Adaptability of Gait in Stroke Survivors

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I, …………………………….…….. (Susanne van der Veen) confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Dedication

Ik zou mijn thesis graag opdragen aan mijn zus Jolijn Kooper-Stoots. In de laatste maanden van mijn Ph.D. maakte zij een beroerte door (13 November 2017). Deze gebeurtenis liet me inzien hoe belangrijk het is om het verslag van mijn onderzoek goed op papier te zetten en door te gaan met deze tak van research. Iets dat ze zei tijdens het etentje met ons gezin om het behalen van mijn verdediging te vieren liet mij inzien hoe voor haar de beroerte haar leven bemoeilijkt en hoe belangrijk het daarom is dat we begrijpen wat voor impact een beroerte kan hebben. Ze zei: **“Het is alsof ik Alice in Wonderland ben. Als ik al weet waar ik heen moet dan nog is alles om me heen onbekend. Tijd is geen constante meer. Hoe weet ik hoe snel een auto bij mij is? Wat is belangrijk om op te letten, en wat kan ik negeren? Het is alsof ik in Wonderland ben maar de deur naar buiten niet kan vinden.”**

I should like to dedicate this thesis to my sister Jolijn Kooper-Stoots. During the last months of my Ph.D. she survived a stroke (13th of November 2017). This event made me all the more determined to make this thesis worth its while. Something she said at the dinner we had with my close family to celebrate my passing my defence really described to me what the stroke did to her and how important research in stroke survivors is and how much we still need to understand something of the deficits that come with a stroke. She said: **“It is as if I am Alice in Wonderland. Even if I know and remember where I am going, all surroundings are hard to determine. Time is not a constant anymore. I don’t know how fast a car moves. I don’t know what I should focus on and what I should ignore. It is if I am in Wonderland and I have not found the door out yet.”**

Abstract

Background: Stroke survivors fall more often, mostly due to stumbling and slipping; which may signify. These causes of falls are hypothesized to be caused by difficulty in controlling and adjusting foot placement in response to the environment. In healthy adults' foot placement control is known to be influenced by balance control, available response time and executive function. All these factors are known to be affected by stroke; however, how these factors affect foot placement accuracy in stroke survivors is largely unknown. The overarching aim of this thesis is therefore to understand the role of these factors in the control of foot placement following stroke and by extension to better understand how foot-placement is controlled, the causes of stroke related impairments and potential reasons for falls.

Methods/Results: Young (n=14) and older healthy adults (n=9) and stroke survivors (n=13) completed a series of experiments on a C-Mill (a force instrumented treadmill with visual projection of stepping targets) designed to assess the role of balance (study 1), response time (study 2) and executive function (study 3) on foot placement control in stroke survivors. Study 1 compared foot placement control in supported versus unsupported conditions; balance support reduced overall error while target stepping (main effect $F(1,30)=18.141$, $p<0.001$), but mostly in stroke survivors. Study 2 compared foot placement control when targets could be seen in advance (planned) with targets appearing at midstance (reactive). Foot-placement error altered according to direction of step but not available response time, with significant increase in error ($F(1,28)=6.013$, $p=0.021$) when adjusting steps medio-laterally but decreased when adjusting steps anterio-posterially ($F(1,28) = 5.932$, $p=0.021$). Overall, stroke survivors missed about 10% of targets and undershot all targets while young healthy adults undershoot only lengthening steps. Study 3 evaluated the use of functional near-infrared spectrometry (fNIRS) to measure activation of prefrontal cortex activation (brain networks responsible for executive function) in target stepping conditions which can be expected to increase challenge to executive function. fNIRS showed high inter person variability and no systematic trends according to walking conditions.

Conclusion: Stroke survivors miss about 1 in every 10 targets; in the real world this may lead to a fall. Balance support may generally help stroke survivors control foot-placement more accurately. However, the lack of difference in accuracy between reactive and pre-planned stepping indicates stroke survivors may respond to all foot-placement adaptations reactively (a "cluttered terrain strategy"). This 'cluttered terrain strategy' is indicative of increased cognitive control, however the use of fNIRS needs development to robustly be assess this during walking.

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The period of my PhD research has been a period of learning, not only of scientific development but also personal development. I would like to thank my supervisors Dr Kristen Hollands for the ongoing support, confidence and motivational ‘slow it down it’ whispers my way. Prof. Ricard Baker I like to thank for his clear view on data and the critical perspective on research methodology. Dr Ulrike Hammerbeck I thank for being such a methodical and straightforward co-worker in the lab during the first part of my Ph.D and taking over the role of Richard Baker in the last. All of you have enriched the journey towards becoming a researcher, a journey which I have truly enjoyed.

Also, I would like to thank the people I have had the pleasure working with during my PhD in various projects. Sultan Alharabi, always two feet on the floor, and always there for data collections, to discuss results, ideas and frustrations with; Ulrike Hammerbeck, Mark Hollands and Jeanine Blaakmeer for working on the project to determine if walking speed had an effect on stepping accuracy. Jevaka Kirilla, it was fun to show you around in Salford and Manchester, and to help you setting up the project on entraining people with different types of noise. Pornprom, it was a blast helping you with recruiting participants and data collection on your balance project in stroke survivors and teaching you ice skating. Lastly, William Royle and Robbert Bendal for providing me with the knowledge and equipment to study the effect on cognition on target stepping in stroke survivors. Thank you for making my time in Salford meaningful and enjoyable.

Kate Siltverthorn, I will always be in debt of massages in return for the tremendous work you have done proofreading this thesis, thank you for all the effort, and if you are close, come and cash a massage or have an easy row with me.

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Lastly, I want to thank my family for supporting me along the way, for the ongoing support, trust and confirmation, you will always be there. The friends I have made in the U.K. for making me feel so welcome and valued, I loved spending time with you and I am looking forward to having these friendships for life. The friends I have in the Netherlands, thank you for coming by, hosting me back home and confirming that friendships are stronger than distance. Thank you all for making me feel so loved and valued, and supporting me during this phase of my life.

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Abbreviations

ADL	Activities of daily living
ANOVA	Analysis of variance
AP	Anterio-posterior
BoS	Base of support
CoM	Centre of mass
CoF	Centre of foot
CoP	Centre of pressure
EEG	electroencephalography
fNIRS	functional near-infrared spectroscopy
HbO	Oxygenated hemoglobin
HbR	Reduced hemoglobin
ML	Medio-lateral direction
N	Number
OH	Older healthy adults (age-match with stroke)
PFC	Pre-frontal cortex
fMRI	functional magnetic resonance imaging
SD	Standard deviation
SE	Standard error
SEM	Standard error of the mean
SS	Stroke survivor
VD	Vertical displacement kinematic gait event detection method
AD	Anterior displacement kinematic gait event detection method
YH	Young healthy adults

Publications in relation to this thesis

Submissions

- Van der Veen, S. M. J., Hammerbeck, U., Baker R.J., Hollands K. L. Validation of Gait Event Detection by Centre of Pressure During Target Stepping in Healthy and Paretic Gait. (in submission)
  The results from this paper are described in Chapter 3.

Conference abstracts

- van der Veen S.M.J., Baker R. J., Hollands K. L. 'How to measure foot-placementaccuracy during target stepping tasks: centre of pressure or centre of foot?', International society of posture and gait, Fort Lauderdale, USA, 25-19 June 2017.
- van der Veen S.M.J., Baker R. J., Hollands K. L. 'Validation of centre of pressuregait event detection in young healthy participants and stroke survivors during target stepping.', International society of posture and gait, Fort Lauderdale, USA, 25-19 June 2017.
- van der Veen S.M.J.,Hammerbeck. U., Hollands. M. A.,Hollands K. L. 'Effects of speed of walking on the accuracy of foot placement control in Stroke Survivors compared to age-matched control', International society of posture and gait, Fort Lauderdale, USA, 25-19 June 2017.
- van der Veen S., Bendel. R. C. A., Hollands K.,"Executive Function During Target Stepping in Young Healthy Adults.", society for the neural control of movement, Dublin, Ireland, 2-5 May 2017.
- van der Veen S., Hammerbeck., Hollands K.,"Reactive vs. Planned Target-Stepping Ability in Stroke Survivors", International society of motor control, Wisla,Poland, 14-16 September2015.
- van der Veen S.,Hammerbeck U., Blaakmeer J., Hollands K.,"Ability to shorten orlengthen StepsVaries According to Walking Speed in Healthy Young Adults",Internationalsociety of motor control, Wisla,Poland, 14-16 September2015.
- van der Veen S., "Adaptation of Gait in Stroke Survivors" Salford, United Kingdom, 14-15 June 2016.
- van der Veen S.,Hammerbeck U., Blaakmeer J., Hollands K., "Reactive stepping ability in healthy adults as a control comparison for stroke survivros", 2015 International Society of Posture and Gait Research, Seville, Spain, June 28-july 2 2015.
- Blaakmeer J., Hammerbeck U., van der Veen S., Hollands K., "Effects of speed of walking on the accuracy of foot placement control", 2015 International Society of Posture and Gait Research, Seville, Spain, June 28-july 2 2015.

1 Introduction

High rates of falls have been reported among stroke survivors (Hyndman, Ashburn, & Stack, 2002; Jorgensen, Engstad, & Jacobsen, 2002; Lamb et al., 2003; Smith, Forster, & Young, 2006; Yates, Lai, Duncan, & Studenski, 2002), mostly due to a trip or a slip during walking (W. P. Berg, Alessio, Mills, & Tong, 1997; Blennerhassett, Dite, Ramage, & Richmond, 2012; Said et al., 2005; Weerdesteyn, de Niet, van Duijnhoven, & Geurts, 2008). These trips and slips may occur when foot placement needs to be adapted (e.g. stepping over obstacles, stepping to safe footfall location in uneven terrain); especially as multiple studies have reported adaptability of stepping in stroke survivors is poor (Den Otter, Geurts, de Haart, Mulder, & Duysens, 2005; K. L. Hollands, Agnihotri, & Tyson, 2014; Nonnekes et al., 2010; van Swigchem, Roerdink, Weerdesteyn, Geurts, & Daffertshofer, 2014). While young or healthy adults are generally able to either avoid a hazard, or recover (Den Otter et al., 2005; Nonnekes et al., 2010), it has been shown that stroke survivors react differently and are less successful in adapting their foot placement. For example, in turning, stroke survivors need to take more time than healthy adults to complete the turn (K. L. Hollands et al., 2014; K. L. Hollands et al., 2010); in obstacle avoidance, stroke survivors are less able than healthy counterparts to lengthen steps when avoiding the obstacle (Den Otter et al., 2005; Said et al., 2005; Said et al., 2008); when narrowing steps, greater error is seen with stroke survivors versus healthy counterparts (Nonnekes et al., 2010). These differences between stroke survivors and their healthy counterparts in control/adaptability of foot placement are likely to be one reason stroke survivors fall more often. One study has made a correlational link between ability to alter foot placement and functional recovery (K. L. Hollands et al., 2015), but beyond this, little is known about the links between falls, functional mobility and adaptability of walking. Being able to change stepping in response to the environment is an essential part of functionally adaptive walking ability (i.e. ability to widen, narrow, shorten, and lengthen steps to target safe footfall locations in uneven/cluttered terrain such as that found in community settings). Therefore, studying the adaptability of foot placement is important to understand the role of foot placement control in functionally adaptive walking ability after stroke. Here we refer to functionally adaptive walking ability as distinct from steady state walking, in which gait has rhythmic cadence with a constant speed, level, and direction. Adaptations to gait are those in which one or more of these factors are interrupted.

1.1 Research aims

The aim of this thesis is to investigate how stroke survivors are limited in foot placement control. Specifically, I investigate how different factors as the direction of adaptation, balance support, and the available response time affect foot placement control. Further I investigate whether the increase of executive function that is necessary to make these changes to steady state gait can be measured with functional near-infrared spectroscopy (fNIRS). The study was designed for moderately affected stroke survivors, as they had to be able to walk for a reasonable amount of time at once. It establishes whether the above factors affect foot placement accuracy, and what the underlying impairment might be.

1.2 Research questions

- Is centre of pressure gait event detection accurate enough for midstance detection in young, older healthy adults and stroke survivors?
- Are centre of pressure and centre of foot both measures of accuracy of foot placement during walking?
- Does the direction of adaptation affect foot placement success during walking?
- Does shortening a step affect foot placement accuracy more than lengthening a step during walking?
- Does narrowing a step affect foot placement accuracy more than widening a step during walking?
- Does balance support make foot placement more accurate than without support during walking?
- Does the time available to adjust foot placement affect success and foot placement accuracy during walking?
- Can we measure executive function increase due to more complicated target stepping paradigms during walking using fNIRS?

1.3 Organization of thesis

This thesis explores the ability and accuracy to adapt foot placement to targets during walking in healthy young and older adults and stroke survivors in three chapters.

1) **Chapter 6** explores the effect of different directions of adaptations on the accuracy of target stepping in young and older healthy adults and stroke survivors
2) **Chapter 7** explores the effect of balance on the accuracy of target stepping in young and older healthy adults and stroke survivors
3) **Chapter 8** explores the influence of response time on the accuracy of target stepping in young and older healthy adults and stroke survivors.
4) **Chapter 9** explores how the measurement of executive function/ oxygenation of the frontal during steady state walking, regular target stepping, and irregular targets stepping.

This thesis contributes to our understanding of foot placement control in as well young and older healthy participants and stroke survivors during walking. It explores the effect of balance, response time, and executive function on the success and accuracy of walking to targets. This thesis will give an idea of what the limiting factors in foot placement control are during walking in stroke survivors, but also young and older healthy adults.

2 Literature review

2.1 A definition of gait adaptability

Gait adaptability has been defined differently in various papers, for example: one's ability to modify walking to meet task goals and demands (Balasubramanian, Clark, and Fox (2014) or 'gait that does not lead to a fall' (Bruijn, Meijer, Beek, & van Dieen, 2013). Because the definition of gait adaptability has to encompass many variations of gait adaptations (e.g. turning, obstacle negotiation etc.), and in doing so, consider the role of internal (body stability, neuromuscular activity, balance, etc.) and external constraints (speeding up to cross a street in time for a traffic light etc.), it must therefore be broad. Additionally, the definition of adaptability has to be one that is operational; allowing measurement identifying impairment clinically and scientifically to measure how the adaptation is achieved and what the cause of impairment is.

Patla and Shumway-Cook (1999) attempted to define adaptability of walking by dividing the adaptations of walking into different domains to allow measurement of the components of safe, adaptable gait. These domains are based on the assumption that mobility is characterised by the ability to respond to environmental demands. This is described by several skills, namely: starts, stops, changes in direction, speed, surfaces with different geometric and physical properties, obstacles in the travel path, and the execution of other tasks such as talking, turning, looking at something, or carrying objects (Patla & Shumway-Cook, 1999). The grouping of these responses to environmental demands are translated into eight domains of adaptability: minimum walking distance, time constraints, ambient condition (i.e. light or whether conditions), terrain characteristics, external physical load, attentional demands, postural transition, and traffic. The process of determining domains of gait adaptability was largely based on the experience and knowledge of the authors, as opposed to formal systematic or objective analytical processes. These eight adaptability domains have recently been modified into nine by Balasubramanian et al. (2014), where traffic density is divided into two new domains: obstacle negotiation and manoeuvring in traffic. The recent work of Balasubramaniam et al. (2014) describes the adaptability domains based on the neuro-control model of functional walking by Forssberg and Nashner (1982) and Grillner and Wallen (1985). These control models of walking contain three levels: 1) basic rhythmic stepping, 2) posture and equilibrium control, and 3) adaptations to goals and environment (figure 2.1). Although the use of a control model to overarch the broad ability to adapt walking can facilitate attempts to base gait adaptability tests on the neuro-motor model of functional walking, the tests currently available are only designed for clinical purposes (i.e. time to perform/success failure which highlight presence or absence of impairment) and do not include measures of how adaptations to environmental demands are achieved or not achieved.

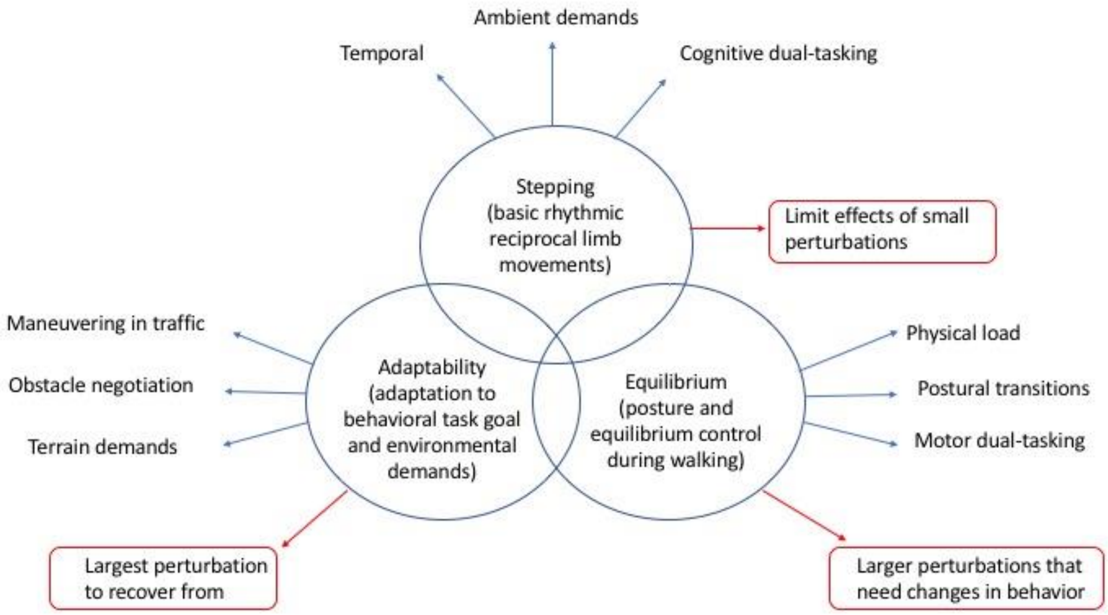

Figure.2.1 *A schematic representation of the original control model of gait with the nine domains of adaptation proposed by Balasubramanian et al. (2014) indicated with the blue arrows, and the three levels of functional walking by Bruijn et al. (2013) indicated with red arrows.*

Alternatively, but similar to previous models of functional walking, Bruijn et al. (2013) proposed a definition of adaptability which is mainly focussed on internal constraints of the body, described as 'gait that does not lead to a fall'. In this definition gait is limited by intrinsic body functions to maintain stable gait. Three mathematical measures reflect levels of functional walking define gait stability:

1) Successful gait adaptability is demonstrated by the ability to recover from, or limit the effect of, small perturbations that occur during every stride.

