a home that has encouraged my curiosity and has helped me develop a love for learning. Thank you for being supportive of my endeavours and my choices, and for encouraging me to reach my goal. Your efforts and patience over the years will remain invaluable to me.

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CONTRIBUTION OF AUTHORS

This thesis is presented in a manuscript format and includes four manuscripts, two of which are already published in peer-reviewed journals. I, Gayatri Aravind, am the main contributor and lead author of all the manuscripts included in this thesis. My contribution includes the research design, data collection and analyses, interpretation of findings, preparation of figures and writing the thesis.

Manuscripts presented in Chapter 3, 5, 6: Study design and experimental set-up were done by Gayatri Aravind and Dr. Anouk Lamontagne. Data collection, data analyses, statistical analyses and manuscript preparation were done by Gayatri Aravind. Dr. Anouk Lamontagne critically reviewed and improved the manuscripts.

Manuscript presented in Chapter 4: Study design and experimental set-up were done by Gayatri Aravind and Dr. Anouk Lamontagne. Data collection, data analyses, statistical analyses and manuscript preparation were done by Gayatri Aravind. Anuja Darekar assisted with the data analyses and critically reviewed the manuscript. Fung and Dr. Anouk Lamontagne critically reviewed the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Post-stroke visuospatial neglect (VSN) is an attentional-perceptual disorder that alters the ability to detect and respond to relevant visual stimuli present in the contralesional space. Since locomotion is highly dependent on visual inputs, VSN may impair the modulation of walking in response to visuospatial cues such as obstacles, especially when located in the “neglected” side of space. Failure to adapt walking in response to obstacles may lead to collisions or falls. Also, since attentional resources are limited in persons with VSN, performing a cognitive task while walking could further alter obstacle avoidance performance. In this thesis, I have utilised a virtual reality paradigm consisting of obstacles approaching from the right, left or head-on, to assess how presence of VSN in stroke survivors interferes with their ability to safely avoid moving obstacles while walking. Stroke survivors with VSN (and without VSN for Manuscript 3 and 4) participated in a series of experiments that involved: (1) detecting moving obstacles; (2) avoiding the obstacle while walking towards a target; (3) using a joystick to navigate around the obstacle and (4) performing a cognitive task along with the obstacle avoidance task. During locomotor (Manuscript 1) and non-locomotor (joystick-driven, Manuscript 2) obstacle avoidance tasks, individuals with VSN (n=12) showed smaller minimum distances and higher collision rates for contralesional and head-on obstacles compared to ipsilesional ones. These results provide evidence that attentional-perceptual deficits due to VSN, independent of post-stroke locomotor deficits, alter obstacle avoidance abilities. In Manuscript 3, 26 stroke survivors (13 with and 13 without VSN) were assessed while concurrently performing the obstacle avoidance and a cognitive task i.e. dual tasking. Compared to the single task, dual tasking caused deterioration of both locomotor (higher collision rate, smaller minimum distances) and cognitive performances (higher error rate) in VSN individuals, suggestive of a “cognitive-locomotor interference”. In contrast, individuals without VSN prioritised the locomotor task (no change in collision rates) over the cognitive task (higher cognitive error rates). In Manuscript 4, we examined kinematic strategies utilised by individuals with and without VSN to safely avoid the obstacles. For individuals free of VSN, deviating to the same-side as the obstacle emerged as a safe strategy to avoid diagonal obstacles, while an opposite-side deviation was riskier and led to collisions. VSN individuals deviated ipsilesionally for all obstacles; displaying same, and opposite-side strategies for ipsilesional and contralesional obstacles, respectively. In this group,

contralesional collisions were frequent, observed for the opposite-side strategy, and associated with a delay in onset-of-heading change. Thus ipsilesional biases arising from VSN influenced the modulation of heading in response to the contralesional obstacle and, along with the adoption of the 'riskier' strategy, contributed to the risk of collisions in individuals with VSN. Collectively, these results reveal that the presence of VSN in stroke survivors puts them at a high risk for collisions with moving obstacles while walking, especially in the presence of increased attentional demands. As avoiding moving obstacles and coping with changing cognitive demands are critical for safe community ambulation, findings of this thesis may explain, in part, the poor community ambulation observed in persons with VSN.

ABRÉGÉ

La négligence visuospatiale (NVS) post accident vasculaire cérébral (AVC) est un trouble perceptuo-attentionnel qui altère la capacité à détecter et répondre à des stimuli visuels du côté opposé à la lésion corticale. Puisque la locomotion dépend fortement de l'information visuelle, la NVS pourrait altérer les comportements de marche en réponse à des stimuli visuo-spatiaux, tel que des obstacles, en particulier lorsqu'ils sont situés du côté 'négligé' de l'espace. Une incapacité à adapter la marche en réponse à des obstacles pourrait engendrer des collisions ou des chutes. De plus, étant donné que les ressources attentionnelles sont limitées chez les personnes avec NVS, l'ajout d'une tâche cognitive durant la marche est susceptible d'altérer leur performance lors de l'évitement d'obstacles. Dans cette thèse, j'ai utilisé des obstacles virtuels approchant de différentes directions (droite, gauche ou de l'avant) pour examiner comment la présence de NVS interfère avec la capacité à éviter des obstacles en mouvement de manière sécuritaire lors de la marche. Des participants post AVC avec NVS (et sans NVS dans les Manuscrits 3 et 4) ont participé à des tâches consistant à : (1) détecter des obstacles en mouvement; (2) éviter ces mêmes obstacles en marchant vers une cible; (3) utiliser une manette de jeu pour naviguer autour des obstacles et (4) exécuter une tâche cognitive en même temps que la tâche d'évitement d'obstacles. Durant la tâche d'évitement d'obstacle à la marche (Manuscrit 1) et dans un contexte non-locomoteur (Manuscrit 2), 12 individus avec NVS ont montré une distance minimale réduite et un taux de collision plus élevé avec des obstacles provenant du côté contralésionnel et de l'avant, comparativement aux obstacles ipsilésionnels. Ces résultats suggèrent que les déficits perceptuo-attentionnels attribuables à la NVS altèrent la capacité d'évitement d'obstacles. Dans le Manuscrit 3, 26 individus ayant un AVC (13 avec et 13 sans NVS) ont été évalués à la marche tout en performant simultanément une tâche cognitive i.e. en double tâche. Comparativement à une tâche simple, la tâche double a causé une détérioration de la performance locomotrice (plus de collisions, distance minimale réduite) et cognitive (taux d'erreur augmenté) chez les participants avec NVS, suggérant une 'interférence cognitive-locomotrice'. Les individus sans NVF ont quant à eux priorisé la tâche locomotrice au détriment de la tâche cognitive. Le Manuscrit 4 décrit les stratégies cinématiques pour éviter un obstacle utilisées par les mêmes participants que le Manuscrit 3. Chez les individus sans NVS, une

déviation du même côté que l'obstacle s'est révélée une stratégie sécuritaire pour éviter les obstacles approchant en diagonale, alors qu'une déviation du côté opposé s'est avéré plus risquée, menant à des collisions. Les individus avec NVS ont dévié du côté ipsilésionnel, démontrant des stratégies 'même côté' ou 'côté opposé' pour les obstacles ipsilésionnel et contralésionnels, respectivement. Dans ce groupe, les collisions avec des obstacles contralésionnels étaient fréquentes, observées avec des stratégies du côté opposé et associées à un délai dans l'initiation d'une stratégie d'évitement. Ainsi, le biais ipsilésionnel découlant de la NVS influence la modulation de la trajectoire de marche en réponse à un obstacle contralésionnel et, avec l'adoption d'une stratégie plus risquée, contribue au risque de collision. Collectivement, les résultats indiquent que la présence de NVS après un AVC hausse le risque de collision avec des objets en mouvement pendant la marche, en particulier en présence d'une demande attentionnelle accrue. L'évitement d'obstacles et la capacité à faire face à des demandes cognitives changeantes sont critiques pour une marche en communauté sécuritaire. Les résultats de cette thèse peuvent expliquer, en partie, la difficulté qu'ont les personnes avec une NVS à marcher dans la communauté.

CHAPTER 1: RATIONALE

1.1 INTRODUCTION

How humans walk and move around in the environment has been of interest to researchers for several decades now. The ability to walk allows humans to move from one place to another, to obtain food or shelter or to avoid danger and is an integral part of the social, cultural and physical activities performed in daily living (Rantanen (2013). The loss of walking independence is therefore considered to be quite debilitating.

Loss of locomotor abilities is commonly witnessed after a cerebrovascular injury i.e. a stroke. Persons with a stroke experience a reduced ability to walk independently due to paresis, impaired balance, spasticity and sensory deficits (Lamontagne et al., 2007b). A reduction of walking independence in individuals with stroke is associated with reduced participation in the society (Rantanen, 2013) and reduced quality of life (Robinson et al., 2011). Hence, the recovery of independence in walking in the community is an important goal for persons who sustained a stroke and is commonly considered to be priority in the rehabilitation process (Lord et al., 2004). In order to achieve independent community ambulation, persons with stroke must be able walk safely in different ambient conditions, on different terrains, under different traffic conditions, and in the presence of other physical and attentional demands (Shumway-Cook et al., 2002). Many individuals with stroke, however, face limitations in their walking independence and safety when faced with such challenges (Balasubramanian et al., 2014; Said et al., 1999; Smulders et al., 2012).

One such group of persons with stroke that are frequently associated with poor independent walking abilities are those with post-stroke visuospatial neglect (VSN) (Oh-Park et al., 2014). In addition to the sensorimotor deficits, stroke often causes attentional-perceptual deficits such as VSN, in which the individual shows a lack of awareness to objects present in the side of space opposite to the brain lesion (Heilman et al., 1985). Consequently, there is a failure in detecting and responding to visual stimuli that are presented in this neglected or contralesional side of space (Heilman et al., 1985). Additionally, VSN causes impairments in the visual exploration of the surrounding space (Sprenger et al., 2002) and in the ability to use spatial information from the neglected side to build cognitive spatial maps (Bisiach et al., 1996). With human locomotion being highly visually reliant, such an impairment in visual attention-perception is likely to have additional damaging consequences on the already limited locomotor ability of individuals with stroke.

Several studies have reported the adverse influence of VSN on the recovery of independent walking after stroke (Oh-Park et al., 2014; Paolucci et al., 2001; van Nes et al., 2009a). Individuals with post-stroke VSN (VSN+) often collide with static objects such as furniture, doorposts and walls, increasing their risk for falls and accidents (Punt et al., 2008; Robertson et al., 1994; Tromp et al., 1995; Turton et al., 2009). This risk of collision may be further heightened while walking in the community in the presence of unpredictable moving objects such as vehicles and pedestrians, especially when these are located on the neglected side.

Negotiation of moving obstacles is a complex task that relies on the interaction of sensory, cognitive and motor systems to detect the obstacle as well as plan and execute an avoidance strategy (Patla & Shumway-Cook, 1999; Shumway-Cook et al., 2002). Since VSN+ individuals may fail to detect an obstacle when it is present in the neglected side of space, they may not make the necessary locomotor adjustments to avoid the obstacle, resulting in collisions. Even though moving obstacles are frequently encountered in the community and may pose a danger to the safety of post-stroke VSN+ individuals, their ability to negotiate such obstacles while walking have not yet been studied. Therefore, in this thesis, I investigated how the presence of VSN impacted the ability of persons with stroke to safely avoid collisions with moving objects in their environment while walking towards a goal.

Studies have also reported that individuals with VSN who are deemed recovered on the common paper-pencil tests display signs of neglect under increased task demands (Bonato & Deouell, 2013; Bonato et al., 2010; Robertson & Frasca, 1992b). The ability to adapt to increased task demands is also an important aspect of community ambulation but its impact on the safety of VSN+ individuals, who already experience attentional deficits, had not yet been understood. Therefore, I also explored how the presence of increased attentional demands would alter obstacle avoidance abilities in VSN+ individuals and whether these changes would be affected by the complexity of the dual-task activity.

Lastly, information regarding the direction of locomotion i.e. heading in space is also obtained through visuospatial cues and is consequently used to control and adjust the ongoing locomotor strategy (Fajen, 2013; Fajen & Warren, 2003; Patla et al., 2004). A deficit in the uptake of the visuospatial cues in VSN+ individuals may therefore impair their ability to modulate their heading in order to steer away from an obstacle or towards a target, as required. Therefore, I also evaluated how persons with and without VSN adapted their heading while walking, in response to an obstacle and a target along with its influence on the success of obstacle avoidance and goal-directed walking.

In the following sections I have introduced and described the phenomenon of VSN keeping in mind its relevance to locomotion, how it is evaluated and what is lacking in the current literature. I have also briefly discussed the concept of obstacle avoidance while walking and how the presence of stroke and more specifically VSN alters the obstacle avoidance abilities. Finally, I have discussed the concepts of dual-tasking, the models of dual-task interference and how different groups of individuals including persons with stroke respond to dual-task demands. The results of this thesis will contribute to understanding the ability of post-stroke VSN+ individuals to cope with frequently encountered demands of community ambulation, and provide insights into their safety and independence while walking.

CHAPTER 2: LITERATURE REVIEW AND OBJECTIVES

2.1 STROKE: PREVALENCE AND CONSEQUENCES

Stroke, also referred to as cerebrovascular accident (CVA), is defined as "rapidly developing clinical signs of focal disturbance of cerebral function lasting more than 24 hours, or leading to death, with no apparent cause other than vascular origin" (World Health Organisation). While sophisticated diagnostic techniques and effective treatment interventions have reduced the number of deaths associated with stroke (Mozaffarian et al., 2016), the number of individuals living with its consequences has increased (Mendis, 2013). Stroke remains a major cause of adult disability with personal, social and economic consequences (Mendis, 2013). A recent statistic by the Centre For Disease Control (2015), has recognized that the cost of health care and lost man hours due to stroke accounts for US$ 34 Billion. The Heart and Stroke Foundation of Canada stated that as of 2011, more than 400,000 Canadians are living with the long-term disabilities associated with stroke and the number of individuals requiring long-term care is steadily increasing. With an increased pressure to discharge patients early, several individuals return to their homes while still unable to perform their activities of daily living independently (Mas & Inzitari, 2015). In order to avoid accidents and subsequent return to rehabilitation, it is important to understand functional abilities before being discharged into independent living (Mozaffarian et al., 2015). One of the consequences of stroke that is frequently related to poor functional abilities is visuospatial neglect (Timbeck et al., 2013).

2.1.1 VISUOSPATIAL NEGLECT

2.1.1.1 Overview

Visuospatial neglect is the inability to attend to or orient oneself to novel or meaningful stimuli on the side of the body contralateral to the side of brain lesion while accurately detecting and responding to stimuli on the ipsilesional side; this inability cannot be attributed to either sensory or motor deficits (Hillis, 2006). It is observed in 12-83% of patients after a right hemispheric stroke and 20-40% of left hemispheric stroke (Pedersen et al., 1997; Ringman et al., 2004; Wertman, 2002). The large variation in the reported prevalence is due to the inherent differences in the understanding of symptoms, subject selection, lesion locations and assessment methods (Bowen et al., 1999; Chan & Man, 2013). Elaborate neural networks in the right hemisphere control the allocation of attention to both the left and right side of space, compensating for right-sided attentional loss in case of a left hemisphere lesion (Bowen et al., 1999; Heilman & Van Den Abell, 1980). The left hemisphere, however, only subserves attention to the right side of space. Therefore, in case of a right hemisphere lesion, the left hemisphere will cause an orientation bias towards the right side i.e. ipsilesional bias, giving rise to left sided neglect (Bowen et al., 1999; Heilman & Van Den Abell, 1980). This lack of compensation of orientation to the left would be responsible for a higher incidence of neglect after right hemispheric lesions (Suchan et al., 2012).

This ipsilesional bias causes visual attention and gaze to be spontaneously oriented towards events and stimuli occurring in the ipsilesional side of space, often at the expense of those located contralesionally (Mark et al., 1988). In fact, patients may experience a *magnetic attraction of gaze* (Bartolomeo et al., 2001), which is associated with a difficulty in disengaging the attention from previously fixed targets to a new target, especially if the shift is from the ipsilesional to the contralesional field (Posner et al., 1982; Posner & Rafal, 1987; Posner et al., 1984). VSN also impairs visual exploration of space with visual search always beginning ipsilesionally before proceeding to the contralesional field (Karnath, 1994; Karnath et al., 1998). Studies that investigated visual attention and reaction times in persons with VSN observed lower detection rate i.e. greater omissions, for contralesional compared to ipsilesional stimuli (Bonato & Deouell, 2013; Bonato et al., 2012; Bonato et al., 2013; Butler et al., 2004; Kinsbourne, 1993) and longer response times for stimuli appearing in the contralesional compared to ipsilesional side (D'Erme et al., 1992; Dvorkin et al., 2012; Dvorkin et al., 2007; van Kessel et al., 2010). Studies that examined visual exploration patterns in persons with VSN observed more fixations and re-fixations with ipsilesionally located stimuli while the number and duration of fixations for contralesional stimuli were significantly lower (Behrmann et al., 1997; Machner et al., 2012; Malhotra et al., 2006; Rossi et al., 1990).

Further, in VSN, there is a failure to centrally process the coordinates of the visual inputs into an egocentric coordinate system (Karnath et al., 1991). This affects the subjective localization of the body orientation, and along with the ipsilesional bias, it causes a shift of the “subjective” midline (i.e. the straight ahead) towards the ipsilesional side (Huitema et al., 2006; Richard et al., 2004). This midline shift also causes the visual representation of the space to be anisometric or asymmetrical across the visual field (Bisiach et al., 1996; Karnath & Ferber, 1999). In fact, Bisiach and colleagues observed that the visual space may be compressed on the ipsilesional side with a pathological expansion on the contralesional side (Bisiach et al., 1996).

This midline, however, is not a definitive distinction between the perceived and the neglected space with studies suggesting that the individual might neglect either a part or the whole of the contralesional hemispace (Eramudugolla & Mattingley, 2008; Heilman & Valenstein, 1979; Kinsbourne, 1993). In fact the border between the neglected and the non-neglected space is not well defined. Rather, a gradient of visual attention is observed where stimuli are increasingly ignored or omitted, as they are located further into the contralesional space away from the midline (Butler et al., 2004; Kinsbourne, 1977; Marshall & Halligan, 1989; Morris et al., 2004).

The effects of the ipsilesional bias and altered spatial representation have also been observed during functional tasks. For example, visually-guided reaches of persons with VSN towards a centrally-located target or between two targets were abnormally curved and deviated to the ipsilesional side, showing an " ipsiversive trajectory" (Goodale et al., 1990; Harvey et al., 1994; Jackson et al., 2000b). Similarly, deviations in trajectories were also observed in persons with VSN as they walked towards a centrally located target, a behaviour that was also attributed to reliance on an altered spatial representation (Berti et al., 2002; Huitema et al., 2006; Punt et al., 2008; Turton et al., 2009). Thus, in addition to the perception of visual information, the subsequent use of the information to execute visually-guided actions also seem to be impaired in persons with VSN.

2.1.2.2 Classification of VSN

VSN is typically classified based on the radial field in which the stimuli are neglected, as personal, near-space extrapersonal or far-space extrapersonal neglect (Kortte & Hillis, 2009; Wertman, 2002). Personal neglect is the neglect of the side of a person's own body, contralateral to the lesion. Individuals with personal neglect may show failure to groom, clean or dress the neglected side of their body. These individuals can also lack awareness or recognize their limbs on the neglected side as their own, a phenomenon referred to as asomatognosia (Kerkhoff, 2001; Kortte & Hillis, 2009; Robertson, 1999).

Peripersonal or near-space extrapersonal neglect involves a lack of awareness of the contralesional side within reaching space and results in clinical signs such as not eating food located on the contralesional half of a plate or seeing only the ipsilesional half or a wristwatch. In far-space extrapersonal neglect, the person neglects the far space or the space beyond one's arm reach. Those having extrapersonal neglect will fail, for instance, to look on the contralateral side when crossing the street or to find the door of a room when located on the contralesional side.

Based on the frames of reference used, the individual may neglect the contralesional part of space that is opposite the eyes head or body, which can be referred to as viewer-centred or egocentric neglect. Here the spatial coordinates are those of the viewer's visual field of peripersonal space (Hillis, 2006). As a result, individuals with viewer-centred or egocentric neglect may ignore objects placed to the contralesional side of their body. Alternatively, individuals with allocentric neglect use an environmental frame of reference and, in the case of a right hemisphere lesion, will ignore the left part of any stimulus irrespective of its location in the visual scene. The stimulus is represented as surfaces oriented with respect to the viewer and it specifies the orientation with respect to the viewer (Hillis, 2006). Here the midline is defined by the midline of the stimulus rather than that of the viewer. For example the west side of a map will be neglected when presented straight and the east will be neglected if the map is presented upside down. In a third type of neglect, referred to as object-centred neglect-, the person with a right brain lesion will ignore the left part of the object irrespective of manner in which the stimuli is presented. Its location with respect to the viewer is no longer represented (Hillis, 2006). For example the west side of a map will always be neglected irrespective of whether the map is in the ipsilateral or contralesional hemisphere or whether the map is held upside down.

Thus the presentation of signs and symptoms of neglect can be varied making their detection challenging, when overt signs are not present.

2.1.2.3 Assessment of VSN

The clinical tests commonly used to assess VSN are summarized in **Table 2-1**.

Test	What does it reveal?	Constructs involved
Line Bisection Test (Schenkenberg et al., 1980)	Indicates a shift in the perception of the midline. A shift of more than 6 mm from the true midpoint or omission of 2 or more lines on one half of the page indicates the presence of VSN	Visual scanning and egocentric representation i.e. subjective midline
Bells Test (Gauthier et al., 1989)	Indicates the presence of spatial neglect in the near-extrapersonal space. Omission of 6 or more bells on one half of the page indicates the presence of VSN.	Visual scanning and visual attention (to find stimuli among distractors)
Behavioural Inattention Test (Wilson et al., 1987a).	A screening test to assess the presence and extent of VSN. (<196 out of 227 is considered positive for presence of VSN)	Visual scanning, detection of stimuli, visual attention (to find stimuli among distractors), attention to visuospatial features, presence of neglect in functional activities
Star Cancellation Test (Wilson et al., 1987a).	Indicates the presence of spatial neglect in the near-extrapersonal space. (A score of < 44 is positive for the presence of VSN	Visual scanning and visual attention
Apples Test	Distinguishes between egocentric and	Visual scanning, visual

(Mancuso et al., 2015)	allocentric neglect. Six omissions or more is considered pathological for presence of neglect.	attention and spatial representation
Catherine Bergego Scale (Bergego et al., 1995a; Deloche et al., 1996).	Is a checklist to detect the presence and severity of VSN in a range of daily activities and neglect self-awareness. 0 = No behavioural neglect;1-10 = Mild behavioural neglect; 11-20 = Moderate behavioural neglect; 21-30 = Severe behavioural neglect	ADL and self-care activities
Figure copying, reading, writing tasks (Jannink et al., 2009; Wertman, 2002).	Explains the patient's frame of reference.	Spatial representation

Paper and pencil tests such as the Bells test (Gauthier et al., 1989), line bisection (Schenkenberg et al., 1980), star cancellation (Wilson et al., 1987a) have traditionally been used to detect the presence of neglect and are still used in a majority of hospitals in both acute and chronic stages of stroke (Pedroli et al., 2015). While these tests can be administered quickly and easily at the patient's bedside and can identify overt signs of left-right spatial asymmetry, they mostly assess VSN within the peripersonal space, they are limited to the horizontal dimension and they do not allow quantification of performance in the far space or the vertical dimension (Pedroli et al., 2015). Moreover, they involve static stimuli, usually of a geometric shape, present in a two-dimensional space and tend to lose sensitivity along the course of recovery due to their fixed and repetitive nature (Chen et al., 2012; Pedroli et al., 2015). Functional activities often involve both static and dynamic stimuli, in both the near and the far space, and are performed in a three-dimensional environment. Thus, performances on these paper-pencil tests do not necessarily reflect the functional abilities of persons with VSN (Chen et al., 2012; Pedroli et al., 2015). In fact, they often lead to misdiagnosis of milder cases of VSN (Buxbaum et al., 2004; Robertson, 1999; Wilson et al., 1987a) since most of these tests were originally designed to evaluate visual function, manual dexterity or intellectual ability (Chen-Sea, 2000).

Moreover, VSN could present in isolation or along with motor neglect, sensory neglect or imagery neglect and could involve the near and/or the far space, involving the egocentric or allocentric reference frame, making it challenging to confirm its presence or absence based on a single test (Kortte & Hillis, 2009; Wertman, 2002). Therefore, the use of a battery of tests that assess different types of neglect is considered more valid to confirm the presence of VSN (Chen et al., 2012).

Recently, the use of computerized assessments have been on the rise due to their greater sensitivity to detect the presence of VSN, its severity and its progression over time (Bonato & Deouell, 2013) and due to their benefits over the limitations of paper-pencil type evaluations (Bonato et al., 2013; van Kessel et al., 2010). However, they present with logistical limitations related to costs, technical usability in clinical settings and yet unproved transferability of performances to real-world functional tasks such as walking (Pedroli et al., 2015; van Kessel et al., 2013a).

Some of these limitations are overcome to an extent by evaluations such as the Behavioural Inattention Test (BIT) and the Catherine Bergego scale (CBS). The BIT includes six conventional tests (cancellation, bisection etc.) and nine behavioural items which examine the presence of neglect during activities such as picture scanning, telephone dialling, map navigation etc. (Wilson et al., 1987b). However, the test is very time consuming and expensive (Teasell et al.) and the items are still restricted to the personal and near-extrapersonal space and are not the ideal measure for detection of VSN (Lezak et al., 2012).

The Catherine Bergego scale in particular is useful as it detects the manifestation of neglect in various activities of daily life and assesses the disability induced by neglect (Azouvi et al., 1996; Bergego et al., 1995b; Chen et al., 2012). However, it does not distinguish motor and sensory contributions to the functional impairments and tracking improvements in specific functional items remain challenging (Plummer et al., 2003).

Despite recovery of independent walking being a critical goal for persons with stroke, measures that assess safety and independence of VSN+ individuals while walking in community settings are rather limited. This is especially pertinent since walking in the everyday environment involves challenges such as avoidance of obstacles, walking on different terrains, or performing dual-tasks while walking (Shumway-Cook et al., 2003). This thesis focuses on two of the demands frequently encountered during community ambulation: *obstacle avoidance* in response to moving objects and *dual-tasking*.

Despite the limitations mentioned earlier concerning the clinical measures for VSN, the participants included in the studies of this thesis were recruited based on clinical observations and/or paper-pencil test performances, as routinely performed in our rehabilitation centres. After providing informed consent, participants were re-tested for VSN on at least two clinical measures: the Bells test, the Line bisection test (and the Apples test in case of the dual-task study in Chapter 5). Recruitment into the VSN+ or VSN- group was thus based on initial diagnosis and confirmed (or refuted) before performing the obstacle avoidance assessment. While walking includes interaction in the personal near and far extrapersonal spaces, it was not possible to classify participants based on these criteria, due to a lack of standardized and valid measures distinguish far space vs. near space VSN.

2.1.2 REQUIREMENTS OF OBSTACLE AVOIDANCE

The environments we walk in are frequently cluttered with various obstacles, such as trees, benches, pedestrians and vehicles, i.e. obstacles that need to be safely avoided in order to proceed towards our intended goal. In fact, the ability to meet internally generated goals (for example, reaching a desired destination) and adapt to externally enforced demands (such as avoiding obstacles in the walking path) is an important requirement for successful locomotion (Patla, 1999; Patla et al., 1991; Patla, 1997). The act of walking towards a goal while avoiding obstacles in the path is complex and requires an integrated functioning of different systems including the sensory, motor and cognitive systems to detect the presence of the obstacle, and subsequently plan and execute the appropriate avoidance strategy.

Specifically, the visual system plays a prominent role in the control of heading and obstacle avoidance as it provides information about self-motion and the environment, which is used for the production of anticipatory locomotor adjustments (Harris & Bonas, 2002; Warren et al., 2001a, 2001b). Visual exploration of the space provides obstacle or target related information such as its size and its dimension, its egocentric location, instantaneous distance of the obstacle/target, as well as its speed and direction of movement (in case of a moving obstacle or target). Along with the proprioceptive and vestibular system, the visual system also inform the observer about its position and orientation in space and in relation to objects in the environment (Patla et al., 2004). Information regarding self-motion can also be obtained through optic flow, which is the visual movement pattern projected on the retina while walking though an environment (Gibson, 1958; Warren et al., 2001b),.

As walking continues, the spatial relationships with the obstacles or the target are constantly changing, necessitating frequent monitoring and updating of this information. Such "spatial updating" is also undertaken the visual system. This visual information is used to determine the risk of collision, and whether the current trajectory must be continued or modified in order to avoid the obstacle or reach the target. For example, based on the size of the obstacle and the velocity and direction of its movement, time to collision (TTC) can be calculated, which in turn provides information about the time available to execute an appropriate avoidance strategy (Carel, 1961; Cutting et al., 1995; Gibson, 1958; Tresilian, 1991). Similarly, based on the angle formed by individuals' heading trajectory with the edge of the object (i.e. gaze-movement-angle) the time to bypass (TTB) can be calculated which is used to estimate the speed and direction of the trajectory that needs to be adopted to avoid the obstacle (Cutting et al., 1995; Peper et al., 1994; Tresilian, 1994)

Some authors have also suggested the concept of a personal space which is a protective or 'buffer' zone maintained by the person that provides sufficient time to perceive environmental hazards as well as plan and execute gait adaptations (Gerin-Lajoie et al., 2005; Templer, 1992b).

An intention to maintain this distance from the obstacle at all times could be used to modulate the future walking path and successfully avoid an obstacle (Gerin-Lajoie et al., 2005).

The control of heading in space and in relation to the obstacle or target can be used to modulate the walking trajectory in order to avoid an obstacle. Fajen et al. (Fajen & Warren, 2003, 2007; Fajen et al., 2003) proposed a *dynamic behavioural model* for obstacle avoidance in humans where the intended goal acts as an attractor such that in order to reach the goal, an individual must minimize the error in heading with respect to the goal. Contrastingly, the object to be avoided, for example, an obstacle, acts as a repeller, entailing an increase in heading error to avoid a collision. This balance of attraction and repulsion determines the final walking trajectory.

The *bearing angle model* (Cutting et al., 1995) discusses how walking trajectories are modulated in order to intercept moving targets or avoid moving obstacles. The bearing angle is the angle subtended between the instantaneous heading of the individual and that of the obstacle, at a given point of observation. According to this model if a continuously moving individual maintains a constant bearing angle with a moving object, a collision is likely to occur. The observation of a constant bearing angle with an obstacle should trigger a modification of the locomotor strategy, for example, by changing the current direction of heading and/or speed of walking to avoid a collision. Information regarding bearing angle is obtained to a large extent from visual cues such as optic flow, egocentric motion cues, and other non-visual cues such as proprioception, vestibular information, inertial cues or motor references (Fajen et al., 2013; Fajen & Warren, 2003; Fajen et al., 2003).

Thus, visuospatial attention plays a critical role in anticipatory and online locomotor control and the ability to obtain pertinent visuospatial information important for successful obstacle avoidance. The presence of VSN in persons with stroke, however, interferes with the ability to obtain the relevant visual information, especially when the objects of interest are located in the contralesional or neglected side of space and may therefore impair obstacle avoidance abilities.

2.1.2.1 Influence of post-stroke VSN on mobility and obstacle avoidance abilities

Locomotion after stroke is characterised by slow gait speed (Vonschroeder et al., 1995), poor endurance(Dean et al., 2001), poor walking balance (Michael et al., 2005), altered movement coordination (Lamontagne et al., 2007a) and a reduced ability to adapt to the task and environmental constraints (Lamontagne et al., 2003; Said et al., 1999). These deficits may interfere with the ability to safely execute the planned avoidance strategy within the time available. However, walking abilities of persons with VSN are significantly poorer than those of persons with stroke without VSN and the presence of VSN is considered as a negative prognostic factor for recovery of walking independence in the acute, sub-acute and chronic stages post-stroke (Nijboer et al., 2013; Oh-Park et al., 2014; Paolucci et al., 2008a).

VSN+ individuals demonstrate significantly lower levels of functional ambulation, slower walking speeds, poorer walking balance with a greater need for supervision, a greater use of assistive devices and a greater risk for falls compared to individuals without VSN (VSN- individuals) (Chen et al., 2015; Friedman, 1990; Paolucci et al., 1996; Paolucci et al., 2001; Stein et al., 2009; van Nes et al., 2009a; van Nes et al., 2009b). Statistics on mobility status at discharge from rehabilitation hospitals are quite astounding, with only 3.6% of VSN+ individuals walking independently outdoors and on uneven surfaces, or climbing stairs independently compared to 32.1% of VSN- individuals (Paolucci et al., 2001). Other studies indicate that VSN+ individuals require a significantly longer period of time in order to achieve comparable levels of walking independence (Jackson et al., 2000a; Stein et al., 2009; van Nes et al., 2009b). On the longer term, however, VSN+ individuals still remain at a disadvantage in terms of community mobility relative to VSN- individuals (Goto et al., 2009a; Jackson et al., 2000a; Suzuki et al., 1997).

Further, their ability to modulate heading while walking can also be impaired. This was observed by Berard and Lamontagne (Berard et al., 2012), and Aburub and Lamontagne (Aburub & Lamontagne, 2013) where persons with VSN failed to utilize visuospatial cues such as optic flow to guide locomotion. In fact, even individuals with a history of neglect i.e. those individuals no longer displaying signs of neglect on the paper-pencil tests, also showed persistent deficits in their ability to use optic flow to “steer” towards a target. Several studies have also observed that in persons with VSN, walking straight ahead to a target or between doorposts resulted in trajectories that were deviated either to the contralesional or the ipsilesional side of the midline (Huitema et al., 2006; Robertson et al., 1994; Tromp et al., 1995; Turton et al., 2009). The side to which they deviated depended on whether they relied on their subjective midline to walk straight ahead, therefore causing an ipsilesional deviation, or aligned their subjective midline to the target resulting in a contralesional deviation of their walking trajectory (Huitema et al., 2006). Thus, a walking strategy planned on the basis of a distorted spatial map was also altered. For obstacle avoidance, an impaired walking strategy executed in response to an obstacle may therefore be ineffective in negotiating the obstacle safely, resulting in collisions.

Finally, due to the ipsilesional bias, the exploration of contralesional side is affected. Thus, the monitoring and tracking of spatial relationships with the obstacles on the contralesional side too may be impaired in persons with VSN. For a constantly moving object whose movements in space may be unpredictable, a failure to update the relevant spatial information will hinder making the necessary modifications to the walking trajectory, increasing the risk of collision. A tendency to collide with objects has, in fact, been reported by a few studies that assessed the ability of persons with VSN to walk in the presence of obstacles (Robertson et al., 1994; Tromp et al., 1995; Turton et al., 2009; Webster et al., 1989). Turton et al. (Turton et al., 2009) observed that while walking in a hospital corridor persons with VSN often collided with the walls while Tromp et al. (Tromp et al., 1995) observed that persons with VSN often collided with static objects that were placed along side the walking path. The collisions were observed with objects in contralesional and/or ipsilesional side of space and were attributed to a deviation in the walking trajectory (Robertson et al., 1994), failure in detection of these objects (Tromp et al., 1995; Turton et al., 2009) and to the lack of readiness to avoid the collision (Webster et al., 1989). Even associated movements such as shoulder and trunk rotations that are required while passing through a narrow aperture are absent in persons with VSN (Tromp et al., 1995), resulting in collisions with doorposts. *However, there have been no studies that had evaluated ability of persons with VSN to negotiate moving obstacles while walking.*

Moving obstacles are potentially more susceptible to collisions since their movements in space are unpredictable and require frequent visual exploration and updating in order to avoid collisions. Considering that the avoidance of moving obstacles, such as navigating through a crowded place, is an important component of community ambulation and has implication on the safety and independence of persons with VSN, it is important to understand whether or not persons with VSN after a stroke are able to safely negotiate such obstacles when they approach from different sides of space. Therefore, the focus of our first study was on the ability of VSN+ individuals to avoid moving obstacles while walking.

2.1.3 DUAL-TASK WALKING

In daily life, we frequently perform more than one task at a time (Bowen et al., 2001; Kizony et al., 2010; O'Shea et al., 2002; Yang et al., 2007a). For example, walking is often performed in conjunction with other tasks such as carrying loads, scanning the environments, changing directions, negotiating obstacles, or engaging in social interactions (Patla & Shumway-Cook, 1999; Shumway-Cook et al., 2002). Such an ability to perform more than one task at a time i.e. dual-tasking, is advantageous during walking because it allows for communication between people, transportation of objects from one location to another and monitoring of the environment so that threats to balance can be avoided (O'Shea et al., 2002).

Dual-task performance involves the execution of a primary task (such as walking) and a secondary task (of equal or unequal importance) performed at the same time (O'Shea et al., 2002). The secondary task could be a motor task (such as carrying a tray or buttoning up of a shirt), a cognitive task (such as performing an arithmetic calculation), a memory task (remembering a shopping list), or a more ecological task (talking or responding to a set of questions).

2.1.3.1 Dual-task interference

Often during dual-tasking, the performance of one or both tasks may be different than when each task is performed individually. This change in the performance of the components of the dual-task relative to the single task performance is known as *dual-task interference or cognitive-motor interference* (when the competing task is a cognitive task) (Della Sala et al., 1995). This change in the performance for each task is often quantified as the dual-task cost and is the percent change in the performance measure during the dual-task, relative to the single task performance.

Dual-task cost (%) = (single task- dual-task)/single task x 100

The main framework underlying dual-task interference or cognitive motor interference is that (a) the capacity of the central information processing is limited, (b) performance of any task imposes demands on a certain portion of this processing capacity and that (c) if the processing demands of all the tasks performed together exceed this total processing capacity, deterioration of one or more tasks will be observed (Abernethy, 1988; Siu & Woollacott, 2007). Such dual-task interference while walking is, therefore, likely to be greater when walking control is altered (e.g. after a stroke) or if attentional deficits (such as VSN) are present.

2.1.3.2 Dual-task walking abilities in persons with stroke

A majority of studies that evaluated the ability of persons with stroke to perform a dual-task while walking observed a deterioration of their walking performance i.e. a *posture-second* strategy. Performing a cognitive, verbal or a motor task while walking mainly led reductions in walking speed, stride length, step length, increased double support time and an increased risk for falls (Bowen et al., 2001; Hyndman et al., 2002; Hyndman et al., 2006; Plummer et al., 2013; Plummer-D'Amato et al., 2008). Tatakori and colleagues found that performing a verbal fluency task resulted in an increase in the time taken to clear obstacles and an increase in the failure to clear obstacles while stepping over them, even while walking at self-selected speeds, putting them at an increased risk of falls (Takatori et al., 2012a; Takatori et al., 2012b). Contrastingly, Smulders and colleagues found no change in the rate of failures to step over an obstacle while walking, but observed that persons with stroke made more errors on an Auditory Stroop task when performed along with the obstacle avoidance task (Smulders et al., 2012).

In other studies involving stroke survivors, a deterioration of performances for both the walking and the competing tasks was observed. Kemper and colleagues observed a reduction in walking speed, cadence and stride length while walking and talking but also showed a greater number of pauses and reduced utterances per narrative (Kemper et al., 2006). Patel and colleagues too observed that in a dual-task situation, along with slower walking speeds, persons with stroke showed larger reaction times on a visuomotor reaction time task and fewer correct responses on a serial subtraction and Stroop task (Patel et al., 2014).

Thus, among persons with stroke, the type and the extent of interference varied between studies. Dennis et al. suggested that the type of interference was dependent on the nature of the tasks being performed (Dennis et al., 2009). They observed that walking while performing a serial subtraction task led to slower walking speeds and a prioritization of the cognitive performance in persons with stroke i.e. a *posture-second strategy*; while walking while performing a visuospatial task led to more errors on the visuospatial task and a maintenance of the walking performance i.e. a *posture-first strategy.* Additionally, Yang et al. observed that the extent of interference was also task dependent; tasks with a higher balance requirement led to greater deterioration of the walking performance compared to those that involved fine motor activities (balancing glasses on a tray vs. buttoning up a shirt) (Yang et al., 2007a).

In summary, performing a dual-task while walking is challenging for persons with stroke and leads to a worsening of their locomotor and/or cognitive performances. These dual-task decrements can be attributed to the impaired walking control resulting from the stroke-related sensorimotor deficits, requiring greater attention to be diverted to the control of walking. Given that the attentional resources are limited, the addition of a second task competes with the control of walking for these resources, leading to the interference (Plummer et al., 2013).

Persons with VSN after a stroke experience attentional deficits in addition to stroke-related sensorimotor deficits, further burdening the already limited attentional resources. Therefore it is likely that they will experience a greater impact of dual-tasking compared to persons with stroke free of VSN. While there have been no studies that have specifically evaluated dual-task walking abilities in VSN+ individuals, evidence from other paradigms are supportive of this claim.

2.1.3.3 Responses to dual-task conditions in individuals with VSN

Robertson and Fresca (Robertson & Frasca, 1992a) hypothesized that individuals with VSN are vulnerable to a deterioration in performance when faced with additional attentional loads since they experience both lateralized (attentional bias, orientation bias) and non-lateralized attention (reduction in attentional capacity and arousal) deficits. In support of these assumptions, several studies involving VSN participants have reported greater omissions of contralesional stimuli and reduced exploration of the contralesional space when the attentional demands were increased by the addition of a secondary task (Bonato, 2012; Bonato et al., 2013; Eramudugolla et al., 2010; Marshall et al., 1997; Rapcsak et al., 1989). Robertson and Frasca (1992) and Van Kessel et al. (2013) observed that the left-right asymmetries on a reaction time task greatly increased when the reaction time task was combined with a cognitive(Robertson & Frasca, 1992a) or motor task (van Kessel et al., 2013b).

Interestingly, as task demands increase or the task becomes more complex, symptoms of VSN become more apparent (Pillon, 1981), sometimes resulting in a re-emergence of well compensated neglect (Robertson & Manly, 2004) and revealing even mild signs of inattention in patients who did not show neglect (Bonato, 2012; Buxbaum et al., 2006; Buxbaum et al., 2008; Pillon, 1981; van Kessel et al., 2013a; van Kessel et al., 2013b; Webster et al., 1995). Bonato et al. proposed that the absence of signs or symptoms of neglect during the single task may reflect the availability of resources just enough to perform one task (Bonato et al., 2010). An assessment of performance on a dual-task condition may therefore be able to identify otherwise subtle signs of neglect that may be missed by clinical evaluations and making them more informative than single tasks in the assessment of recovery from VSN (van Kessel et al., 2010). In addition, the greater sensitivity of dual-task assessments in identifying risk of falls and other functional limitations encourage their use over single task assessments (Li et al., 2005).

Based on these results and on the performance of persons without VSN after a stroke, it is likely that dual-task walking will cause a worsening of the neglect symptoms as well as a deterioration of the walking performances in persons with VSN. In the context of obstacle avoidance, such dual-task decrements will increase their risk for collisions with the obstacles, compromising their safety and independence while walking.

Considering that challenges such as dual-tasking and negotiating moving obstacles are frequently encountered while walking in the community, it becomes imperative to the investigate whether persons with VSN are be able to cope with these task demands. Therefore, in our second study we attempted to study the influence of dual-tasking on the obstacle avoidance abilities, in post-stroke VSN+ individuals.

2.1.4 USE OF VIRTUAL REALITY TO ASSESS OBSTACLE AVOIDANCE, NEGLECT AND DUAL-TASKING

The ideal, ecological scenario for the assessment of obstacle avoidance and dual-task abilities would be an assessment of walking in the community setting, with real physical obstacles approaching from different directions and while simultaneously carrying out a meaningful cognitive task. Such a setting, however, cannot be controlled and repeatedly reproduced in the real world, and it involves an inherent risk of accident with the objects. Virtual reality offers a safe, controlled and realistic environment in which testing can be performed and the performances can be recorded in a standardized manner (Milhejim et al., 2013). It allows for the environment to be manipulated to present different stimuli (Fink et al., 2007) and is a strong tool for perception-action studies (Olivier et al., 2014).

Virtual reality can be defined as a "range of computing technology that present computer-generated images to user that are perceived as being similar to real world objects and events" (Holden & Dyar, 2002; Kalawsky, 1993; Rheingold, 1991). It acts as a user computer interface that involves real-time simulation of a real or imagined environment or world(Fitzgerald & Riva, 2001) that allows for interaction via multiple sensory channels(Burdea, 2003). Virtual reality (VR) presents richly complex multimodal sensory information to the user and can elicit a substantial feeling of realness and agency, despite its artificial nature (Riva et al., 2006). Fink et al. (Fink et al., 2007) recognize the use of virtual reality as providing us with an *"…opportunity to bring naturalistic visual–motor behaviour into the laboratory and study it experimentally, with informational manipulations and proper controls. In particular, ambulatory virtual environments in which the participant can walk freely while wearing a head-mounted display (HMD) provide a new tool with which theories of visually guided locomotion can be rigorously tested."*

Virtual reality technology has been successfully utilized to demonstrate human locomotor behaviour as a part of crowd dynamics, human motion and pedestrian navigation including obstacle avoidance situations (Corbetta et al., 2015; Fink et al., 2007; Olivier et al., 2014; Sloot et al., 2014). Concerns regarding the difference in scaling and underestimation of distance judgment have been resolved by studies that demonstrated no statistical difference in spatial measures such as margins of safety or personal space and path curvatures between the real and the virtual world (Gerin-Lajoie et al., 2008a; Gerin-Lajoie et al., 2005). Thus, locomotor performances observed in a virtual world can be considered to be similar to real world responses (Gerin-Lajoie et al., 2008a; Gerin-Lajoie et al., 2005), supporting the generalization of findings in the virtual world to the physical world. In addition, VR offers the advantage that the obstacles do not pose any real physical danger to the participants even in case of collisions, encouraging its use for assessment of locomotor obstacle avoidance behaviour (Fink et al., 2007).

Virtual reality and other computerized assessments have also been extensively used to detect the presence of neglect and understand exploration patterns in persons with VSN (Plummer et al., 2006) (Erez et al., 2009; Halligan & Marshall, 1989) and even used to mimic ambulation with the use of a joystick (Bonato et al., 2013; Buxbaum et al., 2012b; Buxbaum et al., 2006; Katz et al., 2005; van Kessel et al., 2013a; van Kessel et al., 2013b). Our group was among the first to utilize the technology to assess overground, non-restrictive locomotion in VSN+ individuals. Recent reviews (Ogourtsova et al., 2015; Pedroli et al., 2015) found evidence to support that VR based VSN assessments were more sensitive in identifying the presence of VSN in individuals who were judged as not having neglect based on the conventional paper pencil tests. These reviews also emphasized the need to perform more functional assessments to identify the presence of neglect on functional tasks that mimic challenges faced by the individual on a day-to-day basis.

Keeping in mind advantages offered by the use of VR technology a virtual environment setup was used in the present thesis to assess the locomotor obstacle avoidance and dual-task behaviour in post-stroke individuals with and without VSN.

2.2 OBJECTIVES AND HYPOTHESES OF THE THESIS

The overarching aim of this thesis was to evaluate the influence of post-stroke VSN on the ability to negotiate moving obstacles while walking and to further assess the impact of dual-tasking on these obstacle avoidance abilities. This was addressed in two main sets of experiments that yielded findings presented in four different manuscripts. The first set of experiments evaluated the influence of VSN on the ability to *perceive* and *avoid* collisions with moving obstacles during overground *walking* and during a *joystick-driven navigation* task. In the second set of experiments, I assessed how obstacle avoidance performance of post-stroke individuals with and without VSN is influenced by the *addition of a simultaneous cognitive task*.

The specific objectives and hypotheses of the four manuscripts are presented below.

2.2.1 CHAPTER 3: PERCEPTUAL AND LOCOMOTOR FACTORS AFFECT OBSTACLE AVOIDANCE IN SUBJECTS WITH VISUOSPATIAL NEGLECT

Several studies have shown the tendency of VSN+ individuals to collide with static objects placed alongside their walking path (Tromp et al., 1995; Turton et al., 2009; Webster et al., 1989), but their response to moving obstacles remains unexplored. ***The main objective of this study was to evaluate the ability of persons with VSN to detect moving obstacles (perceptuo-motor task) approaching from different directions and to avoid collisions with such obstacles during a goal directed locomotor task performed in a virtual environment (VE). The second objective was to explore the relationship between clinical evaluations of VSN and the obstacle avoidance performances***. Since VSN+ individuals demonstrate an impairment in obtaining relevant visual information from the contralesional side of space, I hypothesized that in VSN+ individuals, the detection and avoidance of a contralesionally-approaching obstacles would be impaired compared to ipsilesionally-approaching obstacles. I further hypothesized that the clinical evaluations of VSN, which are limited to evaluating the near-space and involve static stimuli, would not be associated with the obstacle avoidance performance.

2.2.2 CHAPTER 4: A VIRTUAL REALITY BASED NAVIGATION TASK TO UNVEIL OBSTACLE AVOIDANCE PERFORMANCE IN INDIVIDUALS WITH VISUOSPATIAL NEGLECT.

In order to understand the contribution of attentional-perceptual deficits resulting from VSN and stroke-related sensorimotor deficits to the obstacle avoidance behaviour observed in Manuscript 1 (Chapter 3), VSN+ individuals were further evaluated in a seated, joystick-driven obstacle avoidance task which minimized the biomechanical demands of locomotion. ***The primary objective of this study was to estimate the ability of VSN+ individuals to detect and avoid moving obstacles approaching from different directions, in a joystick-driven navigation task. The secondary objective was to estimate the extent to which obstacle detection time and clinical evaluations of VSN were related to the obstacle avoidance performance during the joystick navigation task***. I hypothesized that due to the ipsilesional bias introduced by VSN, the detection and avoidance of obstacles approaching from the contralesional side and from head-on would be altered, and would result in higher collision rates for the contralesional obstacles compared to the ipsilesional obstacles. I also hypothesized that the VSN+ participants would maintain asymmetrical spatial relationships with the obstacles, similar to those observed during the locomotor obstacle avoidance task (Manuscript 1). I further expected that the joystick-driven obstacle avoidance performance would be explained by the performance on the obstacle detection task, but not the clinical measures of VSN.

2.2.3 CHAPTER 5: DUAL-TASKING NEGATIVELY IMPACTS OBSTACLE AVOIDANCE ABILITIES IN POST-STROKE INDIVIDUALS WITH VISUOSPATIAL NEGLECT: TASK COMPLEXITY MATTERS!

Avoiding obstacles and coping with changing cognitive demands are two essential requirements of independent community ambulation. Performing a cognitive task while walking often causes worsening of locomotor abilities in post-stroke individuals due to the increased attentional demands of performing two tasks at once. The impact of dual-tasking on the locomotor obstacle avoidance abilities of VSN+ individuals, who already experience attentional-perceptual impairments, was not known. ***The main objective of this study was to estimate the extent to which the addition of a cognitive task during obstacle avoidance, i.e. dual-tasking, alters the obstacle avoidance abilities of post-stroke individuals with and without VSN. The secondary objective was to understand the impact of task complexity on the dual-task performance of VSN+ and VSN- individuals.*** I hypothesized that the concurrent performance of a locomotor and cognitive task would cause cognitive-motor interference both in VSN+ and VSN- individuals. The extent of interference, however, would be larger in VSN+ individuals than in VSN- individuals. Also, since VSN symptoms become more apparent with increases in task complexity (Bonato, 2012), I hypothesized that the interference would be greater when exposed to a more complex cognitive task.

2.2.4 CHAPTER 6: POST-STROKE VISUOSPATIAL NEGLECT INTERFERES WITH THE MODULATION OF HEADING REQUIRED FOR SUCCESSFUL OBSTACLE AVOIDANCE AND GOAL-DIRECTED WALKING.

In VSN, the ipsilesional bias and the altered egocentric representation of the environment impair the utilization of visuospatial cues such as position or orientation in space, or heading in space which are used to guide locomotion. As a consequence, the ability of VSN+ individuals to modulate their locomotor heading relative to objects of interest such as obstacles in the walking path or the final target may be impaired. ***The main objective of this study was to compare, between VSN+ and VSN- stroke individuals, changes in heading and head orientation in space while a) avoiding obstacles approaching from different directions and b) reorienting towards the final goal i.e. target. Secondary objectives were to evaluate the influence of direction of obstacle approach on measures of obstacle avoidance and alignment with the target and to examine the relationship of clinical measures of VSN and cognitive function with locomotor measures related to obstacle avoidance and alignment with the target.*** I hypothesized that VSN+ individuals, compared to VSN- individuals, would show a preference to orient their heading and head towards the ipsilesional side in response to approaching obstacles, and would display larger heading errors with respect to final destination (target); these alterations would be more pronounced for obstacles approaching from the neglected (left) side than for obstacles approaching from the right side or from head-on. I further hypothesized that the clinical measures of VSN, cognitive status and balance confidence would not be associated with locomotor measures reflecting obstacle avoidance or target alignment performance.

CHAPTER 3

3.1 PREFACE

The study of VSN in humans is marked by an abundance of static perceptual studies, but very few of them address this syndrome in the context of ambulatory navigation, especially for complex tasks such as obstacle avoidance. The studies that did investigate walking and obstacle avoidance conducted the assessments with static obstacles that were placed outside the walking path and had several limitations with regards to their study design and study population. There have been no studies that investigated how VSN+ individuals negotiate moving obstacles, even though such obstacles are commonly encountered in the community and may pose an additional risk of accidents and falls due to their unpredictable nature and their constantly changing spatial relationship

MANUSCRIPT 1: PERCEPTUAL AND LOCOMOTOR FACTORS AFFECT OBSTACLE AVOIDANCE IN PERSONS WITH VISUOSPATIAL NEGLECT

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3.2 ABSTRACT

Background: For safe ambulation in the community, detection and avoidance of static and moving obstacles is necessary. Such abilities may be compromised by the presence of visuospatial neglect (VSN), especially when the obstacles are present in the neglected, i.e. contralesional field. **Methods**: Twelve participants with VSN were tested in a virtual environment for their ability to a) detect moving obstacles (perceptuo-motor task) using a joystick with their non-paretic hand, and b) avoid collision (locomotor task) with moving obstacles while walking in the VE. The responses of the participants to obstacles approaching on the contralesional side and from head-on were compared to those during ipsilesional approaches. **Results**: Up to 67 percent of participants (8 out of 12) collided with either contralesional or head-on obstacles or both. Delay in detection (perceptuo-motor task) and execution of avoidance strategies, and smaller distances from obstacles (locomotor task) were observed for colliders compared to non-colliders. Participants' performance on the locomotor task was not explained by clinical measures of VSN but slower walkers displayed fewer collisions. **Conclusion**: Persons with VSN are at the risk of colliding with dynamic obstacles approaching from the contralesional side and from head-on. Locomotor-specific assessments of navigational abilities are needed to appreciate the recovery achieved or challenges faced by persons with VSN.

Key words: Circumvention, Collisions, Hemineglect, Perception, Stroke, Virtual reality, Walking.

3.3 INTRODUCTION

Visuospatial neglect (VSN) is an attentional-perceptual disorder affecting 25% to 30% of persons living with the consequences of a stroke (Appelros et al., 2002; Buxbaum et al., 2004). It alters the detection and utilization of relevant visual information from the side opposite to the brain lesion (Guariglia et al., 2005). It is best described as a failure to report, respond to or orient to novel or meaningful stimuli presented to the side opposite the brain lesion(Heilman et al., 1985). VSN has been shown to impact motor performance in a variety of tasks (Cherney et al., 2001; Edmans & Lincoln, 1990), including locomotion (Chen-Sea et al., 1993; Paolucci et al., 2001). While independent walking is one of the main goals of rehabilitation post stroke (Lord et al., 2004), persons with VSN demonstrate a poor walking recovery (Kollen et al., 2005). They show deviations in their walking trajectory (Huitema et al., 2006), collide with walls and furniture (Turton et al., 2009) and present with an increased risk of falls (Alexander et al., 2009; Jehkonen et al., 2000), making independent walking unsafe (Zihl, 1994). Attentional bias to the ipsilesional side due to lack of inhibition by the affected hemisphere (Kinsbourne, 1993), distorted space representations (Bisiach et al., 1996) and a lack of visual exploration on the contralesional side (Sprenger et al., 2002) have been suggested as explanations for their colliding behaviours.

Community ambulation involves challenges of different terrains and entities that may enter into one’s walking path (Gerin-Lajoie et al., 2005). Dynamic obstacles, which are commonly encountered in community environments such as malls and crowded streets, are especially challenging in that they have constantly changing spatio-temporal characteristics. Avoidance of dynamic obstacles demands the retrieval and processing of information obtained from the environment as well as the planned and coordinated execution of online locomotor adjustments (Iaria et al., 2008). This requires simultaneous and coordinated functioning of attentional, sensory and motor systems, which can be compromised in post-stroke VSN. To our knowledge, the ability of persons with VSN to negotiate dynamic obstacles while walking remains unexplored but is highly pertinent to rehabilitation of such individuals (Peskine et al., 2011). In a recent report, participants who were apparently completely recovered from VSN based on standard ‘paper and pencil’ assessments were shown to display altered walking trajectory adjustments in response to changing visual motion information (Berard et al., 2012). It was suggested that clinical assessments may not be adequate to identify deficits in processing visual motion and far space stimuli. Furthermore, a complex and challenging task such as walking may lead to the neglect symptoms becoming more apparent (Buxbaum et al., 2008). These observations raise the question as to whether conventional clinical assessments for VSN can explain functional performance while walking. In this study, we examined the ability of persons with VSN to detect moving obstacles (perceptuo-motor task) and to avoid collisions with such obstacles during a goal directed locomotor task performed in a VE. The VE provided the ideal setting given that it is safe, controlled and ecological while yielding behaviours similar to what is observed in the real world (Gerin-Lajoie et al., 2005). We hypothesized that in individuals with VSN, the abilities to detect and circumvent moving obstacles approaching from the neglected (contralesional) side are altered as compared to the non-neglected (ipsilesional) side. We further hypothesized that the performance in the perceptuo-motor task better explains obstacle avoidance behaviours while walking than that on clinical VSN assessments.

3.4 METHODS

Sample size was estimated using GPower 3.1.2, for the *analysis of variance for repeated measures* with the 3 directions of approach as a "within" subject factor, assuming a large effect size (0.40) and moderate correlation (0.50) between directions of obstacle approaches. A sample size of 12 participants was obtained at a power of 80 % and a type 1 error of 0.05.

Twelve participants with VSN following a first time unilateral supratentorial stroke (Table 3-1) were recruited from an inpatient rehabilitation centre based on the following inclusion criteria: a stroke confirmed by a CT scan/MRI; a clinical diagnosis of VSN based on the motor free visual perceptual test (MVPT) and/or the Star Cancellation test; an ability to walk independently with or without a walking aid over 10 metres; and motor recovery scores ranging from 3 to 6 out of 7 on the leg and foot impairment inventories of the Chedoke McMaster Stroke Assessment. Individuals with a diagnosed visual field defect (Goldman perimetry test), cognitive deficits (scores <26 on the Mini-Mental State Examination) or other co-morbid conditions (musculo-skeletal, cardiovascular, neurologic) interfering with locomotion were excluded. Participants varied in their comfortable walking speed with values ranging from 0.45 to 1.02m/s (0.74 ±0.17m/s, mean±1SD). Six of them used a cane during the experiment. The study was approved by the ethics committee of the Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal and all participants gave their informed consent.

3.4.1 EXPERIMENTAL SET-UP AND PROCEDURES

Participants took part in two evaluation sessions taking place no more than one week apart and which included, in a random order, clinical tests, the perceptuo-motor task and the locomotor task. Clinical assessment comprised tests for visuospatial neglect (Bells (Gauthier et al., 1989) and Line Bisection (Schenkenberg et al., 1980) tests), cognitive/executive function (Montreal Cognitive Assessment, Trail Making B) and comfortable walking capacity over 10m. All participants were identified as right handed on the Edinburg Handedness Inventory.

The perceptuo-motor and locomotor tasks were conducted while the participants viewed the VE in an nVisor SX60 HMD (NVIS, USA). The VE consisted of a room with dimensions matching that of the physical room (12m x 8m). A blue circular target was present on the wall at the far end (11m) of the virtual room and three red cylinders (obstacles) were positioned in front of a theoretical point of collision in an arc of radius 3.5m at 0° (middle) and 30° right and left (Figure 3-1). The theoretical point of collision (TPC) is the point where the participant and the obstacle paths, if left unaltered, would meet and collide together. Participants were positioned at the beginning of the virtual room facing the centred target. After advancing forward by 0.5m, one of the 3 obstacles randomly started moving in the direction of the TPC and beyond at a speed of 0.75 m/s. A fixed speed and a fixed angle of approach was chosen in order to keep the walking distance to the target consistent. The diagonal obstacles crossed the midline (straight path from starting position to the target) after crossing the TPC.

3.4.1.1 Locomotor task

In the locomotor task, participants were instructed to walk at comfortable speed towards the blue target. They were instructed to avoid a collision with an approaching obstacle, if any, but were not given any instructions on how to avoid the obstacle. A trial could present one of the four conditions randomly: obstacle approaching from the centre, left or right, as well as a control trial which was devoid of any moving obstacle. Control trials were used to determine baseline walking speed and trajectory in the absence of moving obstacles. In case of a collision, visual feedback was provided in the form of a flashing "Collision" sign. Participants were provided with 2 practice trials per condition and 4 to 7 trials per condition were collected, depending on endurance.

Positions of 3 reflective markers placed on the HMD were tracked by a 12-camera Vicon-512™ motion capture system (UK) and fed to the CAREN 3™ virtual reality software (Motek BV, Amsterdam) to provide the real-time update of the participants' perceived position and orientation in the VE. Markers were also placed on specific body landmarks specified in the full body maker set of the Plug in Gait model from Vicon (Appendix A), with 2 additional markers placed on the walking aid when applicable. Data were recorded at 100Hz in CAREN 3™ and at 120Hz in Vicon™.

3.4.1.2 Perceptuo-motor task

For the perceptuo-motor task, participants were seated and responded using a joystick (Attack3, Logitech, USA) held by the non-paretic hand and placed at a comfortable height, while viewing the VE in the HMD. The forward motion of the obstacle was set at 0.75 m/s, a speed representative of ambulatory stroke population (Vonschroeder et al., 1995). A forward displacement of 0.5m triggered one of the 3 obstacles to move, or a catch trial with no moving obstacle. The catch trials were aimed at preventing anticipatory responses. The participants were instructed to press the joystick button as soon as they perceived the onset of obstacle motion, or to withhold any response in the absence of an obstacle. In the failure to press the button in the presence of a moving obstacle, the obstacle continued to move ahead and a collision ensued. The participant was not informed about the collision event. Participants were provided 2 practice trials for each condition and performed 10 trials for each of the 4 conditions for a total of 40 condition

3.4.2 DATA ANALYSIS

For the purpose of the analyses, obstacles were identified as approaching from the contralesional side, the middle and the ipsilesional side. For the perceptuo-motor task, the detection time was calculated as the time taken after the movement onset of the obstacle for the subject to press the button. For the locomotor task, the minimum absolute distance was calculated as the minimum distance maintained between the participant and the obstacle, before the obstacle passed beyond the participant. The number of trials in which a collision was detected was divided by the total number of trials for each of the conditions to give the percent collision. In order to determine the presence of a collision, a critical distance was set for each participant, calculated as the sum of the radius of the obstacle and the distance between C7 and the lateral-most marker on the body or walking aid. When the distance between the participants and the obstacle dropped below this critical distance, a collision event was detected. Onset of an avoidance strategy was measured as the time at which a medio-lateral displacement (of the head markers) exceeding 0.25m (half of average shoulder width) on either side was detected. Preferred sides of avoidance strategy were also noted.

3.4.3 STATISTICAL ANALYSIS

The effects of direction of obstacle approach (i.e. contralesional, head on, ipsilesional) on detection time, minimum absolute distance and onset of avoidance strategy were examined using separate repeated measure analyses of variance (ANOVAs), followed by Tukey post-hoc comparisons with Bonferroni adjustments. Probability level was set at $p<0.05$. Collision rates were compared across conditions using a non-parametric Kruskall-Wallis test. Pearson correlation coefficients were used to quantify the relationship between measures of obstacle avoidance performance (minimum distance, percent collision, onset of avoidance strategy) and performance on the perceptuo-motor task (detection time) as well as on clinical assessment of neglect (Bell's Test, Line Bisection Test), executive function (Trail Making B) and walking capacity (walking speed). Correlations were carried out separately for each obstacle approach.

3.5 RESULTS

3.5.1 VSN AND PERCEPTUO-MOTOR PERFORMANCE

Presence of VNS was confirmed in all 12 participants, with positive results on the Bells and/or Line Bisection tests. Participants scoring positive (>6 omissions (Gauthier et al., 1989)) on the Bell's test (n=4), showed 6 to 18 omissions. Those positive (error >0.6cm (Schenkenberg et al., 1980)) on the line bisection test (n=12), showed errors between 0.9 and 4.8cm. On the perceptuo-motor task, there was a significant difference in detection times across directions ($F(3, 35) = 20.72$; $p=0.01$) with participants taking significantly longer times ($p<0.05$) to detect contralesional than ipsilesional obstacles (Figure 3-3A).

3.5.2 LOCOMOTOR PERFORMANCE

No falls occurred during the testing and none of the participants reported any discomfort or dizziness due to the VE. Figure 3-2 represents walking trajectories of two participants, one collider and one non-collider, in response to different obstacle approaches. Both participants showed a clear preference to deviate to the ipsilesional side, sometimes even in the absence of an obstacle i.e. in the control trials (see non-collider). The collider participant repeatedly collided with the contralesional obstacle, which caused him to stop walking, and showed no collision for the middle and ipsilesional obstacles.