2) Successful gait adaptability requires that large perturbations have to be overcome, which necessitates a change in behaviour.

3) The largest recoverable perturbation, specified by the limits of one's constraints must be larger than the perturbations encountered in daily life, i.e. when the

perturbations encountered in daily life are larger than one is able to recover from it will lead to a fall.

This framework (Bruijn et al., 2013) describes the requirements for gait stability during adaptations, but lacks to take into account adaptations to environmental demands. In addition, the measures and methods used by (Bruijn et al., 2013) are highly mathematical and not user-friendly or translatable into clinical practice.

The control model of gait (Grillner & Wallen, 1985) and the level of functional walking (Bruijn et al., 2013) described in the previous two paragraphs are combined in figure 2.1. Firstly, stepping and basic rhythmic reciprocal limb movements allows us to get in a steady state walking rhythm in which the steps are placed seamlessly into reoccurring gait cycles. This steady state of walking is important to be stable, so attention can be directed to the environment and other tasks while walking. In stroke survivors these basic rhythmic reciprocal movements are often disturbed; as stroke survivors tend to have asymmetric gait and impaired relative timing in interlimb coordination, leading to greater variability in step lengths and times (Kwakkel, Kollen, & Wagenaar, 2002; Wagenaar et al., 1990). Often quality of gait is focused on by physiotherapists to train stroke survivors gait for "normal" looking gait patterns. Further in line with recovering steady state rhythm is the issue of walking speed. Virtually every physio approach studied reports significant improvements in speed. However, many systematic reviews show that the effects on gait speed/steady state progression/rhythm of the vast majority of treatment approaches do not translate to functional improvements in activity or participation (K. L. Hollands, Pelton, Tyson, Hollands, & van Vliet, 2012; Krishnamoorthy et al., 2008; Moseley, Stark, Cameron, & Pollock, 2005).

Secondly, equilibrium and posture control involve the force and coordination needed to adapt the initial steady state walking to the environment. For example, when we adjust a step to be slightly shorter, the forward momentum created at push off will initially be slowed down by the heel contact and will have to be slowed down with a plantar flexion movement to keep recovering the steady state walking speed. In many stroke survivors the hemiplegic side is associated with strength and coordination loss (Arene & Hidler, 2009), sometimes even leading to the need for wearing foot orthoses, preventing stroke survivors from using ankle strategies to correct the CoP under the foot. Lastly, adaptability and being able to recover from the largest perturbation encountered in daily life is the function in the control model that will be focussed on in this thesis the most. This combination of the two factors above, being able to make adjustments during walking that are greater than the ones occurring in daily movement. This could vary per person, as one might be house bound and have smaller perturbations on a daily basis than one still being an independent outside walker. However, generally healthy adults are able to walk while doing double tasks and avoid an obstacle without tripping or target a specific foot placement. Stroke survivors have been shown to have more difficulty adjusting gait, stopping more often when they talk during walking (Hyndman & Ashburn, 2004), are less successful in obstacle avoidance (Den Otter et al., 2005; van Swigchem, van Duijnhoven, den Boer, Geurts, & Weerdesteyn, 2013) and less accurate in foot fall targeting (Nonnekes et al., 2010). Generally, these three levels of functionality are treated uni-dimensional aspects of gait as speed and balance, but how do these uni-dimensional training transfer into function? Maybe to be functional in the environment you need more than the ability to maintain progression, you need the ability to change the steady state rhythm to the environment. To really understand why stroke survivors fall more often than healthy adults, how these factors/levels of the model of stable gait are affected and how that interferes with gait adaptability in daily life needs to be investigated.

Therefore, the development of a definition of gait adaptability that is applicable and measurable in both clinical and research contexts is required to describe adaptations in response to the internal and environmental demands while maintaining stability including the functions ad sections as in the model for stable gait. Besides the lack in either clinical applicableness or information about what limits the person in adapting gait, both approaches described above do not include the importance of maintaining forward progression during the adaptation of walking. However, stopping and pausing have been shown to be a sign of pathology (Buckley, Pitsikoulis, & Hass, 2008; Frykberg, Aberg, Halvorsen, Borg, & Hirschfeld, 2009; Malouin, McFadyen, Dion, & Richards, 2003). For instance, people with a stroke who stop walking when talking, and people who need to stop to adapt their walk were less fluent, walked slower, and showed less coordination (Buckley et al., 2008; Frykberg et al., 2009; Malouin, McFadyen, et al., 2003) which is likely to make them more prone to falling. Therefore, previous definitions of gait adaptability have limitations, which complicate the transition of knowledge and research needs between research and clinical practice.

The following definition of gait adaptability is proposed, for a clinically and scientific setting with definable measures, and will be used throughout the work that follows: **The ability to alter walking in response to environmental demands while maintaining stability and forward progression.** This definition is particularly strong because it captures both environmental and internal demands for safe walking, where previous definitions focussed either on the environmental or internal demands. Also, it is important to note that these demands have to be met during walking, so forward progression has to be maintained.

2.2 Fall prone populations

Stroke survivors are at high risk of falls in all stages of recovery (acute, inpatient care, chronic) (Weerdesteyn et al., 2008). About 18-40% of stroke survivors regain independent walking mobility and about 60% of stroke survivors could still access places of interest such as shopping malls etc. (Lord, McPherson, McNaughton, Rochester, & Weatherall, 2004). While community-dwelling stroke survivors fall less often than those in inpatient rehabilitation, the incidence of falls is still high with 43-70% of community-dwelling stroke survivors reporting falls within 1-year following discharge (Andersson, Kamwendo, Seiger, & Appelros, 2006; Hyndman et al., 2002; Lamb et al., 2003; Watanabe, 2005). Stroke survivors who do regain independent mobility most often fall during walking (Forster & Young, 1995; Jorgensen et al., 2002; Lord et al., 2004) and falls occur during trips, slips and misplaced steps. Therefore, it is likely gait adaptability is a meaningful factor in fall risk in **independently** mobile stroke survivors.

2.3 Why foot placement control may be the essential element to support ability to adapt gait?

Many manoeuvres are encompassed under this proposed definition of adaptability including changes to rhythmic cadence, walking speed, level of terrain, and/or direction, either separately or in a combination (i.e. stepping over obstacles, speeding up to make the green light, step up a curb, etc.). The multitude of different experiments to study gait adaptability reinforces the broadness of the term gait adaptation, however, the factor they all have in common is that placement of the foot has to be adapted to fulfil the task.

What all these gait adaptability studies (i.e. tripping, slipping, turning, obstacle avoidance, targeting) have in common is that they research limitations or interruptions of foot placement position, the largest perturbation to recover from (figure 2.1). A 'new' foot placement position has to be decided on and carried out after tripping, slipping, turning, or obstacle avoidance. This new foot placement is guided by internal and environmental limitations. Tripping and slipping conditions require a recovery step that restores balance (Pijnappels, Bobbert, & van Dieen, 2005). Turning requires steps that drive the person in the desired direction while maintaining balance with either widening foot placement or crossing over foot placement that catch the body falling in this new direction (K. L. Hollands et al., 2014). Obstacle avoidance has a risk for both the leading and the trailing limb to trip, therefor an appropriate step has to be made beyond the obstacle to avoid catching the obstacle with the trailing limb (Den Otter et al., 2005). pre of gait adaptability, foot placement is critical. Indeed, proper foot placement is the most effective means of balance control, as foot placement determines the plane of progression the centre of mass without imbalance (MacKinnon & Winter, 1993). Also, motor control of the upper limbs is studied in reaching studies (Day & Brown, 2001; Hammerbeck et al., 2017) and target stepping could be seen as the lower limb equivalent for these reaching studies. Therefore, it makes sense to investigate the lower limbs' primary function, namely targeting safe foot placement.

The base of support defines the area within which the centre of mass can travel and maintain stability. This centre of mass can be vertically projected on the centre of pressure on the ground (Winter, 1995). This centre of pressure is the location of the vertical ground reaction force vector. When standing on one foot this vector is located under that foot, and when standing on two feet it is somewhere between the two. So, it is important to keep this centre of pressure within the base of support to stay stable. However, after foot placement, the centre of pressure can be altered using ankle or hip strategies to keep the centre of pressure within the base of support. With these ankle and hip strategies, only small changes in the position of the centre of pressure over the foot can be made by repositioning the weight of the body (MacKinnon & Winter, 1993). Because these changes can only be small and require more force than initial foot placement (Townsend, 1985), control over where the foot lands is the most effective way to maintain an appropriate size and shape of the base of support and therefore balance. Given the importance of foot placement in maintaining balance, measuring the ability to adapt foot placement may help identify the risk factors for increased falls risk in stroke survivors.

2.4 How is foot placement assessed?

Because foot placement is critical to adjust your path, to avoid an obstacle, etc., and in the meantime, maintain balanced during walking, understanding, through measurement, how foot placement is controlled can provide insight into the cause of clinical problems. Currents tests mainly asses time to perform or success/failure of a particular gait adaptation, which lacks indication of the cause the inability to adapt foot placement. Individuals may appear to be successful in placing their foot in challenging circumstance i.e. in sufficient time, or hitting a target, or clearing an obstacle; however, these measures might not be sensitive enough to measure impairments in how steps adjustments are made. From obstacle avoidance studies, it is known stroke survivors and older people prefer a lengthening strategy (91.4% in stroke and 74.8% in healthy over all steps (Den Otter et al., 2005), older females 62% when 10%-20% of control step length Weerdesteyn, Nienhuis, Mulder, and Duysens (2005)) when there is sufficient time to adapt foot placement; this lengthening strategy also showed to be a more successful avoidance strategy in healthy older woman, they failed 10% of the obstacles using a lengthening strategy and 87% using a shortening strategy (Weerdesteyn, Nienhuis, Mulder, et al., 2005). Avoidance of obstacles allows for multiple foot placement options, so limiting individuals to only one foot placement during walking will allow for more specific analysis. However, the limitation of one specific foot placement might change the strategy. A more recent paper by Hoogkamer, Potocanac, and Duysens (2015) shows that, similarly to obstacle avoidance, participants are more successful when targets are placed to elicit lengthening (20%-80%) rather than shortening (0%-50%) steps for the available response distances of 0.5-0.7m. This preference and increased ability to lengthen rather than shorten steps suggests there is a direction-dependent difference in the control of foot placement alteration. Currently the only biomechanical explanation specifically for foot placement control is the throw-and catch model (Bancroft & Day, 2016) which states that a specific direction and momentum of the body is determined before foot-off to reach a target. Bancroft and Day (2016) showed the pre-step postural activity (body kinematics and kinetics) was significantly different for the different step directions, and when the target position changed pre-step activity was unchanged while foot positioning changes allowing flexibility in the model. This throw and catch model specifically for foot placement is in line with the uncontrolled manifold hypothesis; which explains control of movement towards an endpoint in terms of performance variables (joint angles, moments etc.) which are allowed to vary (uncontrolled manifold) while still reaching the desired endpoint and those variables which must be tightly controlled to achieve the task(Latash & Anson, 2006; Scholz & Schoner, 1999). The UCM hypothesis is a general motor control model explaining all movement whereas the throw and catch model could be argued to be a specific example of a UCM which describes foot placement control.

Therefore, the variables that play a role in successful foot placement, such as endpoint (foot) trajectory, acceleration, force to maintain single leg stance, and sufficient push off are determined before a step is made. All these variables together create multiple degrees of freedom, so there is an abundance of ways to achieve a successful foot placement. One way to measure control/performance in foot placement is to measure the error of foot placement in relation to a target (visual or auditory). Target stepping can give a measure how a specific foot placement is achieved in time and/or space. Both auditory and visual cueing/targeting can be used to identify impairments and train the gait in clinic (Bank, Roerdink, & Peper, 2011; Heeren et al., 2013; Roerdink, Bank, Peper, & Beek, 2011; Roerdink, Lamoth, Kwakkel, van Wieringen, & Beek, 2007).

Auditory cueing (synchronising steps to a beat) has shown to be effective in changing gait parameters such as walking speed, cadence, and swing time symmetry during walking (Ford, Malone, Nyikos, Yelisetty, & Bickel, 2010; K. L. Hollands et al., 2012; Hurt, Rice, McIntosh, & Thaut, 1998; Langhorne, Coupar, & Pollock, 2009; McIntosh, Brown, Rice, & Thaut, 1997; Nascimento, de Oliveira, Ada, Michaelsen, & Teixeira-Salmela, 2015; Nieuwboer et al., 2007; Roerdink et al., 2007; Suteerawattananon, Morris, Etnyre, Jankovic, & Protas, 2004; Thaut et al., 2007; Thaut, McIntosh, & Rice, 1997) or stepping in place (R. L. Wright, Brownless, Pratt, Sackley, & Wing, 2017). This demonstrates that temporal control of gait can be adjusted. As audio cueing is known to bring temporal (R. L. Wright, Bevins, Pratt, Sackley, & Wing, 2016; Rachel L. Wright et al., 2013) and spatial (R. L. Wright et al., 2016; Rachel L. Wright et al., 2013) gait variability down shown in a decline in the coefficient of variation of step length, step and stance time (R. L. Wright et al., 2016), audio cues are likely to perturb (changes as phase delay and enhance) or substitute (when continuous cueing) the basic reciprocal rhythm needed for stable gait (as seen in figure 2.1). Using auditory cues has shown to affect both temporal and spatial gait variability, while step length has shown to be adjusted to acoustic pacing (Roerdink et al., 2007) as well as temporal gait parameters. Audio cues have shown to be beneficial in affecting gait parameters, and when comparing audio cues to visuals cues, as both have been used to synchronise movements, inconsistent results are found. R. L. Wright and Elliott (2014) showed synchronising to audio cues in response to a perturbation was faster than the response on the visual metronome (flashing light), but Bank et al. (2011) showed participants responded faster to visual cues projected on a treadmill than audio cues. The point can be made a visual metronome is less intuitive to synchronise to than visual cues which specify where we are supposed to place out feet in. However, audio cueing has shown to be successful in the regulation of temporal gait rhythm, and with that decrease variability of gait parameters, rhythm is the predominant target and the hypothesized mechanism of the effect of auditory cueing. Because only an audio cue is given, only the temporal error to that cue could be calculated.

In daily life, gait adaptations are generally visually guided. Walking people spend the majority of the time looking at their goal (M. A. Hollands, Patla, & Vickers, 2002) or an obstacle ahead (Grasso, Prevost, Ivanenko, & Berthoz, 1998; Reed-Jones, Hollands, Reed-Jones, & Vallis, 2009). Generally, foot placements are planned about two steps ahead for steady state walking, and closer for more cluttered terrains where foot placement adaptations are required, as M. A. Hollands and Marple-Horvat (2001) showed that when walking to continuous targets people fixate on the next target of footfall just before they lift their foot to be repositioned and walking movements are synchronized with eye movements. The position of foot placement therefore, is likely to be based on sight rather than hearing, which might explain why synchronization responses are faster to spatial and temporal visual cues (in two steps) than to auditory cues (taking about 5 steps) (Bank et al., 2011). So, visually guided cues are likely to be more reflective of adaptations made in daily life and provide more detailed information about both temporal and spatial control than auditory guided stepping (Bank et al., 2011). Therefore, to comprehensively test control of foot placement in both temporal and spatial domains, a visual paradigm is likely to be more effective than an auditory paradigm.

Visual target stepping paradigms can allow assessment of foot placement control under different conditions. For example, medial and lateral stepping from standing in a balance supported and unsupported condition (Nonnekes et al., 2010), step lengthening, shortening, and widening during walking on a treadmill with a declining response time (Hoogkamer et al., 2015), and adaptability training either over ground or on the treadmill (K. L. Hollands et al., 2015). Target stepping is a frequently used tool to assess control of foot placement and gait adaptability in research (Bank et al., 2011; K. L. Hollands et al., 2015; Hoogkamer et al., 2015; Lindemann, Klenk, Becker, & Moe-Nilssen, 2013; Mazaheri et al., 2014; Nonnekes et al., 2010; Peper, Oorthuizen, & Roerdink, 2012; Reynolds & Day, 2005b; van Swigchem et al., 2013; Yamada et al., 2011; Young, Wing, & Hollands, 2012). This allows performance measurement during target stepping by establishing the number of missed targets (Hoogkamer et al., 2015; Yamada et al., 2011; Young et al., 2012), the magnitude of error from the middle of the target (Hoogkamer et al., 2015; Lindemann et al., 2013), and the variability of the foot placement (Mazaheri et al., 2014). Target stepping allows exploration of foot placement control and allows this to happen while walking (maintaining forward progression) either over ground or on a treadmill. Foot placement error is related to stability (because balance is represented in foot placement) and can be done clinically (hits/misses/time) and kinematically (identify cause of impairment) under different conditions (limiting response time, selecting directions to adapt in etc.). This again allows identification of causes of impairment to establish the treatment target. Using these measures of target stepping performance, healthy young and older adults have shown differences in the ability to adapt foot placement, which is associated with risk of falls and declining cognitive function (Lindemann et al., 2013; Mazaheri et al., 2014; Peper et al., 2012; Yamada et al., 2011; Young et al., 2012).

Target stepping has been shown to be feasible over ground and on the treadmill (K. L. Hollands et al., 2015) and measuring and evaluating target stepping recently became readily available with the development of devices like the C-Mill. Treadmills are known to affect walking through slower self-selected walking speed, shorter step length, higher step frequency, shorter swing phase and longer double support phase (Alton, Baldey, Caplan, & Morrissey, 1998; Murray, Spurr, Sepic, Gardner, & Mollinger, 1985), and may enforce consistency (Dingwell & Cusumano, 2015). This consistent pacing offers scientific benefit in terms of controlling the potential confound of speed-accuracy trade off. Over-ground participants may slow down to negotiate targets, and in fact the speed at which they do so relates to balance problems (K. L. Hollands, Pelton, van der Veen, Alharbi, & Hollands, 2016). However, treadmills, when holding speed constant, may offer the chance to elucidate impairments in accuracy and control of foot placement. Also, new, larger (wider and longer) devices designed to train and assess gait adaptability (like C-Mill) afford the opportunity to allow more "natural" gait or at least for gait to vary more than on other treadmills.

The control of movement in general, and specifically foot placement, can be described in how well a target is reached. The factors representing the control of foot placement are bias (mean or constant error), magnitude of error (mean absolute distance from the target), and consistency (variability between attempts to hit the target) errors (R. A. Schmidt & Lee, 1999). The constant error represents the average magnitude and direction of movement error, while positive and negative values might even each other out. However, a global overview of foot placement location in respect to the target is given. Absolute error represents the average magnitude of the movement error, so, the magnitude of the movement error is represented. Lastly variable error reflects the variability/consistency of the movement error, which would be represented in a wide spread of foot placement positions (figure 2.2).

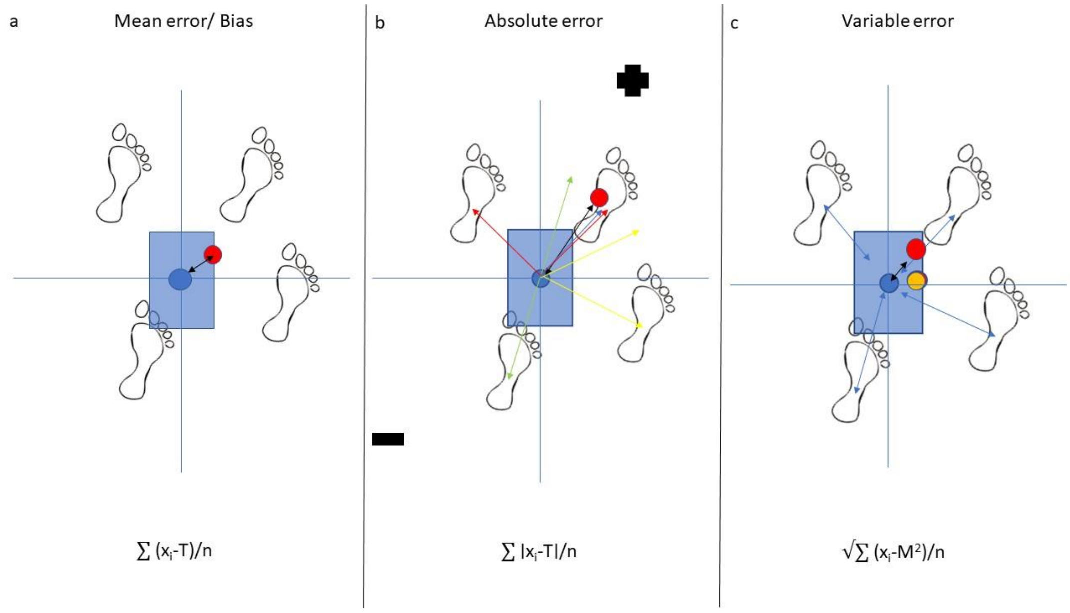

Figure.2.2 *Schematic representation of* the three measures of foot placement error. The blue circle shows the centre of target (T), the feet represent example endpoints of foot placement indices(xi), the red circle represents the mean endpoint position (M) in either x or y direction. Figure inspired by Reynolds and Day (2005b). In figure a) the mean error or the bias is represented by taking the sum of the mean foot placement errors (xi) and divide them by the number of foot placements (n) resulting in the average deviation from the target (T). Figure b) represents the mean absolute error of foot placements (xi), where negative values are transformed into positive values to make the measure absolute (as represented in the colored lined representing the foot placement error being flipped positively), to the target (T) divided by the number (n) representing the average distance the foot is placed from the target. Figure c) represents the variation of foot placement is made around the mean deviation from the error.

2.5 What do we know about foot placement control?

Multiple factors have been shown to have a detrimental effect on the ability to successfully step to targets, such as: executive function, visual spatial attention, available response time, and motor control (direction of adaptation). Different forms of target stepping paradigms have been used to address these factors of gait adaptation. Simple, more complex, double-tasks, or probe response time tasks have been used to examine executive function and attention (Mazaheri et al., 2015; Mazaheri et al., 2014; Peper et al., 2012). Visual spatial attention has been tested by occluding visibility of the targets at certain times during targeting (Rietdyk & Drifmeyer, 2010) and the time or distance available to react to a target (Den Otter et al., 2005; Hoogkamer et al., 2015; van Swigchem et al., 2013) have been used to test how well we react to sudden foot placement adaptations. The control of adaptation in different directions has been tested by positioning the targets at specific locations (Hoogkamer et al., 2015; Nonnekes et al., 2010). The plethora of manipulations show that target stepping can be a very powerful tool in understanding how foot placement is controlled and also highlights that multiple factors are interlinked in the successful control of foot placement.

2.5.1 How does the direction of adaptation affect foot placement?

Considering that in older adults the variability of gait parameters has been shown to increase (Brach et al., 2010; Hausdorff, Rios, & Edelberg, 2001; Verghese, Holtzer, Lipton, & Wang, 2009), young healthy adults have more stepping error lengthening than shortening steps (Hoogkamer et al., 2015) and more stepping error narrowing steps than widening (Nonnekes et al., 2010). The control of a movement is captured well in the error measures proposed above (mean, absolute and variable error). The theory of the throw-and-catch model suggests the endpoint of the foot is directed with a pre-step activation, then the body is 'thrown' in the direction of the desired foot placement where it is 'caught' (Bancroft & Day, 2016; Lyon & Day, 1997). This would mean that the take-off would be specific to the target location, and only small adjustments to the endpoint of the foot can me made during swing, as confirmed by Bancroft and Day (2016) meaning that people carefully plan their foot placement. When something changes in this ability to regulate foot placement, as shown in aging and stroke survivors, one of the factors in control is likely to be affected. Therefore, investigating how people control their foot placement, and how this changes in ageing or due to a pathology may provide insights for treatment and training.

2.5.1.1 Anterior-Posterior directions of adaptation

Lengthening and shortening a step is necessary in daily life, for example to avoid a puddle or reach a curb to safe position the foot closer or further than the natural stride length. A study by Hoogkamer et al. (2015) compared healthy young adults' ability to lengthen or shorten their steps while walking on a treadmill. Participants were more accurate at step lengthening (20%-80%) than shortening (0%-50%) when available response distance was between 0.5-0.7m (Hoogkamer et al., 2015).

Similar outcomes are found in a study by Bank et al. (2011), where participants walked synchronizing steps with either a metronome or visual cues. Timing of metronome beats and location/time of stepping-stones were occasionally delayed or advanced to either elicit a step lengthening or shortening, respectively. Healthy older adults were able to adapt their foot placement more rapidly (within 5 steps) to a delay applied at mid-swing (i.e. longer time to the next beep of distance to the next target), than stepping to an advance (about 7 steps) (shorter time or distance to the next cue) received from either auditory or visual cues (Bank et al., 2011). The fact that a phase advance (which equates to a fast cue to shorten a step) is more difficult is in line with obstacle avoidance studies in which participants increasingly favour lengthening over shortening their steps with progressing age (Weerdesteyn, Nienhuis, & Duysens, 2005; Weerdesteyn, Nienhuis, Mulder, et al., 2005).

Different theories could explain the potential benefits of lengthening as opposed to shortening a step. Firstly, lengthening a step increases the available response time and provides more time to adjust the trajectory of the foot up until foot placement (Patla, Adkin, & Ballard, 1999). Secondly, biomechanically, a lengthening step is more similar to ongoing gait than a shortened step. Although lengthening a step prolongs the single support phase and could therefore be argued to compromise balance, the centre of mass is allowed to continue forward progression, and the base of support will become larger after foot placement to compensate for the extra forward velocity. In contrast, when shortening a step, the foot and therefore centre of pressure, is placed closer to the body than it otherwise would have been while the centre of mass is still moving forward. This creates a greater separation between the centre of mass and centre of pressure, which requires a decrease of forward momentum to keep balanced. If the definition of adaptable gait (proposed above) is the ability to maintain forward progression and balance while accommodating the change required by the environment, then step shortening may limit the maintenance of forward progression (Hof, Gazendam, & Sinke, 2005).

2.5.1.2 Medial-Lateral directions of adaptation

There is some evidence that medial target stepping when no support for balance (i.e. crutches) were provided induces greater errors than lateral target stepping in young healthy adults (Reynolds & Day, 2005a) and older healthy adults age-matched with stroke survivors (Nonnekes et al., 2010). However, when participants were stabilized (i.e. holding on to crutches) the difference between step narrowing (medial) and widening (lateral) became negligible. These narrowing and widening target steps were executed from standing and the fact that stepping errors were reduced with support of crutches implied that balance is important when aiming for targets, even from a standing position. However, these observations could not be extrapolated into how step widening and narrowing would affect walking. To the knowledge of the author, only one study has investigated medio-lateral adaptations during walking; a recent study by Hoogkamer et al. (2015) examined lateral step adjustments (+20% of step length in a lateral direction) during walking on a treadmill in healthy adults and found these were more challenging (with greater error of foot placement) than step lengthening adjustments (+40% of step length in anterior direction), but less challenging than step shortening adjustments (-40% of step length in posterior direction). However, it may not be fair to compare lateral adjustments to adaptations in anterior-posterior direction, based on proportions of step length, and no studies have yet investigated medial as well as lateral gait adaptations during walking. The preference for step widening (Nonnekes et al., 2010) over narrowing likely reflects an increased base of support with the wider step, which makes it easier to keep the centre of mass within the margins of stability.

Because studies in humans are limited, theoretical frameworks have been used to generate evidence, where passive bi-pendulum walkers were introduced to medio-lateral tilting (Kuo, 1999). Passive bi-pendulum walkers are two-legged system that can walk down an incline without any control or actuation. This study showed that tilting movements from side to side bring passive walking closer to that observed in real life; however, the investigators found that the walkers became more instable with the sideways tilting movements. In addition, a study by Rankin et al.(2014) proposed that healthy people have to actively stabilize lateral placement of the foot by controlling the medial-lateral trajectory of the swinging leg with the hip muscles. This suggests that small medial-lateral adjustments may require more active control than anterior-posterior adjustments, that could be achieved passively (or without additional muscular activation). Therefore, the assumption is made that medio-lateral adjustments cost more energy than anterio-posterior adaptations and may be more challenging to make. Besides medio-lateral adaptations need more muscle activation, the base of support is affected as well. When narrowing steps the base of support will be reduced, which challenges balance, where widening the base of support will be increased. In conclusion, narrowing steps are thought to be more challenging than widening steps, because limiting the base of support challenges balance.

2.5.2 When do we need to see the target to respond accurately?

We know young healthy people can alter foot placement with very short notice. Healthy young adults were able to recover within a single step from trips in which they had to avoid a projection on to their preferred landing spot at the time of the trip (Potocanac, de Bruin, et al., 2014). During walking foot placement adjustments could be made up until contralateral late stance (in accordance with the swing phase of the targeting foot) when slowing down (M. A. Hollands & Marple-Horvat, 2001; Matthis, Barton, & Fajen, 2015; Reynolds & Day, 2005b).

However, the moment information is gained about the need to adapt gait, and the time allowed to adjust to this information have shown to affect the success of the adaptation.

Normally foot placement is planned about two steps ahead for steady state walking, and closer for more cluttered terrains where ongoing foot placement adaptations are required as shown in continuous target stepping (M. A. Hollands & Marple-Horvat, 2001). However, it has been shown that visuomotor control changes with age. Older adults look sooner towards a target and maintain gaze at a target for longer than young adults (Chapman & Hollands, 2007; Lindemann et al., 2013; Yamada et al., 2011). If there is a second obstacle ahead, participants with high risk of falls (berg balance scale 45<) would look away from the initial target early, which correlated with the amount of stepping error (Chapman & Hollands, 2006a, 2007). This shows that the way vision is used to scan the environment and plan our steps directly affects how successful the actual foot placement will be. Falls could be related to either looking at the wrong moment or a not processing the visual information into a motor plan. So, where and when we look at a target is related to the success of target stepping and fall risking older adults.

In addition to looking at the target until foot placement is achieved, the time available (and therefore distance) to alter foot placement is known to affect the success of obstacle avoidance and target stepping (Hoogkamer et al., 2015). This implies that, when walking adaptions have to be made rapidly and suddenly, people become less successful and have a higher fall risk than when more time is available. Hoogkamer et al. (2015) showed a decline in the success of on-going target stepping while walking with a declining available response distance. The available distances were set at 0.7-0.4m; as gait speed was set to 1m/s, the distance available corresponded with available response time. Success in the longest (700ms or 0.7m) available response distance/time was greater than 50%, and declined to less than 20% for the shortest available response distance (400ms or 0.4m). Very rapid foot placement adjustments can be made, even when balance has to be recovered after a trip; however, during ongoing target stepping, success declines with the distance/time available to respond. Therefore, when we look at something, and how long we get to respond, has seems to affect the accuracy of foot placement.

2.5.3 The role of executive function in target stepping

The model explaining control of walking by Grillner and Wallen (1985) was based on the idea that the first two components of walking (stepping and equilibrium) can be done subcortically, whereas the third component of walking (adapting gait) must be controlled cortically, as it involves behavioral task goals and environmental demands. This is also shown in animal studies, where rhythmic walking movement can be evoked in spinal and decerebrate preparations without involvement of the cortex, but when gait has to be adapted the cortex takes control (Drew, Prentice, & Schepens, 2004). In human walking, we know that stepping to visual targets is an attention-demanding task for healthy young adults (Mazaheri et al., 2015; Mazaheri et al., 2014; Peper et al., 2012). Even when targets coincide with natural foot placement, young healthy adults reduce their walking speed (Peper, de Dreu, & Roerdink, 2015) and increase their reaction time when performing dual tasks (Mazaheri et al., 2014). This is surprising, given that if participants had continued to walk normally their feet would have landed in the target locations. Therefore, the observation that participants slow down to step to targets, and double tasks reaction times increase, even when targets coincide with their usual foot placement, may indicate that longer time is needed to process visual information of foot placement in relation to the target, in order to monitor success (Peper et al., 2012). Planning and monitoring foot placement against the external demands of a target requires both visuo-motor control and attention.

2.6 What do we know about foot placement control after stroke?

Adaptation of gait is important in daily life, stepping up a curb, avoiding a puddle, or maneuvering trough crowded streets is something we do on a daily basis. Stroke survivors have a high falls incidence (Hyndman et al., 2002; Jorgensen et al., 2002; Lamb et al., 2003; Smith et al., 2006; Yates et al., 2002), which indicates treatments and falls prevention may be effective in reducing falls. Current treatments seem to be effective in increasing gait speeds (Dickstein, 2008), however quality and/or robustness of gait, allowing people to be safe in ADL, is not really aimed on, or assessed. The need to gain a better understanding of how to provide effective interventions to improve gait adaptability is shown in the number of recent studies assessing the feasibility of target stepping to asses and train gait adaptability (Heeren et al., 2013; K. L. Hollands et al., 2016; K. L. Hollands et al., 2015; Timmermans et al., 2016; van Ooijen et al., 2015; van Ooijen et al., 2013).

Gait adaptability has shown to be feasible for testing and training gait (Heeren et al., 2013; K. L. Hollands et al., 2016; K. L. Hollands et al., 2015; Timmermans et al., 2016; van Ooijen et al., 2015; van Ooijen et al., 2013) however, the knowledge of the factors that reduce the ability to adapt gait in stroke survivors are limited. Two features of target stepping performance in stroke survivors have been shown to be related with clinical measures of functional recovery after stroke. Firstly, the number of targets missed by the paretic limb is associated with the Fugl-Meyer score (which indicates motor recovery); secondly, speed of target stepping can be predicted using the Berg balance scale, (a measure for balance) (K. L. Hollands et al., 2016). Furthermore, stroke survivors have shown to have greater foot placement error when narrowing gait while they have to maintain balance in comparison to when they are stabilized by crutches (Nonnekes et al., 2010). Target stepping therefore could be indicative of how impaired balance and motor recovery would affect gait and be a valuable measure to assess safe gait in stroke survivors.