When considering all participants, the minimum distance maintained from the obstacle differed across obstacle directions [$F(3, 35)=8.133$; $p=0.0114$]. Compared to the ipsilesional obstacle, participants maintained smaller distances from the contralesional ($p<0.005$) and middle obstacles ($p<0.05$) (3- 3B). This difference was maintained when the collision trials were excluded from the analysis ($F(3, 35)=9.159$; $p=0.001$). Five participants out of 12 collided with the contralesional obstacle and 8 collided with the middle obstacle, while no collisions occurred with the ipsilesional obstacle in any of the participants. Average percent collisions were 48.11% (12% to 70% of trials) and 49.34% (40% to 65% of trials), respectively, for participants showing collisions with the contralesional and middle obstacles (Figure 3-3C).

3.5.3 COLLIDERS VS. NON-COLLIDERS

To understand the factors that differentiate participants who collided from those who did not collide in the locomotor task, their performances were examined and qualitatively compared for the contralesional and middle approaches. A statistical approach was not feasible due to the small number of participants in each group. In the perceptuo-motor task, detection times for the contralesional and middle obstacles, expressed as a ratio of the ipsilesional obstacle detection time, revealed that colliders with contralesional and middle obstacles took longer to detect the obstacles compared to non-colliders (Figure 3-4). In the locomotor task, colliders maintained smaller minimum distances from the obstacles and initiated their avoidance strategies later compared to non-colliders for the contralesional and middle obstacles. All participants showed a preference to deviate their trajectories to the ipsilesional side, with no clear differences between the colliders (Contralesional obstacle: 83%; Middle obstacle: 78%) compared to the non-colliders (Contralesional obstacle: 71%; Middle obstacle: 91%). Note that for ipsilesional approaches and for control trials where no obstacles were moving, participants veered ipsilaterally in 86% and 74% of the trials, respectively.

Colliders and non-colliders showed similar results on the Bells, Line Bisection and Trail Making B tests (Table 3-2). However, colliders with the contralesional obstacles walked faster (0.56±0.08m/s) than non-colliders under the same condition (0.31±0.08m/s), as well as in control trials. No speed differences between middle obstacle colliders and non-colliders were observed during the middle obstacle approach and control trials.

Finally, while the contralesional colliders tended to present a better motor recovery of the paretic leg and foot compared to contralesional non-colliders (mean difference of 1 unit on the Chedoke McMaster Stroke Assessment), the head-on colliders and non-colliders did not show much difference (See Table 3-2).

3.5.4 RELATIONSHIP BETWEEN PERCEPTUO-MOTOR AND WALKING PERFORMANCES

No significant associations were observed between detection times on the perceptuo-motor task and the participants' performance on the locomotor task, as measured by minimum distances maintained from the obstacle, percent collisions and onset of trajectory deviation ($p>0.57$). Performances on the perceptuo-motor and locomotor tasks did not correlate with the results on the Line Bisection Test, Bells Tests and Trail Making B ($p>0.5$). Walking speed during the trials was not related to percent collisions but it was, however, negatively associated with the minimum distance for contralesional ($r=-0.761$, $p=0.004$) and ipsilesional obstacles ($r=-0.878$, $p<0.0001$). Smaller minimum distances were associated with larger percentage of collisions for contralesional and middle obstacles (Contralesional: $r=-0.6366$, $p=0.013$; Middle: $r=-0.622$, $p=0.0155$).

3.6 DISCUSSION

Previous navigation studies involving persons with VSN have aimed at understanding trajectories of walking (Huitema et al., 2006; Robertson et al., 1994; Tromp et al., 1995), object recognition (Dawson et al., 2008; Kim et al., 2007) and collision with static objects present on the side of the walking path (Tromp et al., 1995; Turton et al., 2009). A significant body of literature is also concerned with computer based navigation tasks, where the challenges of locomotion itself are not present (Iaria et al., 2008; Kim et al., 2007; Weiss et al., 2003). The present study adds to previous knowledge by addressing a functional task commonly encountered in daily life using a locomotor-specific evaluation and by investigating the perceptuo-motor and locomotor factors affecting obstacle avoidance abilities. Our results demonstrate, for the first time, that persons with VSN are at greater risk of colliding with moving obstacles approaching contralesionally and from straight ahead, as opposed to obstacles approaching ipsilesionally. Colliders, while displaying a similar severity of neglect on clinical assessments compared to non-colliders, take longer to identify approaching obstacles and display altered steering behaviours. The implication of such findings as well as the contribution of perceptual and locomotor factors are discussed below.

3.6.1 VSN IS ASSOCIATED WITH HIGH RATES OF COLLISIONS WITH MOVING OBSTACLES

One of the most striking findings of this study is that up to 67% of participants (8 out of 12 participants) collided with either or both the contralesional and the head on obstacle, with collisions occurring in almost 1 out of 2 trials in some of the participants. While persons with VSN are reported to bump into stationary objects (Punt et al., 2008; Turton et al., 2009), present collision rates with moving obstacles cannot be compared with previous studies given that collision rates are typically not reported. These high collision rates may compromise safety while walking in community environments where moving obstacles are present. Limited community ambulation, in return, may further delay the recovery of independent walking (Kollen et al., 2005) and reduce quality of life (Pound et al., 1998). These observations highlight the importance of addressing obstacle avoidance abilities in persons with VSN.

3.6.2 INTERACTION OF PERCEPTUAL AND LOCOMOTOR FACTORS

The perceptual deficits in our participants were evident through larger detection times and subsequent delays in onset of avoidance strategy for the contralesional and middle obstacles. These variables also differentiated the colliders from the non-colliders. Since the joystick was held with the non-paretic hand, the results were not biased by the presence of any upper-extremity motor impairment. Moreover, due to the task being a simple joystick-button click, we believe that the handedness would not invalidate the results. Similar to other studies in VSN (Butler et al., 2004; Dvorkin et al., 2012), a gradient of increasing detection times was observed from the ipsilesional to the contralateral visual field. Minimum distances from the obstacles maintained by participants in the present study were also smaller for contralesional and middle approaches, suggesting that their ‘personal space’, defined as the perceived safe distance an individual maintains from another object/person while walking (Gerin-Lajoie et al., 2005; Templer, 1992a), is contracted on the contralesional side. Other possible explanations include an altered internal representation of space that is compressed towards the ipsilesional side (Halligan & Marshall, 1991), an altered sense of position with respect to objects (egocentric coordinates) located in the neglected field (Karnath, 1997) and an ipsilesional shift of the subjective midline(Huitema et al., 2006) which could cause the contralesional and the middle obstacle to remain unattended in the contralesional field.

Healthy young and elderly individuals (Gerin-Lajoie et al., 2006), and individuals with stroke but no VSN (Darekar et al., August 2013), tested on a similar obstacle-avoidance paradigm, were shown to increase their ‘safety margins’ when additional attentional challenges were introduced. Older adults were also shown to slow down their gait when confronted with moving obstacles (Gerin-Lajoie et al., 2006). Conversely, VSN participants in the present study maintained smaller distances from middle and contralesional obstacles. They also maintained walking speeds similar to that adopted during the control trials where no obstacles were approaching. This absence of an adaptive response to a perceived threat is consistent with an attentional-perceptual disorder that is characteristic of VSN (Guariglia et al., 2005; Heilman et al., 1985).

Although no direct relationships were observed between collision rates and gait speed, faster walkers maintained smaller minimum distances compared to slower walkers for the diagonally approaching obstacles. Furthermore, a qualitative comparison of colliders vs. non-colliders revealed that for the contralesional approach, colliders displayed faster walking speeds and higher level of lower-extremity motor recovery. It is interesting to note that these observations contrast with the common presumption that persons with slower walking speeds or poorer motor recovery present with a compromised walking capacity and should be at higher risk of collisions. We hypothesize that slow walking may have served as a protection by allowing diagonal obstacles passing in front of the participants, therefore preventing a collision. Slow walking speed, however, was not a 'strategy' or context-specific adaptation adopted by the non-colliders since their speeds were similar in the control trials. The unintentional protection offered by the fixed-speed obstacle to the slower walkers can be viewed as a limitation of the experimental design. We predict that greater collision rates may have been observed for the contralesionally-approaching obstacles, had the obstacle speeds matched the walking speeds. Also, this protective effect cannot operate for middle obstacles where directional changes of the walking trajectory are required to avoid a collision.

Given the absence of a comparison group of non-VSN stroke participants, one may debate whether the altered perceptuo-motor and locomotor strategies observed in the present study are attributed to VSN, or to stroke-related sensorimotor deficits. In an other study from our laboratory (Aravind et al., 2015; Aravind & Lamontagne, 2014), participants with VSN were evaluated on a joystick-driven obstacle avoidance task, using their non-paretic hand to manipulate the joystick while seated. In such context that minimized postural and locomotor demands, participants demonstrated collisions with contralesional and middle obstacles, as in the locomotor task described in this study. This observation supports the hypothesis that attentional-perceptual deficits of VSN influence obstacle avoidance abilities. Rates of collision in the joystick-driven task (21% to 26 %), however, were smaller than those observed during walking. This may be due to the influence of stroke-related sensorimotor impairments on locomotion and defective sensorimotor integration processes (for a review (Lamontagne et al., 2007b)), as well as to the increased complexity of the locomotor task that results in VSN becoming more apparent (Buxbaum et al., 2012b; Buxbaum et al., 2006; Webster et al., 1989). Therefore, the additional burden of locomotion may make the task more complex, increasing the rate of collisions.

Additionally, Darekar et al. (Darekar et al., August 2013), using a similar paradigm with obstacles approaching from the middle, ipsilesional and contralesional directions, have shown that individuals with stroke without VSN demonstrated i) no collisions with any of the three obstacles and ii) a tendency to maintain larger distances from obstacles compared to healthy controls, a behaviour that is contrasting to our participants with VSN Thus the presence of sensorimotor deficits post-stroke alone cannot explain the tendency to collide with moving objects.

3.6.3 NEED FOR TASK-SPECIFIC ASSESSMENTS OF AMBULATION ABILITIES

Contrary to our expectations, no associations were observed between the participants' performance on the locomotor task and that on the perceptuo-motor task. This is somewhat surprising given that colliders performed worse, on average, compared to non-colliders on the perceptuo-motor task. We suggest that the participants' locomotor and perceptuo-motor abilities have interacted in generating altered obstacles avoidance strategies, a hypothesis that may be further verified in a larger sample of participants. The perceptuo-motor task also differed from the locomotor tasks in that the participants were seated and responded with a single-alternative button press, facing none of the complex locomotor demands. Persons with VSN may prioritize the limited attentional resources to the control of walking, hence compromising the attention diverted to extrinsic stimuli (Huitema et al., 2006) . Responses on the perceptuo-motor task may not entirely reflect perception while walking.

A lack of relationship was also observed between the participants' performance on the laboratory tasks and clinical scores of VSN, which support previous observations that paper-pencil tests fail to predict performance on visually-guided functional tasks (Buxbaum et al., 2008; Peskine et al., 2011). These clinical tests are limited to near space (Robertson & Halligan, 1999) and static visual stimuli (Berard et al., 2012) and they lose sensitivity for milder cases (Dvorkin et al., 2007) with many of them being originally designed for visual attention and cognitive assessments rather than VSN (Chen-Sea, 2001). Therefore it is essential to carry out a functional, task-specific assessment to appreciate the recovery achieved and the challenges faced by the individuals. The obstacle avoidance behaviours observed in the VE are closely related to the real-world strategies (Fink et al., 2007; Gerin-Lajoie et al., 2008b; Gerin-Lajoie et al., 2005).

Therefore, the performance of individuals with VSN in our study can provide information regarding their safety during community ambulation, lending support to the external validity of our findings. This experimental paradigm can be used to assess and potentially train individuals with neglect after stroke to avoid moving obstacles while walking.

3.7 CONCLUSIONS

Persons with post-stroke VSN show a delayed perception and experience collisions with obstacles approaching from the contralesional side and from straight ahead, as opposed to obstacle approaching from the ipsilesional side. The longer obstacle detection times in the colliders compared to non-colliders suggest that attentional-perceptual deficits, along with sensorimotor impairments and altered sensorimotor integration processes due to the stroke, influence obstacle avoidance strategies and lead to collisions. The failure of clinical tests of VSN to predict the participants' performance on the obstacle avoidance task emphasizes the need for a task-specific assessment of ambulation abilities.

3.8 LIST OF ABBREVIATIONS USED

VSN, Visuospatial neglect; VE, Virtual environment; CT, Computerized Tomography; MRI, Magnetic Resonance Imaging; MVPT, Motor free visual perceptual test; SD, Standard deviation; HMD, Helmet mounted display; ANOVA, Analysis of variance

3.9 COMPETING INTERESTS

The author (s) declare that they have no competing interests.

3.10 AUTHORS' CONTRIBUTION

GA conceived, collected and carried out the experiments. She also carried out the data reduction, analyses of the data and drafting of the manuscript. AL contributed to the design of the study, data analysis, interpretation of results and revision of the manuscript. All authors read and approved the final manuscript.

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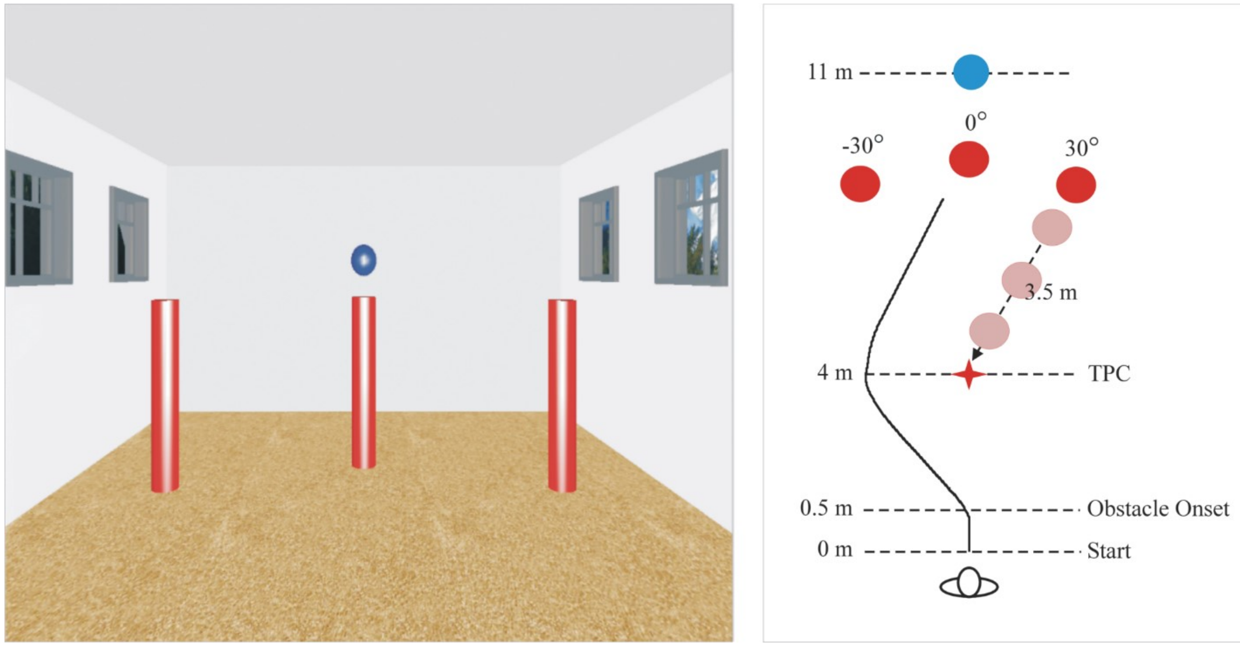

Figure 3-1: Schematic representation of the virtual scene. The left panel shows the screenshot of the virtual scene with the three red cylindrical obstacles and the blue target. The right panel illustrates the dimensions of the testing area and the relative positions of the participant and the obstacles. The red star symbol represents the theoretical point of collision (TPC).

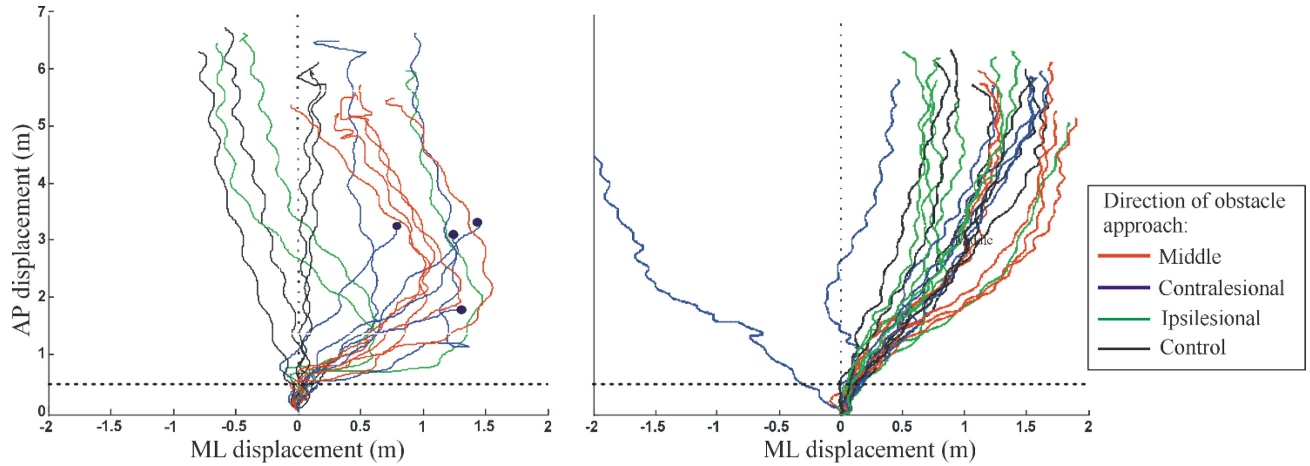

Figure 3-2: Representative diagram of walking strategies adopted by 2 participants. The left panel is the walking pattern of a collider while the right panel consist of walking pattern of a non-collider. Note the collisions experienced by participant #12 [# omissions on Bells test = 9] (see left panel), which are represented by the black dots, and the absence of collision for participant #6 [# omissions on Bells test = 0] (see right panel).

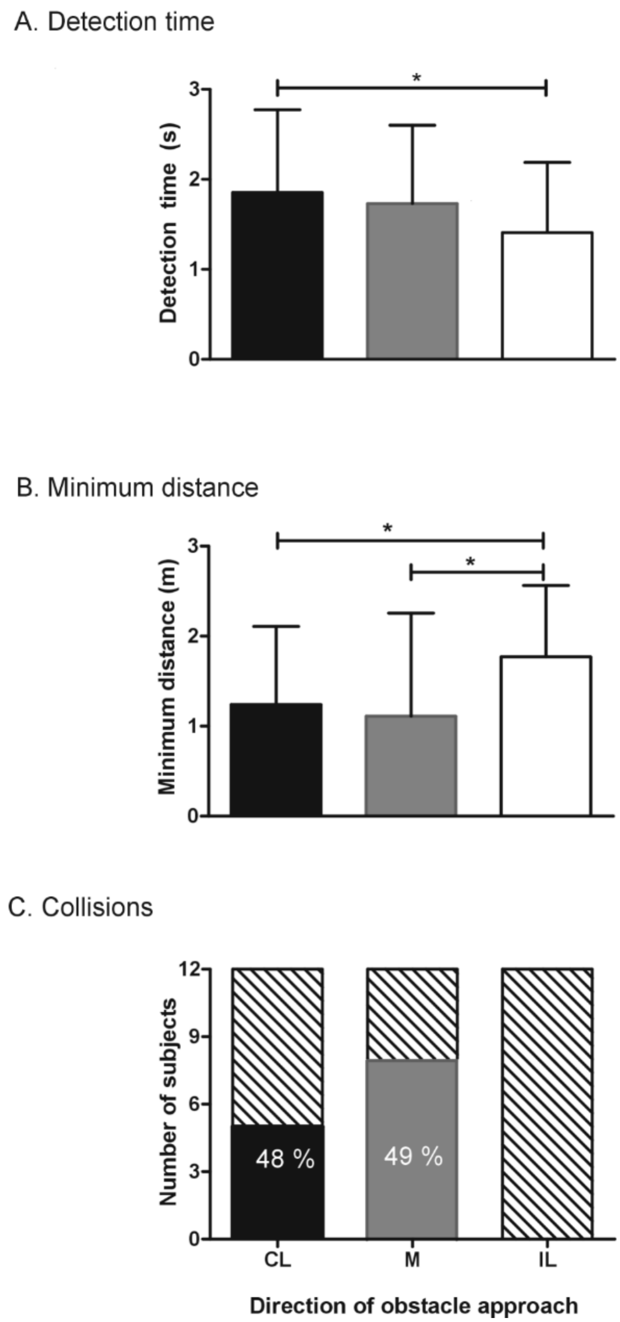

Figure 3-3: Mean ± 1SD values of all participants for A) detection times [perceptuo-motor task] B) Minimum absolute distances maintained between the participants and the obstacles as well as C) the distribution of colliders (solid) and non-colliders (lined) [locomotor task] for the contralesional (CL), middle (M) and ipsilesional (IL) obstacles. The digits in the solid columns indicate the average percentage of trials in which collisions were recorded for the specific obstacle direction. * $p<0.05$.

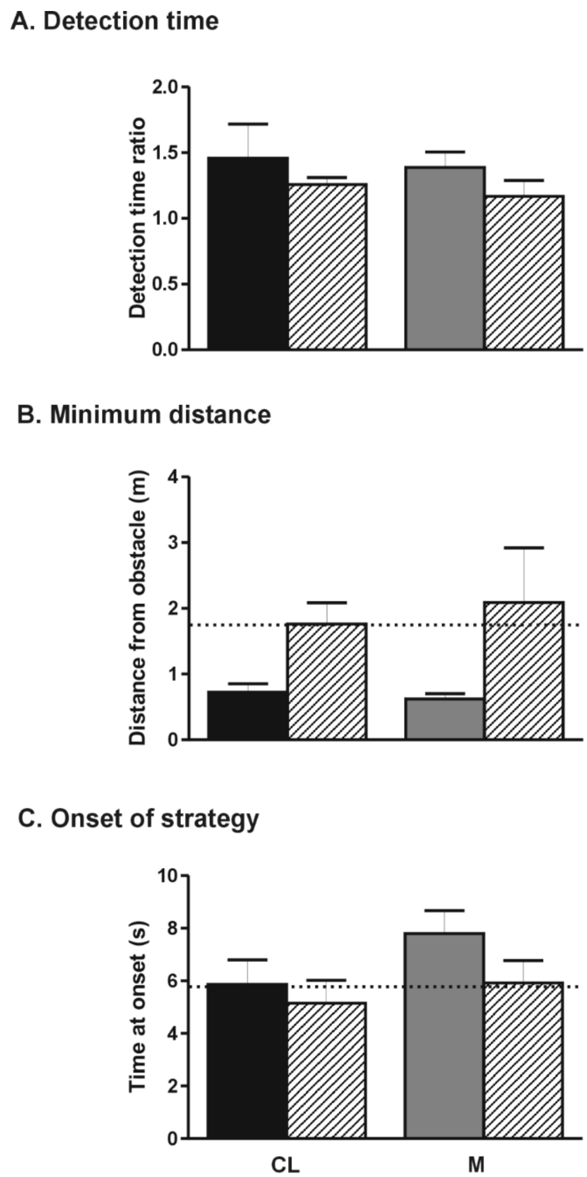

Figure 3-4: Mean (±1SD) values for obstacle detection times [perceptuo-motor task], minimum distances and onset time of avoidance strategy for the colliders (solid bars) and non-colliders (lined bars) [locomotor task] are represented for the contralesional (CL) and middle obstacle (M). Mean values across all participants for the ipsilesional obstacle approach are represented by the dotted line to provide a reference value.

ID	Age (yrs)	Gender	Cane	VSN (MVPT+)	MoCA (/30)	CMMSA leg,foot (/7)	Chronicity (months)	Etiology of CVA	Site of lesion	Collisions
1	50	F	N	+	28	6,5	90	Ischemic	Unspecified right MCA supplied territories	CL + M
2	63	M	Y	+	28	4,3	10	Hemorrhagic	Right subcortical regions, internal capsule, thalamus	M
3	67	F	N	+	23	5,3	6	Ischemic	Unspecified right subcortical regions	None
4	52	F	N	+	27	4,3	4	Ischemic	Right temporo-parietal, frontal	None
5	57	M	Y	+	23	4,3	5	Hemorrhagic	Left internal capsule	M
6	57	F	Y	+*	25	5,3	7	Ischemic	Unspecified right MCA supplied territories	None
7	57	M	N	+	27	5,4	4	Ischemic	Right internal capsule, thalamus & basal ganglia	CL + M
8	72	F	Y	+	-†	4,3	6	Ischemic	Left MCA supplied territories	None
9	65	M	N	+	24	6,4	10	Ischemic	Right MCA supplied territories, watershed areas of ACA and MCA	CL + M
10	72	F	N	+	24	5,4	3	Ischemic	Right Internal capsule, Posterior parietal area with diffuse cerebral atrophy	CL + M
11	69	F	Y	+	24	4,3	13	Ischemic	Right MCA including temporal areas, corona radiata, grey nucleus	M
12	47	F	Y	+	28	5,5	4	Ischemic	Unspecified right MCA supplied territories	CL + M

Table 3-1. Participant characteristics. * Only Cancellation Test was reported in the chart; † Could not assess due to language barriers. Abbreviations: VSN, Visuospatial neglect ; MVPT, Motor Free Visual Perceptual Test; MoCA, Montreal Cognitive Assessment ; CMMSA, Chedoke-McMaster Stroke Assessment (CMMSA); MCA, Middle cerebral artery; CVA, cerebrovascular accident, ACA, Anterior cerebral artery; M, middle ; CL, contralesional; SD, standard deviation.

	CL Obstacle		M Obstacle	
	Colliders (n=5)	Non-Colliders (n=7)	Colliders (n=8)	Non-Colliders (n=4)
Bells Test	6 (3.1)	4.5 (1.8)	5.4 (2.0)	4.7 (3.1)
Line Bisection	1.2 (0.5)	1.8 (0.5)	1.4 (0.5)	1.9 (0.5)
Trail Making B	159.2 (32.8)	189.7 (31.2)	173.3 (28.4)	184.5 (40.5)
CMMSA (Leg)	5.2 (0.4)	4.3 (0.5)	4.8 (0.9)	4.5 (0.5)
CMMSA (Foot)	4.0 (0.7)	3.0 (0)	3.6 (0.7)	3.0 (0)
Walking speed*	0.56 (0.08)	0.31 (0.08)	0.41 (0.08)	0.44 (0.13)
Walking Speed for Control Trial	0.51 (0.12)	0.28 (0.19)	0.37 (0.20)	0.38 (0.23)

Table 3-2. Characteristics of Colliders and Non Colliders for the contralesional (CL) and middle (M) obstacle approaches. Mean values (one standard deviation) are presented. In the Bells test, the values reflect the average number of omissions. In the Line Bisection Test, the values are the error (deviation from the midpoint) in cm. For the Trail Making B, the values indicate the time taken to complete the test, in seconds. CMMSA, Chedoke McMaster Stroke assessment level of motor recovery for the leg and foot components (/7). * Walking speed during the specified obstacle condition in meters/second.

CHAPTER 4

4.1 PREFACE

In the locomotor obstacle avoidance study presented in Chapter 3, we were unable to comment on whether the locomotor behaviours observed were due to VSN itself or to sensorimotor deficits caused by the stroke. In this second manuscript, VSN+ participants were assessed while seated on an obstacle avoidance task which was performed using a joystick held in the non-paretic hand. The main assumption behind this paradigm is that the manipulation of the joystick with the non-paretic upper extremity while seated minimizes the demands of locomotion, thus allowing us to investigate attentional-perceptual demands associated with obstacle avoidance.

Also, for the locomotor study presented in Chapter 3, the obstacles approached at a speed of 0.75 m/s while the participants walked at their preferred walking speeds. Due to their slow walking speed, some VSN participants could thus avoid collisions with diagonally approaching obstacles without implementing any avoidance strategy. With the joystick-driven task used in this manuscript, the participants' speed of progression was matched to the obstacle speed i.e. at 0.75 m/s in order to impose a collision unless an avoidance strategy was initiated.

MANUSCRIPT 2: A VIRTUAL REALITY BASED NAVIGATION TASK TO UNVEIL OBSTACLE AVOIDANCE PERFORMANCE IN INDIVIDUALS WITH VISUOSPATIAL NEGLECT.

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4.2 ABSTRACT

Background: Persons with post-stroke visuospatial neglect (VSN) often collide with moving obstacles while walking. It is not well understood whether the collisions occur as a result of attentional-perceptual deficits caused by VSN or due to post-stroke locomotor deficits. We assessed individuals with VSN on a seated, joystick-driven obstacle avoidance task, thus eliminating the influence of locomotion. **Methods**: Twelve participants with VSN were tested on obstacle detection and obstacle avoidance tasks in a virtual environment that included three obstacles approaching head-on or 30° contralesionally/ ipsilesionally. **Results**: In the detection task, the contralesional and head-on obstacles were detected at closer proximities compared to the ipsilesional obstacle. For the avoidance task collisions were observed only for the contralesional and head-on obstacle approaches. For the contralesional obstacle approach, participants initiated their avoidance strategies at smaller distances from the obstacle and maintained smaller minimum distances from the obstacles. The distance at detection showed a negative association with the distance at the onset of avoidance strategy for all three obstacle approaches. **Conclusion**: The observation of collisions with contralesional and head-on obstacles, in the absence of locomotor burden, provides evidence that attentional-perceptual deficits due to VSN, independent of post-stroke locomotor deficits, alters obstacle avoidance abilities.

Index Terms— Hemineglect, Locomotion, Stroke, Virtual environment

4.3 INTRODUCTION

Commonly after a cerebrovascular accident or stroke, there is a reduction of locomotor control due to various factors including neuromuscular weakness (Lamontagne et al., 2007b; Nadeau et al., 1999), sensory disturbances (Lamontagne et al., 2005), and cognitive factors (Regnaux et al., 2005). Since walking is one of the main determinants of independence (Paolucci et al., 2008b), patients as well as therapists consider the recovery of independent community ambulation as a crucial goal of post-stroke rehabilitation (Patla, 1997). The presence of visuospatial neglect (VSN) is known to worsen this prognosis and slow down the process of recovery of walking (Paolucci et al., 2001).

VSN is often described as an attentional-perceptual disorder in which both the uptake and utilization of visual information on the side opposite to the brain lesion are impaired (Butler et al., 2004; Kinsbourne, 1977). Clinically, the effects of VSN have been observed in many ways such as a complete omission (Hillis, 2006) or a delay in the reaction to relevant stimuli on the contralesional side (Dvorkin et al., 2012; Dvorkin et al., 2007), a shift in the midpoint on line bisection tests (Marshall & Halligan, 1989) and difficulty in utilizing visual information which can alter functional tasks such as eating (Heilman et al., 2003) or navigation (Huitema et al., 2006; Turton et al., 2009).

While 68-82% of individuals without VSN after stroke recover independent walking abilities, less than 40% of individuals with VSN after a stroke are able to walk independently at home or community settings (Goto et al., 2009b). Yet the literature discussing the effects of VSN on walking abilities is rather limited.

So far, navigation studies involving individuals with VSN report deviations of walking trajectories while walking towards a target (Huitema et al., 2006; Punt et al., 2008; Tromp et al., 1995; Turton et al., 2009). Collisions with static objects placed alongside the walking path have also been observed (Buxbaum et al., 2008; Tromp et al., 1995; Turton et al., 2009). Recently, we have demonstrated that persons with post-stroke VSN also collide with moving obstacles approaching from the contralesional (neglected) side and from head-on, while displaying no collision for the ipsilesional (non-neglected) side approach (Aravind & Lamontagne, 2014).

Whether such collisions occur due to the attentional-perceptual deficits associated with VSN or due to postural and locomotor deficits attributed to post-stroke sensorimotor impairments remains unresolved.

In the present study, we propose to assess participants with VSN on an obstacle avoidance task while navigating in a VE with the use of a joystick. The main assumption behind this paradigm is that the manipulation of the joystick with the non-paretic upper extremity while seated minimizes the biomechanical demands of locomotion, thus allowing us to investigate attentional-perceptual demands associated with obstacle avoidance. The primary objective of this study was to estimate the ability of individuals with VSN to detect and avoid moving obstacles approaching from different directions. The secondary objective was to estimate the extent to which obstacle detection time and clinical evaluations of VSN were related to the obstacle avoidance performance. We hypothesized that the detection and avoidance of obstacles approaching from the contralesional side and from head-on would be altered, compared to the ipsilesional approach. Such asymmetry in the detection and avoidance behaviour would be similar to what was observed during locomotion on foot (Aravind & Lamontagne, 2014) and provide further evidence that VSN, independently of post-stroke sensorimotor impairments (hemiparesis), does play a role in the altered obstacle avoidance behaviour. We also expected that obstacle detection time, but not clinical measures of VSN, would be associated with joystick-driven obstacle avoidance performance.

4.4 METHODS

4.4.1 PARTICIPANTS

A convenience sample of 12 participants (8 females, 4 males) with VSN following a first time unilateral supratentorial stroke (10 ischemic, 2 haemorrhagic) was recruited from an inpatient rehabilitation centre (Table 4-1). They presented with a stroke confirmed by a CT scan/MRI and a clinical diagnosis of VSN based on age related norms on the Motor Free Visual Perceptual Test (MVPT) (Colarusso & Hammill, 1972) and/or 4 or more omissions on the Letter Cancellation Test (Diller et al., 1974) which are routinely performed in the hospital. As participants were also involved in a locomotor study (Aravind & Lamontagne, 2014), they were required to have an ability to walk independently with or without a walking aid over 10 metres (Graham et al., 2008) and to present motor recovery scores ranging from 3 to 6 out of 7 on the leg and foot impairment scale based on the Chedoke McMaster Stroke Assessment (Gowland et al., 1993). Individuals with a diagnosed visual field defect (Goldman perimetry test (Zhang et al., 2006)), cognitive deficits (scores <26 on the Mini-Mental State Examination (Folstein et al., 1975)) or other co-morbid conditions (musculoskeletal, cardiovascular, neurologic) interfering with locomotion were excluded.

4.4.2 EXPERIMENTAL SET-UP AND PROCEDURES

Participants were evaluated on clinical assessments and performed three laboratory tasks, an *obstacle detection task, a joystick-driven obstacle avoidance task* and *a locomotor obstacle avoidance task.* The evaluations were randomized in order and conducted in two sessions over two separate days within one week. In this paper we discuss the results for the *obstacle detection task* and the *joystick-driven obstacle avoidance task*, which will hereafter, simply be referred to as the *obstacle avoidance task*. For a detailed description of the *locomotor task,* see our previously published article (Aravind & Lamontagne, 2014).

The clinical assessments comprised of clinical tests commonly used to assess (1) VSN: Bells Test- 6 or more omissions indicate the presence of VSN while 3 or more omissions indicate the presence of a lateralized inattention (Gauthier et al., 1989), Line Bisection test- errors of 0.6 cm or more is indicative of a midline shift (Schenkenberg et al., 1980), (2) cognitive/executive motor function: Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005), Trail-making B test (Reitan, 1958) and (3) hand dominance: Edinburgh Handedness Inventory (Oldfield, 1971)).

Both laboratory tasks were conducted while the participants were seated in a comfortable chair and viewed the VE in a HMD with a 40° horizontal and 60° diagonal field-of-view and a resolution of 1280 x 1084 pixels (nVisor SX60, NVIS, USA). The VE, controlled with CAREN-3^{TM} virtual reality software (Motek BV, Amsterdam), consisted of a room (12 m x 8m) with a blue circular target on the wall at the far end (11m) and three red cylinders (obstacles), 0.5 m in diameter and matched to the participant's height, positioned in front of a theoretical point of collision in an arc of radius 3.5m at 0° (middle) and 30° to the right and left. The theoretical point of collision (TPC) is the point where the participant and the obstacle paths, if left unaltered, would meet (See Figure 4-1). The participants were asked to sit erect facing forwards and responded using a joystick (Attack3, Logitech, USA) held by the non-paretic hand and supported on a table of a comfortable height.

Participants were positioned at the beginning of the virtual room facing the centred target. The forward motion of the subject was set at 0.75 m/s for both tasks, a speed representative of ambulatory stroke population (Vonschroeder et al., 1995). After advancing forward by 0.5m, one of the 3 obstacles started approaching the midline along a straight path, at a speed of 0.75 m/s, or a catch/control trial was introduced, for a total of 4 conditions presented randomly. The catch/control trials were aimed at preventing anticipatory responses. Participants' responded by using a joystick (Attack3- Logitech, USA) held in the non-paretic hand and placed at a comfortable height. Their performance in both laboratory tasks was recorded at 100Hz in CAREN 3™.

4.4.2.1 Obstacle detection task

In this task, the participants were instructed to respond as soon as possible, by clicking a joystick button, on perceiving the onset of obstacle motion. In case of the catch trial, where none of the obstacles moved, the participants were instructed to withhold any response. The failure to respond to the obstacle motion would result in a collision but the participant did not receive feedback about the collision event. All obstacles remained in view during the trial to necessitate visual scanning to identify moving obstacle.

4.4.2.2. Obstacle avoidance task

In the obstacle avoidance task, participants were instructed to proceed towards the target and avoid the oncoming obstacles, if any, by manipulating the joystick. Once the obstacle started moving, the other obstacles disappeared from the participants view. This was designed to isolate responses to one obstacle at a time and bring the target into attention. In the control trials all obstacles disappeared and only the target remained in view. The joystick could be moved forward, backward, to the right or the left in order to move faster, slower and to the right or left direction in the VE. The joystick can be moved from the centre to each extreme position in 64 steps. Each step of the joystick in the medio-lateral (ML) and antero-posterior (AP) direction changes speed of progression by 0.0156 m/s and 0.0117 m/s respectively. In the absence of joystick movement, the participant would proceed in the VE at the speed of 0.75 m/s. The maximum speed of 1.5 m/s and a minimum speed of 0 m/s can be achieved by manipulating the joystick. This differed from the locomotor task where the participant walked at a self-selected speed. By matching the participant and obstacle speed we presented a 'forced-collision' paradigm where a collision would occur unless the participant executed an avoidance strategy. In case of a collision with the obstacle, the participants received feedback in the form of a flashing "collision" sign. The control trial consisted of no obstacles and the participants were instructed to proceed towards the target.

For each task, eight practice trials (2 for each condition) were provided before the start of the experiment. Ten trials for each of the 4 conditions were collected in five blocks of 8 trials each, for a total of 40 trials per task. Participant 1 was a part of a previous protocol where obstacles approached at different speeds. This was then modified to matching speeds for participant and obstacle in order to impose collisions. Only six of those trials were at obstacle speeds of 0.75 m/s and were included in the analysis for participant #1.

4.4.3 DATA ANALYSIS

Primary outcomes for the obstacle detection and obstacle avoidance tasks were, respectively, the distance from the obstacle at detection time and percentage of collision with the obstacle. Secondary outcomes for the avoidance task included the distance at onset of strategy and the minimum absolute distance maintained from the obstacle.

The results of the obstacle detection task were interpreted using a time-based outcome from a previous locomotor study (Aravind & Lamontagne, 2014). As we wanted to explore whether the altered obstacle avoidance behaviour was related to the participants' obstacle detection abilities, it was essential to include also results from the obstacle detection task in the present manuscript. The *distance at detection* was noted as the distance between the participant and the obstacle at the instant when the joystick button was clicked after the obstacle onset. Instead of the time-based outcome used in the locomotor study, we used absolute distances from the obstacle as a measure of detection as it allows us to understand the participants' spatial relationship with the obstacle, which is relevant to a condition like VSN where the spatial orientation with respect to objects is altered especially on the neglected side.

For the obstacle avoidance task, a critical distance from the obstacle calculated as the sum of the radius of the obstacle and half the shoulder width of the participant was set. When the distance between lateral borders of participant's avatar and the obstacle dropped below this critical distance, a collision event was detected. The number of trials in which a collision was detected was divided by the total number of trials for each approach to provide a *percentage of collision*. Any participant who experienced a collision was considered a collider. A change in ML displacement exceeding 0.25 m (half of average shoulder width) on either side was used to identify the initiation of a ML strategy. Similarly, a change in speed of forward progression exceeding or below the average speed ± 2SD during control trials was used to identify the initiation of a speed strategy. The distance between the participant and the obstacle at this instant was used as the *distance at the onset of strategy*. The type of strategy utilized (speed change vs. medio-lateral deviation) and the side to which the navigational strategy occurred were also noted. The *minimum absolute distance* was calculated as the minimum distance maintained between the participant and the obstacle before the obstacle passed beyond the participant. The directions of obstacle approach were termed as contralesional, head-on and ipsilesional, relative to the side of lesion for all participants. Minimum distance was calculated for the three obstacle conditions in trials that did not conclude in a collision. All analyses were done in Matlab.

4.4.4 STATISTICAL ANALYSIS

The effects of direction of obstacle approach (ipsilesional, contralesional, head-on) on average values of distance at detection, minimum absolute distance and distance at onset of avoidance strategy were examined using separate repeated measures one-way analyses of variance (ANOVAs) followed by Tukey post-hoc comparisons with Bonferroni adjustments. Three levels of comparison (contralesional, head-on, ipsilesional) were used for the analysis of distance at detection, distance at onset of strategy and minimum absolute distance. One-sided Pearson correlation coefficients were used to quantify the relationship of obstacle avoidance performance (percent collision, minimum distance, distance at onset of strategy) with the performance on the obstacle detection task (distance at detection), clinical assessments of neglect (Bell's Test, Line Bisection Test) and executive function (Trail-making B). Correlations were carried out separately for each obstacle direction. Outliers, when present, were identified and excluded from the analysis if having a leverage effect greater than p/n, where p= number of independent variables and n= number of observations. The probability level was set at $p<0.05$. All analyses were done in SPSS v.17.0.

4.5 RESULTS

4.5.1 CLINICAL TESTS AND OBSTACLE DETECTION TASK

The participants' performances on the clinical evaluations of VSN and executive cognitive functions are shown in Table 4-1. The participants, who were recruited on the basis of a positive score on the MVPT or Letter Cancellation test, showed a wide range of scores on the Bells test, with some displaying less than 3 omissions (i.e. negative for presence of lateralized inattention (Gauthier et al., 1989)). The time taken to complete the Trail Making B test was, for most participants (except # 12), greater than the age and education related normative values (Tombaugh, 2004). On the obstacle detection task, the participants successfully detected approaching obstacles for all three conditions. However, there was a significant difference in distances at detection time across obstacle approaches ($F (3, 35) =19.11$; $p<0.0001$) with participants detecting obstacles at closer proximity ($p<0.05$) for contralesional (4.6 ± 0.8 m, mean ± 1SD) and head-on (4.6 ±0.7 m) approaches as compared to the ipsilesional approach (5.0 ±0.6 m) (Figure 4-2A).

4.5.2 OBSTACLE AVOIDANCE TASK

Representative traces of the trajectory adopted during the obstacle avoidance task are presented for a collider (left panel) and a non-collider (right panel) participant in Figure 4-3. It can be observed from the top row panels that the collider showed collisions with obstacles approaching contralesionally and from head-on, but not with ipsilesionally-approaching obstacles. Compared to the non-collider participant, the collider showed more variability across trials in terms of direction and extent of ML deviation from the central path. The bottom-row panels are traces of the control trials demonstrating that participants deviated from the central path even when there were no obstacles in their path, but this deviation is of a lesser extent than that observed with an obstacle approaching.

When considering all participants, 5 of them demonstrated collisions with the contralesional obstacle and 9 collided with the head-on obstacle (see Table 4-1). The average collision rates for colliders were 21.2% and 26.2 % for the contralesional and head-on obstacles, respectively, with individual collision rates varying from 10% to 50% of trials. No collisions occurred with obstacles that approached from the ipsilesional side. The minimum distance maintained from the obstacle differed across the directions of obstacle approach ($F(2,35)=36.08$; $p<0.0001$). Post-hoc analysis revealed that participants displayed smaller minimum distances when the obstacle approached contralesionally ($p<0.05$) or head-on ($p<0.05$), as opposed to when it approached ipsilesionally (Figure 4-2C).

In all participants, the initiation of the avoidance strategy during the trial was characterized by a joint increase in speed of progression and ML deviation for all three obstacle approaches, with the ML deviation occurring before or at the same time as the speed change. Hence, ML deviation was used to identify onsets of strategies. The distance at onset of a ML avoidance strategy was found to be significantly different across directions of obstacle approach ($F(3, 35) =13.34$; $p<0.01$) (Figure 4-2E). Participants showed smaller distances from the obstacle at onset of an avoidance strategy for contralesional obstacles compared to ipsilesional obstacles ($p<0.05$), while other comparisons were not statistically significant.

The use of ML deviation as a strategy was associated with a deviation to the same side as the approaching obstacle for the diagonally approaching obstacles. Out of the 12 participants, 11 preferred to deviate ipsilesionally for IL obstacles (82% of trials) and 9 preferred to deviate contralesionally for CL obstacles (87% of trials). For the head-on obstacle an equal number of participants preferred to deviate ipsilesionally (in 81% of trials) and contralesionally (in 91% of trials). For the no obstacle condition, five participants showed a preference to deviate to the contralesional side (72% of trials) while seven participants showed an ipsilesional deviation in a majority of trials (77% of trials).

In a majority of trials, the participants also showed an increase in the speed of forward progression in response to obstacle onset for contralesional (93 ± 10% trials), head-on (96 ± 13% trials) and ipsilesional (93 ± 15% trials) approaches. For the remaining trials, a reduction in speed was observed in response to the onset of obstacle motion.

For non-collision trials, comparing the relative AP positions of the obstacle and the participant at minimum distance allowed us to determine whether the obstacle passed in front or behind the participant for diagonally approaching obstacles, taking into account the side of deviation.

These behaviours are similar to those seen for individuals with right-sided stroke and left-sided VSN. As for individuals with a right-sided stroke, collision rates varied between the two individuals with a left-sided stroke.

4.5.3 COLLIDERS VS. NON-COLLIDERS

To compare the behaviours of the colliders and the non-colliders, we analyzed their performances on the obstacle perception and the obstacle avoidance tasks. Since the number of colliders and non-colliders are small, only observational comparisons are presented. Since no collisions were observed with the ipsilesional obstacle, all participants are classified as non-colliders. In the obstacle detection task, the colliders showed smaller distances at detection for the contralesional and head-on approaches, compared to the non-colliders (Figure 4-2B). In the obstacle avoidance task, colliders displayed smaller distances at onset of ML deviation and maintained smaller minimum distances from the obstacle for the contralesional and head-on approaches, as compared to the non-colliders (Figure 4-2 D & F).

4.5.4 RELATIONSHIP BETWEEN CLINICAL, OBSTACLE DETECTION AND OBSTACLE AVOIDANCE MEASURES

Smaller distances at detection on the obstacle detection task were associated with smaller distances at onset of the strategy in the avoidance task for all three obstacle approaches (contralesional $r = 0.65$; head-on $r=0.72$; ipsilesional $r=-0.55$, $p \leq 0.03$) (Figure 4). Neither the distance at detection nor the distance at onset of strategy, however, showed a significant association with the minimum distance maintained from the obstacle (r= -0.12 to 0.32) or the percentage of collisions (r=-0.41 to -0.27) for any obstacle approach (p> 0.05).

For the detection task, smaller distances at detection was in general associated with greater deficits on the clinical assessments of VSN- the Bells test (r values; c contralesional r= -0.51, head-on r= -0.43 and ipsilesional r= -0.23) and Line bisection test (contralesional r= -0.65, head-on r =-0.61 and ipsilesional r =-0.40). However, these relationships lost significance when one participant (participant #7) who presented with the largest number omissions on the Bells (18 omissions) and largest error on the line bisection test (error=4.8 cm), was identified as an outlier (leverage effect of 47% and 37%, for the Bells and Line bisection test respectively) and was excluded from the analyses. No significant relationships were observed between the clinical measurements of VSN and distance at onset of strategy or the collision rates. In fact, some participants (e.g. Participant #1) who did not demonstrate the presence of neglect on the clinical evaluations (<0.6 cm on the line bisection test and <6 omissions on the Bells test) showed collisions with obstacles, while others (e.g. participant #10) who showed the presence of VSN on clinical assessments did not collide.

Longer times of completion on the Trail-making B test were found to be associated with smaller distances at detection for all three obstacle conditions. The relationship between Trail Making B and distance at onset of strategy was significant for the contralesional approach and tended towards significance for head-on and ipsilesional approaches.

Table 4-2 summarizes the correlation coefficients observed between clinical assessments (VSN and executive function) and the performance of the participants on the obstacle detection and obstacle avoidance tasks. For the associations involving the Bells and Line bisection test the reported r values were obtained after excluding the outlier from the analyses.

4.6 DISCUSSION

This study is a continuum to the study of obstacle avoidance abilities while walking in individuals with post-stroke VSN (Aravind & Lamontagne, 2014). The results of this study show similarities with the locomotor task such as collisions with contralesional and head-on approaches, delay in initiation of an avoidance strategy and smaller minimum distances for CL and HO obstacle approaches. However, the responses in the joystick task differed in their preferred side of strategies, and rate of collisions. Present findings show that the ability to detect and avoid obstacles approaching from the neglected side and head-on is altered in individuals with VSN, even during tasks that minimize locomotor demands.

4.6.1 VSN LEADS TO ALTERED OBSTACLE PERCEPTION AND AVOIDANCE

Visual attention and perception are crucial during obstacle avoidance as they function to detect the obstacle, track its approach and provide feedback about the success of the adopted navigation strategy. Attentional-perceptual deficits in our participants were observed in the form of smaller distances at detection for contralesional and head-on obstacles compared to ipsilesional obstacles. Since the obstacle was moving at a constant speed, smaller distances at detection indicate that participants took a greater amount of time to detect them.

Despite being a seated task where the locomotor and postural demands were minimized, smaller distances at onset of strategy, and smaller minimum distances were observed for contralesional and head-on obstacles in the obstacle avoidance task. Collisions were also observed for the latter two obstacle approaches, but not for the ipsilesional approach. Based on the concept of *'personal space'* (Gerin-Lajoie et al., 2008a), the minimum distance outcome reflects the participants' perception of a safe distance from the obstacle at which sufficient time and space is available to avoid a collision. Smaller distances from the obstacle at initiation of strategy or smaller minimum distances will provide less time and space to plan and execute a safe and effective avoidance strategy, putting participants at risk for collisions. The presence of a direction-specific pattern of collisions on a joystick-navigation task and the presence of a positive association between the distance at detection (perceptual task) and distance at onset of strategy (obstacle avoidance task) further support a specific involvement of VSN in the altered obstacle avoidance behaviour.

Our findings also revealed the presence of a gradient in the performance of the participants, where the distances at detection and distances at onset of strategies were the largest for the ipsilesional approach and decreased i.e. worsened, for the head-on and contralesional approaches. The observation of such a gradient, which is demonstrated for the first time with moving stimuli, is in agreement with many studies in VSN showing gradients of increasing reaction times to static stimuli, as one proceeds from the ipsilesional field towards the midline and into the contralesional field (Butler et al., 2004; Deouell et al., 2005; Dvorkin et al., 2007; Smania et al., 1998). In fact, computerized reaction time tasks have been found to be more sensitive compared to paper and pencil evaluations of VSN; being able to detect the presence of even mild or sub-clinical VSN even in chronic post-stroke stages (Bonato et al., 2012; Rengachary et al., 2009) The ipsilesional attentional bias and/or the predisposition to initiating visual scanning of the environment from the ipsilesional side, commonly seen in individuals with VSN, may be responsible for this gradient (Dvorkin et al., 2012; Smania et al., 1998). The rightward shift of the egocentric representation which is commonly observed in VSN, may also be responsible for the delay in detection and initiation of response to the obstacles observed for the CL and HO obstacles (Richard et al., 2004).

The spatial asymmetry across the three directions of obstacle approach, observed for minimum distance and distance at onset of strategy, could be attributed to the asymmetrical representation of visual space seen in VSN (Bisiach & Luzzatti, 1978; Karnath & Ferber, 1999) where the representation of the space is considered to be pathologically expanded on one side and contracted on the other. While there remains a controversy in literature about whether or not the representation of space is altered in VSN, our results are consistent with a compression of the contralesional space resulting in an under-estimation of spatial relationships between self and the surrounding objects located on the neglected side. As a result, the objects or obstacles end up being much closer to the individuals before they are perceived as being threatening. Alternatively, the shift of ER may explain the spatial asymmetry of the minimum distance across the three directions of obstacle approach. The failure to centrally process sensory inputs coordinates from the visual field into an egocentric body-centred coordinate system (Karnath et al., 1991) is observed in VSN. This affects the subjective localization of body orientation and may cause a shift of the 'midline' towards the ipsilesional side and alter the judgment of distance from the obstacle. These spatial relationships, along with the global optic flow caused by self-motion and the local optic flow generated by the moving obstacle, when altered could affect obstacle avoidance abilities and goal-directed locomotion (Warren & Rushton, 2009; Warren & Fajen, 2008). Non-lateralized deficits of attention (Robertson et al., 1995), arousal (Heilman et al., 1978), working memory and processing (Husain & Rorden, 2003) observed after stroke may also affect the detection of obstacles, and planning and execution of avoidance strategies and when co-existing with spatially lateralized deficits, may further impact the ability to avoid obstacles .

Buxbaum et al. [59] observed that 20 out of 25 participants with VSN collided with left-sided objects while propelling themselves in a virtual environment using a joystick, compared to only 1 out of 31 post-stroke participants without VSN. Additionally, in a case study involving a joystick-driven obstacle avoidance task by Darekar et al.(Darekar et al., 2015) post-stroke individuals free of VSN showed no collisions with objects that approached from different directions, and maintained a symmetrical clearance between contralesional and ipsilesional obstacle approaches. These observations are consistent with findings of the present study and, taken together, support the presence of a VSN-specific alteration in obstacle avoidance abilities, which may be attributable to an altered spatial representation.

On analyzing the types of strategies utilized, we observed that a combination of change in ML deviation and an increase in speed was adopted in a majority of trials. The observation that participants deviated to both ipsilesional and contralesional sides is consistent with other VSN studies involving walking and wheelchair navigation (Huitema et al., 2006; Tromp et al., 1995; Turton et al., 2009). Interestingly, the deviations to both sides were observed for control trials as well. One explanation for this behaviour could be that, participants who were aware of their neglect compensated by deviating to the contralesional while those who were influenced by the ipsilesional bias or midline-shift deviated to the ipsilesional side.

The increase in speed along with the ML deviation was used to pass in front of the obstacle, which contrasts with results from our walking experiment (Aravind & Lamontagne, 2014) where the obstacles passed in front of the participants. We suggest that, as the participants were not limited by their walking and balance capacity in this joystick-driven task, they were able to take advantage of the speed and direction changes allowed in our experimental design. As a result, a delay in the detection of the obstacle and a delay in the initiation of an avoidance strategy did not necessarily lead to a collision. This may explain, to some extent, the lack of relationship observed between obstacle movement perception and collision rates in the present study. However, as no relationships were observed between the detection and avoidance of moving obstacles while walking in the same group of participants (Aravind & Lamontagne, 2014), other factors such as choice of strategy, and executive cognitive skills may influence the avoidance strategy. Further comparisons of the results on the joystick-driven task presented in this study vs. our previous study on locomotor obstacle avoidance (Aravind & Lamontagne, 2014) show the presence of larger collision rates, longer latencies for onset of strategy and smaller minimum distances during the locomotor task. Walking trajectory and speed adjustments are further affected by post-stroke sensorimotor impairments (Darekar et al., August 2013; Lamontagne & Fung, 2009; Marshall & Halligan, 1989; Nadeau et al., 1999). In the presence of obstacles, attentional resources also need to be divided between the control of locomotion, and detection and avoidance of obstacles. Altogether, this challenges the attentional resources that are already limited in individuals with VSN (Huitema et al., 2006). Therefore, complex tasks such as obstacle avoidance that compete for attentional resources can make the neglect symptoms more apparent (Buxbaum et al., 2012a).

4.6.2 CLINICAL MEASURES OF VSN ARE NOT REFLECTIVE OF OBSTACLE DETECTION AND AVOIDANCE ABILITIES

Paper-and-pencil tests such as the Bells test and the Line bisection test are often used clinically to evaluate the presence of VSN and its recovery post-stroke. For our participants, the results on these tests did not show any association with the outcomes such as rates of collisions, or distance at onset of strategy (joystick-navigation task). Interestingly, we observed that performances on these paper-and-pencil tests of VSN were negatively associated with distances at detection but the association lost significance with the exclusion of an outlier (participant # 7) who showed greatest deficits amongst our participants on the Bells and Line bisection tests. The disparity between performance on clinical tests of VSN and performance on the obstacle detection and avoidance task could be caused by the difference in the types of stimuli and the nature of the task experienced by the individuals. On the one hand, the paper-and-pencil tests are limited to near space, consist of static stimuli and are performed in a two-dimensional space (Aravind & Lamontagne, 2014; Buxbaum et al., 2008; Deouell et al., 2005). Our test in the VE, on the other hand, incorporates moving stimuli in the 3-dimensional space, which enables recognition of more subtle effects of neglect (Dvorkin et al., 2012) and also presents the danger of a collision.

Other studies have also observed that participants who are considered to have recovered based on paper-and-pencil tests of VSN continue to show neglect symptoms during more challenging tasks such as walking or wheelchair navigation (Berard et al., 2012; Buxbaum et al., 2012a; Buxbaum et al., 2008). In fact, similar to previous studies using computerized assessment to detect VSN, (Bonato & Deouell, 2013; Bonato et al., 2012; van Kessel et al., 2010) we too were able to detect asymmetries across the visuospatial field in the obstacle detection task even in participants who did not show deficits on clinical evaluations (e.g. participants # 1, 5, 11 and 12). Moreover, the navigation task involves more complex processes such as route navigation and planning that are not accounted for in the paper-and-pencil tests leading to the lack of an association. Thus we can confirm our hypothesis that the clinical tests of VSN are insufficient to reflect impairments in complex activities such as the avoidance of moving obstacles. These findings are in agreement with the results of our previous study on locomotor obstacle avoidance (Aravind & Lamontagne, 2014) where we reported a lack of association between clinical tests and detection time. Post-stroke individuals who do not show deficits on paper-and-pencil tests of VSN may show signs of neglect on more complex and demanding tasks and therefore must be evaluated on complex tasks that mimic functional demands.

The detection of the obstacle and the initiation of a strategy involve visual attentional and executive skills that are assessed by the Trail-making B test. Individuals with poorer executive functioning showed smaller distances at detection and at onsets. The minimum distance and rates of collision, however, are more complex outcomes that are influenced by detection of obstacle and initiation of strategy but also factors such as choice of avoidance strategies that are not evaluated by the Trail making B, which may be the reason for the absence of an association between this test and obstacle avoidance performance outcomes. This finding differs from our previous study (Aravind & Lamontagne, 2014) where we did not find an association between Trail making B and detection time. We attribute it to the use of a distance-based outcome instead of time-based outcome, which allowed us to better understand spatial relationships between the participant and the obstacle given that the uptake of spatial information, especially from the neglected side is altered in individuals with VSN. Due to the position of the obstacles along an arc around the TPC, the distance of the participant from the obstacle was different for diagonally approaching obstacles (contralesional and ipsilesional) and head-on obstacles, so that they arrive at the TPC at the same time. As a result, for a given detection latency, distances between the participant and obstacle for a diagonally approaching obstacle is not the same as for an obstacle approaching head-on. This may be one reason for observing a relationship between Trail making B and distance at detection even though we did not observe a relationship between Trail making B and detection time in the previous study (Aravind & Lamontagne, 2014).

4.7 STUDY LIMITATIONS

One limitation of this study is the degrees of freedom assigned to the participant via the joystick control. The joystick does not allow rotation along the vertical axis to mimic horizontal rotation of the head/body that are used as strategies during obstacle avoidance (Patla et al., 1999). Additionally, the range of speed (0 to 1.5 m/s) provided to the participants was not reflective of their overground walking speed ranges. Together these may limit the generalization of the findings to actual locomotion. VSN is considered to be more severe in the far extra-personal space compared to the near space (Butler et al., 2004; Cowey et al., 1994a). Since obstacle avoidance involves interaction mainly within the far space, including an assessment for far space VSN may help further explain collision behaviours.

4.8 CONCLUSIONS

The key implication of the findings in this study is that attentional-perceptual deficits contribute to poor obstacle avoidance performance in individuals with VSN. Individuals with VSN showed a delay in detection of obstacles approaching from the contralesional and head-on directions and also collided with these obstacles, even in the absence of a locomotor burden. Since moving obstacles are commonly encountered during community ambulation, it is important to assess the risks involved with independent ambulation in the presence of VSN post-stroke. The experimental paradigm used in this study could be used as a quick and easy, task-specific assessment to examine the ability of VSN individuals to safely negotiate obstacles before a more detailed walking assessment is conducted.

4.9 ACKNOWLEDGEMENT

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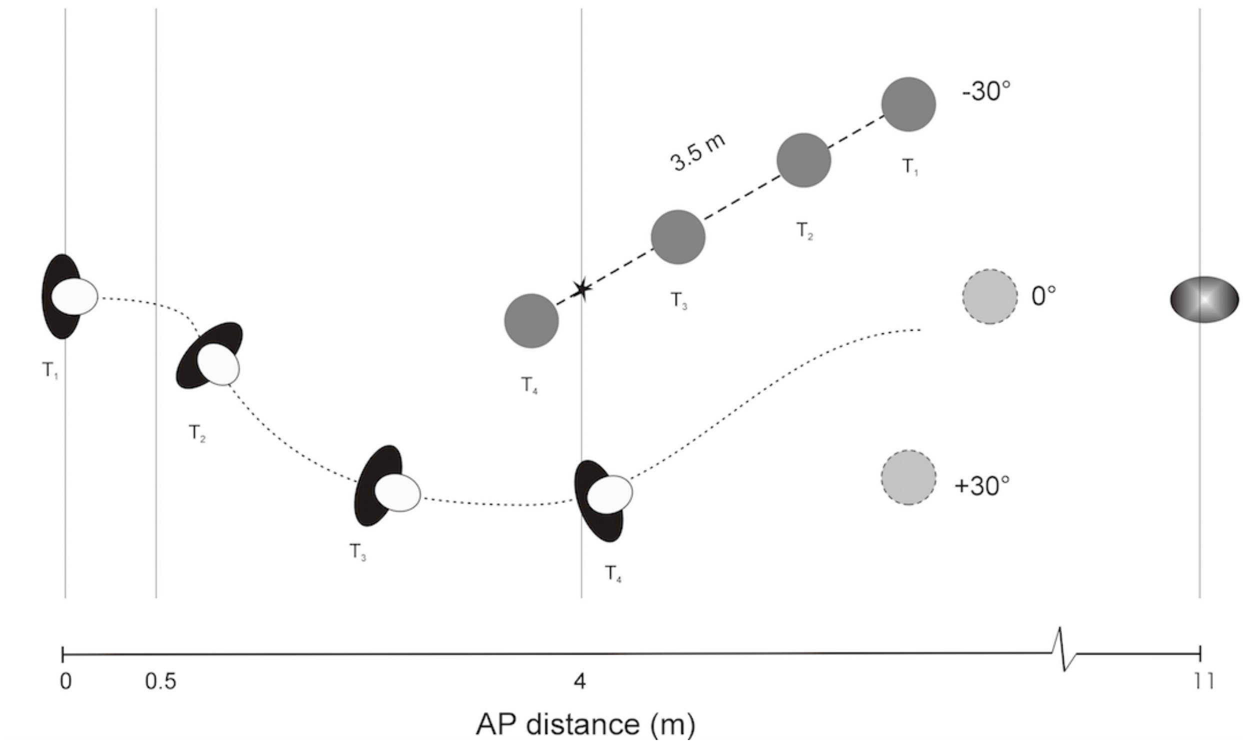

Figure 4-1. Schematic representation of the top-view of the experimental setup and the virtual scene. The trajectory of participant (black and white bonhomme) is shown as a dotted line while the trajectory of the obstacle (grey circle) is shown as a dashed line. In the avoidance task the other two obstacles (light grey) do not remain in view once an obstacle has started moving. T_1: Starting position, T_2: after onset of obstacle, T_3: random position along the trajectory, T_4: position after crossing the Theoretical point of Collision (black star).

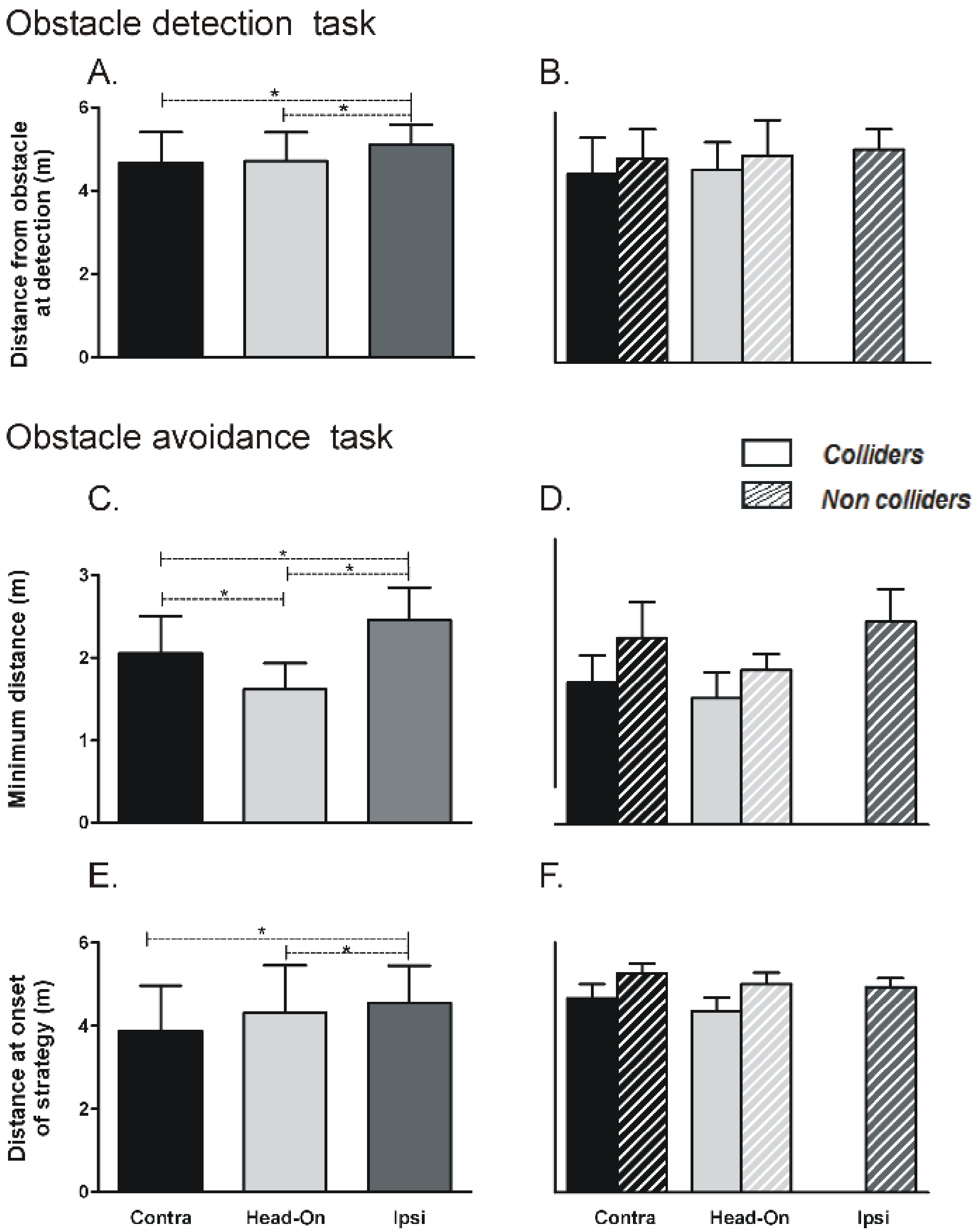

Figure 4-2: Mean ± 1SD values of all participants for distance from obstacle at detection in (A) all participants, (B) colliders vs. non colliders; for distance from obstacle at onset of strategy in (C) all participants, (D) colliders vs. non colliders; minimum absolute distances maintained between the participants and the obstacles in (E) all participants, (F) colliders vs. non colliders. *p<0.05.