The factors that are likely to affect foot placement control in healthy young and older adults are likely to deteriorate more in stroke survivors. The direction of adaptation is expected to be affected as stroke survivors prefer lengthening over shortening when avoiding an obstacle (Den Otter et al., 2005), and are less accurate stepping medially than laterally (Nonnekes et al., 2010). The fact that medial stepping is more challenging than lateral, and this difference is reduced when stroke survivors are stabilized with crutches, indicates balance affects foot placement accuracy as well (Nonnekes et al., 2010). Also, the time stroke survivors got to avoid an obstacle showed to affect how successful stroke survivors were at obstacle avoidance (van Swigchem et al., 2013). And lastly, stroke survivors are known to have executive function deficits (Ballard et al., 2003; Zinn, Bosworth, Hoenig, & Swartzwelder, 2007). Therefore, investigating how stroke survivors are affected in their foot placement control may provide insights for treatment and training.

2.6.1 How does the direction of adaptation affect foot placement in stroke survivors?

Stroke survivors have difficulty adjusting foot placement, part of this difficulty could lie in the motor control of the limb. Two factors due to stroke affect the motor control directly. Firstly, the hemiparesis affects the descending activation from the motor cortex to the spinal tracts, resulting in the inability to voluntarily contract or relax muscles (Arene & Hidler, 2009). Secondly, tone, which is defined as the resistance against passive movement, which is often negligible, or totally absent, during the acute phase after stroke. In the chronic phase it either stays reduced or tone can increase. Both situations severely affect the coordination of a movement, both reduced or no tone and increased tone will limit the effectiveness of the movement, if movement is even possible. Lastly, spasticity, where tone is a constant resistance against passive movement in a hemiparesis, spasticity appears in stretch reflexes; the resistance is dependent on the stretch speed (Arene & Hidler, 2009). If and how spasticity affects gait is still unknown, as multiple studies have shown contradicting results, either saying spasticity is affecting (McLellan, 1977; Sahrmann & Norton, 1977) or not affecting (Ada, Vattanasilp, O'Dwyer, & Crosbie, 1998; Yelnick, I, & I, 1999) gait. Many factors may affect the motor control of the foot placement. All of these factors could singularly or in combination affect, by degrees of severity, how well the planned endpoint of the foot can be reached, which could not only considerably influence how safely the current step is made, but also impact on the base of support and balance for the upcoming steps. Therefore, it is important to study the effect of stroke on foot placement accuracy in as well the paretic and non-paretic limb, as both limbs might be affected by different factors, which might induce different limitations.

2.6.1.1 Anterior-posterior direction of adaptation in stroke survivors

From studies in healthy young and older adults we know that lengthening steps can be achieved with more accuracy than shortening steps (Hoogkamer et al., 2015), which implies shortening is harder either due to the forward momentum during walking, a shorter time to react, or the smaller base of support. In stroke survivors, no studies have investigated anterio-posterior stepping adjustments to targets; from obstacle avoidance studies it is known however that stroke survivors are less successful at avoiding an obstacle during treadmill walking than their healthy counterparts (van Swigchem et al., 2013), and that they are more successful at using a lengthening strategy, which they use more often and with longer time to adapt, than their healthy counterparts (Den Otter et al., 2005; van Swigchem et al., 2013). This increased success and preference for the lengthening strategy in obstacle avoidance suggests that stroke survivors may be more successful in lengthening steps than shortening steps, similar to young and older adults. In addition, it might even be that the control to shorten a step is more limited in stroke survivors, slowing down the forward momentum in single stance requires foot-ankle strategies that require high forces (MacKinnon & Winter, 1993), which only leaves them with the option to lengthen when avoiding an obstacle.

2.6.1.2 Medial-lateral adaptation

As poor balance has shown to be a limiting factor in target stepping among stroke survivors (Nonnekes et al., 2010), it is likely that narrowing gait, which reduces the base of support, will affect gait. However, no studies have investigated step narrowing and widening during walking in stroke survivors. Nonnekes et al. (2010) showed that step narrowing from standing makes stroke survivors' foot placement less accurate than when widening. When support for balance (i.e. crutches) was allowed, the narrowing steps would be as accurate as the widening steps (Nonnekes et al., 2010). Stepping accuracy can be affected by a paretic leg in both the stance and step phase. During stance phase on the paretic leg weakness limits balance and drive in the targeting direction, affecting foot placement of the non-paretic limb. During Swing phase motor control affects the aim of the paretic leg. While no differences in error in foot placement or success have been found between paretic and non-paretic legs (Den Otter et al., 2005; Nonnekes et al., 2010; van Swigchem et al., 2013), Said et al. (2008), investigated balance during obstacle avoidances and did find a difference between paretic and non-paretic obstacle negotiation. A greater separation between CoP and centre of mass (CoM) during paretic stance compared to non-paretic stance. The separation between centre of pressure and CoM reflects an aspect of balance, as the CoM has to stay within the base of support to maintain stability. However, this balance deficit in stroke survivors does not seem to affect the success of obstacle avoidance and target stepping, it indicates underlying mechanisms for the overall declined success in stroke survivors is different for the paretic than the non-paretic limb. The increase in separation between CoM and centre of pressure during paretic stance and the decrease of stepping error when support for balance is offered supports a theory that weakness in the affected limb causes balance problems.

Besides the deficit of balance in stroke survivors, van Swigchem et al. (2013) proposed that motor control impairments, as reduced and delayed electromyogram responses, may underlie the diminished adaptability during walking. When motor control of the paretic leg affects targeting, a greater foot placement error on the paretic side would be expected. Accordingly, a study investigating over-ground target stepping found a greater time taken to walk over (and hit) stepping stones correlated with poorer balance scores (K. L. Hollands et al., 2016). In turn poor balance scores have been associated with high risk of falling, showing, albeit indirectly, that control of foot placement/adaptability of walking may be related to falls risk. The correlation between the success of stepping to targets on the paretic side and motor function corroborates evidence from previous studies (Den Otter et al., 2005; Nonnekes et al., 2010) which found that impairments in the control of paretic limb foot placement may be a limiting factor in gait adaptations, which will affect adaptations in the anterio-posterior direction as much as in the medio-lateral direction. Therefore, it is understood that balance and motor control affect the medial stepping adjustments, although which of these represents the greater fall risk during walking is yet unknown.

2.6.2 When do stroke survivors need to see the target to respond accurately?

It is known that young healthy adults become less successful in target stepping with a shorter available response distance or time to adjust the foot placement (Hoogkamer et al., 2015). However, in stroke survivors no studies to identify the time required to step to a target have been performed. Obstacle avoidance studies have shown that stroke survivors become less successful in avoiding the obstacle when they have less time to do so (Den Otter et al., 2005; van Swigchem et al., 2013). In tests with a short (150-300ms) available response time, a step-shortening strategy was preferred, but stroke survivors often failed to sufficiently shorten their step, resulting in hitting the obstacle (van Swigchem et al., 2013). One of the factors that could underlie this deficit is delayed and reduced muscle activations resulting in slower limb acceleration compared to healthy older adults (Nonnekes et al., 2010; van Swigchem et al., 2013). Both paretic and non-paretic sides are affected when adjusting foot placement, the cause however it is yet unclear whether the underlying cause is the same. Considering that young healthy adults are less successful in target stepping with a shorter available response distance/time, and stroke survivors hit more obstacles when they have less time to respond, it is likely that stroke survivors will have difficulty with target stepping under time pressure.

2.6.3 The role of the executive function lobe in target stepping in stroke survivors

Impaired executive function is common following stroke; in acute stroke 50% suffers from cognitive impairments, especially in left cortical strokes where declined executive function is found to be present in 60-70%, is present 8-10 days after stroke (G. M. S. Nys et al., 2007; Zinn et al., 2007). These executive dysfunctions have also been found three months after stroke (Vataja et al., 2003). Executive function has been associated with the functional recovery post stroke (Hayes, Donnellan, & Stokes, 2013; Lesniak, Bak, Czepiel, Seniow, & Czlonkowska, 2008; G. M. Nys et al., 2005), Hayes et al. (2013), suggesting that stroke survivors might be more reliant on executive function abilities during less complicated tasks then healthy counter parts, which could affect the available executive function in walking in busy environments or performing double tasks. This difficulty in performing double tasks has been shown in reduced success rates of stepping tasks during obstacle avoidance (van Ooijen et al., 2015), decline in remembering a shopping list while walking (Hyndman, Ashburn, Yardley, & Stack, 2006), and a decline in walking parameters while turning during a cognitive dual-task subsequently subtracting threes from hundred (K. L. Hollands et al., 2014). In addition, stroke survivors with increased functional disability tend to stop walking when talking (Hyndman & Ashburn, 2004). This increased load of the cognitive function in stroke survivors and in other neurological diseases like Parkinson's Disease, multiple sclerosis and Alzheimer's Disease, could be the reason they fall more often (Segev-Jacubovski et al., 2011), and are less able to adjust foot placement.

2.7 Can we train gait adaptability?

If we know what limits gait adaptability and how to establish this, we would expect that we could treat limited adaptability and/or high falls risk. In previous studies, target stepping paradigms have shown to be feasible and potentially successful for training (Heeren et al., 2013; K.L. Hollands et al., 2013; K. L. Hollands et al., 2015) and testing (K. L. Hollands et al., 2016) gait in stroke survivors in clinical settings. Also, two features of target stepping performance have been shown to be related with clinical measures of functional recovery. Firstly, the number of targets missed by the paretic limb is associated with the Fugl-Meyer score (which indicates motor recovery). Secondly, speed of target stepping can be predicted using the Berg Balance Scale, (a measure for balance) (K. L. Hollands et al., 2016). This indicates that good motor function of the paretic limb is needed for target stepping. Adjusting footfall location at higher speeds challenges balance more than at lower speeds, and might be trainable by repetition of the task. Task-specific training including practice of walking adaptability, is one of the most promising interventions (Weerdesteyn et al., 2008). Several studies have shown the benefits of these task specific rehabilitation training among stroke survivors (Stretton, Mudge, Kayes, & McPherson, 2017). In this review by Stretton et al. (2017) show that real world practice is likely to be more effective than physical training alone at improving real world walking after stroke. However, real world training is not always feasible, as location, weather and time do not always allow for functional training, and safe for early or severely impaired patients. The addition of treadmill training could increase intensity (Hornby et al., 2011), which could be made specific with adaptability training which is in preparation for randomised clinical trials (K.L. Hollands et al., 2013; Timmermans et al., 2016). A suggestion can be made that gait adaptability training using treadmills will be successful, based on the facts that it is task-specific training with easy adjustable intensity, besides the implementations.

2.8 Gaps in the literature

Motor impairment, balance, time pressure, attention and executive function are known to play a role in the ability to adapt gait in the healthy young and ageing population. Impairment in any of these factors, due to stroke, may be expected to influence all aspects of gait adaptability (i.e. ability to maintain posture, basic stepping rhythm and largest possible adaptation – figure 2.1). However very little is known about how these factors affect foot placement control and how they affect equilibrium, rhythm and/or limit the largest adaptation possible (figure 2.1). This is an important question because these same factors are very likely to contribute to increased falls risk.

It is likely that foot placement control is a major factor in the increased number of falls among stroke survivors. However, as laid out in the literature review, the control of foot placement is an interlinked ability that involves a number of skills. Understanding why stroke survivors fall more often therefore involves studying how foot placement is achieved, and which skills affect the success of the foot placement the most. Few studies have investigated how stroke survivors are limited in adapting their foot placement, and these studies mostly focus on the adaptability part of the model for stable gait (figure 2.1) by testing the involvement of motor-control, balance, response time, and executive function. We know in general stroke survivors recover more poorly from perturbations during gait than healthy older and younger adults, as shown in the obstacle avoidance studies. Different aspects of adapting gait have been studied among healthy participants, which showed that the direction of adaptation matters in addition to the time available to adapt. However, how these factors affect foot placement control is largely unknown, especially in stroke survivors.

The limited knowledge we have on target stepping accuracy nowadays has been collected with very diverse methods and measures. The error of foot placement has been based on either centre of foot (Nonnekes et al., 2010; Reynolds & Day, 2005a) or centre of pressure (Hoogkamer et al., 2015; Mazaheri et al., 2015; Potocanac, Hoogkamer, et al., 2014). These measures are described as the same in literature, but are they? There is a possibility that these measures do not represent the same control mechanism. Also, the time point these measures are taken are not validated yet, which might affect the reliability of the measure. Where it might be less limiting to take foot placement error in one step from standing paradigms, as in the two studies that used centre of foot as an accuracy measure (Nonnekes et al., 2010; Reynolds & Day, 2005a), the CoP characteristically not only moves during the full gait cycle (Roerdink, Coolen, Clairbois, Lamoth, & Beek, 2008), but also moves under the foot during single support (Nolan, Yarossi, & McLaughlin, 2015; Wong et al., 2004). However centre of pressure gait event detection, which is often used in target stepping paradigms, has been validated for steady state walking in healthy young adults, gait adaptability tasks and hemiparetic gait. These are likely to affect centre of pressure trajectory, and therefore gait event detection. Methodology of how foot placement accuracy is measured therefore lacks ambiguity and needs clarity on what is measured and what those measures represent.

The aims in this thesis will be to investigate the limitations in foot placement adaptations in stroke survivors while focussing on the adaptability part of the model for stable gait (figure 2.1). Participants in this study are community-dwelling stroke survivors known to fall mostly during walking due to trips, slips and misplaced steps, implying that the ability to respond to the environment may be a key factor in falls risk. Further, the ability to alter steps in response to the environment requires good regulation of the relationship between the BoS and CoM (as explained by the catch and throw model) and therefor provides a window into dynamic balance regulation (maintenance of equilibrium Fig 2.1). The factors that will be investigated after methodological preparatory work are 1) the differences in foot placement accuracy between stroke survivors, young and older healthy adults. 2) The effect of motor control deficits, by investigating the differences between different directions of adaptations. 3) The effect of balance on foot placement accuracy, by targeting in a supported and unsupported condition. 4) The effect of limiting available response time on foot placement accuracy, by targeting in a planned and reactive condition. 5) The involvement of the pre-frontal cortex/ executive function in simple and more complicated target stepping tasks. To be substantial in how the above factors affect foot placement accuracy, a chapter validating the measures used to describe foot placement accuracy is included.

3 Validation studies

3.1 Introduction

In older adults and patient groups high rates of falls are reported (Hyndman et al., 2002; Jorgensen et al., 2002; Lamb et al., 2003; Smith et al., 2006; Yates et al., 2002); mostly due to a trip or a slip during walking (W. P. Berg et al., 1997; Blennerhassett et al., 2012; Said et al., 2005; Weerdesteyn et al., 2008). The nature of falls therefore indicates that many may be due to difficulties adapting walking in response to the environment (i.e. gait adaptability). A recent review (Balasubramanian et al., 2014) highlighted the current lack of measurements for gait adaptability and the importance of establishing better measures to identify difficulties and inform appropriate treatments. Target stepping is one method proposed to be able to measure and train gait adaptability, and the use therefore is increasing (Balasubramanian et al., 2014; Bank et al., 2011; K. L. Hollands et al., 2015; Hoogkamer et al., 2015; Lindemann et al., 2013; Mazaheri et al., 2014; Peper et al., 2015; Peper et al., 2012; Reynolds & Day, 2005b; van Swigchem et al., 2013; Yamada et al., 2011; Young & Hollands, 2012). Accuracy of foot placement is potentially a strong indicator of the ability to adapt gait because of strong associations between the ability to control foot placement to targets and clinical measures of balance, lower limb motor control and walking speed (K. L. Hollands et al., 2016).

Instrumented treadmills are useful equipment to study foot placement control, as indicated by increased use (Heeren et al., 2013; K.L. Hollands et al., 2013; K. L. Hollands et al., 2015; Mazaheri et al., 2015; Mazaheri et al., 2014; Timmermans et al., 2016). These devices facilitate a high volume of training and/or data acquisition in a safe (e.g. intensity controlled and safety harnesses available) and efficient way (time, space, and financial). Most research on these treadmills is focussed at training and assessing gait in older adult or patient groups (Bank et al., 2011; Duysens, Potocanac, Hegeman, Verschueren, & McFadyen, 2012; Heeren et al., 2013; K.L. Hollands et al., 2013; K. L. Hollands et al., 2015; Mazaheri et al., 2015; Mazaheri et al., 2014; Peper et al., 2015; van Swigchem et al., 2013; Weerdesteyn et al., 2006). Besides examinations of steady-state gait, they also allow examination of how adjustments of gait are achieved with the use of virtual targets, obstacles, and asymmetric gait using split belts (Duysens et al., 2012; Hoogkamer et al., 2015; Potocanac, Hoogkamer, et al., 2014). In many of these studies centre of pressure (CoP) gait event detection (GED) is used to determine gait phases and analyse gait as a proxy for gold standard kinetics from force plates under individual steps (Ghoussayni, Stevens, Durham, & Ewins, 2004; Hreljac & Marshall, 2000) or for kinematic based GED (Mickelborough, van der Linden, Richards, & Ennos, 2000; Pijnappels, Bobbert, & van Dieen, 2001; Zeni, Richards, & Higginson, 2008) In addition, these systems can be used by clinicians because provided software allows for delivering training and testing paradigm with limited need for set-up, and with an easy and fast way to analyse gait and assessing the ability to adapt gait.