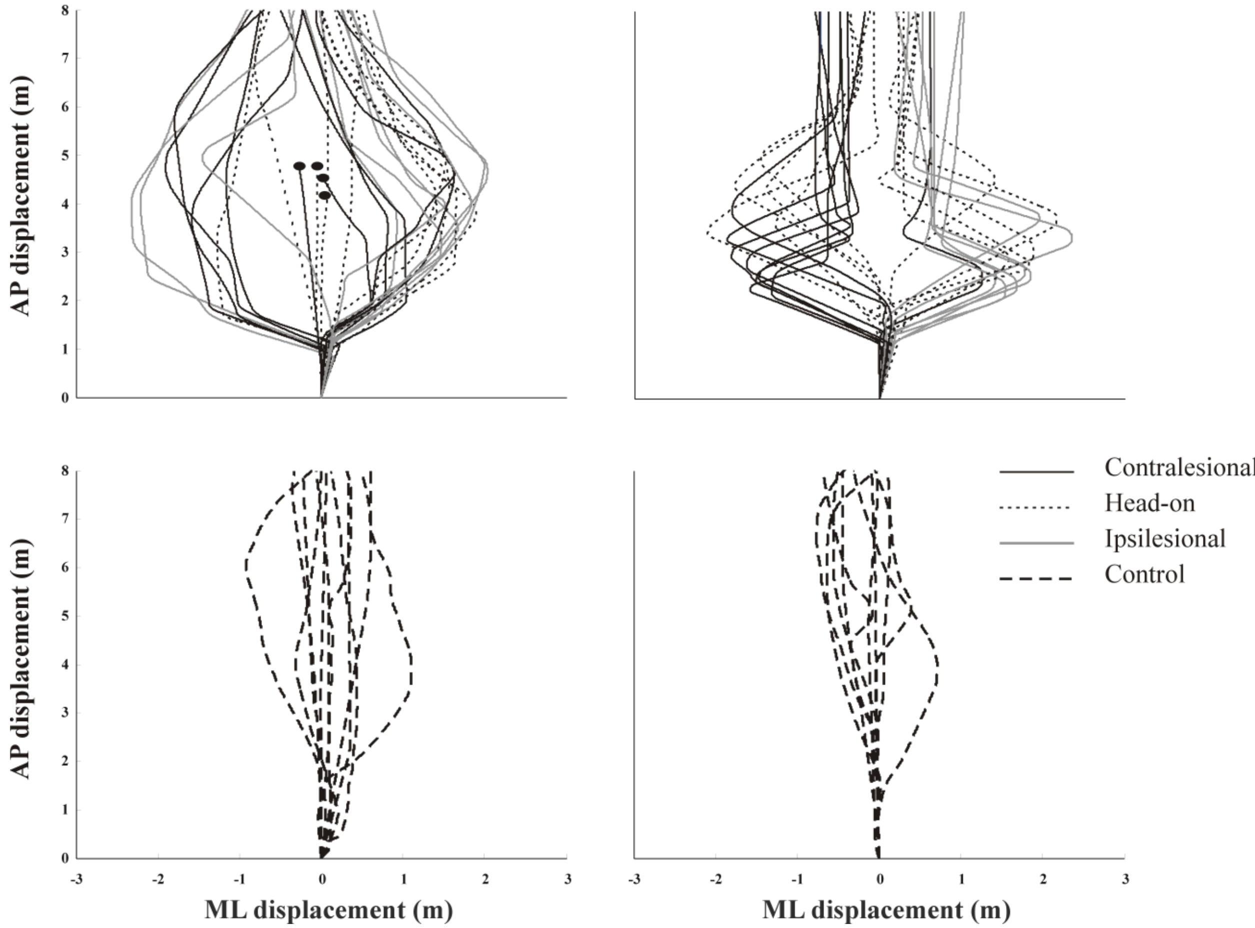

Figure 4-3: Representative traces of navigational strategies adopted by 2 participants. The left panel is the walking pattern of a collider while the right panel consist of walking pattern of a non-collider. Note the collisions experienced by participant #7 (left panel), which are represented by the black dots, and the absence of collisions for participant #10 (right panel).

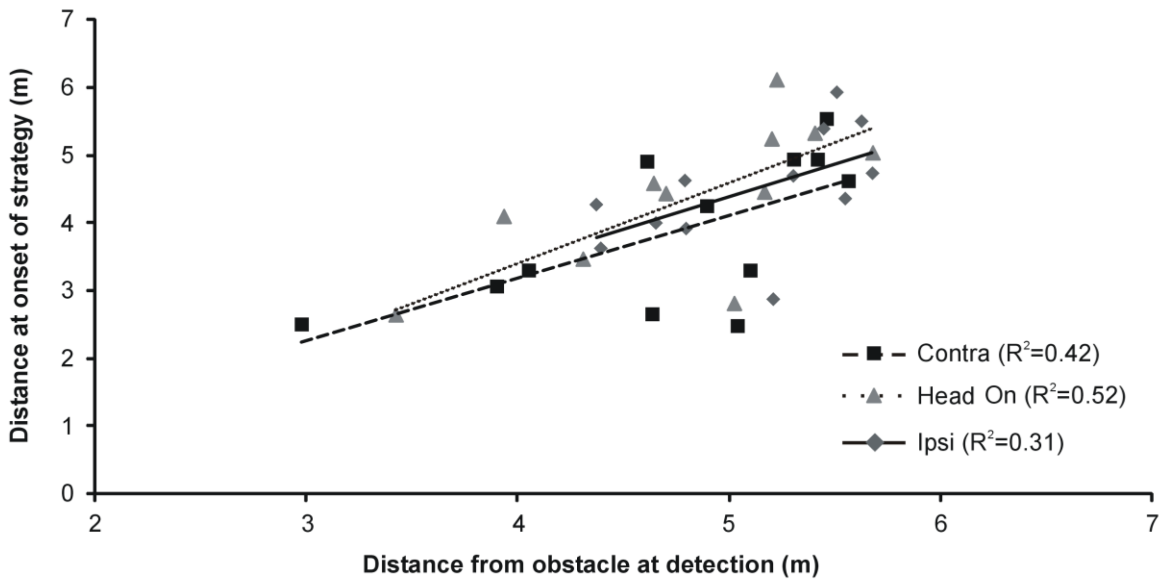

Figure. 4-4. Relationship between distance from obstacle at detection and the distance from obstacle at onset of strategies for the various directions of obstacles.

Participant	Age (yrs)	Lesion Side	Chronicity (months)	# of Bells omission	Error on Line Bisection (cm)	Trail Making B	MoCA (/30)	Collision CL (%)	Collision HO (%)
1	50	R	90	0	0.5	180	28	16.66	16.66
2	63	R	10	4	1	135	28	20	30
3	67	R	6	13	2.3	180	23	10	10
4	52	R	4	0	1.32	140	27	0	30
5	72	L	6	0	1.32	300	†	0	10
6	65	R	10	4	0.94	229	24	10	40
7	72	R	3	18	4.8	240	24	50	50
8	69	R	13	9	3.2	315	24	0	30
9	47	R	4	6	1.98	120	28	0	20
10	57	L	5	3	0.94	120	23	0	0
11	57	R	7	0	0.98	138	25	0	0
12	57	R	4	2	0.94	69	27	0	0

Table 4-1: Participant characteristics. * Only Cancellation test was reported in the charts. + could not assess due to language barriers. Abbreviations: VSN, Visuospatial neglect,; MVPT, Motor free Visual Perceptual test; MoCA, Montreal Cognitive Assessment; CL, Contralesional; HO, Head-on; IL, Ipsilesional.

Laboratory assessment	Clinical assessment	Direction of obstacle approach		
		Contra	Head-on	Ipsi
Obstacle Detection				
Distance at detection	Bells Test	0.02	-0.07	-0.02
	Line Bisection Test	-0.17	-0.26	-0.27
	Trail Making B Test	-0.55*	-0.70**	-0.60*
Obstacle avoidance				
Rate of collisions	Bells Test	0.17	0.27	NA
	Line Bisection Test	-0.30	0.17	NA
	Trail Making B Test	0.17	0.46	NA
Distance at onset of strategy	Bells Test	0.26	-0.25	-0.04
	Line Bisection Test	-0.34	-0.38	0.08
	Trail Making B Test	-0.63**	-0.48	-0.38

Table 4-2: Correlation (r values) between the performances on laboratory assessments and clinical measures. Note: For the associations involving the Bells and Line bisection tests reported r values were obtained after excluding the outlier (participant # 7). Contra: contralesional, Ipsi: ipsilesional. * = $p < 0.05$, **= $p \leq 0.01$, (1-tail probability levels).

CHAPTER 5

5.1 PREFACE

In the previous chapters we have demonstrated how VSN altered the ability to perform one of the common demands of community ambulation: obstacle avoidance. However, walking is often, if not always, performed while thinking, planning, talking or listening. This act of performing a simultaneous task while walking, i.e. dual-task walking, is time efficient but also increases cognitive load while walking. Considering that the presence of VSN is associated with reduced attentional resources, the addition of another task that competes for attention will likely worsen the symptoms of VSN and increase the risk of collisions during obstacle avoidance. Hence, in the next part of this thesis we investigated how the addition of a cognitive task would alter obstacle avoidance capabilities of individuals with vs. without VSN.

MANUSCRIPT 3: DUAL-TASKING NEGATIVELY IMPACTS OBSTACLE AVOIDANCE ABILITIES IN STROKE INDIVIDUALS WITH VISUOSPATIAL NEGLECT: TASK COMPLEXITY MATTERS!

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5.2 ABSTRACT

Performing a cognitive task while walking i.e. dual-tasking is challenging for stroke individuals. The presence of perceptual-attentional deficits associated with post-stroke visuospatial neglect (VSN) may further compromise the ability to dual-task while walking. We compared participants with and without VSN on their ability to negotiate moving obstacles while walking and concurrently performing a cognitive task. **Methods**: Twenty-six post-stroke individuals with VSN (VSN+, n=13) and without VSN (VSN-, n=13) were assessed on their ability to (a) avoid collisions with moving obstacles while walking (locomotor-single-task); (b) perform a simple and complex cognitive task (cognitive-single-task) and: (c) simultaneously perform the walking and cognitive tasks (dual-task). We compared the two groups on locomotor (collision rates, minimum distance from obstacle, and onset of strategies) and cognitive (error rates) outcomes. **Results and Discussion**: For both single and dual-task walking, VSN+ individuals showed higher collision rates compared to VSN- individuals. Compared to single task performances, dual-tasking caused deterioration of locomotor (more collisions, delayed onset of strategies and smaller minimum distances) and cognitive performances (increased error rate) in VSN+ individuals who demonstrated a "cognitive-locomotor interference". Contrastingly, VSN- individuals maintained collision rates, increased minimum distance, but showed higher cognitive error rates, prioritizing their locomotor performance. An increase in cognitive task complexity caused greater deterioration on locomotor outcomes for the VSN+ group and greater cognitive deterioration for both groups. **Conclusions**: Avoiding obstacles and attending to changing attentional demands are essential requirements of community ambulation. The inability to adapt to these demands while walking can compromise safety and walking independence in VSN+ individuals.

5.3 INTRODUCTION

Visuospatial neglect (VSN) is a common and disabling condition frequently observed in persons with stroke (Heilman et al., 2000; Ringman et al., 2004; Wertman, 2002). It is an attentional –perceptual disorder which impairs the ability to orient towards and/or respond to relevant stimuli on the side opposite to the brain lesion (i.e. contralesional side) (Heilman et al., 2000). During walking, such attentional-perceptual deficit could affect the ability to attend to visuospatial information such as the location of the intended goal or the presence of obstacles in the walking path, especially if these features are present in the contralesional side of space. Consequently, the planning and execution of adaptive strategies could be impaired leading to falls and collisions.

Successful community ambulation involves walking safely under different spatial and temporal constraints, in the presence of static and moving obstacles (Shumway-Cook et al., 2002). In our previous study, we demonstrated that post-stroke VSN+ individuals had difficulty negotiating moving obstacles while walking (Aravind & Lamontagne, 2014), which may hamper safety while walking in the community as moving obstacles are frequently encountered. Community ambulation also involves performing several tasks concurrently, such as walking while making a mental list or talking, which is commonly referred to as dual-task walking. If the total attentional demands of the tasks being performed simultaneously exceeds total processing capacity, it can result in the deterioration of the walking performance (locomotor cost), the cognitive performance (cognitive cost) or both (referred to as dual-task interference or, in this specific case, to cognitive-motor interference) (Rabuffetti et al., 2013).

Such interference is likely to be greater when the locomotor function is already compromised (e.g. after a stroke) or if attentional deficits (such as VSN) are present. Studies involving overground un-obstructed walking while performing a dual-task in post-stroke individuals have observed motor interference (reduction in walking speed, reduction in walking balance, increased risk of falls) or cognitive-motor interference (cognitive errors along with motor interference) during dual-task situations (Rabuffetti et al., 2013). However, effects of dual-task walking during complex locomotor tasks such as obstacle avoidance has not been understood.

Given that VSN+ individuals experience spatially lateralized (attentional bias, reduced contralesional exploration and increased response times) and non-spatially-lateralized (reduced attentional capacity and arousal) attention deficits (Husain & Rorden, 2003; Suchan et al., 2012), along with post-stroke locomotor impairments, they may be more vulnerable to the effects of dual-tasking than VSN- individuals.

In order to understand the implications of dual-tasking on the safety of VSN+ and VSN- individuals while walking in complex environments, such as in the presence of moving obstacles, we assessed their abilities to negotiate moving obstacles while performing a cognitive task simultaneously, in a virtual reality set-up. The VE offers a safe, controlled and realistic environment to assess locomotion while yielding walking behaviours similar to real-world behaviour (Gerin-Lajoie et al., 2008a; Gerin-Lajoie et al., 2005).

We hypothesized that the concurrent performance of a locomotor and cognitive task would cause cognitive-motor interference both in VSN+ and VSN- individuals with stroke. The extent of interference, however, would be larger in VSN+ individuals than in VSN- individuals. Moreover, since VSN symptoms become more apparent with an increase in task complexity (Bonato, 2012), the interference would be greater for a more complex task. VSN+ individuals would further present with an asymmetry in the obstacle avoidance performance where performance on the locomotor and cognitive task are more compromised for obstacle approaching from the neglected (contralesional) as compared to the non-neglected (ipsilesional) side.

5.4 METHODS

Twenty-six participants (Table 5-1) following a first-time right-sided supratentorial stroke (13 VSN+ and 13 VSN-) were recruited from 3 rehabilitation clinical sites of the Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal (CRIR) based on the following inclusion criteria: a right-hemispheric stroke (CT scan/MRI); a clinical diagnosis of VSN (Motor Free Visual Perceptual Test, Letter Cancellation Test, or Bells Test); an ability to walk independently, (speeds > 0.3 and <1.2 m/s, with or without a walking-aid); and motor recovery scores of 3- 6 out of 7 on the leg and foot components of the Chedoke McMaster Stroke

Assessment (CMMSA). Individuals with visual field defects, hearing loss, cognitive deficits (<26 on the Mini-Mental State Examination) or other co-morbid conditions interfering with locomotion were excluded. Recruited participants varied in their comfortable walking speed with values ranging from 0.45m/s to 1.02m/s (0.74 ±0.17m/s, mean±1SD). The study was approved by the Ethics Committee of CRIR and all participants gave their informed written consent.

5.4.1 EXPERIMENTAL SET-UP AND PROCEDURES

5.4.1.1 Locomotor Single Task (LocoST)

The locomotor task was conducted in a VE designed using the CAREN 3^{TM} software (Motek BV, Amsterdam), which the participants viewed through an nVisor SX60 HMD (NVIS, USA). A 12-camera Vicon-512^{TM} motion capture system tracked the position of three reflective-markers affixed to the HMD. This information, fed to CAREN 3^{TM}, provided real-time updates of the participants' position in the VE. Markers were also placed on specific body landmarks as specified in the full-body maker set of the Plug-in-Gait model from Vicon^{TM}. Data were recorded at 300Hz in CAREN 3^{TM} and at 120Hz in Vicon^{TM}.

The VE (Figure 5-1) presented a room (12m x 8m) consisting of a blue target on the far-end wall (11m) and three cylindrical obstacles positioned in front of a theoretical point-of-collision (TPC) in an arc at 0° (Head-on [HO]), 40° right (Ipsilesional side [IL] and 40° left (Contralesional side [CL]). The TPC is the point where the participant and the obstacle paths, if left unaltered, would meet and collide. Participants were instructed to walk towards the target while avoiding a collision with the approaching obstacle, if any. After advancing forward by 0.5m, one of the 3 obstacles randomly moved in the direction of the TPC and beyond, at a speed that matched the participants' overground walking speed. Matched walking speeds ensured that a collision was imposed for every obstacle condition unless an avoidance strategy was executed. When a collision occurred, visual feedback was provided in the form of a flashing “Collision” sign. A control condition, with no obstacles in the walking path, was used to determine walking speed and walking trajectory in the absence of moving obstacles.

5.4.1.2 Cognitive Single Task (CogST)

The cognitive task was an auditory pitch-discrimination (Auditory Stroop) task. Participants were seated and passively observed the VE while responding to the Auditory Stroop stimuli. Two types of tasks were presented: (a) a simple task in which the word "Cat" was presented in a high or low pitch (CogST-CAT) and; (b) a more complex task in which the words "High" or "Low" were presented in a high or low pitch (CogST-HL). The HL task was considered more complex since greater attention and inhibition is required to correctly identify the pitch without being influenced by the sound of the word presented. Meanwhile, participants viewed a scene that simulated the locomotor task but were not required to respond. They were instructed to verbally report the pitch of the sound (High/low). Participants performed four blocks of five trials, resulting in 10 trials each for the CogST-CAT and CogST-HL tasks, with the task order randomized to minimize learning effects.

The auditory stimuli were presented to the participants via seven speakers placed around the room ensuring a uniform sound intensity throughout the walking space. The participants' responses to the Stroop task were entered into the computer by the researcher and verified offline with an audio recording of the performance.

5.4.1.3 Locomotor Dual-task (LocoDT)

During the dual-task obstacle avoidance, participants were instructed to perform the obstacle avoidance and the cognitive tasks simultaneously. Two dual-task conditions were presented: LocoDT-CAT i.e. with "CAT" as the auditory stimulus and LocoDT-HL with "High" and "Low" as the auditory stimuli. The participants were instructed to perform both tasks as well as they could. The performances on the CAT and HL tasks during walking are referred to as CogDT-CAT and CogDT-HL respectively.

For the locomotor tasks (LocoST, LocoDT-CAT and LocoDT-HL), participants were provided with at least 4 practice trials and 4 to 6 trials per condition were collected, depending on the participant's endurance. The tasks were presented in blocks of 8 trials with the task order and obstacle's direction of approach randomized. Participants were given frequent rest pauses to avoid fatigue.

Participants were also evaluated on clinical assessments of VSN, including the Bells test (Gauthier et al., 1989), the Line Bisection test (Schenkenberg et al., 1980), and the Apples test (Bickerton et al., 2011). Executive cognitive function was assessed with the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005), Trail Making Test B (TMT-B) (Reitan & Wolfson, 1985) and Zoo Map test (Allain et al., 2005). Gait speed was assessed with the 10m walk test. All participants were identified as right-hand dominant on the Edinburg Handedness Inventory.

5.4.2 DATA ANALYSIS

For the locomotor tasks, *onset of an avoidance strategy* was measured as the time at which a medio-lateral displacement (of the head markers) exceeded 0.25m (half of average shoulder width) on either side. The *minimum absolute distance* was calculated as the minimum distance maintained between the participant and obstacle, before the obstacle passed beyond the participant. To identify a collision, a critical distance was set for each participant, calculated as the sum of the obstacle-radius and the distance between C7 and the lateral-most marker on the body or walking-aid. When the distance between the participants and the obstacle dropped below this critical distance, a collision event was detected. The number of trials in which collision were detected was divided by the total number of trials for each of the conditions to give the *rate of collision.* The *average walking speeds* were also recorded. Locomotor outcomes are suffixed by ST, CAT and HL depending on the task condition.

The extent of change caused by each type of dual-task (LocoDT-CAT or LocoDT-HL) relative to single task (LocoST), i.e. the *Dual-task cost was calculated as follows:*

$$Dual\ task\ Cost = \frac{LocoDT - LocoST}{LocoST} X\ 100\%$$

For the cognitive tasks, errors in pitch identification or failure to report the pitch were considered as cognitive errors. However, cognitive cost as a percent change from CogST could not be calculated since none of the participants made errors during the CogST-CAT or CogST-HL task. Therefore, actual cognitive error rates under dual-task conditions, as well as differences between CogDT-CAT and CogDT-HL are reported. The rate of cognitive errors was calculated as a proportion of cognitive errors to the total number of stimuli.

5.4.3 STATISTICAL ANALYSIS

We conducted a linear mixed model analysis for repeated measures with unstructured covariance structure, with 1 between subject factor (group: VSN+, VSN-) and 2 within subject factor (task LocoST, LocoDT-CAT and LocoDT-HL; direction of obstacle approach: CL, HO and IL (exception: 4 levels including control condition (C) for the average walking speed outcome)) to assess the influence of VSN and of dual-tasking on locomotor and cognitive outcomes. Significant interaction terms were further elaborated using simple effects where *a priori* identified pairwise comparisons were carried out. Collision rates were not compared statistically due to the presence of many zero-values in the VSN- group. For the cost outcomes, the analysis was conducted with 1 between subject factor (group: VSN+, VSN-) and 2 within subject factors (task: Dual-task Costs with CAT vs. with HL; direction of obstacle approach: 3 or 4 directions). Student t-tests were used to compare the two groups for age, stroke chronicity, MoCA scores, TMT scores. They were also used to compare the average cognitive errors rates during the first 50% of trials and the 2nd 50% of trials in both VSN+ and VSN- groups to confirm the absence of learning effects on the cognitive tasks.

Pearson correlations were carried out between performances on the clinical measures (MoCA, TMT-B, Bells test, Line bisection test, Apples test) or other patient characteristics (age, time since stroke,) and dual-task walking costs. Correlations were carried out separately for each obstacle approach. All statistical analyses were performed in SAS v9.4. The level of significance was set to $p < 0.05$.

5.5 RESULTS

For participants recruited into the VSN+ group, the presence of VSN was confirmed with confirmatory results on at least two of the three tests for VSN (Bells, Line bisection and Apples tests). Positive scores for VSN on each test included 6 or more omissions on the Bells test

(Gauthier et al., 1989), a line bisection error of 6 mm or greater (Schenkenberg et al., 1980) and 6 errors or more on the Apples test (Mancuso et al., 2015). Participant characteristics are presented in Table 5-1. Upon chart review, it was also found that two participants had shown signs of neglect during everyday behaviour and during rehabilitation sessions but did not have any tests performed to confirm the presence of VSN. As they scored positive on at least two of the three VSN clinical tests conducted during this study, they were included into the VSN+ group (participants VSN+10 and VSN+11).

All participants walked independently with two participants (VSN+5 and VSN-7) using a cane. The VSN+ vs. VSN- groups did not differ in age or stroke chronicity, level of motor recovery (CMMSA), walking speed, cognitive status (MoCA, Zoo Map scores) and years of education ($p > 0.05$). The VSN+ group did, however, show significantly larger times on the TMT-B ($p=0.03$) and, as expected, showed larger errors on the Bells test, Line Bisection test and the Apples test ($p<0.001$).

Figure 5-2 shows examples of walking trajectories adopted by VSN+ and VSN- individuals for different tasks and obstacle conditions. As illustrated by these examples, VSN+ participants deviated to the ipsilesional side in most trials during single task walking (Walk ST), regardless of the obstacle condition (mean±1SD= 85.5±9.7% of trials); This preference became more pronounced for LocoDT-CAT (92.1±4.9% of trials) and even more so for LocoDT-HL (98.3±2.8% of trials). For all obstacle approaches and for all task complexities, VSN- participants did not show a preference to deviate to one side.

5.5.1 COLLISION RATES

Collision rates and number of colliders observed during the obstacle avoidance tasks are reported in Table 5-2. Overall, larger proportions of VSN+ individuals than VSN- individuals collided with obstacles, with higher collision rates under both single and dual-task conditions. Within the VSN+ group, a direction-specific gradient was observed during single task walking (LocoST) and to a greater extent during dual-task walking (LocoDT-CAT and LocoDT-HL), where the proportion of colliders and collision rates increased from the IL to the HO and CL obstacle approaches. Additionally, an effect of task complexity was observed in VSN+ individuals, as both the proportion of colliders and collision rates increased from LocoST to LocoDT-CAT and LocoDT-HL. In fact, 92% and 100% of VSN+ participants collided with HO and CL obstacles, respectively, while performing the most complex locomotor task (LocoDT-HL), compared to 46% and 76%, respectively, during single task walking. Within the VSN- group, collision rates did not show the presence of a direction-specific gradient and the number of colliders (range: 18-30%) and collision rates (range: 19-25%) did not drastically differ between the task complexities.

5.5.2 OBSTACLE AVOIDANCE STRATEGIES

For the *minimum distance* maintained from the obstacle (Figure 5-3), a significant interaction effect of Group x Task x Direction was observed ($F(4,96)=3.5$, $p<0.05$) where the VSN+ maintained significantly smaller minimum distances from the obstacle for the dual-task conditions (LocoDT-CAT and LocoDT-HL), regardless of the direction of obstacle approach, compared to VSN- group ($p<0.001$). The VSN+ participants significantly reduced their minimum distances as task complexity increased (LocoST to LocoDT-CAT to LocoDT-HL), while the VSN- participants increased their minimum distances for all obstacle direction ($p<0.05$). Regardless of task complexity, VSN+ participants also maintained significantly smaller minimum distances for CL and HO obstacles approaches compared to IL obstacles ($p<0.05$). Such a direction-specific gradient of minimal distances was not observed for the VSN-group.

The *onset of strategy* showed significant two-way interactions of Group X Task ($F(2,96)=15.42$, $p<0.001$) and Group X Direction ($F(2,96)=52.49$, $p<0.001$). Post-hoc pairwise comparisons indicated that in VSN+ individuals, a greater task complexity led to significantly longer delays in onset of avoidance strategy (significant only for HL tasks), while the task complexity did not affect the onsets of VSN- individuals. Moreover, only the VSN+ group showed a significant effect of obstacle direction with longer onsets of avoidance strategy for CL and HO obstacles compared to IL obstacles ($p<0.05$).

For *walking speed*, a Group X Task interaction ($F(2,96)=11.97$) and an effect of Direction ($(F=1,48)=38.67$, $p<0.001$) emerged as significant. The difference between walking speeds for VSN+ and VSN- groups was evident only for the LocoDT-HL task (Figure 5-3 c). Furthermore, in the VSN+ group, the effect of task complexity translated to significantly slower walking speeds for the LocoDT-HL task compared to the LocoST task. Note that both groups walked significantly slower during trials with moving obstacles compared to control trials devoid of obstacles. Other main or interaction effects not specified above were not significant.

5.5.3 DUAL-TASK COSTS

The cost outcomes compared changes observed during the simple dual-task (LocoDT-CAT) and the more complex dual-task waking condition (LocoDT-HL) relative to single task walking (LocoST). A significant Group X Task interaction was observed for all the locomotor cost outcomes, including: minimum distance cost ($F(2,48)=14.73$), onset of strategy cost ($F(2,48)=13.15$) and walking speed cost ($F(2,48)=9.61$) (Figure 5-4). Overall, VSN+ participants demonstrated greater locomotor costs for both dual-task conditions (LocoDT-CAT and LocoDT-HL), compared to VSN- participants ($p<0.05$).

Within the VSN+ group, a significant effect of Task was observed, with individuals showing larger onset of strategy costs (increase in onsets), larger minimum distance costs (decrease in minimum distances), larger speed costs (reduction in walking speeds) in LocoDT-HL compared to LocoDT-CAT ($p<0.01$). In addition, a significant Group X Direction interaction ($F(2,48)= 3.14$) was also observed for the onset of strategy cost outcome, as VSN+ individuals showed greater costs, i.e. greater delay in onset of strategy for CL and HO obstacles compared to IL obstacles. Among VSN- individuals, the minimum distance cost was greater for LocoDT-HL compared to LocoDT-CAT task ($p < 0.05$). There were no significant effects of the direction of obstacle approach on any of the locomotor cost outcomes for the VSN- group.

5.5.4 COGNITIVE OUTCOMES

None of the participants made errors in pitch-recognition during the CogST-CAT and the CogST-HL tasks. Twelve out of the 13 VSN+ participants demonstrated errors in pitch recognition during for the CogDT-CAT (error rate= 16.01±8.93% of stimuli) and the CogDT-HL task (27.24±9.77% of stimuli). In the VSN- group, 9 and 10 out of the 13 participants made errors in the CogDT-CAT (7.96±4.87% of stimuli) task and CogDT-HL (in 16.9±17.43% of stimuli) task respectively.

A significant group X task interaction emerged for cognitive errors (F(2,48)=8.41) with a more errors for the CogDT-HL task compared to CogDT-CAT and for the VSN+ group compared to the VSN- group ($p<0.05$). There was no influence of direction of obstacle approach on cognitive errors and the extent of change caused by the complexity of the auditory task (CogDT-HL – CogDT-CAT) did not differ between the two groups ($P>0.05$). Note that no learning effect in dual-task cognitive performance (e.g. CogDT-CAT and CogDT-HL) were observed in the VSN+ and VSN- groups who showed no difference in cognitive performance in the first and second 50% of trials ($p>0.05$).

5.5.5 RELATIONSHIP BETWEEN LOCOMOTOR AND COGNITIVE COSTS AND CLINICAL EVALUATIONS

The locomotor cost and cognitive cost outcomes did not show significant relationships with clinical measures of executive function (TMT-B test), overground walking speed, cognitive function (MoCA) or VSN assessments (e.g. Bells, Line bisection and Apples tests) ($p>0.05$).

5.6 DISCUSSION

The ability to cope with different traffic levels and with changing attentional demands are two essential requirements for community ambulation (Patla & Shumway-Cook, 1999). Poor dual-tasking and poor obstacle avoidance abilities are also associated with an increased risk of falls and accidents (Hegeman et al., 2012). Results of this study confirm the hypothesis that VSN+ individuals show a deterioration in both locomotor and cognitive performances while dual-tasking, and that such deterioration is larger compared to VSN- individuals. In the following sections, we discuss how the presence of post-stroke VSN alters obstacle avoidance abilities and how the simultaneous performance of a cognitive task further compromises these abilities in VSN+ individuals.