This gait event-detection is based on the measured centre of pressure (CoP) within the C-Mill software. While CoP based gait-event detection has been validated by Roerdink et al. (2008) for steady state walking in healthy young adults it still requires validation in patient groups like stroke survivors, especially during target-stepping. Within the C-Mill (C-mill, CueFors1, Motekforce Link, Culemborg, The Netherlands), the trajectory of the CoP, during steady state gait, is measured by the single uniaxial force plate. This trajectory of the CoP has a characteristic butterfly shape pattern in time, called a cyclogram (Figure 3.1). While, based on the results of Roerdink et al. (2008), CoP GED seems reasonably accurate during steady state walking in healthy adults, previous literature has shown the shape of the cyclogram changes with the severity of a stroke (Wong et al., 2004). Because the CoP based GED relies on the butterfly shape of the cyclogram, the gait events of more affected stroke survivors, might be identified with a lower accuracy, or not identified at all. Four categories of cyclogram changes have been used to describe severity of the stroke: a symmetric butterfly pattern, which occurs in normal healthy gait; an asymmetric butterfly pattern, showing mildly affected gait with higher Brunstrom scores; a rectangular shape, for more severe affected gait; and a triangular shaped cyclogram, for the mostly affected gait with low Brunstrom scores (Wong et al., 2004). Abnormalities in the cyclogam arise because of the differences in how stroke transfer bodyweight from the one foot to the other and in the location of the CoP under the foot during stance phase (Nolan et al., 2015). In healthy walking and on the unaffected side in stroke survivors a heel contact is made and the CoP progresses forwards throughout stance. On the affected limb stroke survivors are much more likely to make a mid-foot or forefoot contact. The CoP is thus more anteriorly located under the foot and does not start to progress further forward until around mid-stance. This could affect GED by less clear direction changes of the CoP in the cyclogram. However, during target stepping, the mechanism of foot contact may change from initial heel contact to mid-foot contact for both healthy people and stroke survivors. Therefore, CoP gait event detection is compared with a kinematic gait event detection method previously used to validate CoP gait event detection in healthy young adults (Roerdink et al., 2008) and a kinematic gait event detection method nominated as the gold-standard in stroke survivors (Zeni et al., 2008). The reason we compare to both of these kinematic detections is to establish if we could reproduce the results of Roerdink et al. (2008) in healthy young adults and, secondly, to compare against the nominated gold-standard to validate CoP gait event detection.

Secondly, the accuracy measures of foot placement during target stepping tasks are important. Two methods used are either the distance of the target to the centre of foot (CoF) (Nonnekes et al., 2010; Reynolds & Day, 2005a) or centre of pressure (CoP) (Hoogkamer et al., 2015; Mazaheri et al., 2015; Potocanac, Hoogkamer, et al., 2014) to the middle of the target. If the instructions for target stepping are to place the CoF in the centre of the target (CoT) then location of CoF is a direct reflection of task instructions. With increasing availability of instrumented treadmills to implement and measure precision stepping paradigms, CoP is increasingly used as a convenient measure of target stepping performance. In healthy walking CoP moves forwards under the foot in a consistent manner and at mid-stance it appears reasonable to assume that the CoP will be close to the CoF (Winter, 1990). However, CoP trajectory under the foot is known to alter after stroke (Wong et al., 2004). One of the aims of this study is thus to test the validity of the assumption that CoP at mid-stance coincides with CoF and can be used to measure foot placement accuracy. To achieve this aim we compare the two measurements of foot placement accuracy in young healthy adults and stroke survivors in different target stepping contexts.

The aim of this chapter is to establish whether the use of the software within C-Mill, CueFors1, produces the right measure of accuracy of target stepping. To answer this aim three studies have been carried out: 1) A validation of the GED, where CoP GED will be compared with two kinematic GED methods, a kinematic algorithms used in a previous study to validate CoP GED in young healthy adults (Roerdink et al., 2008) that has previously being developed by Pijnappels et al. (2001), and a kinematic algorithm suggested as the most appropriate for stroke survivors walking on treadmills (Zeni et al., 2008). 2) A validation of the representation of the target, where the position of the targets in Qualisys environment will be compared with Cue positions registered in the output of CueFors1. 3) Having established in the previous two studies/sections that CoP derived gait events are sufficiently accurate to deliver targets/obstacles according to the gait cycle and that the centre of the target can be determined with similar accuracy in both CMill and Kinematic systems, we will perform an additional study to determine how well foot placement accuracy can be measured by both CoP and CoF (relative to CoT).

3.2 Methods

3.2.1 Participants

Young healthy adults between the age of eighteen and thirty-five were recruited by poster advertisement and email invitations sent to University staff and students. Stroke survivors were recruited from community stroke support and exercise groups in Greater Manchester. Participants were included if they: were able to complete the ten-meter walking test within 30s (to ensure sufficient independent mobility to safely take part in the study) and had no severe visual impairments that would prevent sight of stepping targets. Potentially eligible participants were excluded if their mobility was limited by factors other than their stroke.

Demographic and anthropometric data were taken including: date of birth, date of stroke, side and site of paresis, height, weight, and leg length. The University of Salford, College of Health and Social Care Research Ethics Committee approved the study, and all participants provided written informed consent.

3.1.2 Kinetics

Within the C-Mill, CueFors1 (the software incorporated in the machine), signals from a single large (0.8x3m) uniaxial force plate are passed through an analogue signal conditioner (100Hz low pass filter) before being recorded at 500Hz. The program automatically analyses the vertical forces and generates the CoP cyclogram to detect gait events and generate an output. The main characteristics of the cyclogram are two vertical lines linked by two diagonal lines (Fig. 3.1). The vertical lines represent the foot position during single support. The CoP is under the stance foot which travels backwards on the treadmill belt over the force plate. Single support ends when contact is made with the opposite foot. From that point load is transferred from the trailing limb to the leading limb and the CoP, which represents the average of the CoP under both feet, moves forward and across (the diagonal lines). Foot off (FO) ends double support and the CoP then starts moving vertically down the opposite vertical line. The timing of the minimum of the right-side curve is thus assumed to represent left foot contact (FC) and the maximum of the left side curve to represent right foot off (and vice versa).

For the calculation of CoP error the CoP position is taken at midstance, reported by CueFors1. This midstance is determined as the temporal midpoint between unilateral FC and

FO. The position of the CoP at this time of midstance is used to determine the distance between the centre of the target and the CoP; CoP error.

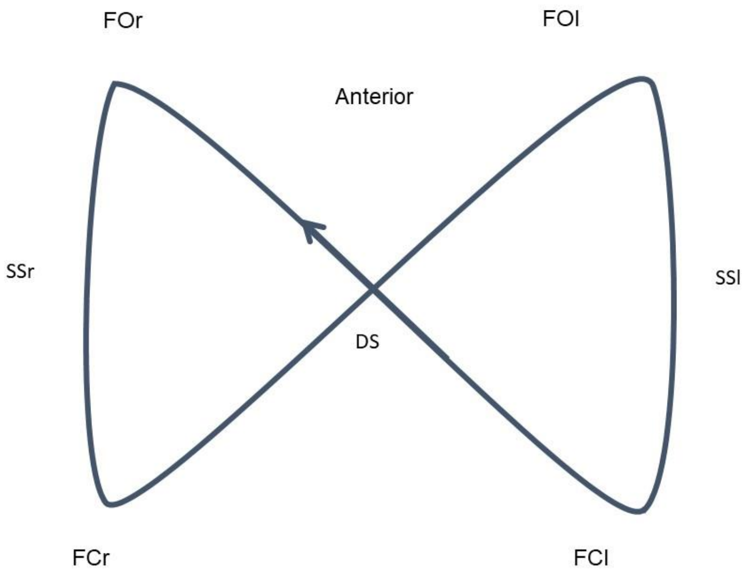

Figure 3.1 Representations of a CoP cyclogram. The blue line represents the optimal CoP trajectory. FC_l and FC_r represent left and right foot contacts, as FO_l and FO_r represent left and right foot off. The FC and FO of one side are connected by the single support phase of each foot (SSl and SSr) and the FO and FC are connected by the weight transition from the one foot to the other in double support (DS).

3.1.3 Kinematics

Kinematic data were collected with a six-camera motion capture system (Qualysis, Sweden) for all young healthy participants at 126Hz and stroke participants at a minimum sampling rate of 31Hz. The variation in sampling frequency is due to limited processing speed of the collection computer when synchronizing motion capture with high speed video collection. However, this difference in capture rate between participants, a capture rate of 31Hz is still effective for walking speeds below 9km/h (Padulo, Chamari, & Ardigo, 2014), to report outcomes similarly for the different capture rates, kinematic data were equalized by reporting outcomes in real time as opposed to number of frames. A heel and toe marker on the 2nd distal phalangeal head and the calcaneus were used for kinematic GED with Qualisys (Inc., Gothenburg, Sweden). Kinematic gait events were identified offline after interpolating (max of 5 frames) and filtering the data (2th order bidirectional 6Hz low pass Butterworth filter). Because filtering could affect local maximum and minima of the data it could affect GED, pilot work for this study found no relevant differences between using these on non-filtered, 20HZ or 6Hz cut off frequency filtered data.

Two GED algorithms where used to determine gait events: the first, vertical displacement (VD) determined foot contact (FC) as the minima of the vertical displacement of the heel marker (VFC), and foot off (FO) on the maxima in vertical velocity of the heel marker (VFO) (Roerdink et al., 2008). The second, anterior displacement (AD) (Zeni et al., 2008), determines FC as the maximum anterior displacement of the heel marker (AFC) and FO as the instant that the anterior velocity of the toe marker is zero (AFO) when it transitions from posterior to anterior velocity.

To calculate CoF error, the CoF location was taken at the instant of treadmill determined mid-stance. The CoF was determined as the middle of markers placed at: 1st and 5th metatarsals, 2nd distal phalange head, and the calcaneus.

$$CoF(i,x:y) = [\text{1st Met}(I,x) - ((\text{1st Met}(1,x) - \text{5th Met}(1,x)) * 0.5), \text{Calcaneus}(I,y) + ((\text{1st Met}(1,y) - \text{Clacaneus}(1,y) * 0.5)]$$

3.1.4 Synchronization

The synchronisation of kinetic and kinematic data in time is done by a continuous pulse at 500Hz in CueFors1 sent via the USB6211 port which is used to start the Qualisys capture. Kinematic gait events are matched within 200ms of the CoP gait events. The 200ms is chosen as a precaution measure to match gait events of the same gait cycle, when gait events are separated more than 200ms gait events from contralateral limbs could be confused and lead to mismatches. When gait events could not be matched they were recorded as a percentage of steps that could not be matched (no-match) (see table 3.2).

The space calibration is done by aligning the two origins of the Qualisys and C-Mill. The origin of the C-Mill force plate is at the left bottom corner of the treadmill, as this is also the origin of the force plate (figure 3.2). For Qualisys an origin was selected where coverage of the kinematic volume was optimal, specifically 0.77, 1.20m according to the C-Mill origin (Figure 3.2). These differences in physical locations of origins between the systems were corrected by transferring the X direction of Qualysis data by -0.77*-1 and Y+1.2. The success of aligning the two origins was determined by visual inspection of data showing the CoP fell in between feet markers.

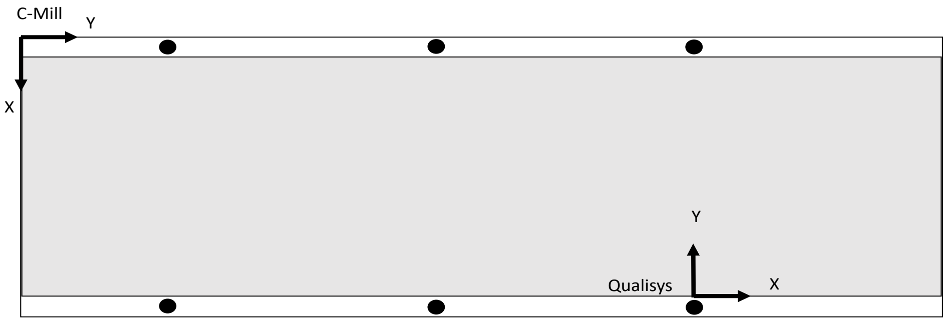

Figure. 3.2 *Representation of the C-Mill treadmill with the force plate origin in the left top and calibrated origin of Qulalisys (in C-Mill coordinates X=0.77m Y= 1.20m).*

3.1.5 Procedures

Clinical assessments were carried out with stroke survivors in order to document recovery and mobility status including: Self-selected walking speed and functional mobility: 10m walking test (Green, Forster, & Young, 2002); Timed Up and Go (Hiengkaew, Jitaree, & Chaiyawat, 2012) and Dynamic Gait Index (Jonsdottir & Cattaneo, 2007).

Participants were familiarized with walking on the treadmill without stepping targets for approximately three minutes. Each participant's (SSWS) was determined by increasing speed from 1km/h until participants felt they were walking faster than preferred, then decreasing the speed to a comfortable pace. Participants then walked to targets located at their usual step lengths and widths (based on walking during previous no target acclimatisation period) for one minute, to become acquainted with target stepping. Step characteristics such as speed, step length and width where recorded during this last minute of target-stepping as a basis for programming the location of targets for the subsequent protocol of personalized target-stepping tasks.

Participants stepped to the targets located according to their personalized protocol projected on the treadmill belt while walking at SSWS (figure 3.3) according to a previously described non-random stepping paradigm (K. L. Hollands et al., 2015), consisting of 60 targets per task in 6 blocks of 10 targets as shown in figure 3.3. 12 targets (8cmx40cm wide) were projected at normal step length and 12 of the same size for both shorter and longer steps (±25% of baseline step length). A further 24 targets of different shape (20x15cm wide) were projected on the midline of the treadmill to elicit more medial foot placements. Targets were delivered in six sets of ten as in figure 3.3. All targets where visible for at least two steps ahead. Participants were not allowed to use the handrail for stability, however stroke survivors wore a harness to prevent falls. There was the opportunity to take a rest in-between every block, six sets of ten steps, resulting in a block of 60 steps.

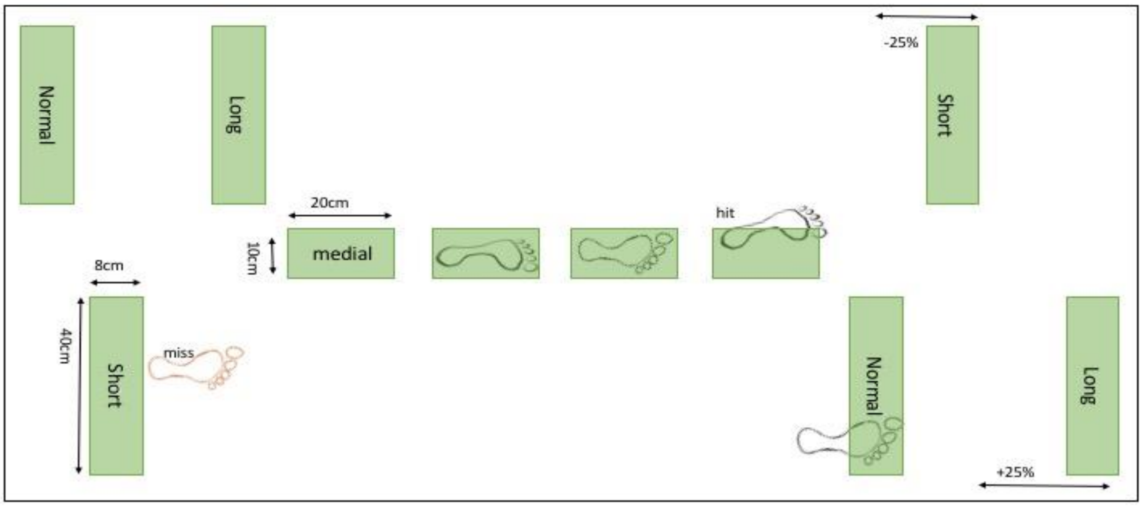

Figure 3.3 Schematic representation of the layout of stepping targets (normal, short, long, and medial).

3.1.6 Target validation

The target positions in the output of CueFors1 are reported alongside the gait events. Because the targets are moving objects on the belt (with self-selected walking speed mean 2.93km/h ± STD 1.20) and the exact time they are of interest is not predictable by CueFors1, the positions of the targets are registered at left mid stance after a full stride has past. To establish the accuracy of the position of the targets in Qualisys environment reflective markers were placed by hand in the right top corner of targets (length 20cm and width 10cm). This procedure was performed at intervals of 0.5km/h speed increases for speeds from 0.5km/h to 5.5km/h. This allowed calculation of the centre of target position in Qualisys space. A minimum of 20 calculated centre of target positions per speed were compared between Qualisys and the centre of target position in the CueForec1. The synchronisation of the environments was checked in a measurement with static markers on the treadmill placed on landmarks (figure 3.2 the 6 black dots representing screws on the treadmill) which overlapped in both C-Mill and Qualisys space. Synchronisation in time has been covered in validation of GED, as gait events matched within 200ms.

3.1.7 Statistical analysis

For experiment one, a comparison is made between CoP gait events and matched (within 200ms, see synchronisation section) kinematic GED algorithms (VD and AD). At least thirty gait events (FC and FO) per participant per foot, consisting of at least ten normal steps (10 steps without targets), for some participants the pre block walking took longer and provided more than ten steps) and sixty target steps (thirty per side) of CoP and kinematic gait events paretic and non-paretic and the left and right side of stroke survivors and healthy young adults were compared using a one-sample (two tailed) t-test against a reference value of 0ms (i.e. no difference between CoP GED and reference comparators) (Roerdink et al., 2008).

For experiment two, the Qualysis and C-Mill centre of target are compared and correlation and best fit linear trend line is calculated with Microsoft Excel.

In experiment 3, foot placement accuracy (CoF and CoP error) was defined as the distance from CoF or CoP to CoT at mid-stance. Mean difference between CoP and CoF error for each step adjustment was compared in a repeated measures ANOVA, with Bonferroni correction for multiple comparisons, individually, for AP and ML directions. Within subject factors were: step type (4) (preferred, shortening, lengthening, and narrowing steps), limb (2) (paretic and non-paretic instroke survivors and left and right in healthy young adults). Between subject factor was group (stroke survivors and young healthy). If CoP and CoF error are comparable then it would be expected that either there would be no significant differences between groups for any stepping condition or that there would be a systematic and constant, significant, offset between the measures in all step conditions and between groups.

3.3 Results

Participant characteristics are detailed in table 3.1.

Table 3.1 *Participant demographics, represented in Mean± SD when not specified differently.*

	Young healthy	Stroke Survivors
Number (Female)	9(5)	13(3)
Age (years)	26.44± 4.22	66.77±8.67
Time since stroke (month)	-	86.54±134.43
Paretic Right	-	5 (23.1%)
SSWS (m/s)	1.11± 0.14	0.46± 0.19
Berg Balance Scale	-	53.31± 5.54
Fugl-Meyer Assessment	-	25.92± 3.90
Dynamic Gait Index	-	17.92± 5.62
10m-walking speed (s)	-	13.13± 4.07
Timed Up and Go (s)	-	14.55± 5.11
Montreal Cognitive Assessment	-	25.08± 4.37
Apples test	-	46.85± 4.52
Falls reported in the last year	-	
No fall		69.2%
1 fall		7.7%
1< fall		23.1%

3.3.1 Gait event detection

No abnormalities in cyclograms which would have prevented CoP GEDs were found on visual inspection of individual participant data (figure 3.4).

3.3.1.1 Foot contact

Detailed timings of gait events are reported in table 3.2. VFC detected FC significantly earlier than CoP in YH ($p<0.001$) but there were no differences between methods in FC detection for SS (on either paretic and non-paretic side). FC via AFC was detected significantly earlier than CoP in healthy participants ($p<0.001$) and in SS on both paretic and non-paretic sides ($p<0.001$ for both).

A significant interaction effect between limb, GED method and group ($F(18) = 4.960$, $p=0.039$) indicates that the difference between COP and AFC GED is smaller on the non-paretic side than the paretic side. Additionally, FC identified in stroke survivors using VFC were matched with CoP detections less often (P 20% and nP 9% was unmatched), than AFC across all participants (YH 3%, SS P 7% and nP 4%).

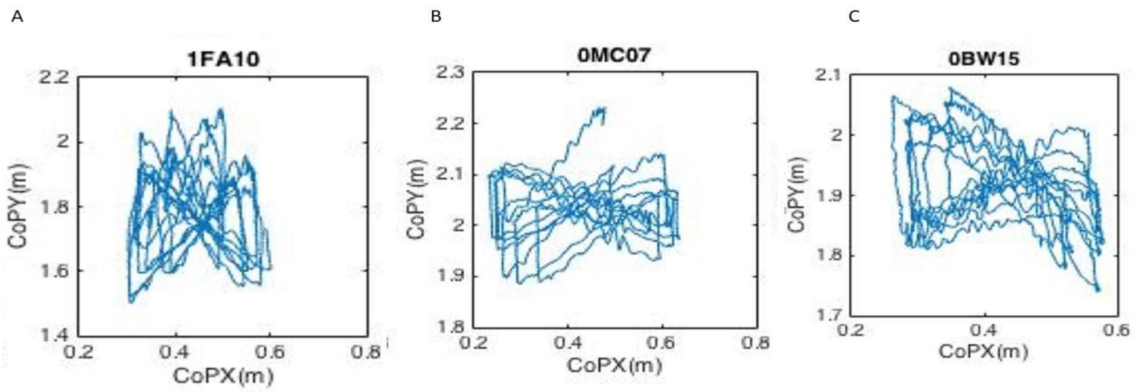

Figure 3.4 *Representations of a CoP cyclogram for A) a representative young healthy adult. B and C) two representative stroke survivors. The two vertical lines linked by two diagonals, represented by the blue line, describe the CoP trajectory in healthy participants. In single limb support, the CoP travels backwards on the treadmill belt over the force plate, creating the vertical lines. At the end of single support, the load transfers from the trailing limb to the leading limb and the CoP moves forward and across (diagonal lines) during double support. At the end of double support, CoP then starts moving vertically down the opposite vertical line. The timing of the lowest point in the curve on the right-side represents left foot contact (FCl) and the highest point of the left side curve to represent right foot off (FOr) (and vice versa).*

3.3.1.2 Foot off

The AFO algorithm worked with similar success in both groups and sides (3% unmatched FO). The VFO was less successful with 7% and 11% unmatched FO in SS and YH subsequently. FO was detected earlier in VFO than CoP in all participants (p<0.001). FO was detected earlier in AFO compared with CoP in YH and in SS for both paretic and non-paretic sides (P<0.001).

A significant interaction effect between limb, GED method and group (F (1,18) =9.173, p=0.007) was found indicating the difference between CoP and AFO GED is significantly larger on the non-paretic than paretic limbs.

3.3.1.3 Step times

Phase durations (e.g. swing, stance and step times) calculated using the time of foot contact and foot off identifications are similar if foot contact and foot off are identified with kinematic algorithms for stroke survivors treadmill walking (AFC, AFO) (Zeni et al., 2008) or CoP. In contrast, temporal gait parameters using VFC and VFO (Roerdink et al., 2008) kinematic criteria yield a significantly shorter stance and longer swing phase (figure 3.5), as a result of slightly later foot contact identification in stroke survivors and earlier foot off identification (see Table 3.2)

Table 3.2 *Difference between kinematic gait event detections relative to CoP detection in ms. Means and SDs and the percentage of matches within 200ms of 38-51 strides per participant are provided for each gait event detection method. A negative sign indicates the kinematic method identified the event before the CoP method. *P<0.05 **P<0.001.*

	AFC			**VFC**			**AFO**			**VFO**		
	mean	IC	Unmatched %	mean	IC	Unmatched %	mean	IC	Unmatched %	mean	IC	Unmatched %
Stroke survivors (N=13, 10 male, 8 left paretic, 67 Mean± 9 SD years, 87±134 months since stroke, SSWS0.47± 0.19, DGI 17.9±5.6, TUG 14.5± 5.1)												
Paretic	-80*	-95 to -64	7	-1	-17 to 15	20	-49**	-59 to -38	3	-92**	-105 to -80	7
Non-paretic	-36*	-48 to -23	4	-5	-17 to 26	9	-69**	-79 to -59	3	-87**	-98 to -76	7
Young Healthy (N=7, 3 male, 27 ± 5 years, SSWS 1.11± 0.15m/s)												
Left	-62**	-83 to -40	3	-29**	-50 to -7	9	-42**	-57 to -28	3	-72**	-63 to -37	11
Right	-63**	-81 to -46	4	-28**	-58 to 1	5	-42**	-56 to -28	3	-74**	-59 to-42	11

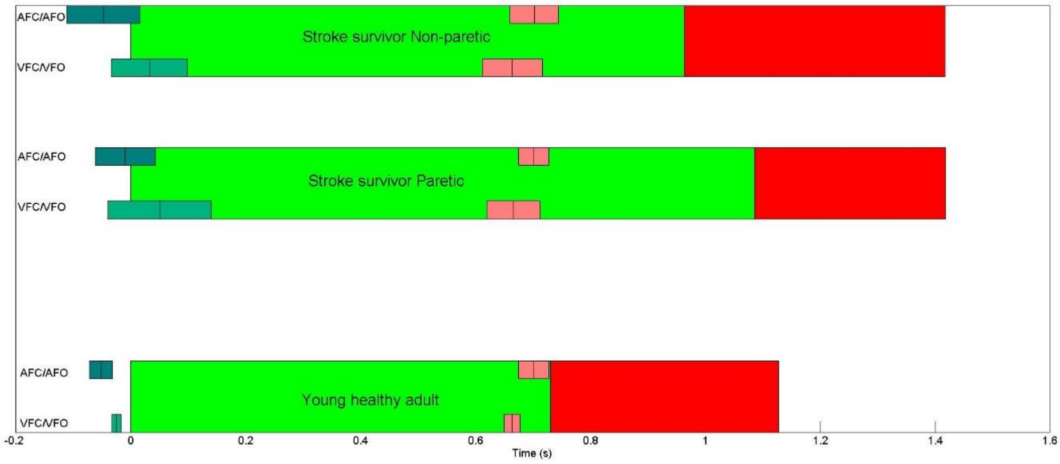

Figure 3.5 *Schematic representation of the stance and swing phases derived from CoP and kinematic gait event detection criteria. Green represents the mean duration(s) of stance phase determined by CoP gait event detection, with mean of matched kinematic foot contact detection in dark green surrounded by ± 1SD bars. Red represents the mean duration(s) of swing phase*

determined by the CoP gait event detection, with mean of matched kinematic foot off detection in orange surrounded by ±1SD bars.

3.3.2 Target validation

We found an offset linear progressing with walking speed between Qualisys and C-Mill target position (See figure 3.6), however, this offset can be successfully (R^2=0.94) corrected by calculating the real position in space (Qualisys position) from the C-Mill position with the following

Equation 3.1: $(treadmill\ speed * -1.33) - 0.39$ *(figure 3.5).*

Where the -0.39cm is the constant offset of the system and -1.33cm is the linear offset adding per km/h speed difference. Overall standard deviations (SD) are low with the method we have used, but with increasing speed the variability increases too probably owing to less accurate placement of markers at higher speeds.

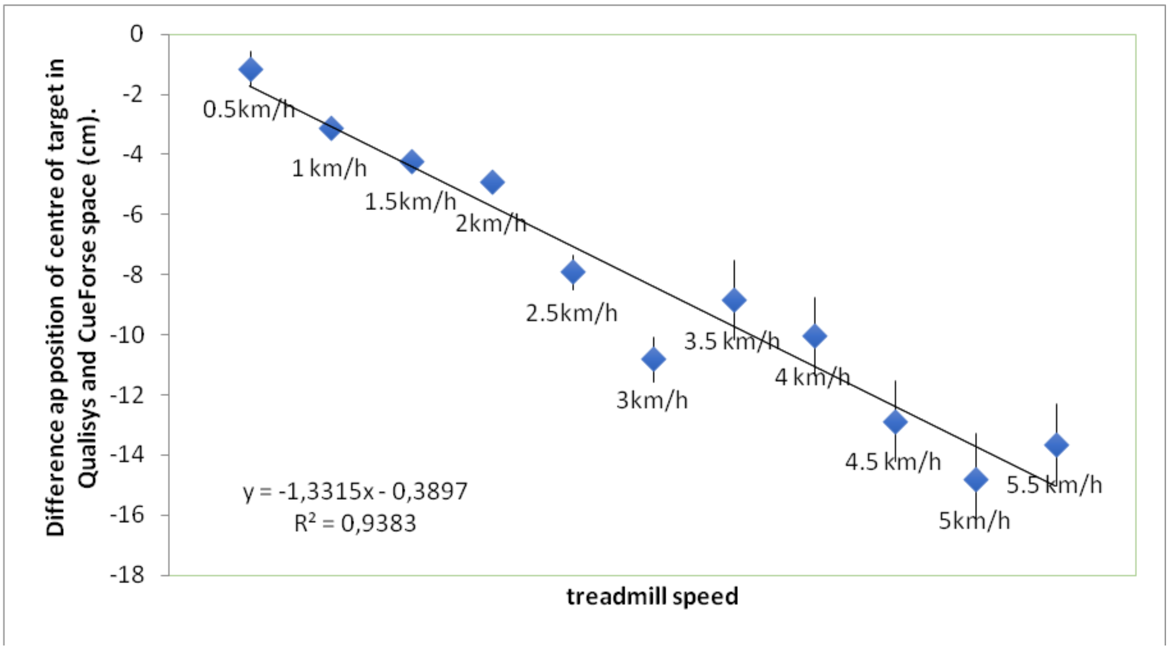

Figure 3.6 *Difference between CueFore1 registered centre of target positions and the Qualisys centre of target at the time of registration in CueFors1 over the range of speeds from 05.5km/h to 5.5km/h. Diamond shaped represent the differences at the different speeds, black line represents the linear relationship. Error bars represent standard deviation.*

3.1.3 Error measures: CoP or CoF error?

3.3.3.1 Anterior posterior CoP positioning

Figure 3.7 shows significant interaction effects between CoP and CoF error measures for particular step types and groups and side. Stroke survivors (-4.1± 0.6cm) have significantly less difference between CoP and CoF error in AP direction (F (1,20)=23.011, p<0.000) in comparison to young healthy (-8.6± 0.7cm). Additionally, for both groups AP difference between CoP and CoF error is greater (p= 0.007) when shortening steps (-6.7± 0.6cm) compared to preferred steps (-5.6± 0.5cm).

3.3.3.2 Medio-lateral CoP positioning

Figure 3.7 shows in both groups, ML CoP error was more medial than CoF error for narrowing (0.6± 0.2cm) steps than lengthening (p=0.021, -0.9± 0.2cm), preferred (p=0.017, -0.6± 0.2cm), and shortening (p= 0.016, -0.3± 0.2cm) steps. Also, both groups have a more lateral position of CoP position on the foot in long steps than in short steps (p=0.009).

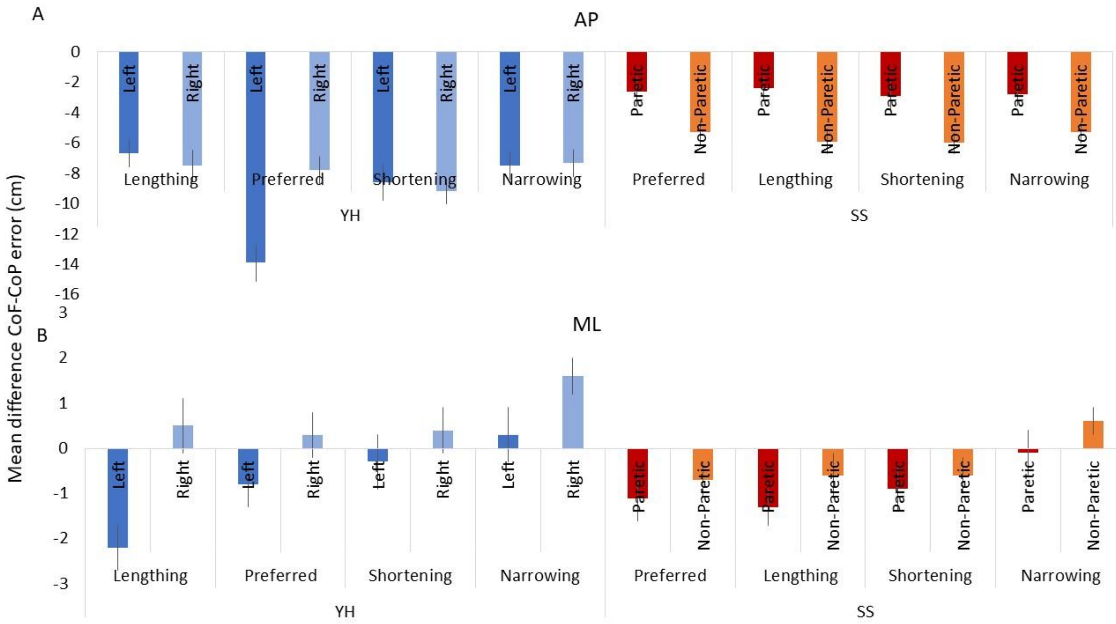

Figure.3.7 *Mean position of CoP on the foot (difference between CoF and CoP) for lengthening, preferred, shortening and narrowing steps in young adults (YH, blue), paretic (SSP, orange), and non-paretic leg (SSnP, grey) of stroke survivors. a) anterio-posterior difference between CoF and CoP error. Negative values reflect CoP located anterior on the foot. b) medio-lateral CoP position on the foot, negative values represent a lateral CoP position on the foot. Statistically significant (p<0.05) differences are denoted by brackets and asterisk, error bars represent standard errors.*

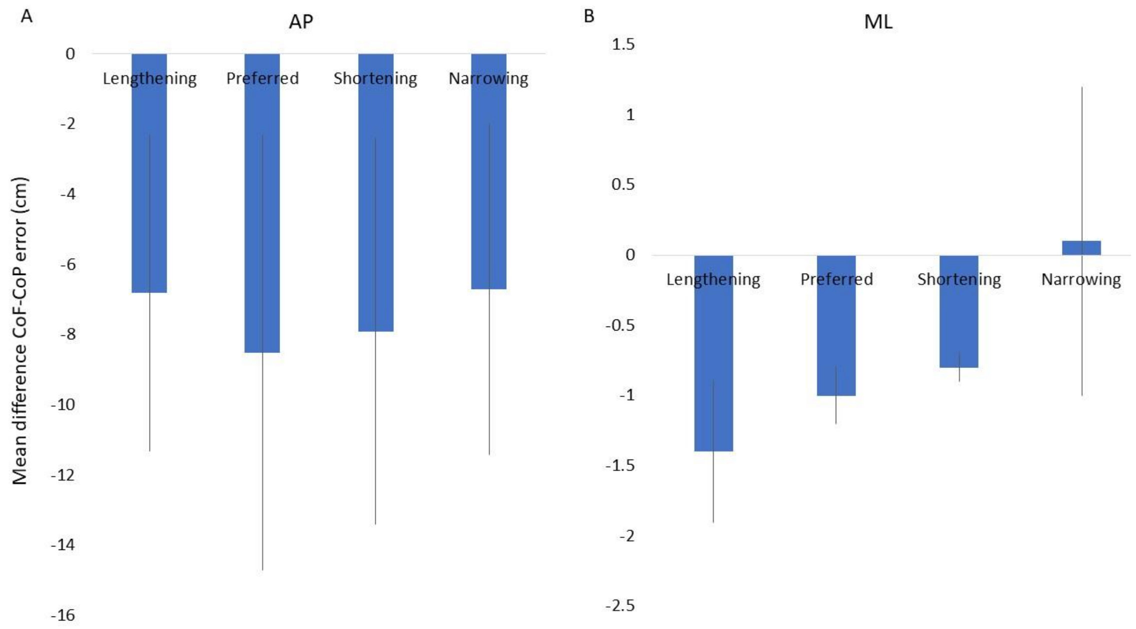

Figure 3.8 *Mean difference between CoF and CoP error reflecting the CoP position on the foot for lengthening, shortening, and narrowing steps for all participants.* ***a)*** *anterio-posterior position on the foot, negative values represent an anterior position on the foot.* ***b)*** *medio-lateral position on the foot, negative values represent a lateral position on the foot. Error bars represent standard errors.*

3.4 Discussion

In this chapter, multiple facets of the use of a target stepping paradigm on an instrumented treadmill were validated. Firstly, GED based on CoP was compared to kinematic GED algorithms (Roerdink et al., 2008; Zeni et al., 2008) during target stepping for as well stroke survivors as young healthy adults. Secondly, the positioning of targets within CueFors1 was compared to the position in Qualisys space, over a range of speeds between 0.5 and 5.5km/h, to determine any offset between the two systems. Lastly, a comparison between CoP and CoF error was made to establish whether they could be used as the same measure, as both measures are reported in a similar way in literature.