5.6.1 VSN ALTERS THE SPATIOTEMPORAL RELATIONSHIPS WITH THE OBSTACLE DURING THE AVOIDANCE STRATEGY AND LEAD TO INCREASED COLLISION RATES

Obstacle avoidance is a complex task which requires processing of visuospatial information obtained from the environment and a planned and coordinated execution of locomotor adjustments that are in line with body capabilities (Iaria et al., 2008). Sensorimotor impairment resulting from a stroke could therefore compromise the ability to safely avoid obstacles leading to collisions (Darekar et al., August 2013). In the present study, we showed that VSN+ and VSN- individuals who had similar level of motor recovery (CMMSA scores) differed in their ability to negotiate obstacles under single and dual-task conditions. Overall, a greater proportion of VSN+ individuals collided with obstacles, at higher collision rates, compared to VSN- individuals. Other studies too have documented the tendency of VSN+ to collide with static and moving objects while walking (Aravind & Lamontagne, 2014; Punt et al., 2008; Robertson et al., 1994; Tromp et al., 1995) and have mainly attributed this to the ipsilesional bias of attention and perception commonly observed in VSN (Kinsbourne, 1970a, 1987). This bias causes a spontaneous orientation of attention and gaze to ipsilesionally occurring events (Kinsbourne, 1970b, 1994). Therefore, contralesional stimuli are ignored or detected after a delay. For a moving object, this delay would bring the individual within close proximities of the obstacle, effectively reducing the time and distance available to plan and execute an avoidance strategy. In support of this idea, our team has previously shown that the perception of moving obstacles is indeed delayed in VSN+ individuals and is associated with obstacles being at closer distances at the onset of strategies, in a joystick-driven navigation task (Aravind et al., 2015). This increases the risk of collision with the obstacle.

In the present study, the attentional-perceptual bias towards the ipsilesional side was evident in the delayed onsets of strategies, smaller minimum distances and higher collision rates observed for the CL and HO obstacle approaches compared to the IL approach. Moreover, a preference to deviate ipsilesionally, irrespective of the direction of obstacle approach, and in the absence of an obstacle, support the idea of such an ipsilesional bias. The VSN- group did not show direction-specific difference in their locomotor responses, deviating to both their ipsilesional and contralesional sides and did not show large deviations from the midline when no obstacles were present. Collectively, these observations support the idea that the attentional-perceptual deficits involved in VSN are the main factor explaining the altered obstacle avoidance strategies and increased risk of collisions.

5.6.2 VSN+ INDIVIDUALS EXPERIENCE GREATER COGNITIVE-LOCOMOTOR INTERFERENCE COMPARED TO VSN- INDIVIDUALS

It is widely accepted that the ability to dual-task while walking is impaired in post-stroke individuals, leading to deterioration of walking performance (Baetens et al., 2013; Bowen et al., 2001; Plummer-D'Amato et al., 2008; Yang et al., 2007b) or a deterioration of the competing cognitive/motor performance (Kizony et al., 2010; Plummer-D'Amato & Altmann, 2012; Smulders et al., 2012). However, the impact of dual-tasking on the locomotor behaviour of VSN+ individuals had never been established. In this study, we demonstrated for the first time that dual-task walking dramatically compromises both locomotor and cognitive performances in individuals with VSN.

During dual-task walking, the VSN- participants adopted larger minimum distances from the obstacles compared to the single task condition but did not alter their onsets of strategy, walking speeds or collision rates. However, similar to VSN+ individuals, VSN- individuals did not successfully attend to the cognitive task, demonstrating high error rates for both the simple and complex cognitive task. Thus, VSN- individuals appear to adopt a *safety-first* strategy by prioritizing their attention to safely avoid obstacles at the expense of the cognitive performance, which can be referred to as a motor-related cognitive interference (Rabuffetti et al., 2013). This prioritization may have been influenced by the threat of an imminent collision and by the fact that the cognitive task itself does not inform the walking task (e.g. not providing information about turns, stops or goals).

In contrast, under dual-task conditions, VSN+ participants of this study experienced further delays in initiating an avoidance strategy, reduced minimum distances with respect to the obstacle and more frequent collisions. A reduction of walking speed was also observed for the LocoDT-HL task, which could interpreted as an attempt to increase stability (Dingwell & Marin,

2006) and divert attention towards the cognitive task. Nevertheless, the high rates of cognitive errors observed under dual-task conditions suggest that attentional resources were not prioritized towards one task over the other. Such “mutual interference” (Rabuffetti et al., 2013), that is a worsening of both the locomotor and cognitive performance in VSN+ individuals, might have resulted from the demands of the walking and cognitive task exceeding the already limited attentional resources associated with VSN.

Overall, cost (locomotor and cognitive) of dual-tasking was greater for VSN+ individuals compared to VSN- individuals. In addition to the attentional deficits in VSN, this could be attributed to the deficits in executive functioning. The TMT-B test is a good measure of working memory, attention switching and response inhibition, which are important components of dual-tasking (Coppin et al., 2006). The VSN+ participants in our study showed TMT-B completion times that were not only longer than normative values (age and years of education based) (Tombaugh, 2004), but were also significantly greater than those of VSN- group, suggesting that their ability to flexibly allocate attention between tasks is impaired. In agreement with findings in our previous studies (Aravind et al., 2015; Aravind & Lamontagne, 2014) clinical evaluations of neglect, motor recovery and walking speed did not predict single task or dual-task performances in either group, emphasizing the need for task-specific assessments of obstacle avoidance abilities.

The complexity of the competing tasks is an important determinant of the extent of dual-task interference (Plummer-D'Amato et al., 2008). It can be inferred that the HL cognitive task used in this study imposed a greater attentional load than the CAT cognitive task due to the need to discern the pitch of the stimuli while ignoring the meaning of the announced word. For both groups, increased task complexity led to increased rates of cognitive errors under dual-task conditions. An effect of task complexity on walking performance, however, was observed only for the VSN+ group, with higher locomotor costs (e.g. smaller minimum distances and delayed onsets of strategies) and more numerous collisions being observed under the more complex (LocoDT-HL) vs. the simpler dual-task condition (LocoDT-CAT task). The latter observations indicate that task complexity matters for VSN+ individuals, with more complex tasks leading to greater cognitive locomotor interference.

Another factor that could influence the type of interference was the feedback provided to the participants during the task. For the obstacle avoidance task, participants received feedback for unsuccessful obstacle avoidance in the form of a flashing "collision" sign but did not receive any feedback for incorrect responses to the cognitive stimuli. Given that there were more obvious consequences in case of a failure in avoiding the obstacles, the type of feedback may also have influenced the prioritization of the locomotor task seen in VSN- participants, even when participants were instructed to prioritise both tasks equally. However, the type of feedback did not appear to influence the dual-task responses of VSN+ individuals.

In the context of community ambulation where obstacle and attentional distractors are frequently encountered, deterioration of locomotor performance could lead to falls or accidents while the inability to cognitively process information, highlights their inability to attend to extrinsic stimuli, making walking less efficient, limiting interaction and participation in society.

5.7 CONCLUSION

In this study we have presented a novel approach of understanding the limitations faced by post-stroke individuals with VSN while walking in the community, faced with different demands. For the first tine, we showed that individuals with post-stroke VSN demonstrate a dramatic deterioration of both their locomotor as well as cognitive performance during dual-task walking in comparison to stroke individuals without VSN who prioritized their safety while walking. The dual-task paradigm was able to reveal deficits faced by individuals with VSN in adapting to complex environmental demands which were not evident on clinical evaluations of neglect, reinforcing its usefulness in understanding functional status of stroke individuals. The virtual reality set-up used in this study has the potential to be used as tool for evaluation and training of complex locomotor tasks in stroke survivors with and without perceptual-attentional deficits.

5.8 CONFLICT OF INTEREST

The authors declare that there is not conflict of interest.

5.9 ACKNOWLEDGMENT

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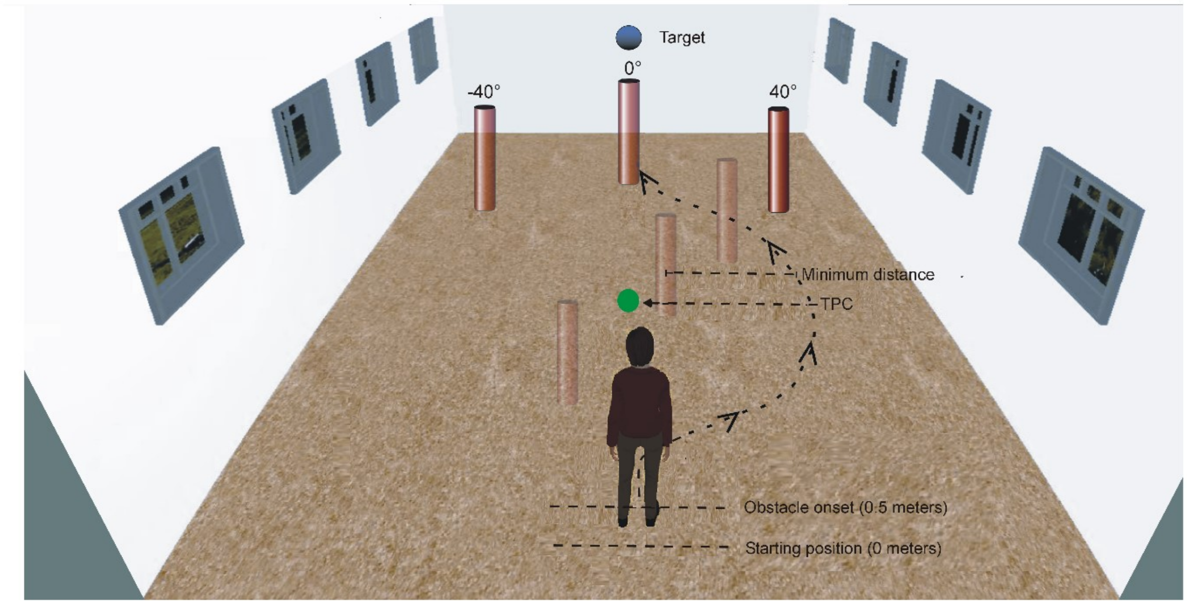

Figure 5-1: Schematic representation of the virtual scene. The figure shows an overhead view of the virtual scene with the three red cylindrical obstacles and the blue target. The transparent cylinders represent the path taken by the ipsilesional (right) obstacle when approaching the participant. The avatar is for representational purposes only and is not viewed in the scene. The dotted trace is an example of a path taken to avoid the obstacle. Abbreviations: TPC, theoretical point of collision.

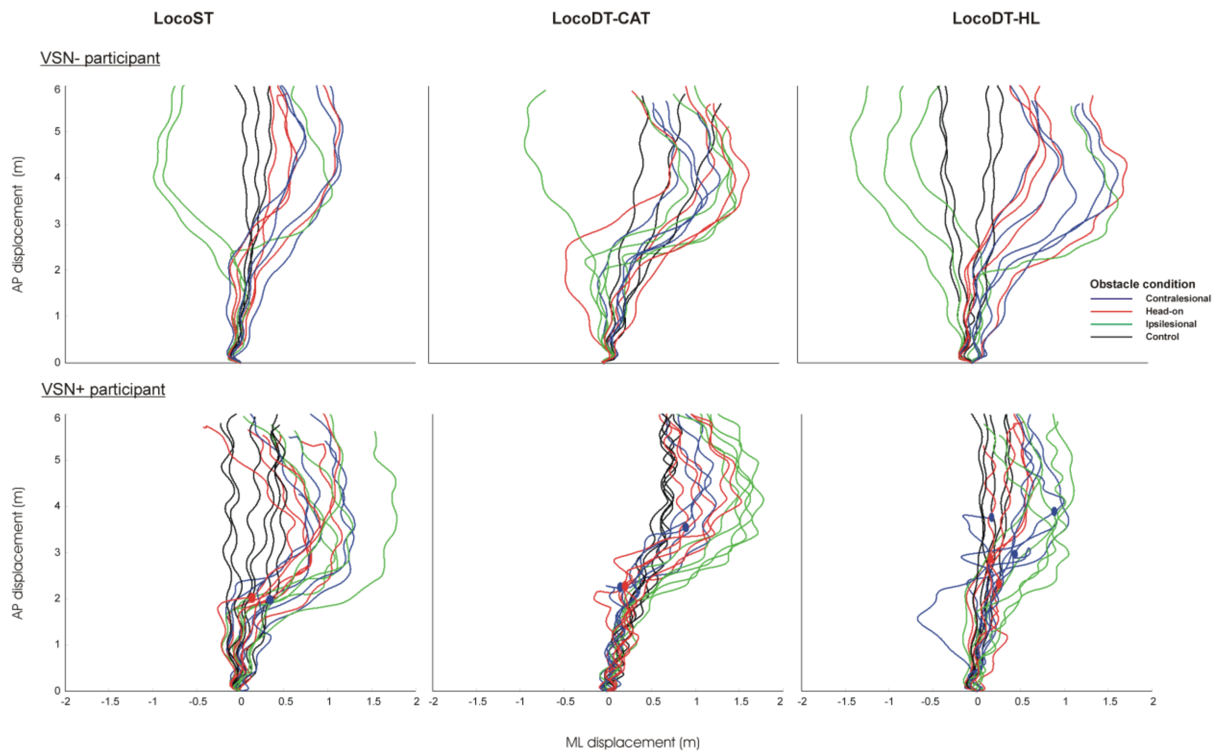

Figure 5-2: Representative diagram of walking strategies adopted by 2 participants. The top row shows the walking trajectories of a VSN- participant, while the bottom row shows the walking trajectories of a VSN+ participant during the LocoST, LocoDT-CAT and LocoDT-HL task. For the VSN+ participant, note the presence of collisions which are represented by red dots (collisions with head-on obstacles) and blue dots (collisions with contralesionally approaching obstacle).

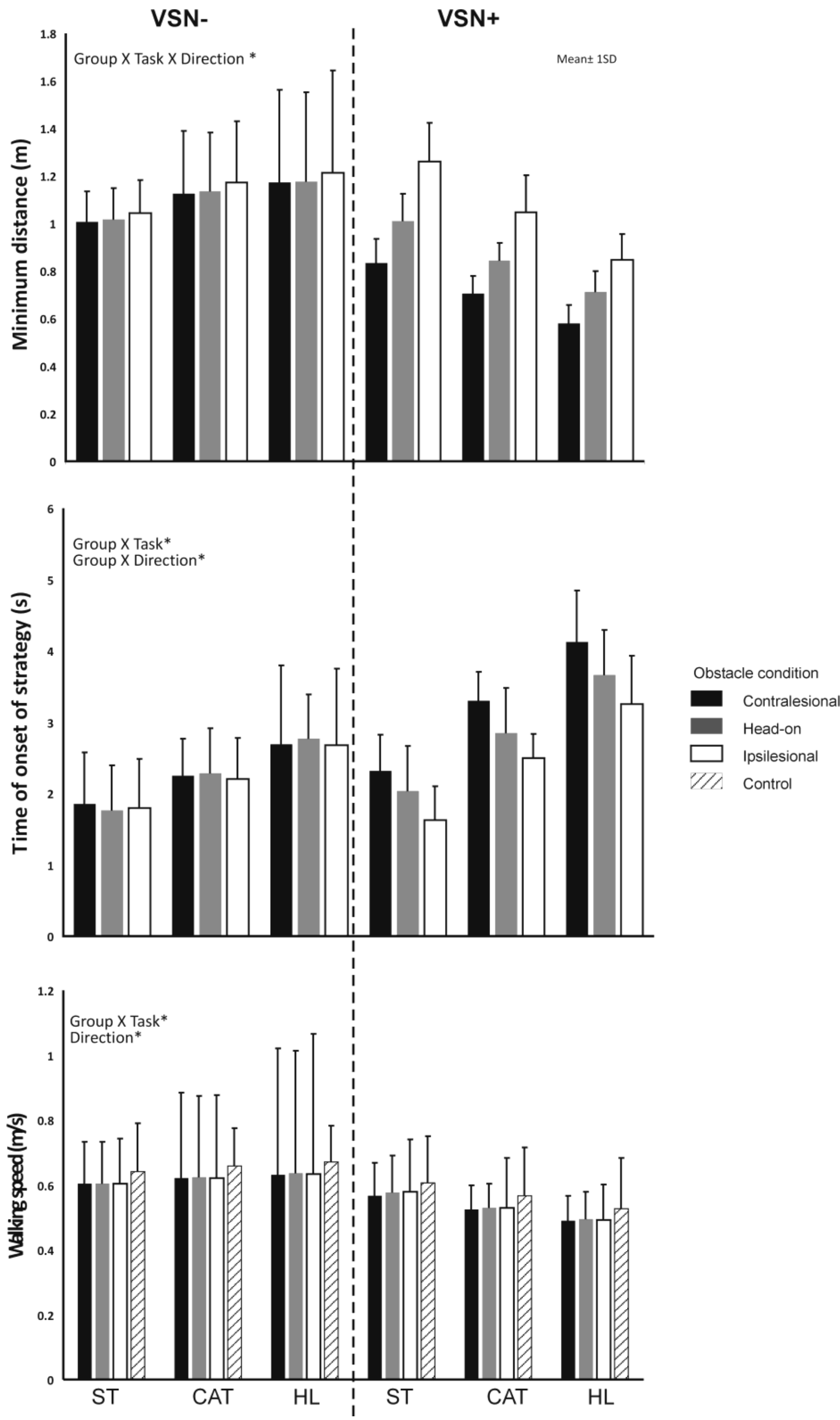

Figure 5-3: The figure shows mean (± 1SD values) of time of onset of strategy (top row), minimum absolute distances maintained between the participants and the obstacles as well (middle row) and walking speed (bottom row) for the VSN- and VSN+ participants during single-task walking (ST) as well as walking while performing the CAT and the High-Low (HL) cognitive tasks. Statistically significant interaction terms are specified in the text inserts. * $p<0.05$.

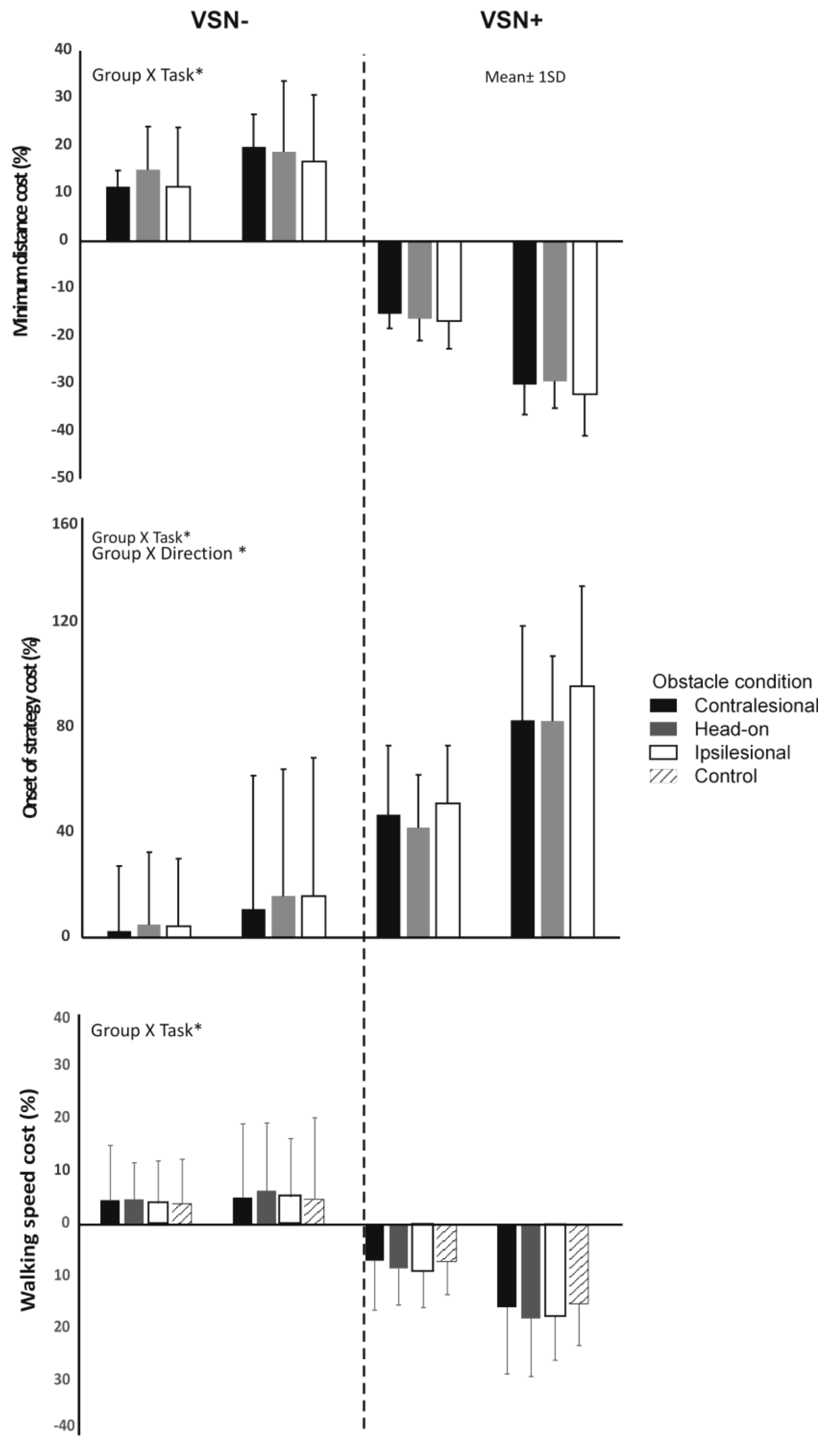

Figure 5-4: The figure shows mean (± 1SD values) for dual-task costs of time of onset of strategy (top row), minimum absolute distances maintained between the participants and the obstacles as well (middle row) and walking speed (bottom row) in the VSN+ and VSN- participants. Here CAT denotes the cost of performing LocoDT-CAT relative to LocoST task while HL denotes the cost of performing LocoDT-CAT relative to LocoST task. Statistically significant interaction terms are specified in the text inserts. * $p<0.05$.

Subject ID	Age (yrs)	MoCA	Chronicity (months)	CMMSA	TMT-B (seconds)	Bells omission	Line bisection	Apples
VSN-1	72	28	13	6,6,	101	5	28.5	0
VSN-2	60	28	18	5,5	40	2	60	5
VSN-3	53	25	6	6,5	104.3	4	43	0
VSN-4	64	29	18	6,5	100	2	75	4
VSN-5	68	26	20	6,6	88	4	64	5
VSN-6	65	27	8	6,6	76	0	68	2
VSN-7	58	28	7	5,4	92	0	62.5	0
VSN-8	53	27	5	6,5	48	1	86	1
VSN-9	64	26	7	6,6	109	1	26	1
VSN-10	51	28	10	6,6	92	0	109.5	0
VSN-11	57	26	11	6,6	60	4	46.5	0
VSN-12	69	30	12	5,5	79	1	40	1
VSN-13	56	24	19	6,5	60	1	40	1
Mean	60.8	27.1	11.8	-	80.7	1.9	57.6	1.5
SD	6.5	1.6	5.1	-	21.6	1.7	22.8	1.8
VSN+1	72	24	13	5,5	263	5	128.5	6
VSN+2	69	28	12	6,5	135	5	68	7
VSN+3	66	25	10	6,6	438	6	216	0
VSN+4	54	28	13	6,5	154	6	65	6
VSN+5	58	25	1	6,6	146	5	88	6
VSN+6	54	25	20	5,5	65	7	208	8
VSN+7	63	26	6	5,5	324	6	138	7
VSN+8	53	26	8	5,5	192	11	72.5	4
VSN+9	67	25	8	6,5	81	7	79	0
VSN+10	49	27	17	5,5	91	7	64.5	6
VSN+11	48	28	8	6,6	141	5	76.5	6
VSN+12	57	24	10	5,4	86	9	70.5	8
VSN+13	67	28	10	6,6	58	11	75	4
Mean	59.8	26.1	10.5	-	159.5	6.9	103.8	5.2
SD	7.7	1.5	4.6	-	113.3	2.1	51.2	2.5

Table 5-1: Participant characteristics: Abbreviations: VSN, Visuospatial neglect ; MoCA, Montreal Cognitive Assessment ; CMMSA, Chedoke-McMaster Stroke Assessment (CMMSA); TMT-B, Trail making test-B; SD, standard deviation.

Group	Task	CL Colliders	Collision rate	HO Colliders	Collision rate	IL Colliders	Collision rate
VSN+	LocoST	76.9	34.4±8.1	46.2	24.7±6.5	0.0	NA
	LocoDT-CAT	92.3	48.2 ±11.6	76.9	30.6 ±10.6	15.4	24.3 ±4.3
	LocoDT-HL	100.0	61.3 ±14.4	92.3	39.6 ±11.9	38.5	30.6 ±9.1
VSN-	LocoST	30.8	33.3±8.2	30.8	24.5±5.4	7.7	16.7
	LocoDT-CAT	23.1	36.6±3.3	15.4	18.9 ±1.6	0.0	NA
	LocoDT-HL	23.1	32 ± 11.2	15.4	23.3±2.4	0.0	NA

Table 5-2: Number of colliders and collision rates: Number of colliders as a percentage of total participants are presented (n=13 for each group). Mean collision rates (as a percentage of trials) ± one standard deviation are presented. CL, HO and IL indicate the direction of obstacle approach, contralesional, head-on and ipsilesional, respectively.

CHAPTER 6

6.1 PREFACE

When walking towards a goal, we normally chose the safest and the shortest route. The presence of an obstacle in the walking path means that this route needs to be modified in order to accommodate this new object in the environment and to preserve safety. How we modulate the walking trajectory (e.g. heading) in response to the obstacle and the goal determine the success of obstacle avoidance and ability to reach the intended goal. In persons with VSN, the impairments in the perception of contralesional and head-on obstacles may interfere with their the ability to appropriately modulate the walking strategies and consequently lead to collisions with the obstacle or a failure to reach a goal.

In this chapter we have evaluated the locomotor strategies (e.g. adopted by VSN+ and VSN- individuals in response to the approaching obstacle and compared strategies that led to successful or unsuccessful obstacle avoidance (i.e. collisions). Moreover, since the final purpose of any goal-directed locomotion is to reach the intended destination, we evaluated the two groups on their ability to align themselves to the final target, subsequent to the obstacle avoidance.

MANUSCRIPT 4: POST-STROKE VISUOSPATIAL NEGLECT INTERFERES WITH THE MODULATION OF HEADING REQUIRED FOR SUCCESSFUL OBSTACLE AVOIDANCE AND GOAL-DIRECTED WALKING.

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6.2 ABSTRACT

The control of locomotor heading can be impaired by the presence of post-stroke visuospatial neglect (VSN), which alters the perception of visuospatial information on the contralesional side of space. In this study we assessed how the presence of VSN influenced the ability of post-stroke individuals to modulate their heading in response to moving obstacles when walking towards a stationary target. **Methods**: Twenty-six post-stroke individuals (13 VSN+ and 13 VSN-) were assessed while walking in a virtual environment visualized in a helmet-mounted display. They were instructed to avoid a collision with a moving cylinder that approached either ipsilesionally, contralesionally or from head-on while walking towards a centrally-located target. Measures related to obstacle avoidance (onset-of-heading change, maximum mediolateral (MaxML) deviation, walking speed) and target alignment (heading and head rotation errors with the target) were compared across groups and directions of obstacles. Relationships between aforementioned measures with clinical measures of neglect severity were also examined. **Results**: Seventy-five percent of VSN+ compared to 38% of VSN- individuals collided with the contralesional and head-on obstacles. For individuals free of VSN, deviating to the same-side as the obstacle emerged as a safe strategy to avoid diagonal obstacles while deviating to the opposite-side was riskier and led to occasional collision. Individuals with VSN deviated to the ipsilesional side for all obstacle conditions, hence displaying same-side vs. opposite-side strategies for ipsilesional and contralesional obstacles, respectively. In this group, collisions with the contralesional obstacles were frequent, invariantly observed for the opposite-side strategy, and were associated with large delays in onset of heading reorientation. Overall, VSN+ individuals showed significantly greater delays in onsets and smaller MaxML deviations in response to obstacles, and significantly larger errors in target alignment compared to VSN- individuals. **Conclusion**: The ipsilesional bias arising from VSN influences the modulation of heading in response to contralesional obstacles and, along with the adoption of the 'riskier' opposite-side strategy, contribute to the higher number colliders and poor goal-directed walking abilities in post-stroke VSN.

6.3 INTRODUCTION:

The environments within which we walk are rarely clutter-free and are often interspersed with static and moving objects that require us to adapt our walking trajectory in order to prevent collisions. As such, obstacle avoidance is an important component of independent community ambulation (Patla & Shumway-Cook, 1999) which is a critical goal of rehabilitation among post-stroke individuals (Lord et al., 2004). In our previous studies we have shown that obstacle avoidance abilities are altered by the presence of stroke and to a greater extent by the presence of visuospatial neglect (VSN) (Aravind & Lamontagne, 2014, 2016; Darekar et al., 2015). What characterizes the obstacle avoidance strategies that lead to successful vs. unsuccessful avoidance of a collision in these individuals, however, remains unclear.

In human locomotion, information regarding self-motion is derived from both visual and non-visual sensory inputs (vestibular, proprioceptive, inertial) (Fajen & Warren, 2007). However, the visual system assumes a central role in providing information necessary for obstacle avoidance and goal-directed locomotion (Harris & Bonas, 2002; Warren et al., 2001a). Studies conducted in healthy adults have also revealed that for obstacle avoidance and goal-directed walking, information regarding the heading in space and heading in relation to objects of interest (e.g. obstacles and target) are key factors in route selection and planning of the locomotor trajectory (Fajen, 2013; Fajen & Warren, 2003; Patla et al., 2004). The spatial relationships maintained with visuospatial cues such as obstacles or a target would determine the success of the locomotor activity i.e. obstacle avoidance or target interception. Obstacle/target related information such as its size and its dimension, instantaneous distance of the obstacle/target, as well as speed and direction of its movement would be used to prospectively determine whether a collision is likely to occur (Carel, 1961; Cutting et al., 1995) and the time available to safely bypass the obstacle. As walking continues, these relationships are constantly changing, necessitating frequent monitoring and updating of this information. Such “spatial updating” is used to determine if the current trajectory should be maintained or if changes are needed in order to avoid the obstacle or reach the target. Under such dynamic conditions, the walking trajectory would not be pre-planned and would rather develop in an online fashion, contingent on the participant’s interaction with the environment (Fajen, 2013; Fajen & Warren, 2003). Thus, the role of visuospatial attention in the online control of locomotor trajectory cannot be understated.

Visuospatial neglect is an attentional-perceptual disorder commonly observed in stroke individuals. It is characterized by a reduced ability to uptake visuospatial information from the contralesional side of space and to use this information into action (Booth, 1982; Heilman et al., 2000). As the visual attention is preferentially oriented towards events and stimuli present in ipsilesional side of space, stimuli occurring contralesionally are ignored or detected after a delay (Booth, 1982; Heilman et al., 2000). In an obstacle avoidance paradigm, a delay in detection of the obstacle reduces the time and distance available to perform an avoidance strategy (Aravind et al., 2015; Aravind & Lamontagne, 2014). Moreover, VSN also results in the subjective midline, i.e. egocentric midline which provides a framework for spatial orientation and goal-directed walking, to be shifted ipsilesionally (Richard et al., 2004). Consequently, coding the coordinates of visuospatial cues such as obstacles or targets in such an altered frame of reference leads to incorrect subjective localizations and judgments of distances from objects (Karnath et al., 1991). Finally, previous studies have shown that the use of self-motion cues such as optic flow, used to guide locomotion, can be impaired in VSN+ individuals (Berard et al., 2012). Thus, the altered utilization of visuospatial cues in VSN+ individuals would subsequently interfere with their ability to modulate locomotor heading with respect to targets and/or obstacles.

The main objective of this study was to compare, between VSN+ and VSN- stroke individuals, changes in heading and head orientation in space while: (a) avoiding obstacles approaching from different directions and; (b) reorienting towards the final goal i.e. target. Secondary objectives were to evaluate the influence of direction of obstacle approach on measures of obstacle avoidance and alignment with the target and to examine the relationship between locomotor outcomes related to obstacle avoidance and alignment with the target with clinical scores of VSN, cognitive function and balance confidence. To this end, we used a virtual reality set-up which permitted testing obstacle avoidance behaviour in a safe, and realistic environment.

We hypothesized that VSN+ individuals, compared to VSN- individuals, would show a preference to orient their heading and head towards the ipsilesional side in response to approaching obstacles, and would display larger heading errors with respect to final destination (target); these alterations would be more pronounced for obstacles approaching from the neglected (left) side than for obstacles approaching from the right side or from head-on. As suggested by results from our previous studies (Aravind & Lamontagne, 2014), we further hypothesized that the ability to avoid the obstacle avoidance and to align with the target would not be explained by clinical measures of VSN severity, cognitive status and balance confidence.

6.4 METHODS

Twenty-six participants (2 female, 24 male) following a first time right-sided supratentorial stroke (13 VSN+ and 13 VSN-) were recruited from 3 rehabilitation clinical sites of the Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal (CRIR) based on the following inclusion criteria: a right-hemispheric stroke (confirmed by CT /MRI); a clinical diagnosis of VSN based on the Motor Free Visual Perceptual Test (MVPT)(Colarusso & Hammill, 1972), or Letter Cancellation Test (Diller et al., 1974), or Bells Test (Gauthier et al., 1989); an ability to walk independently at speeds less than 1.2 m/s, with or without a walking aid; and motor recovery scores ranging from 3 to 6 out of 7 on the leg and foot impairment inventories of the Chedoke McMaster Stroke Assessment (CMMSA) and right-handed dominance (see Table 6-1). Individuals with a visual field defect, hearing loss, cognitive deficits or other co-morbid conditions (medical charts), interfering with locomotion were excluded. Five healthy control (CTL) participants (2 female, 3 male) were also recruited to understand the locomotor behaviours of individuals without stroke-related sensorimotor deficits, but were not included in the analysis.