3.4.1 Gait event detection

Measurement of walking using force instrumented treadmills is increasingly pervasive. Here a comparison between CoP data obtained using CueFors1 on a C-Mill (Motek, The Netherlands) with established kinematic GED algorithms (Roerdink et al., 2008; Zeni et al., 2008) indicated as most appropriate during treadmill walking in stroke survivors and young healthy participants. Traditionally GED is validated during walking in a straight line. However, owing to the importance of being able to adapt steps in response to the environment and the increasing use of instrumented treadmills to measure gait adaptability, we robustly tested the performance of GED methods while people were making step alterations (lengthening, shortening, and narrowing).

In healthy young participants both kinematic GED methods where evenly successful in means of low percentage of unmatched gait events. In stroke survivors however, the VD GED method failed frequently (VFC 20% paretic 9% non-paretic, VFO 7% in both paretic and non-paretic), and the reliability of this method should therefore be questioned. In comparison using the AD GED method using, AFC and AFO to detect FC and FO, was more successful (failure rate of 3-7%). It is important to consider the effect that a failed detection of a gait event will have on the data, without elimination of these data points the gait parameters will be affected and large errors can occur. Where kinematic GED was successful, there was agreement across all methods to within 100ms (summarised in Table 3.2). This suggests CoP GED has sufficient resolution for GED in many applications beyond steady state walking, as the comparison between GED methods here is carried out during gait adaptation target stepping. Statistical analyses suggest systematic differences between the techniques, and, for work requiring greater levels of accuracy than 100ms, further consideration of possible explanations of these differences is important.

Although the kinematic algorithms seem quite plausible as originally described (Pijnappels et al., 2001; Zeni et al., 2008), neither paper provides a thorough justification or statement of any limitations. The FC detection based on VFC is determined as the local minimum in the heel marker height. Whilst there is evidence of a systematic difference between VFC and CoP methods in the data this difference is small (CoP detection is around (-1ms paretic and -5ms non-paretic) for stroke survivors and (-28 right and -29ms left) young healthy, than kinematic measures) and of little practical significance. More importantly many stroke survivors have abnormalities in foot and ankle movement (Burridge & McLellan, 2000; Stein et al., 2010) which often result in a mid-foot contact with the heel continuing to move downwards after contact. This would lead to the minimum heel marker height occurring after FC, as has also been observed here. Such abnormalities may also explain why the VFC method appears to fail more frequently against CoP detections in approximately 20% for paretic and 9% for non-paretic of steps taken by stroke survivors.

The AFC method determines FC as the most anterior position of the heel marker (with respect to the sacrum). In most people, however, knee flexion commences before initial contact (Winter, 1992) resulting in the heel moving posteriorly at initial contact leading to an early detection compared to CoP methods. This agrees with our data and might suggest that the CoP method is more accurate than AFC for FC detection.

The FO detection by VFO identifies the maximum vertical velocity of the heel marker which starts at heel off, which is quite a bit earlier than toe off and will lead to an early detection of FO (as can be seen in Table 3.2). Foot off detection AFO is based on the zero-crossing point of the forward velocity of the toe marker. For both these algorithms differences could be explained by the difference between marker movement and actual weight transfer. In AD the AFO is identified by the zero crossing of the anterior velocity, with the marker on the 2nd phalangeal, this marker mover forward as the shoe rotates forward when the heel lifts. For VD VFO is determined by maximal vertical velocity, which occurs during push off. However, weight is not fully transferred to the next leg during push off. Both leading to an earlier GED than intended (the original description was with a more anterior toe marker) as observed.

The differences we observed in detection of gait events between CoP and kinematic detections might be expected to affect calculations of gait phase durations. However, early detection of FC would lead to a shorter stance phase which, in turn, would be offset by a longer swing phase (figure 3.4). This pattern has been observed both in this study of stroke survivors target stepping and in previous validations of CoP GED in healthy adults (Roerdink et al., 2008), and is likely to be due to late detection in kinematic algorithms, as marker movement is less accurate than kinetic data. Given the consistency and similarity of our results with those of Roerdink et al. (2008), it is a strong suggestion CoP GED is more robust, for both walking with and without targets, than kinematic GED based on minimum heel vertical displacement and maximum heel velocity, particularly in stroke survivors with hemi paretic gait.

While the GED based on CoP trajectory seems to be a reliable way of detecting FC and FO in stroke survivors, the stroke survivors who participated in this study all had butterfly shaped cyclograms. It must be noted therefore, that CoP GED algorithm might not work for stroke survivors with cyclograms shaped differently (patterns 3 and 4)(Wong et al., 2004). For future work, CoP GED for these more severely affected gait patterns could be validated by using a (fore aft) split-belt treadmill. The cyclogram could be computed by combining signals from the two force plates but the gait detection could be done on the basis of the magnitude of the ground reaction under each foot separately.

3.4.2 Target position

The comparison between CueFors1 target position and Qualisys target position at the time of registration in CueFors1 show a linear offset for treadmill speed. However, an increase in standard deviation at the faster speeds is shown, it is likely this is due to less accurate reaching movements of the arms to place markers at faster movement speeds (Fitts, 1954). The linear offset described in the results can be corrected for, and will be corrected for in the work of this Ph.D., with the linear equation derived at previously (treadmill speed x -0.0266) – 0.0039). $(treadmill\ speed * -1.33) - 0.39$. This equation represents the static offset between both systems (-0.39cm), and the linear offset due to the speed of the treadmill (treadmill speed * -1.33), which means that per km/h the treadmill is moving faster the target position in CueFors1 is represented 1.33cm more forward than in Qualisys representation.

3.4.3 Error measures

The results of the experiment to define the differences between CoP and CoF error and participant group indicate that the measures cannot be considered comparable. The question then arises as to which measure is a correct reflection of foot placement control? Target stepping is an essentially kinematic task - the foot is to be placed over a target – and thus CoF error is therefore a direct indication of how well the participant is fulfilling the required task. However, it seems unlikely that people use CoF to steer footfall location (as opposed to the edge of the foot or toes). CoF may therefore lack the desired insight into the cause of balance problems and falls, which could inform targeted treatments. Measures based on CoP error have been introduced largely because the measurement can be made with an instrumented treadmill without the requirement for an optoelectronic tracking system or the placement of markers on the participant. But beyond the convenience of measurement, given the tight coupling between foot placement and control of centre of mass acceleration (Bancroft & Day, 2016) there is theoretical reason to believe that CoP may be an informative performance measure of how foot placement is altered.

The difference we observed between the measures of CoF and CoP arises because the CoP moves differently in relation to the foot in the different participants, sides and tasks. Nolan et al. (2015) has previously shown differences in CoP trajectory between stroke survivors and healthy controls and between the sides in stroke survivors, and Wong et al. (2004) further demonstrated that different Brunstrom scores are related to different shaped cyclograms in stroke survivors. However it would appear that although CoP measurments are easier to make, they have potential to give mis-leading results when used to quantify foot placement accuracy and make comparisons between step types or patient groups. Although CoP might be informative in how foot placement and balance are perturbed by the target stepping task, CoF error is representative of how well one has placed their foot on the target an therefore is the most direct measure of target stepping acurracy, reflecting the task to fit the foot into a target. However, it is unclear if (indeed unlikely) that the variable used to aim foot-placement is the CoF. So, while this measure reflects performance of the task, it may not reflect control mechanisms or the reason for poor control (when this exists). CoP error may better reflect the role of balance in foot-placement control but our pilot work showed the response of CoP to different gait adaptations was not systematic and so it is unclear what CoP error represents in the task. For this reason we have focussed on using the most clear and direct measure of task performance and then conducted a series of studies to investigate the roles of different factors on that task performance as a way of determining the nature and cause of stroke survivor impairments.

3.5 Conclusion

Firstly, the CoP GED agrees within 100ms to kinematic algorithms suggested for use with stroke survivors walking on a treadmill. However, when greater time resolution is required, in, for example, response time tasks, even a 100ms difference in GED may be important and care should be taken to use the most robust method for these applications. Detailed comparison of the different algorithms suggests that CoP GED may actually be more accurate than kinematic methods for stroke survivors during target stepping tasks. For the means of this thesis, determining mid stance to calculate target stepping error and present reactive targets, CoP GED is accurate enough, within 100ms.

Secondly, the representation of target position in the registration of CueFors1 in C-Mill has a linear offset with the representation in Qualisys space at the time of registration in CueFors1. This linear offset can be corrected for, and will be corrected for in the work of this Ph.D., with the linear equation derived at previously $(treadmill\ speed * -1.33) - 0.39$.

Lastly, our results indicate the most apropriate measure for foot placement accuracy (i.e. fulfillment of task requirments) is CoF error, which is not equivalent to CoP position under the foot. However, CoF may not be the method by which people control their foot placment onto targets. Conversely, because foot placement is closely linked with centre of mass acceleration (and therefore maintenance of balance) CoP position on the foot may reflect mechanisms of balance impairement in participant groups. However,within this thesis CoF error will be used as the measure of foot placement accuracy.

4 Pilot study

4.1 Introduction

The understanding of foot placement control and adaptations during walking is important because altering foot placement is the most effective means of balance control when walking (Winter, 1995; Winter, Mackinnon, Ruder, & Wieman, 1993). Stroke survivors have difficulty adjusting foot placement to step over obstacles as well as with narrowing steps, and performance worsens under time pressure (Nonnekes et al., 2010; Weerdesteyn, van Swigchem, van Duijnhoven, & Geurts, 2007). However, evidence on how foot placement is controlled during walking post-stroke is incomplete. Current knowledge is largely derived from studies in standing investigating obstacle avoidance or target stepping during walking and predominantly focused on most directions except step narrowing during walking. A recent systematic review of gait adaptability (Balasubramanian et al., 2014) has called for the development of measures which capture all aspects of gait adaptability. Therefore, a need exists for a feasible testing paradigm to obtain robust measures of foot placement to investigate foot placement control.

Current gait rehabilitation programs and measures are mainly focussed on walking speed (Dickstein, 2008). However, being able to walk fast does not necessarily mean improved quality and safety of walking. Recently, many studies are investigating feasibility and success of gait adaptability training (Heeren et al., 2013; K. L. Hollands et al., 2015; Timmermans et al., 2016; van Ooijen et al., 2015; van Ooijen et al., 2013). Multiple attempts have been made to investigate the mechanisms limiting gait adaptability by target stepping when walking. In these studies multiple methods and measures have been used to asses stepping accuracy. Stepping from standing (Nonnekes et al., 2010; Reynolds & Day, 2005a), over ground walking to targets (K. L. Hollands et al., 2016; Lindemann et al., 2013) and treadmill walking to targets (Hoogkamer et al., 2015; Mazaheri et al., 2015; Mazaheri et al., 2014; Peper et al., 2015). Target stepping paradigms have been used mainly with healthy adults, using various outcome measures such as walking speed (K. L. Hollands et al., 2016; Lindemann et al., 2013), task success (K. L. Hollands et al., 2016; Hoogkamer et al., 2015), stepping error normalized to step length (Mazaheri et al., 2015), variable error (Lindemann et al., 2013; Mazaheri et al., 2014) and absolute error (Nonnekes et al., 2010; Reynolds & Day, 2005a). This great spread of methodologies and use of measures makes it complicated to compare results and gain definite understanding of limitations of foot placement control in stroke survivors, but also in other populations that are prone to falls.

Current evidence (reviewed in Chapter: Literature review) indicates that stroke survivors may have difficulty adapting their foot placement in response to the environment. Several studies have documented that, similar to healthy older adults, stroke survivors prefer to lengthen rather than shorten their steps when avoiding obstacles (Den Otter et al., 2005; van Swigchem et al., 2013). Stroke survivors hit more obstacles, which means they are less successful, than healthy adults when the obstacles appear with limited response time; at the time of transition from stance to swing of the avoiding leg (Den Otter et al., 2005; van Swigchem et al., 2013). The preference for step lengthening rather than shortening and a decline in performance under time pressure have also been seen in healthy young adults during target stepping while walking (Hoogkamer et al., 2015). Nonnekes et al. (2010) found narrowing foot placement targets had large foot placement errors in stroke survivors. So, evidence indicates that stroke survivors may have diminished ability to adapt foot placement in some directions; particularly narrowing steps and especially under time pressure, as Den Otter et al. (2005) and van Swigchem et al. (2013) showed success declined with time pressure. Therefore, foot placement accuracy in stroke survivors is likely to be affected by the direction of adaptation and the available response time more so than in healthy young and older adults.

In the present study, the first aim is to test feasibility and robustness of the current target stepping paradigm. Secondly, this study evaluates foot placement for reactive and planned conditions as the direction of foot placement adjustment during walking. How stroke survivors and healthy adults make step length and width adjustments under time pressure. The data from this study will give a strong basis for completing a powered study to test target stepping; providing more insight in how stroke survivors adapt their gait and what factors limit accurate foot placement adaptation during walking.

4.2 Methods

4.2.1 Participants

9 Young healthy adults aged between 18 and 35 were recruited by poster advertisement and email invitations to University staff and students. 12 Stroke survivors were recruited from community stroke support and exercise groups in Greater Manchester. Both the data of young

healthy and stroke survivors was also used in chapter 3 Validation studies. Participants were included if they were able to complete the 10-metre walking test within 30s (to ensure sufficient independent mobility to safely take part in the study) and had no severe visual impairments that would prevent sight of stepping targets. Potentially eligible participants were excluded if their mobility was limited by factors other than their stroke.

Demographic and anthropometric data were taken, including date of birth, date of stroke, side and site of paresis, height, weight, and leg length. The University of Salford, College of Health and Social Care Research Ethics Committee approved the study, and all participants provided written informed consent.

4.2.2 Procedures

Clinical assessments were carried out with stroke survivors in order to document recovery and mobility status, including self-selected treadmill walking speed (SSWS) and functional mobility using the 10m walking test (Green et al., 2002),Timed Up and Go (Hiengkaew et al., 2012) and Dynamic Gait Index (Jonsdottir & Cattaneo, 2007).

Participants were familiarised with walking on the treadmill without stepping targets for approximately three minutes. Each participant's SSWS was determined by increasing speed from 1km/h with increments on 0.1km/h until participants felt they were walking faster than preferred, then decreasing the speed to a comfortable pace. Participants then walked to targets located at their usual step length and width (based on walking during a previous no-target acclimatisation period) for one minute, to become acquainted with target stepping. Step characteristics such as speed, step length and width, were recorded during this last minute of target-stepping as a basis for programming the location of targets for the subsequent protocol of personalised target-stepping tasks.

Participants stepped to the targets located according to their personalised protocol projected onto the treadmill belt while walking at SSWS (figure 4.1) according to a previously described paradigm (K. L. Hollands et al., 2015). Twelve targets (8cm long x 40cm wide) were projected at preferred step length and 12 of the same size were projected for both shortening and lengthening steps (±25% of baseline step length). A further 24 targets of a different shape (20cm long x 15cm wide) were projected onto the midline of the treadmill to elicit more narrowing foot placements. These targets were delivered in six blocks of ten as in figure 4.1. Targets where visible for either at least two steps ahead (planned) or at contra lateral mid stance, when the aiming limb is about mid swing (reactive). Participants were not allowed to use a handrail for stability, however stroke survivors wore a harness to maintain safety. There was the opportunity to take a rest between every trial of 60 steps.