6.4.1 EXPERIMENTAL SET-UP AND PROCEDURES

This study was part of a larger project designed to evaluate the ability of post-stroke individuals with and without VSN to perceive and actively avoid moving obstacles while walking and performing a simultaneous cognitive task (Aravind & Lamontagne, 2016). In this manuscript, we are presenting the findings related to the kinematic strategies adopted by the participants to avoid the approaching obstacle under a single-task condition.

The experiments were conducted using a VE designed using CAREN 3^{TM} (Motek BV, Amsterdam) software, which the participants viewed through an nVisor SX60 ^{TM} HMD (NVIS, USA). A 12-camera Vicon-512™ motion capture system tracked the position of three reflective markers affixed to the HMD. This information was fed to the CAREN 3™ to provide real-time updates of the participants' head position and orientation in the VE. Reflective markers were also placed on specific body landmarks as specified in the full body maker set based on the Plug-in-Gait model (Appendix A) from Vicon™, with 2 additional markers placed on the walking aid when applicable. Data were recorded at 300Hz in CAREN 3™ and at 120Hz in Vicon™.

6.4.1.1 Locomotor obstacle avoidance task

The VE set-up for the locomotor task included a room (12m x 8m) with a blue circular target on the wall at the far end (11m) and three red cylinders (obstacles) positioned in front of a theoretical point of collision (TPC) in an arc at 0° (Head-on), 40° right (ipsilesional side) and 40° left (contralesional side) (see VE in our previous publication (Aravind & Lamontagne, 2016)). The TPC is the point where the participant and the obstacle paths, if left unaltered, would meet and collide together. Participants were positioned at the beginning of the room facing the target and were instructed to walk towards the target while avoiding a collision with the approaching obstacle, if any. After advancing forward by 0.5m, one of the 3 obstacles randomly moved in the direction of the TPC and beyond, at a speed that matched the participant's unobstructed overground walking speed. Matched walking speeds ensured that a collision was imposed for every obstacle condition unless an avoidance strategy was executed. In the event of a collision, visual feedback was provided in the form of a flashing "Collision" sign. A fourth condition, which consisted of control trials with no obstacles in the walking path, was used to determine unobstructed walking speed and walking trajectory. At least 4 practice trials were provided and 4 to 6 trials per condition were collected, depending on the participant's endurance.

6.4.1.2 Perceptual task and clinical assessment

For this task, the participants were seated in a chair and held a joystick (Attack3- Logitech USA) in their right (ipsilesional) hand. The joystick and the forearm were rested on a table at a comfortable height. The VE and obstacle conditions were identical to the locomotor task. The perceived speed of self-motion and the speed of the obstacles, however, were set to 0.75 m/s, a speed that is representative of the average ambulatory stroke population (Ringman et al., 2004). Unlike the locomotor task, head-movements were not tracked and did not influence the view of the scene so that movement detection could occur only by visual exploration of the space. Forward displacement of 0.5m triggered the movement of one of the three obstacles or a control condition in which all obstacles remained stationary. The catch trials, with no moving obstacles, were aimed at preventing anticipatory responses. The participants were instructed to press the joystick button as soon as they perceived the onset of obstacle motion, or to withhold any response in case of a catch trial. When one obstacle moved, the others remained in view to avoid cuing the participant. No feedback was provided regarding collisions, if any. Participants were provided 8-10 practice trials and performed 10 trials for each of the 4 conditions, for a total of 40 conditions.

Stroke participants were also assessed on various clinical assessments to confirm the presence/absence of neglect (Bells test (Gauthier et al., 1989), Apples test (Mancuso et al., 2015), Line bisection test (Schenkenberg et al., 1980)), cognitive functioning (Montreal Cognitive assessment scale; MoCA (Nasreddine et al., 2005)), balance confidence (Activity specific balance confidence scale; ABC (Botner et al., 2005)) and overground comfortable walking speed (10 m walk test). The study was approved by the Ethics Committee of CRIR and all participants gave their informed written consent.

6.4.2 DATA ANALYSIS

For the *locomotor task*, the variables of interest included the participants' heading in space, horizontal head rotation in space, proportion of right head rotation, maximum mediolateral deviation (Max_ML), distance at onset-of-heading-change, end position errors in heading and head rotation with respect to the target, as well as peak walking speed.

Heading in space was calculated as the instantaneous angular orientation of the person's displacement along the anteroposterior and mediolateral axes, as measured by the 3-D coordinates of the head in space recorded in CAREN-3 (Berard et al., 2012). If someone were to walk perfectly straightforward, they would have a heading of 0˚. Distance at onset-of-heading-change was calculated as the distance after obstacle onset at which a change in the heading angle, greater than mean +2 standard deviations of the heading angles during the control trials (no obstacle), was detected. Head rotation angles were also obtained from the spatial coordinate data recorded in CAREN-3. Heading or head orientation to the right have positive values, while those to the left have negative values.

Heading errors were calculated as follows. First, the instantaneous angle made by the participants heading with the stationary target i.e. participant-target-angle (PTA) was calculated as the angle made by the participant with the target, given the instantaneous heading angle and mediolateral displacement (Fajen, 2013; Fajen & Warren, 2003, 2007). Then, the PTA at 5.5 m of forward displacement was recorded as heading error with respect to the target (Δ_Heading). The head rotation error with the target at 5.5 m of forward displacement was calculated from the difference between the ideal head rotation required at the participant's final position in order to align the head with the target and the recorded head rotation. For example, if at the end position, the target is 30° to the left of the participant, a head rotation of 30 degrees to the left would make the head aligned with the target such that Δ_HeadRotation=0°.

Maximum mediolateral (Max_ML) deviation achieved during the trial and the proportion of time for which the head was rotated towards the right (ipsilesionally) were also calculated. Average walking speed prior to onset and peak walking speed during obstacle avoidance was recorded along with comfortable walking speeds for control trials. The minimum absolute distance between the participant and the obstacle and collision rates, presented in another study (Aravind & Lamontagne, 2016), were used as timestamps and determinants of success of an avoidance strategy, respectively.

For the *perceptual task*, the time taken after onset of obstacle to press the joystick button was recorded as the detection time. The ratio of detection times for the contralesional and ipsilesional obstacles was calculated as an index of the visuospatial perception asymmetry.

6.4.3 STATISTICAL ANALYSIS

For Δ_Heading, Δ_HeadRotation, Max_ML deviation, distance at onset-of-heading-change, proportion of head rotation to the right, we conducted a linear mixed model analysis for repeated measures with unstructured covariance structure, with 1 between subject factor (group: VSN+, VSN-) and 1 within subject factor (direction of obstacle approach: left, head-on, right and none) to assess the influence of direction of obstacle approach on locomotor outcomes. However, for distance at onset-of-heading-change only 3 directions of obstacle approach (left, head-on and right) were compared. Significant interaction terms were further elaborated using simple effects where *a priori* identified specific pairwise comparisons were carried out, adjusting for multiple comparisons. For the visuospatial perception asymmetry measures, 95% Confidence intervals were calculated based on the performance of VSN- and CTL individuals combined ($\alpha = 0.05$). The presence of visuospatial perception asymmetry in VSN+ was confirmed if their scores lay outside the interval. Student t-tests were used to compare the VSN+ and VSN- groups for visuospatial perception asymmetry. Pearson correlation coefficients were used to quantify the relationship of VSN+ participants' locomotor performance (Δ_Heading, Δ_HeadRotation, Max_ML deviation and proportion of IL rotation, distance at onset of strategy) in response to the left obstacle, with visuospatial asymmetry scores and with the clinical assessments of neglect (Bell's Test, Line Bisection Test, Apple's test) and balance confidence (ABC). All statistical analyses were performed in SAS v9.4. The level of significance was set to $p < 0.05$. The performances of the CTL group were not included in the analyses. Only statistical tests with significant results are reported.

6.5 RESULTS

The presence and absence of VSN was confirmed in all participants, based on their performance on the Bells test (Gauthier et al., 1989), Apples test (Bickerton et al., 2011) and Line bisection test (Schenkenberg et al., 1980), with VSN+ individuals showing positive signs of neglect on at least two out of the three tests (Aravind & Lamontagne, 2016). The presence of an ipsilesional bias in VSN+ individuals was also observed and confirmed by our detection time task where visuospatial perception asymmetry scores of all VSN+ individuals (Mean ±1SD= 1.49 ±0.45 seconds) featured outside and above the 95% confidence interval of scores of VSN- and CTL individuals (Mean ±SD= 1.005 ±0.02 seconds) ($p<0.01$). While VSN+ and VSN- individuals did not differ on their levels of motor recovery (CMMSA), cognitive status (MoCA) and comfortable walking speeds, the VSN+ group showed significantly poorer balance confidence as assessed by the Activity-specific Balance Confidence scale, compared to the VSN- individuals ($p<0.05$).

All five CTL participants and eight out of the 13 VSN- participants were able to successfully negotiate the moving obstacles without collisions, compared to only three of the 13 VSN+

participants. Among the VSN- participants, one participant collided only with the head-on obstacle, one participant only with the left obstacle, two participants with left and head-on obstacles while one participant collided with left, head-on and right obstacles. Among the VSN+ participants, six participants collided with both the left and head-on obstacles while four others collided only with the left obstacle; none collided with the right obstacle.

Figure 6-1 shows representative walking traces of a CTL participant, as well as of a VSN- and a VSN+ participant. The healthy CTL and VSN- participants deviated their walking trajectory to both the right (ipsilesional) and left (contralesional) sides while avoiding the obstacles. In comparison, the VSN+ individual consistently deviated towards the right (ipsilesional) side, irrespective of the direction of obstacle approach. The latter behaviour was consistently observed in all VSN+ participants.

Participants were further analyzed on their preferred side of locomotor trajectory deviation in response to diagonally approaching obstacles (i.e. left and right approaching obstacles). Two strategies were observed: (i) the "same-side" strategy where participants veered to the same side as the approaching obstacle (i.e. left deviation for a left obstacle approach and right deviation for a right obstacle) and; (ii) "opposite-side" strategy where participants deviated to the side opposite to the approaching obstacle (i.e. right deviation for left obstacle and left deviation for right obstacle). Participants were classified as displaying the "same-side" or "opposite-side" strategy when their trajectory deviation fitted into one pattern of behaviour for more than 75% of trials. In the following sections we present the locomotor strategies shown by VSN- and VSN+ individuals and compare strategies that led to successful vs. unsuccessful obstacle avoidance.

6.5.1 KINEMATIC STRATEGIES IN VSN- PARTICIPANTS

The use of same-side vs. opposite-side strategies were nearly equally distributed amongst VSN- and CTL participants. Indeed, six of the 13 VSN- participants and three of the five CTL participants demonstrated a same-side strategy while the remaining participants showed an opposite-side strategy. Examples of opposite side and same-side strategies in VSN- participants that led to safe avoidance of obstacles are shown in Figures 6-2a and 2b, respectively. Note that examples of CTL participants are not illustrated, as their behaviour was comparable to that of

VSN- participants, unless otherwise specified. Further, while locomotor adaptations observed for head-on obstacles cannot be classified as same-side vs. opposite-side, observed strategies were consistent with those adopted to diagonal obstacle approaches by the participants and are thus illustrated along with the same-side or opposite-side behaviour set in Figure 6-2.

For the *opposite-side strategy* (Figure 6-2a), a change in heading was initiated soon after onset of obstacle movement, e.g. 0.5m of forward displacement. Peak heading angles occurred early on during the avoidance strategy (e.g. around 2.5 m of forward displacement) and were followed by maintenance of the heading angle until minimum distance from the obstacle was achieved. In contrast, for the *same-side strategy (Figure* 6-*2b)*, participants initiated the heading change later (about 1.5 m of forward displacement) and peak heading angles were observed around the time minimum distance was achieved (e.g. around 4 m of forward displacement). For both strategies, subsequent to minimum distance a reduction in the heading angles was observed leading to reorientation of the trajectory toward the midline. This translated into a reduction of the PTA and ultimately led to small Δ_Heading angles. The orientation of the head (head-rotation) roughly followed the heading orientation, for both strategies, leading to small Δ_HeadRotation.

Along with changes described above, changes in walking speed were also observed (not illustrated in Figure 6-2). While VSN- and CTL participants who deviated to the *opposite-side* sped up following the onset of obstacle movement, participants who deviated to the *same-side* sped up only while initiating a change in heading. For both strategies, however, peak walking speeds occurred around the time minimum distance was achieved following which the participants returned to their walking speeds observed prior to obstacle onset.

Interestingly, all VSN- colliders belonged to the sub-group that adopted the opposite-side strategy, with none of the participants adopting a same-side strategy making any collision. Collisions trials differed from non-collision trials in that they showed a delay in initiation of heading change, a delay in achieving peak heading angles, and smaller peak heading angles in comparison to the non-collision trials or an early reduction of heading angles (Figure 6-2c).

6.5.2 KINEMATIC STRATEGIES IN VSN+ PARTICIPANTS

Since the VSN+ participants consistently deviated towards the right (ipsilesional) side for all obstacle conditions, it could be interpreted that they demonstrated a same-side strategy for the right (ipsilesional) obstacle approach and an opposite-side strategy for the left (contralesional) obstacle approach. Qualitatively, however, their locomotor avoidance strategies substantially differed from those of the VSN- and CTL participants. Indeed, subsequent to the onset of obstacle, VSN+ participants maintained a fairly constant heading with an observable change in heading angles occurring only after a forward displacement of 2m to 2.5m, marginally preceding the achievement of minimum distance (Figure 6-2d). In addition, VSN+ individuals did not demonstrate an observable change in walking speed following the onset of obstacle movement (not illustrated).

In non-collision trials (Figure 6-2d), even after minimum distance was achieved, there were no observable changes in the heading angles i.e. VSN+ participants did not reorient towards the centrally located target. In fact, the PTA increased as the participant proceeded forwards leading to large Δ_Heading angles. In addition, throughout the trial, the head remained rotated towards the right (i.e. facing ipsilesionally), which ultimately led to a large Δ_HeadRotation. Collision trials differed from non-collision trials in that the former had no identifiable changes in heading angle or a change in heading orientation that occurred just before the collision. Similar to the non-collision trials, the head during the collision trials was aligned with the heading and oriented ipsilesionally (Figure 6-2e).

6.5.3 BETWEEN-GROUP COMPARISONS

Mean values of distance at onset-of-heading-change, Max_ML deviation, peak walking speeds, Δ_Heading, Δ_HeadRotation and collision rates for non-collision trial of each group and the different obstacle directions are shown in Figure 6-3. The mixed-model analysis revealed significant group-by-direction interactions for distance at onset-of-heading-change ($F_{(2,48)}=70.28$, $p<0.001$) and Max_ML deviation ($F_{(3,143)}=3.85$, $p<0.01$). Compared to VSN- group, the VSN + group showed larger distances at onset-of-heading-change and smaller Max_ML for the left and head-on approach, but not the right obstacle approach ($p<0.05$). An asymmetry was evident in the VSN+ group, with larger distances at onset-of-heading-change for the left compared to right obstacle-condition and smaller Max_ML deviations for left, head-on and control trials compared to right obstacle-condition ($p<0.05$). Contrastingly, VSN- and CTL participants showed comparable distances at onset-of-heading-change and Max_ML deviation across obstacle directions ($p<0.05$).

A significant main effect for group but not for direction was observed for peak walking speed (Figure 6-3c) and proportion of right head rotation (not illustrated in Figure 6-3), with VSN+ individuals achieving significantly smaller peak walking speeds ($F (2,48)=13.61$, $p<0.05$) and demonstrating a rightward head rotation for a greater proportion of the trial ($F (2,24)=24.6$, $p<0.05$) compared to VSN- individuals. A significant main effect for group, but not for direction, was also observed for the Δ_Heading ($F (3,143)=18.34$, $p<0.01$) and the Δ_HeadRotation ($F (3,143)=10.95$, $p<0.01$), with larger values (greater errors) being observed in VSN+ individuals compared to VSN- individuals for each of the obstacle approaches ($p<0.05$).

6.5.4 BETWEEN-STRATEGY COMPARISONS

To help understand the impact of the choice of strategy on the spatial relationships with the obstacle and target, mean values for the different locomotor outcomes in individuals who adopted the same vs. opposite side strategy are shown in Figure 6-4. Note that since the distribution of participants between the two strategies was unequal across the groups, no statistical analyses were performed. Results indicates that individuals of the VSN- and CTL groups who adopted the opposite-side strategy showed smaller distances at onset-of-heading-change, larger Max_ML deviations and larger peak walking speeds compared to the individuals who adopted the same-side strategy; Collisions were observed only for the opposite-side strategy (both left and right obstacles) but Δ_Heading and Δ_HeadingRotation were comparable for the two types of strategies. VSN+ individuals, however, showed larger distances at onset-of-heading-change and smaller Max_ML for opposite-side strategy (i.e. in response to left obstacles) compared to the same-side strategy (i.e. in response to the right obstacle); their peak walking speeds were similar for the two strategies. As observed for VSN- individuals, collisions were observed only for the opposite-side strategy (i.e. for left obstacles) and the choice of strategy did not influence Δ_Heading and Δ_HeadingRotation.

6.5.5 RELATIONSHIP BETWEEN CLINICAL ASSESSMENTS AND WALKING PERFORMANCES

No significant associations were observed between the participants' performances on the locomotor task (distance at onset-of-heading-change, Δ_Heading Δ_HeadRotation, Max_ML deviation) and their scores on the visuospatial asymmetry test, clinical tests of VSN, cognitive status and balance confidence ($p>0.05$).

6.6 DISCUSSION

The main purpose of this study was to understand how post-stroke individuals with and without VSN adapt their kinematic strategies to avoid a moving obstacle while walking and align with a final goal, and to compare strategies that led to successful and unsuccessful obstacle avoidance. The results of this study suggest that the presence of VSN alters the ability of post-stroke individuals to modulate their locomotor heading in response to visuospatial cues such as obstacles and targets, leading to collisions and large errors in aligning with the desired destination.

6.6.1 SAME-SIDE STRATEGY PRESENTS A 'SAFER' AND MORE 'EFFICIENT' STRATEGY FOR OBSTACLE AVOIDANCE COMPARED TO OPPOSITE-SIDE STRATEGY

During goal-directed walking, individuals steer towards an end-goal so as to minimize the error between the heading angle and the angle with the target(Fajen, 2013; Fajen & Warren, 2003, 2007). The presence of an obstacle in the walking pathway, however, necessitates an intermediate change in the heading in order to avoid a collision. In our study, participants that were devoid of VSN (VSN- and CTL) executed this intermediate change of heading while using two strategies, when exposed to diagonal obstacle approaches: (a) by deviating to the same-side as the obstacle; or (b) by deviating to the opposite-side of the obstacle.

Overall, the use of a same-side strategy appeared to be safer method to avoid diagonally approaching obstacles compared to the opposite-side strategy. Indeed, by deviating to the same side, participants almost immediately avoided the need to cross the obstacle's path in order to reach the target, thereby reducing the risk of collision. In fact, VSN- and CTL participants who adopted this behaviour were able to safely avoid collisions despite showing larger distances-at-onset-of-strategy (i.e. delayed onsets), staying closer to the midline (smaller MaxML deviations, smaller peak headings) and relatively smaller speed changes (lower peak walking speeds) in comparison to the opposite-side strategy.

The use of the opposite-side strategy also led to successful obstacle avoidance. However, unlike the same-side strategy, we suggest that it does not minimize the risk of a future collision. In order to proceed towards the target, an opposite-side approach necessitates the interception of the obstacle's future path. If this interception occurs when the obstacle is in close proximity such that no further changes to heading can be executed, then a collision will occur. In trials that led to successful obstacle avoidance, VSN- individuals who deviated to the opposite side displayed small distances-at-onsets-of-heading-changes (early onsets), larger Max_ML deviations, larger peak headings and greater speed changes (higher peak walking speeds) compared to the same-side strategy.

A failure to make such adaptations, for example a delay in onsets of heading change, smaller deviations to the side, or an early re-orientation of heading towards the midline, led to collisions with the approaching obstacles. Moreover, since energy expenditure increases with increased walking distances and speeds (Hall et al., 2004; McArdle et al., 2015), modulations such as larger Max_ML deviations and faster peak walking speed, although allowing the participant to avoid a collision, are likely to exert greater energy demands. Thus the opposite-side strategy may not only be more risky for collisions but also less efficient compared to the same-side strategy.

Another interesting observation of this study is that for both same-side and opposite-side strategies, the head orientation was aligned with that of the heading. Therefore, for the same-side strategy, the head was rotated in the direction of obstacle approach, and the obstacle was likely to remain in the field-of-view, potentially favouring an enhanced uptake of visual information about the relative obstacle position. Contrastingly, for the opposite-side strategy, the head was rotated away from the obstacle during the avoidance strategy, potentially minimizing the uptake of visual information about the obstacle. Thus, the orientation of the head towards the approaching obstacle during the same-side strategy may further contribute to make this strategy safer, compared to the opposite-side strategy. In fact, an absence of visual feedback about the obstacle could also explain why, in some trials, VSN- participants who adopted the opposite-side strategy performed an early reorientation towards the midline, leading to collisions. However, an objective measurement of gaze, which was not performed in this study, would be required to confirm this hypothesis. Collectively, aforementioned observations suggest that the choice of strategy influences the success of obstacle avoidance while walking.

6.6.2 VSN ALTERS THE CONTROL OF HEADING AND HEAD ORIENTATION, LEADING TO COLLISIONS

Compared to 38% of VSN- individuals and 0% of CTL individuals, 75% of VSN+ individuals demonstrated collisions for left and head-on obstacles, with none of VSN+ individuals colliding with the right obstacle. Such locomotor behaviour where VSN+ individuals collide with objects present on the neglected side of space has been observed for both static(Tromp et al., 1995; Turton et al., 2009) and dynamic obstacles(Aravind & Lamontagne, 2014) and can be attributed to an ipsilesional (right) bias observed in VSN and a visual attention that is preferentially directed towards the ipsilesional side of space(Dvorkin et al., 2012; Kinsbourne, 1993; Posner et al., 1984). Consequently, visual exploration of the contralesional side is limited and stimuli located on the contralesional side may be omitted or detected after a delay(Rizzolatti & Berti, 1990, 1993; Robertson et al., 1994). In support of this hypothesis, all VSN+ individuals tested in this study did show an asymmetrical performance in detecting approaching obstacles, with longer detection times for left (contralesional) compared to right (ipsilesional) obstacles. Further, as they walked, they spent a greater proportion of the trial time with their head rotated towards the ipsilesional side compared to VSN- individuals. We suggest that this bias of perceptual-attentional resources towards the ipsilesional side delayed the detection of contralesionally approaching obstacle and the initiation of an avoidance strategy (Aravind et al., 2015; Aravind & Lamontagne, 2014) thereby reducing the time and distance available to execute the avoidance strategy and leading to collisions. At variance, the detection of and initiation of the avoidance strategy in response to the ipsilesionally approaching obstacle for VSN+ individuals were comparable to those of VSN- individuals and, as observed in our earlier work (Aravind et al., 2015; Aravind & Lamontagne, 2014), no collisions were observed.

In the present study, the influence of ipsilesional bias was also evident in the preference of VSN+ participants to deviate to the right while walking, for all obstacle conditions. In VSN, there is a rightward shift of the egocentric midline, causing a rightward shift of the “straight ahead”. Since we rely on egocentric frames of reference to specify our location and orientation in space (Ruotolo et al., 2015), a “rightward-shifted” midline results in a walking trajectory that is also deviated to the right. This was supported by the observation that an ipsilesionally-deviated trajectory was observed even when no obstacles were present in the path i.e. control trials. This ipsilesional deviation of walking trajectory resulted in a same-side strategy for ipsilesional obstacles and an opposite-side strategy for contralesional obstacles. Considering the higher demands, greater risks and reduced uptake of obstacle-related visual information associated with the opposite-side strategy, the preferential adoption of the opposite-side strategy for *all* VSN+ individuals is likely to have contributed to the larger proportion of colliders for this group.

Present findings further revealed that kinematic patterns leading to collisions in VSN+ vs. VSN- individuals differed. When adopting the opposite-side avoidance strategy, for instance, VSN+ individuals showed delayed onset-of-heading-change (larger distances), smaller deviations from the midline (Max_ML deviations) and minimal change in walking speed compared to VSN- individuals. Thus, despite the risk of collision associated with the opposite-side strategy, VSN+ individuals did not make early enough nor large enough changes to their heading or speed for contralesional obstacles, thereby increasing the risk of collisions. In fact, trials that ended in collisions did not demonstrate an identifiable onset-of-heading direction change until just prior to minimum distance, with the individual maintaining a small, constant heading angle as they proceeded in space leading to collisions. A similar pattern was observed for collision trials in presence of obstacles approaching from head-on. This contrasts with the collision trials in VSN- individuals that were rather characterized by an early reorientation of the heading towards the midline.

Findings or this study also show that the ability to reorient towards the final goal was dramatically altered in VSN+ individuals, as evidenced by large Δ_Heading and Δ_HeadRotation errors compared to individuals without VSN. This can, once again, be attributed to the ipsilesional bias observed in VSN. Since the heading and the head-rotation was ipsilesionally oriented, the target fell in the unattended, neglected side of space and was not used to update and modify the walking strategy, leading to poor alignment with the target.

Finally, in further support our previous findings(Aravind et al., 2015; Aravind & Lamontagne, 2014) and those of other studies(Buxbaum et al., 2006; Buxbaum et al., 2008); the clinical evaluations of VSN did not predict the locomotor responses for the VSN+ individuals. The perceptual task, which was able to reveal the ipsilesional biases in detection of moving obstacles, also failed to explain the locomotor obstacle avoidance performance of VSN+ participants. The latter finding could be explained by inherent differences in the nature of the perceptual task (seated, with no postural demands of locomotion, use of ipsilesional hand to navigate the joystick) and a more challenging task such as locomotion. These observations bolster the need to include complex tasks such as obstacle avoidance in clinical assessments of post-stroke VSN+ individuals, in order to obtain insights into the their capability to adapt to the demands of community ambulation.

6.7 CONCLUSIONS

In this study we demonstrated that individuals with post-stroke VSN fail to adapt their walking strategies when negotiating obstacles approaching from the neglected side and from head-on and show an impaired ability to align their heading with the desired destination. We suggest that the ipsilesional bias arising from VSN resulted in a failure to initiate a timely heading change, in insufficient trajectory deviation from the midline and in a marked preference to orient the head and locomotor heading ipsilesionally. We further suggest that such an ipsilesional bias, along with the adoption of the 'riskier' opposite-side strategy, contributed to the high proportion of colliders observed in participants with post-stroke VSN.

6.8 CONFLICT OF INTEREST

The authors declare that there is not conflict of interest.

6.9 ACKNOWLEDGMENT

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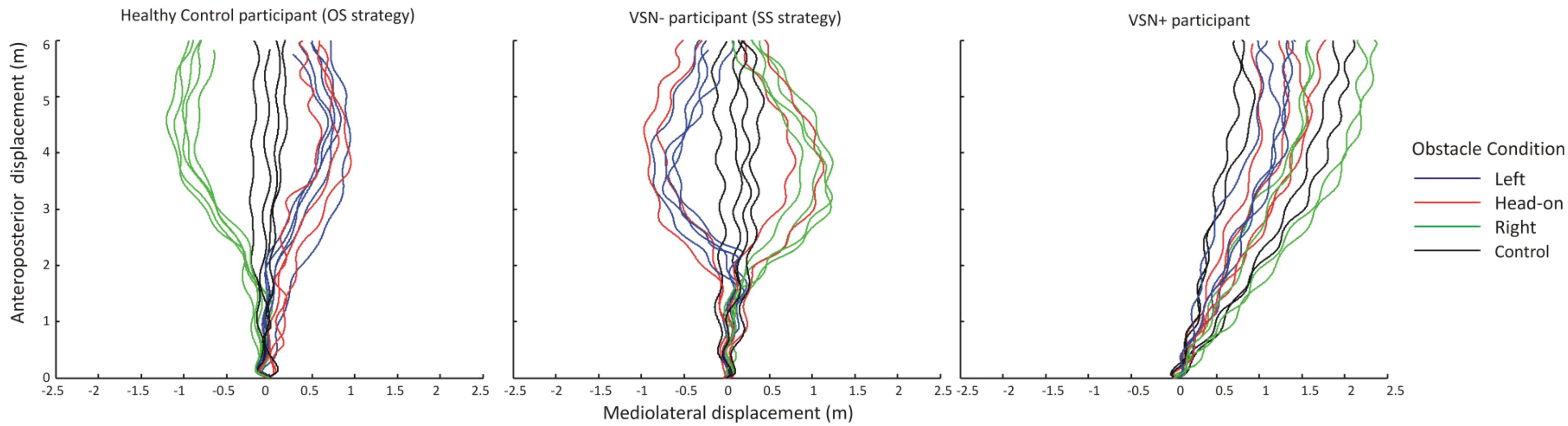

Figure 6-1. Representative traces of walking strategies adopted by (a) CTL (b) VSN- and (c) VSN+ participants. The CTL participant demonstrated the opposite-side strategy (OS) and the VSN- presented a same-side strategy (SS). The VSN+ participant consistently deviated to the ipsilesional side and presented a same-side strategy for the ipsilesional obstacle condition and an opposite-side strategy for the contralesional obstacles condition.

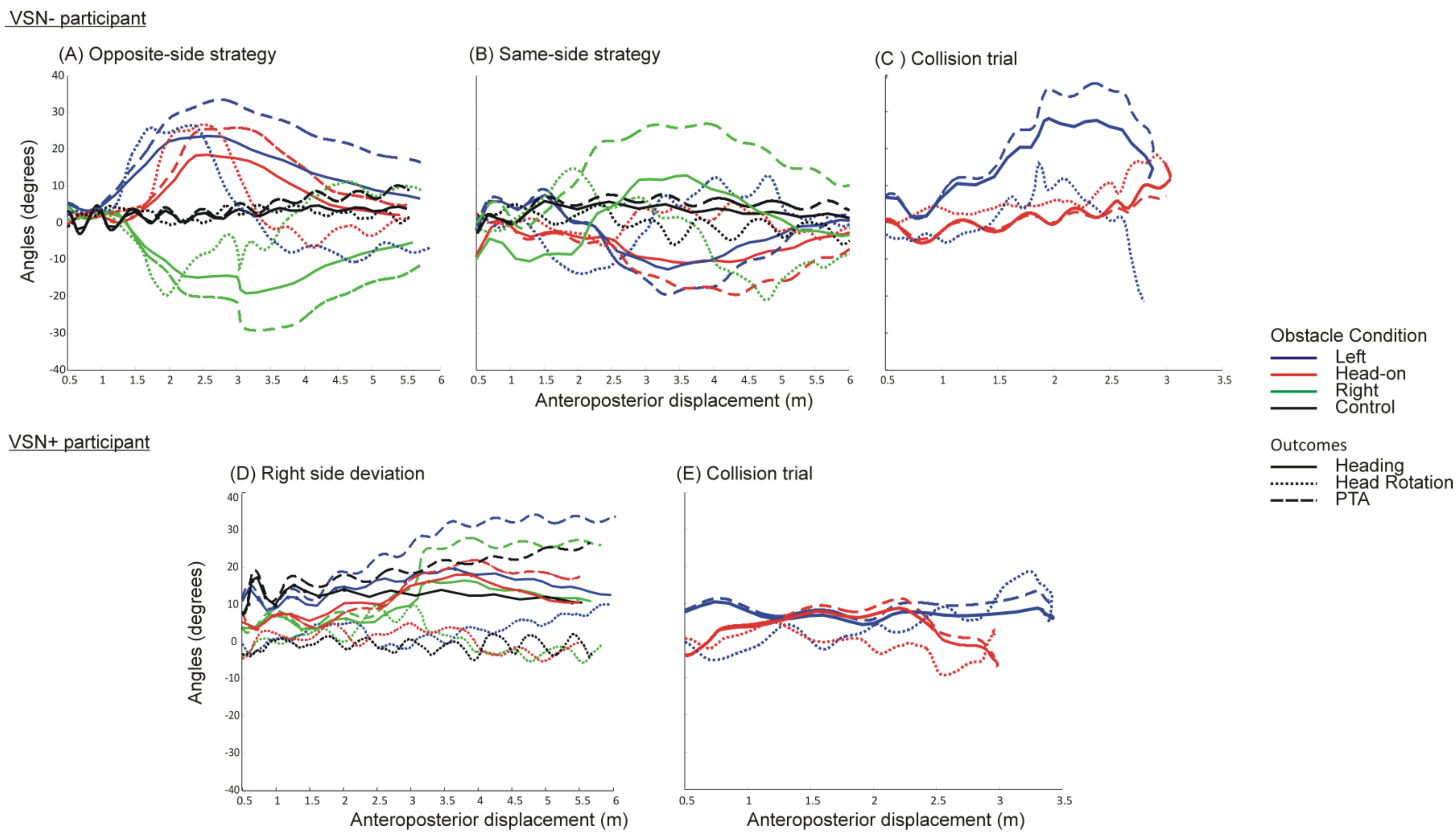

Figure 6-2. The figure shows representative traces for heading orientation, participant-target-angle (PTA) and head rotation angles maintained by the participants. Traces in (a) and (b) represent, respectively, a VSN- participant who adopted an opposite-side strategy and a same-side strategy; Traces in (c) represent a VSN- participant who collided with the obstacles; Traces in (d) represent a VSN+ participant who deviated to the right side for all obstacle conditions and traces in e) are representative traces of VSN+ participant who collided with the obstacles.

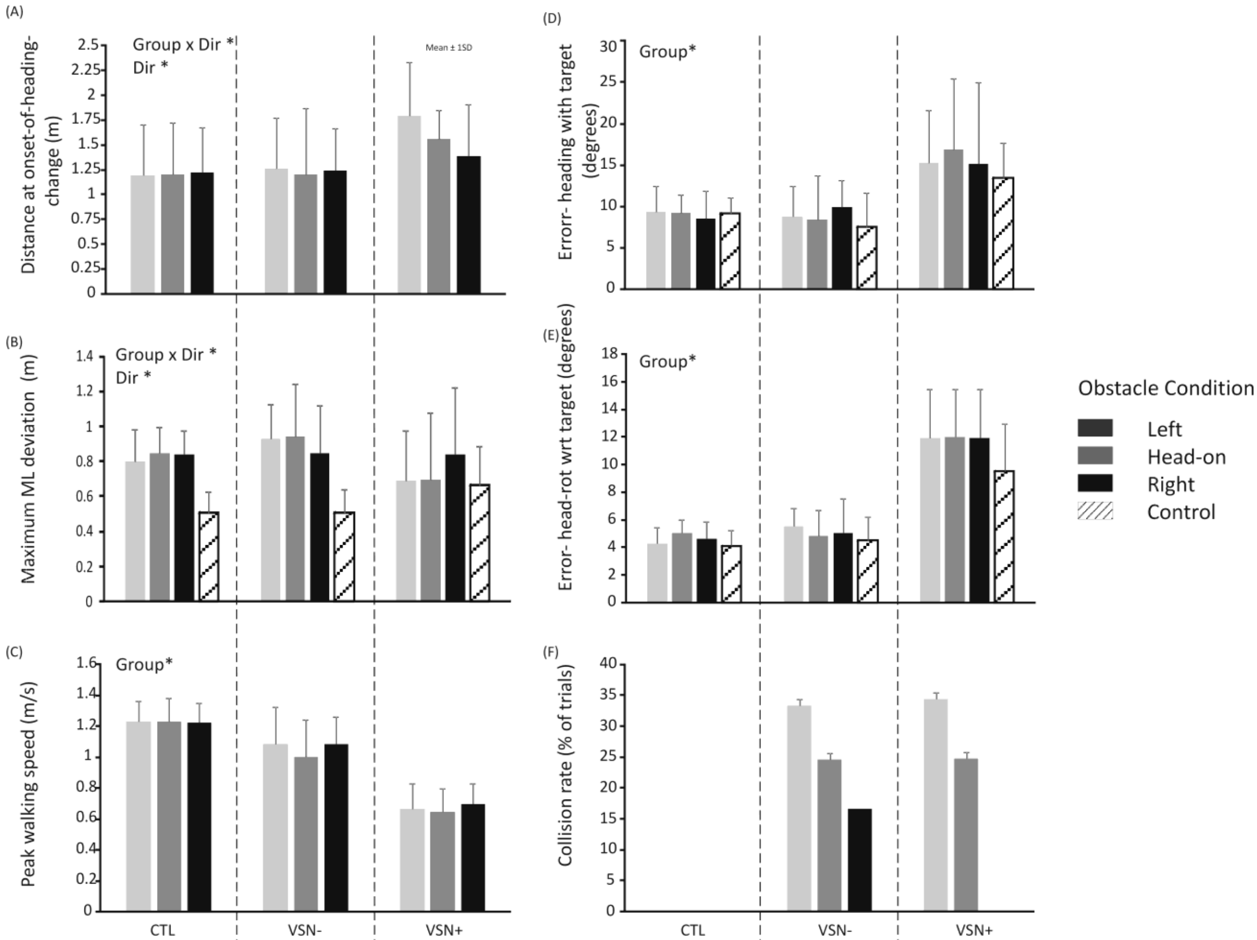

Figure 6-3: The figure shows mean ± 1SD values of CTL , VSN- and VSN+ participants for distance at onset-of-heading-change (3a); Maximum mediolateral deviation (3b); Peak walking speeds (3c); Δ_Heading (3d), Δ_HeadRotation (3e) and Collision rates (3f). Statistically significant interaction terms are specified in the text inserts. * $p<0.05$.

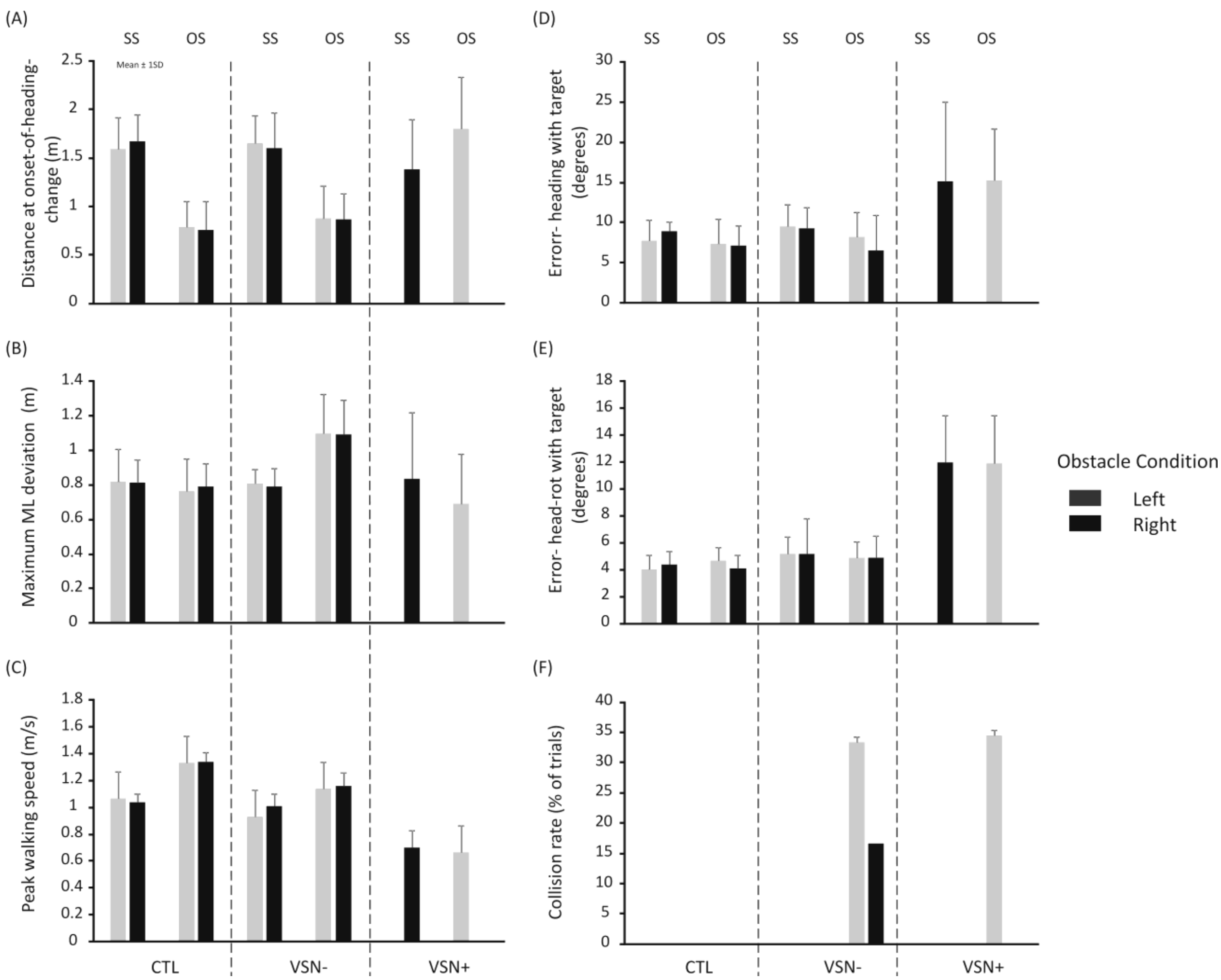

Figure 6-4. The figure shows mean ± 1SD values of CTL, VSN- and VSN+ participants' responses to diagonal obstacles (i.e. left and right), divided into the type of strategy adopted i.e. same-side or opposite-side, for (a) distance at onset-of-heading-change; (b) maximum mediolateral deviation; (c) peak walking speeds; (d) Δ_Heading; (e) Δ_HeadRotation and; (f) collision rates. Note that due to uneven distributions, no statistical comparisons were performed between the two types of strategy.

CHAPTER 7: GENERAL DISCUSSION

7.1 SUMMARY OF RESULTS

The aims of this thesis were two fold: to investigate how the presence of VSN in post-stroke individuals influence the ability to perceive and safely avoid moving obstacles while walking, and to assess the impact of simultaneously performing a cognitive task (i.e. dual-tasking) on obstacle avoidance abilities. It was hypothesized that due to the ipsilesional bias in visual perceptual-attentional abilities that characterize VSN, VSN+ individuals would display an altered detection of obstacles that approached from their contralesional side compared to their ipsilesional side. It was also hypothesized that VSN+ individuals would display altered spatial-temporal relationships, and ultimately collisions, with obstacle approaching from the contralesional but not ipsilesional side while walking. These hypotheses were confirmed in Chapter 3 (manuscript 1) where we observed that the detection and avoidance of contralesional obstacles (and head-on) obstacles were compromised in VSN+ individuals, compared to ipsilesional obstacles.

In order to ascertain the contribution of VSN related attentional-perceptual deficits and stroke-related sensorimotor deficits, obstacle avoidance behaviour was re-evaluated in a joystick-driven task. We hypothesized that even when the biomechanical burden of locomotion was minimized, VSN+ individuals would continue to demonstrate more collisions and maintain altered spatial-temporal relationships with the contralesional and head-on obstacles compared to the ipsilesional obstacles, as observed during locomotion. This was confirmed in Chapter 4 (Manuscript 2) where, despite performing the obstacle avoidance with a joystick held in the ipsilesional hand, VSN+ individuals showed smaller distances from obstacle at onset, smaller minimum distances and higher collision rates for contralesional and head-on obstacles compared to ipsilesional ones. However, the collision rates for the joystick-driven task were smaller than for the locomotor task, suggesting the additional burden placed by the demands of locomotion contribute to, but are not solely responsible for, the collisions observed in VSN+ while walking.

Next, we evaluated the impact of performing a simultaneous cognitive task i.e. dual-tasking on the obstacle avoidance performance of VSN+ and VSN- individuals. We hypothesized that the burden on the attentional resources would cause a cognitive-motor interference in both VSN+ and VSN- individuals, but the superimposed deficits in visuospatial attention in VSN+ individuals would lead to greater interference in the VSN+ individuals compared to VSN- individuals. This was confirmed in Chapter 5 (Manuscript 3) where VSN+ individuals demonstrated a decline in locomotor (delayed onsets, smaller minimum distance, higher collision rates) and cognitive (higher cognitive error rates) performances during the dual-task condition, relative to the single task performances. In contrast, VSN- individuals prioritized their locomotor performance (larger minimum distances but no change in collision rates) during the dual-task condition but deteriorated in their cognitive performance (higher cognitive error rates). Overall, VSN+ individuals fared worse for both the locomotor and cognitive performance than the VSN- individuals. We had also hypothesized that interference would be greater for a more complex cognitive task. Confirming this hypothesis, it was observed that an increase in task complexity led to greater decline in the cognitive performances for both groups and to a greater decline in the locomotor performance for the VSN+ group only.

Further, we evaluated the premise that the ipsilesional bias resulting from VSN would impair the control of heading while negotiating obstacles and walking towards a target. It was expected that VSN+ individuals would demonstrate a preference to orient their heading and head towards the ipsilesional side and would display larger errors in aligning with the target and that these alterations would be more pronounced for the contralesional and head-on obstacles compared to the ipsilesional ones. This was confirmed in Chapter 6 (Manuscript 4) where we observed that the modulation of heading in response to an approaching obstacle in VSN+ individuals was greatly influenced by the ipsilesional bias of VSN, with delays in initiating a heading change, smaller maximum mediolateral deviations and greater proportion of colliders for the contralesional and head-on approach and a greater preference to orient the heading and head ipsilesionally for all obstacle conditions, compared to the VSN- group. The direction of deviation emerged as an important determinant for the risk of collision for both VSN+ and VSN- individuals with deviation to the same-side as the obstacle leading to safer and more efficient obstacle avoidance while deviation to the side opposite to the obstacle putting the individuals at a greater risk for collision. For VSN+ individuals, adoption of a riskier strategy along with the altered modulation of heading in response to the obstacle, contributed to the risk of collisions. The ipsilesionally oriented heading and head rotation also resulted in larger errors when aligning with the final target, for VSN+ individuals in comparison to VSN- individuals, revealing impairment in aligning with the final goal.

Altogether, these findings support the view that obstacle avoidance while walking is challenging for persons with post-stroke VSN, putting them at a risk for collisions with obstacles that approach from their neglected side of space or head-on. This risk of collision further increases when attentional burdens are increased such as in a dual-task situation. Finally, the lack of significant relationships between clinical assessments of VSN and obstacle avoidance outcomes that was consistently observed across manuscripts (1-4) suggests the need for task-specific assessments of VSN to help determine the impact of VSN on functional tasks such as locomotion.

7.2 GENERAL DISCUSSION

The world we walk in is cluttered with both static and dynamic objects that we need to safely avoid as we continue to walk to our destination. The ability to avoid obstacles while walking is therefore a skill necessary for maintaining safety and independence. The ability to dual-task is another common demand of community ambulation.

Shumway-Cook and Woolacott describe a movement generated as an outcome of the manner in which an *individual* attempts to fulfil demands of a *task* being performed in a given *environment* (Shumway-Cook & Woollacott, 2007). In the context of this thesis, I examined how these factors interacted to produce a contextually adapted gait and specifically examined how walking (i.e. the *movement)* while exposed to moving obstacles and a target (i.e. the *environment)* is shaped by post-stroke VSN (i.e. *the individual*) during obstacle avoidance task performed under single or dual-task conditions (i.e. *task demands*).

Since the return to independent community ambulation is a major goal of rehabilitation for stroke survivors, it was imperative to understand how persons with VSN after a stroke would cope under the different demands of community ambulation, of which two, obstacle avoidance and dual-tasking, are explored in this thesis. As these demands had never been explored in persons with VSN before, this work therefore contributes to fill a large knowledge gap to the field of rehabilitation, while providing results that should help guiding the development of future VR-based assessment and treatment strategies for mobility in post-stroke VSN.

In humans, vision plays a critical role in the anticipatory locomotor control as it identifies potentially de-stabilizing events such as presence of an obstacle and guides the appropriate locomotor adaptations in order to safely progress towards the goal. Therefore, it was expected that persons with VSN after a stroke, in whom the ability to obtain relevant visual information from the side of space opposite to the lesion is impaired, would have difficulties in producing the necessary locomotor adaptation to safely avoid an obstacle in the contralesional space. Results of this thesis confirm that the presence of post-stroke VSN profoundly affects the ability to successfully avoid moving obstacles while walking, particularly for the obstacles that approach from the contralesional side of space and from head-on. This ability is further impaired when a cognitive task is performed simultaneously with the obstacle avoidance task. Results from this thesis further suggest that this reduced ability to perform obstacle avoidance and dual-tasking are attributed, at least in part, to the attentional-perceptual deficits that characterize VSN.

7.2.1 VISUOSPATIAL NEGLECT INTERFERES WITH DETECTION OF MOVING OBSTACLES APPROACHING FROM THE CONTRALESIONAL AND HEAD-ON DIRECTIONS

Using paper-pencil or computerized tasks, various studies have shown that the presence of VSN negatively influences attention towards events and stimuli occurring on the ipsilesional side, leading to a failure to recognize static stimuli in the contralesional side of space; a phenomenon that is broadly referred to as ‘ipsilesional bias’ (Bonato & Deouell, 2013; Bonato et al., 2013; Dvorkin et al., 2012; Dvorkin et al., 2007; Robertson, 1989). Manuscript 1 (Chapter 3) showed, for the first time, that the detection of moving objects is also affected by this ipsilesional bias. Indeed, in a novel and immersive virtual reality paradigm where obstacles approached from different directions, VSN+ participants demonstrated a significant delay in the detection of obstacles that approached from the contralesional i.e. neglected side compared to the obstacle that approached from the ipsilesional or non-neglected side. Interestingly, we observed that the detection times for head-on obstacles were also longer than those for ipsilesional obstacles but less than that for contralesional obstacles. Therefore, instead of suggesting an absolute distinction between the neglected and non-neglected visual space, present findings are rather supportive of a gradient of neglect in which the detection of stimuli becomes increasingly worse when the location of the stimulus changes from ipsilesional to head-on to contralesional (Butler et al., 2004; Kinsbourne, 1977; Marshall & Halligan, 1989; Morris et al., 2004). Such a direction-specific gradient in detection times was not observed for VSN- individuals or for healthy controls (Manuscript 4, Chapter 6), confirming the hypothesis that VSN does in fact specifically influence the detection of contralesionally-approaching and head-on obstacles. It was also noted that obstacle detection times in VSN+ individuals were generally larger than in VSN- individuals, suggesting that non-spatially lateralized attention-perception deficits also contribute to the altered performance of VSN+ individuals.

For the joystick-driven navigation task (Manuscript 2, Chapter 4), we transformed the obstacle detection time, a time variable, into a distance variable i.e. distance between the obstacle and participant at detection. It was observed that shorter distances from the obstacle at detection were associated with onsets of avoidance strategies that were initiated at closer proximity from the obstacles, thereby reducing the distance (and time) available to bypass the obstacle. While it was expected that a delay in the perception of the obstacle would also be associated with delayed onsets of avoidance strategy during the *locomotor* avoidance task, no such association was observed. It is possible that the nature and demands of the joystick-navigation task (seated, reduced postural demands, response is with less-affected ipsilesional arm) more closely resemble those of the obstacle detection tasks, making the relationship between outcomes on the two tasks easier to unveil. Further, as Huitema and colleagues suggest, VSN interacts with the walking capacity to influence the control of walking trajectory (Huitema et al., 2006), which may explain the absence of relationships between the perception and locomotor performances.

Together, results from manuscripts 1 and 2 confirm that the perception of moving obstacles is altered in persons with VSN and can explain, in specific conditions such as a joystick navigation task, the longer delays in initiating on obstacle avoidance strategy. During walking, however, this relationship between perception and action could be more complex, with possible interactions between perceptual and locomotor factors.

7.2.2 VISUOSPATIAL NEGLECT INFLUENCES THE SPATIOTEMPORAL RELATIONSHIPS MAINTAINED WITH OBSTACLES AND CONTRIBUTES TO THE RISK OF COLLISION

Avoidance of moving obstacles is a complex task that largely relies on the visual system for information regarding the position of the obstacle relative to oneself. Due to the impaired uptake of the visual information from the contralesional side of space, along with the altered spatial representation observed in persons with VSN, we predicted that spatiotemporal relationships maintained with the obstacle would also be altered and would lead to collisions with obstacles approaching from the neglected side of space.

This prediction was confirmed by the results of Manuscripts 1, 2, 3 (Chapters 3, 4, 5 respectively), with the observation of delayed onsets of avoidance strategy, smaller distances maintained from the obstacles and larger collision rates in VSN+ individuals when avoiding contralesional and head-on obstacles, compared to when obstacles were approaching from the ipsilesional side and to the behaviour observed in VSN- individuals. Thus, the gradient observed for the *perceptual task* was also observed in the *locomotor task*, with VSN specifically enhancing the risk of collision with obstacles approaching from the neglected side and from head-on, but not from the non-neglected side.

Interestingly, even in the joystick-driven obstacle avoidance task where the burden of locomotion was minimized, an almost identical proportion of participants (75%) to the locomotor task collided with the contralesional and head-on obstacles. The latter observation, along with the differences in obstacle avoidance performance observed between stroke individuals with vs. without VSN, suggest that the enhanced collision rates in post-stroke VSN cannot be attributed solely to the presence of stroke-related sensorimotor deficits that impair walking abilities, and that the attentional-perceptual deficits related to VSN are very likely to be at cause.

Findings from the different studies of this thesis also point towards a *delayed initiation of avoidance strategy* as being a critical factor inducing collisions with moving obstacles. Indeed, a delay in initiation of an avoidance strategy, when an obstacle is constantly approaching, reduces the time and distance available to execute an avoidance strategy (Manuscript 2, Chapter 4). Given that making sudden changes to the walking behaviour is challenging in persons with stroke (Lamontagne et al., 2007b), the delay in initiation makes obstacle avoidance further challenging for VSN+ participants. This was demonstrated in Manuscript 4 (Chapter 6) where the delay in initiation of a heading change emerged as a contributing factor for collisions in both VSN+ and VSN- group. In fact, the delay in initiation of an avoidance strategy was an important factor that differentiated colliders from non-colliders (Manuscript 1 and 4 (Chapters 3, 6)).

VSN+ participants involved in the present studies also maintained *smaller minimum distances* from the contralesional and head-on obstacles compared to the ipsilesional ones. The minimum distance can be interpreted as a “buffer” or “personal space” which an individual creates between themselves and an object that provides some time and distance to execute a change in the event that the obstacle makes an unpredicted movement (Gerin-Lajoie et al., 2008a). Maintaining larger personal spaces, as observed in participants with stroke free of VSN, would provide more time and distance from the obstacle to safely execute the necessary locomotor adaptations (Darekar et al., 2015). The “contraction” of “personal space” observed on the neglected (contralesional) side and head-on compared to the non-neglected side observed in this thesis (Manuscript 1, 2, 3 (Chapters 3, 4, 5)) is reminiscent of the theory of neglect according to which the representation of space is compressed contralesionally and expanded on the ipsilesional side (Halligan & Marshall, 1991).

A pattern of walking behaviour that was also consistently seen across the VSN+ individuals was the *preference to deviate their walking trajectories* towards the ipsilesional side (Manuscripts 1, 3, 4). This has been observed in previous studies where VSN+ individuals walk towards a central target and has been attributed to the ipsilesional shift of the subjective midline observed in VSN (Huitema et al., 2006; Punt et al., 2008; Tromp et al., 1995; Turton et al., 2009). In addition to the ipsilesional deviation of the walking trajectory, VSN+ individuals also preferentially orient their head towards the ipsilesional side of space, further restricting the exploration of environment and monitoring of the contralesional and head-on obstacle, which now lay in the neglected field-of-view (Manuscript 4, Chapter 6). This may be an additional contributing factor for the collision and may serve to explain why the head-on obstacle is also “neglected”.

As shown in Manuscript 4 (Chapter 6), the *side of strategy* was another factor influencing of the outcome (success vs. failure) of obstacle avoidance. By deviating ipsilesionally for the contralesional obstacle, VSN+ individuals put themselves in the obstacle's path and increase the chances of colliding with it. Moreover, such an "opposite-side" strategy involves greater demands for safe obstacle avoidance such as early onsets, faster speeds and larger deviation from the midline. VSN+ individuals failed to demonstrate these adaptations, which put them at a higher risk for collision with the obstacle. On the contrary VSN- individuals showed a variety in the strategies adopted to avoid the obstacle. VSN- individuals who deviated to the same side as the obstacle in case of the diagonal obstacles demonstrated a more "efficient" strategy and were able to safely avoid collisions despite delayed onsets-of-heading-change and slower walking speeds. VSN- individuals who deviated to the opposite side of the obstacle did not collide so long as they were able to cope with the demands of the opposite-side strategy, and a failure to do so resulted in collisions as well. Considering the higher demands, greater risks and reduced uptake of obstacle-related visual information associated with the opposite-side strategy, the use of the opposite-side strategy in all VSN+ individuals may have contributed to the larger proportion of colliders for this group.

These sets of behaviours collectively resulted in greater collision rates for contralesional and head-on obstacles, compared to ipsilesional obstacles for the VSN+ group. For those trials that did not end in a collision, the influence of ipsilesional bias was observed even in their attempts to align with the target. Subsequent to avoiding the obstacle, VSN+ individuals, unlike the VSN- individuals, did not show a reorientation of their walking trajectory towards the target, displaying larger errors in alignment of their head and heading with respect to the target, compared to VSN- individuals. Thus, in addition to impaired obstacle avoidance abilities, their *ability to align with the intended destination*, which is the main aim of goal-directed locomotion, is also impaired by VSN.

7.2.3 DUAL-TASKING FURTHER IMPAIRS SUCCESS OF LOCOMOTOR OBSTACLE AVOIDANCE IN VSN+ INDIVIDUALS

Dual-task paradigms have been used extensively to understand the role played by attention in performing various tasks of daily living. They reflect the ability of a person to perform concurrent tasks while efficiently allocating attention to both tasks (Bonato, 2012). In this thesis a dual-task paradigm was utilized to further uncover the impact of VSN-related perceptual-attentional deficits on obstacle avoidance while walking. Since VSN is associated with a deficit of visuospatial attention directed towards the contralesional side of space and with a generalized reduction in attentional resources, we expected that the ipsilesional bias of attention and its subsequent effects of locomotor obstacle avoidance would be exaggerated under conditions of increased attentional demands. The observation that VSN+ individuals demonstrated deterioration of their locomotor obstacle performance when simultaneously performing the Stroop task confirmed this hypothesis. The concurrent observation of a cognitive cost along with the locomotor task is indicative of a mutual *cognitive-locomotor interference*.

According to Baltes & Baltes (Baltes & Baltes, 1990), in a dual-task situation, the task that is of immediate importance is often prioritized while walking. Considering that the danger of colliding with the obstacle is of an urgent nature, and that the cognitive task did not provide any useful information, prudence would dictate the prioritization of the walking task, as seen in VSN- individuals. While stroke individuals who were free of VSN increased their margins of safety (minimum distances) to prevent an increase in the collision rates at the expense of the cognitive performance under dual vs. single task condition, VSN+ individuals demonstrated concurrent deteriorations in obstacle avoidance (delayed onsets, smaller minimum distances and more collisions) and cognitive performances (more errors). This suggests that VSN+ participants did not prioritize either task and showed a mutual cognitive-locomotor interference, which is a novel finding of this study. In fact, for the complex dual-task (DTWalk-HL), all VSN+ participants demonstrated collisions with the contralesional and/or head-on obstacles and some even displayed collisions with the ipsilesional obstacle. This may be a reflection of a completely overwhelmed attentional system, compromising even non-spatially lateralized attention leading to collision with obstacles on the non-neglected side of space.

Avoiding obstacles and coping with changing attentional demands are two tasks that are frequently performed concurrently while walking in the community. A deterioration of locomotor performance due to dual-tasking could lead to falls or accidents affecting the safety and independence of persons with VSN. Similarly, the inability to simultaneously process cognitive information while walking could limit the completion of essential tasks in the context community ambulation (e.g. recalling of shopping list items, talking while walking, etc.), reduce attention to extrinsic stimuli, as well as limit the ability of the person to interact and participate to community walking. In fact, rehabilitation for improving gait function often involves the patient walking and the therapist providing feedback, usually in the form of verbal cues. If the VSN+ individual is unable to attend to the feedback while walking or is unable to walk while attending to feedback, the therapeutic session could become less effective.

7.2.4 MOVING AHEAD FROM PAPER-PENCIL TESTS TO FUNCTIONAL, TASK-SPECIFIC EVALUATIONS

A recurring theme through the various studies included in this thesis is the attempt to understand whether the evaluations that are used in the clinical settings to detect the presence and resolution of VSN are in fact capable of reflecting performance on a functional task such as avoiding obstacles while walking.

It was consistently found that the results on paper-pencil tests such as Bells test, Line bisection test or Apples test did not correlate with the measures of obstacle avoidance such as minimal distance, collision rates or even obstacle detection times. In addition, Manuscript 1 (Chapter 3) included participants with a history of neglect, who were deemed "recovered from neglect" based on these paper-pencil based evaluations but they too showed spatially asymmetrical relationships with the obstacles and demonstrated collisions with contralesional and head-on obstacles while walking. Moreover, the exaggeration of signs of neglect under dual-task conditions indicates that the degree of task complexity is also critical to the locomotor behaviour observed. Considering above-mentioned observations, it appears that the demands and challenges of walking in the community are unique, and cannot be reflected by evaluations that are limited to the near-space, with static stimuli involving a 2-dimensional space without time or attentional constraints. In order to understand the safety and level of independence of VSN+ individuals during tasks such as obstacle avoidance or dual-tasking, task-specific assessments that match the complexity and challenges faced in the community must be included in the battery of clinical evaluations. The results of such functional assessments could then be used to design a comprehensive rehabilitation program with the focus of returning stroke individuals to independent community walking.

Virtual reality emerges as an ideal platform for conducting these assessments for stroke with and without VSN. As described in the introduction of this thesis, a VR setup affords several benefits in terms of safety, reproducibility and transferability to real-world behaviour. Our VR paradigm allowed to reveal the presence of a spatial asymmetry in obstacle avoidance, and also demonstrated how changing the attentional demands of a task impact the walking behaviour. For these reasons, such paradigm could be used for gait assessment and treatment. The joystick-driven obstacle avoidance task, while not entirely reflective of the challenge of locomotor obstacle avoidance, did extract similar behaviours (delayed onsets, smaller minimum distance and collisions for contralesional and head on compared to ipsilesional approach). It could thus be used as an alternative to a more costly and complex locomotor set-up for the assessment and training of detection and avoidance of moving stimuli, in the absence of locomotor demands. The advancement in technology and the availability of low-cost devices designed by the games industry will make it easier to expand the use of VR beyond the research setting.

7.3 LIMITATIONS OF THE STUDY

One of the main limitations of this thesis is the absence of measures that detected and distinguished the presence of near and/or far space neglect in our VSN+ participants. Far space neglect is often reported to be more severe than near space neglect (Berti et al., 2002; Cowey et al., 1994b) and cannot be detected in the paper-pencil tests. Often, persons who do not show neglect in one domain could demonstrate it in the other (Berti et al., 2002). Since walking and more specifically obstacle avoidance require the detection of events occurring at a distance to plan avoidance strategies in advance, the presence of far space neglect could be a factor that separated colliders from non-colliders. However, due to the lack of standardized clinical evaluations that are considered sensitive and valid to test for far space VSN, we were unable to identify these deficits in our participants.

Another limitation was the lack of comparison between obstacle-avoidance performance on the joystick-driven avoidance task and the locomotor task seen examined in Manuscripts 1 and 2. The joystick permits motion in two planes, antero-posterior and medio-lateral. It does not allow for rotational movements and therefore cannot replicate the actual walking task in which shoulders and trunk can be rotated to acquire a larger clearance from an object. In addition, the joystick-driven task allowed a greater range of speed variations (0-1.5 m/s), which was beyond the self-selected fast walking speeds for all participants. These affordances were provided with the intention of assessing responses under conditions that minimized the contribution of stroke-related sensorimotor impairments, thereby assessing the contribution of VSN-related attentional-perceptual deficits to obstacle avoidance performance. However, these differences in the nature of the two tasks prevented a direct comparison of the responses in the joystick-driven task and locomotor obstacle avoidance task.

Lastly, the virtual reality environment utilized in this thesis, while deemed ecological, remains simplistic compared to a real community environment as encountered in daily living, due to the presence of a sole fixed target, 'non-reactive' inanimate obstacles moving along a fixed path at a fixed speed and a lack of common environmental features such as auditory and visual distractors. While this limits the generalizability of the findings to other challenges that may be encountered while walking in the community, controlling these variables was judged as essential in order to determine the specific effects of direction of obstacle approach and dual-tasking on the obstacle avoidance strategies while minimizing potential confounds, as well as to characterize behaviour in a less challenging environment before moving on to more complex environments.

7.4 FUTURE DIRECTIONS

The results of this work open up several arenas for future research. The knowledge that VSN+ individuals are unable to modulate their walking strategies in complex environments while facing additional challenges (dual-tasking) highlights the need to evaluate and treat these challenges to community ambulation. Future research should focus on designing a VR-based functional assessment tool, which incorporates obstacle avoidance behaviour and dual-task walking as dimensions of the assessment.

Dual-task training has been shown to be effective in improving the ability to dual-task and reduce dual-task costs while walking in persons with stroke (Ada et al., 2003; An et al., 2014; Kim et al., 2014; Plummer-D'Amato et al., 2012). However, whether such training programs would help reduce the cognitive-locomotor interference observed in persons with VSN is not yet know. Therefore, future studies could also focus on developing an effective VR-based rehabilitation program in which the persons with VSN can be taught to attend to visual information in different regions of the space while performing a goal directed locomotor task and also to concurrently perform a cognitive or motor task. This would prepare the individual for challenges that are faced during community ambulation and enhance their safety and independence.

Further, eye-tracking devices that are compatible with immersive virtual reality setups could be combined with the above-mentioned assessment and treatment protocols to assess visual scanning and gaze fixations on objects of interest (obstacle, target etc.), in order to further understand the visual-guidance of locomotion in persons with VSN after a stroke.

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APPENDICES

APPENDIX A: PLUG-IN-GAIT MODEL FOR MARKER PLACEMENT