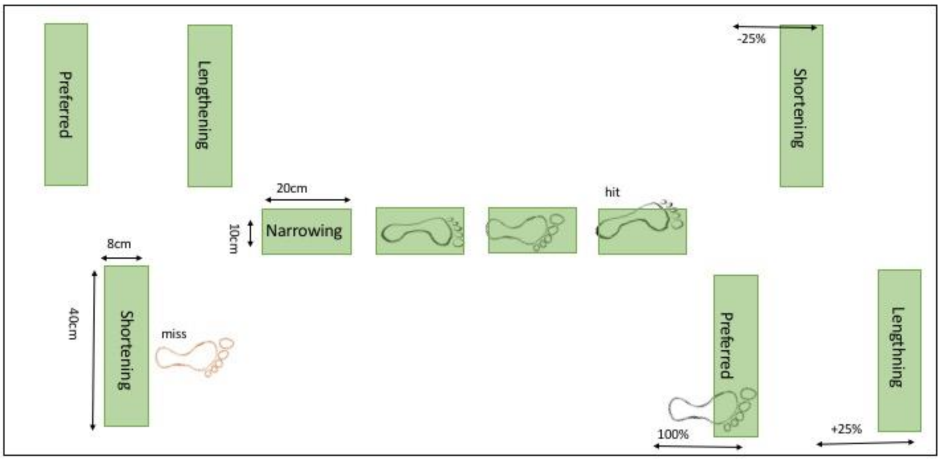

Figure 4.1 *Schematic representation of the layout of stepping targets (preferred, shortening, lengthening and narrowing). Black foot prints represent successful steps, the red one represents a missed step.*

4.2.3 Measures of stepping performance

The percentage of misses was based on CoF position; the size of the foot was projected around the CoF and overlaid on the centre of target, when no part of the foot was touching the target this was considered a miss.

In addition to percentage of target misses, the distance of the centre of foot (CoF) to the middle of the target, as described previously in Chapter 3, was used as a measure of stepping accuracy. The CoF error was analysed separately in medio-lateral (ML) direction and anterior-posterior (AP) direction for all steps. Mean CoF error per participant was used to analyse the direction of error (average tendency to undershoot vs. overshoot targets); absolute CoF error was used to compare the size of error between the target stepping task and adaptation steps (preferred, narrowing, lengthening and shortening); variable CoF error was used as a measure of consistency (R. A. Schmidt & Lee, 1999).

4.2.4 Power calculation

Software package G*power (University Dusseldorf, Dusseldorf) is used to calculate the power based on sample sizes of the stroke survivors and the young healthy adults and the effect size. The effect size is based on the mean of the stroke survivors minus young healthy adults divided by the standard deviation and an α=0.05.

4.2.5 Statistics

Repeated measures ANOVA was conducted for the mean (from 12 steps for planned and 6 steps for reactive stepping) of each measure (percentage misses and CoF), separately for the different directions of error (ML and AP) per participant. As steps of the left and right leg did not show significant differences these data were pooled for further analyses. Post hoc comparisons were assessed using Bonferroni test with adjustment for multiple comparisons. The software package SPSS (version 24.0) was used. A $p< 0.05$ was used for statistical significance.

The percentage of misses was angular transformed [angX=asin (squareroot(X))] to stabilise the variance of percentage data and regain a normal distribution, similar to previous foot placement studies (Hoogkamer et al., 2015; van Swigchem, van Duijnhoven, den Boer, Geurts, & Weerdesteyn, 2012), prior to statistical analysis but untransformed means and SDs are reported in results.

4.3 Results

A total of nine young adults, eight older adults, and 12 stroke survivors took part in the study (see table 4.1 for participant demographics). Of the stroke survivors, six were non-functional walkers (<0.4m/s), six limited outdoor walkers (0.4-0.8m/s), and one was a healthy walker (>0.8m/s) (Schmid et al., 2007). All young and older healthy adults were healthy walkers who exceeded the 0.8m/s threshold.

Table 4.1 *Participant demographics and clinical characteristics represented in mean± SD unless specified differently.*

	Young adults (N=9)	Older adults (N=8)	Stroke Survivors (N=12
Female, n	5	2	3
Mean age in years	26.44±4.22	66.11±9.60	66.77±8.67
Mean SSWS in m/s	1.11± 0.14	0.88±0.19	0.46± 0.19
Berg balance scale	-	55.78±0.67	53.31± 5.54
Dynamic gait index	-	29.67±0.5	17.92± 5.62
10m-walking speed (s)	-	7.23±1.24	13.13± 4.07
Falls in last 12 months	-		
0		7	9
1		2	1
>1		0	3
Mean time since stroke inmonths	-	-	86.54±134.43
Paretic side (Right)	-	-	5 (65%)
Fugl-Meyer assesment	-	-	25.92± 3.90
Timed un and go (s)10m-	-	-	14.55± 5.11
Montreal cognitive assessment			
Timed un and go (s)	-	-	25.08± 4.37
	-	-	14.55± 5.11
Apples test	-	-	46.85± 4.52

4.3.1 Is percentage of misses a sensitive measure for the differences in stroke and healthy participants?

Investigation of the percentage of misses between the three groups showed a main effect (F (2, 26) = 7.536, p=0.003), where stroke survivors missed (Mean 11.6± SEM 2.0%) significantly more targets than healthy young adults and older adults (1.9± 2.3% and 2.5± 2.4%, respectively). A second main effect (F (3, 24) = 3.776, p=0.024) showed narrowing steps were missed significantly more often than short steps for all participant groups (9.0± 2.3%). Lastly, a main effect of condition was found (F (1, 26) = 7.589, p=0.011); reactive targets were missed significantly more often than planned steps (2.4± 0.8% versus 8.2± 2.2%). Interaction effects were found for steps and groups (F (6, 50) =3.428, p= 0.005), stroke survivors (21.9± 19.6%) missed more narrowing steps than young (1.4± 4.7) an older (3.6± 5.8%) healthy adults. See Figure 4.2.

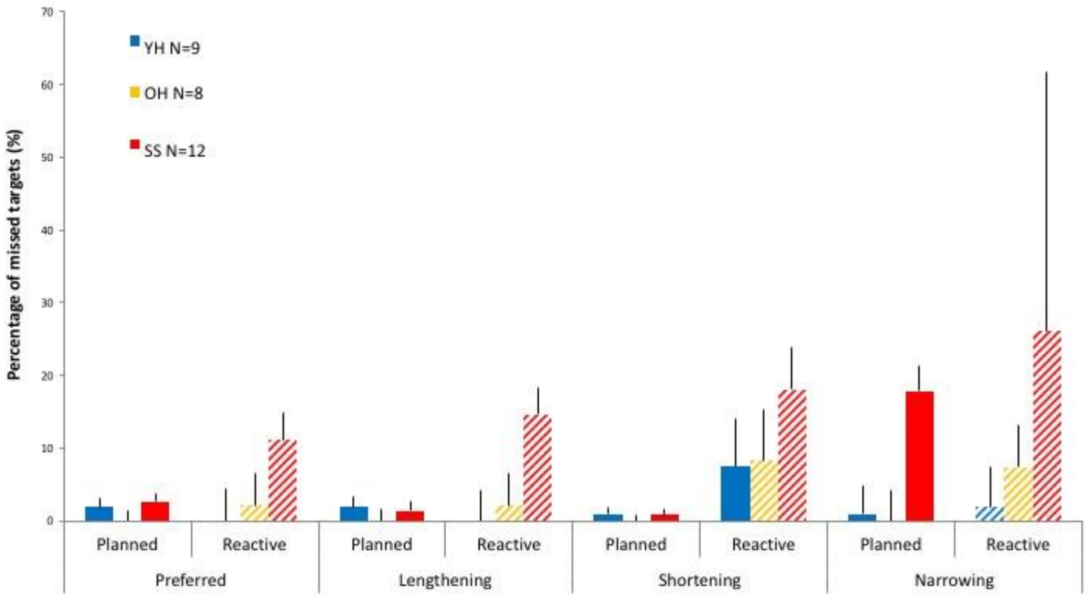

Figure 4.2 *Bars represent the mean percentage of target misses for young healthy adults (YH), older healthy adults (OH) and stroke survivors (SS), for each type of step adjustment (preferred, shortening, lengthening and narrowing) in both planned (solid) and reactive (striped) conditions. Error bars represent standard deviations.*

From figure 4.3 it can be seen that four of the stroke survivors did not miss any targets in the planned condition, whereas only one stroke survivor did not miss a single target in both planned and reactive conditions. None of the older healthy adults missed a target in the planned condition, where three started missing targets in the reactive condition. In contrast to healthy older adults, three of the young healthy adults missed targets in the planned condition; two of the young healthy adults that missed planned targets did not miss reactive targets though. One young healthy adult did not miss planned targets, but missed reactive targets, and three young healthy adults did not miss any targets in both tasks.

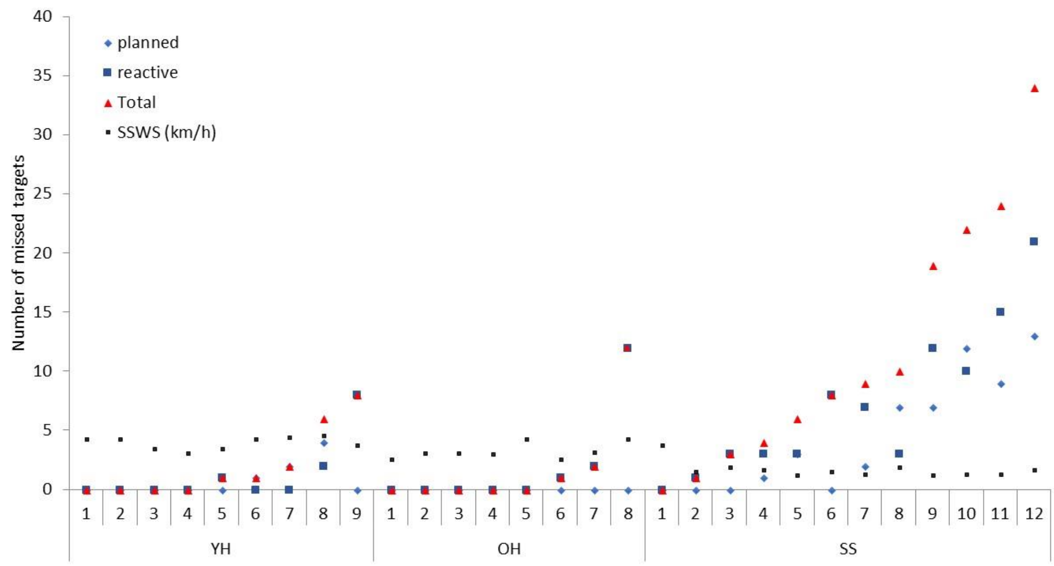

Figure 4.3 *Accumulative number of misses per individual participant (listed as ID number) for the planned , reactive and total (accummulation of planned and reactive) target stepping tasks for young healthy adults (YH), older healthy adults (OH), and stroke survivors (SS). Also the self-selected walking speed is represented (in black).*

4.3.2 Is CoF error a sensitive measure for the differences between groups, steps and conditions)

4.3.2.1 Error in anterior-posterior direction

A main effect of group (F (2, 24) =7.589, p=0.003) indicated that stroke survivors (mean -7.4± SD 0.7cm) undershot targets more than young healthy adults (-3.2± 0.9cm, p=0.003) in all types of stepping adjustments and in both reactive and planned stepping tasks. An interaction effect (F (3, 22) = 8.465, p=0.001) was found for condition and steps which reflects a larger mean undershot error in planned step shortening compared to reactive step shortening (figure 4.4a). A main effect for steps (F (3, 22) = 36.228, p<0.001) showed preferred (-5.6±0.5cm, <0.001) and lengthening (-7.6± 0.6cm, p<0.001) targets are under-shot by all groups (reflected in a negative mean CoF error), whereas shortening (-2.4± 0.5cm) steps are undershot (in the anterio-posterior direction) to a lesser extent and even over-shot by young healthy adults (figure 4.4a).

A main effect of groups was found in the absolute foot placement error (F (2,26) = 13.182, p<0.001) showing stroke survivors had significantly more absolute error (8.5± 0.5cm) than young (5.1± 0.6cm, p<0.001) and older healthy adults (5.3± 0.6cm, p=0.002). A second main effect for steps was found (F (3,24) =20.617, p<0.001), lengthening steps (8.1± 0.5cm) had significantly greater error than preferred (6.3± 0.4cm, p=0.003) and shortening steps (5.0± 0.4cm, p=0.005). Also, a step condition interaction was found (F (3,24) = 8.139, p=0.001) showing lengthening steps had more error in the reactive than planned condition (figure 4.4b).

A main effect for group (F (2, 21) =4.835, p=0.019) showed stroke survivors had significantly more variability (3.3±0.3cm) in anterio-posterior direction than older healthy adults (2.1± 0.4cm, p=0.043). A steps condition interaction effect was found (F (3,19) =3.297, p=0.043), showing the reactive lengthening targets (1.0± 0.5cm) had less variable error than the planned lengthening steps (2.6±2.6cm) (figure 4.4c).

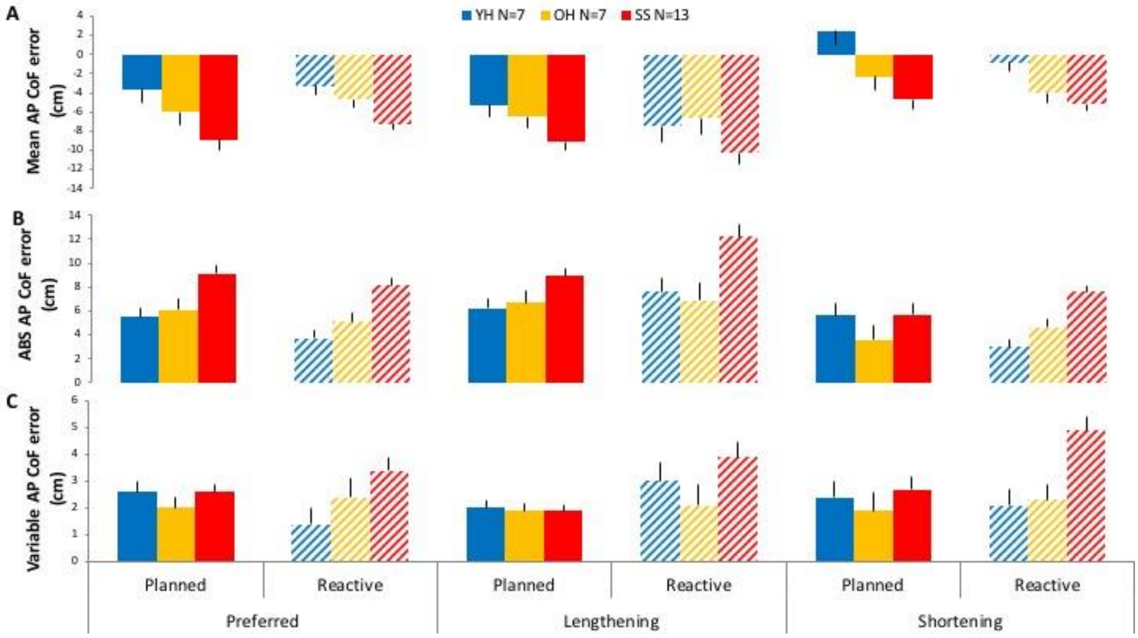

Figure 4.4 *Anterior/ posterior (A/P) Centre of Foot (CoF) mean error (A), absolute (ABS) error (B) and (C) variable error, for young healthy adults (YH), older healthy (OH) and stroke survivors (SS), for each type of step adjustment (preferred, lengthening and shortening) in both planned and reactive conditions. Positive values represent overshoot and negative values undershoot; error bars represent standard deviation.*

4.3.2.2 Error in Medio-lateral direction

A main effect for group was found (F (2, 24) = 6.792, p=0.005), and young healthy adults (6.8± 0.6cm) had more medio-lateral error than older healthy adults (3.9± 0.6cm, p=0.004), but stroke survivors (5.1± 0.4cm) did not have significantly different error in medio-lateral direction than young or older healthy adults (figure 4.5a). A main effect of condition was found (F (1, 24) =10.145, p=0.004), the planned task (4.8± 0.3cm) had less error than the reactive (5.8± 0.4cm, p=0.004). And an interaction effect was found for steps and group (F (6.46) =3.388, p=0.008), stroke survivors (6.1± 0.8cm) had more mean error in narrowing steps than young (3.4± 1.1cm) and older (3.1± 1.1cm) healthy adults (figure 4.5a).

A main effect for groups in the absolute error was found (F (2, 26) =10.692, p<0.001) showing stroke survivors (5.7± 0.3cm, p=0.006) and older healthy adults (4.2± 0.5cm, p=0.005) had significantly more magnitude of error than young healthy adults (0.1± 0.0cm). A main effect for condition (F (1, 26) = 17.184, p<0.001) showed reactive steps (6.3± 0.3cm) had more magnitude of error than planned steps (5.1± 0.2cm, p<0.001). Also, a main effect of steps was found (F (3, 24) = 3.326, p=0.037) lengthening steps (5.6± 0.3cm) had les medio-lateral error than preferred steps 6.2± 0.3cm, p=0.049). An interaction effect of step and group was found (F (6, 50) =4.764, p=0.001), stroke survivors (7.3.1± 0.6cm) had more magnitude of error in narrowing steps than young (3.8± 0.7cm) and older (3.2± 0.8cm) healthy adults. See (figure 4.5b).

No significant main or interaction effects were found in medio-lateral direction for variable error (see figure 4.5c).

4.3.4 Where do people position their foot

Mean CoF foot placement (as a general representation) showed that lengthening steps were slightly under-shot, and shortening steps were slightly over-shot (Figure 4.5a). These results were showed a trend in stroke survivors than young and older healthy adults with planned steps (Figure 4.6a). However, this difference between groups became smaller in the reactive steps (figure 4.6b).

Participants generally step medial of the middle of the target, in preferred, lengthening, and shortening steps. This is expected because of the width of the targets. However, in narrowing targets this means they generally over-shot for medio-lateral adaptations (figure 4.6 a/b).

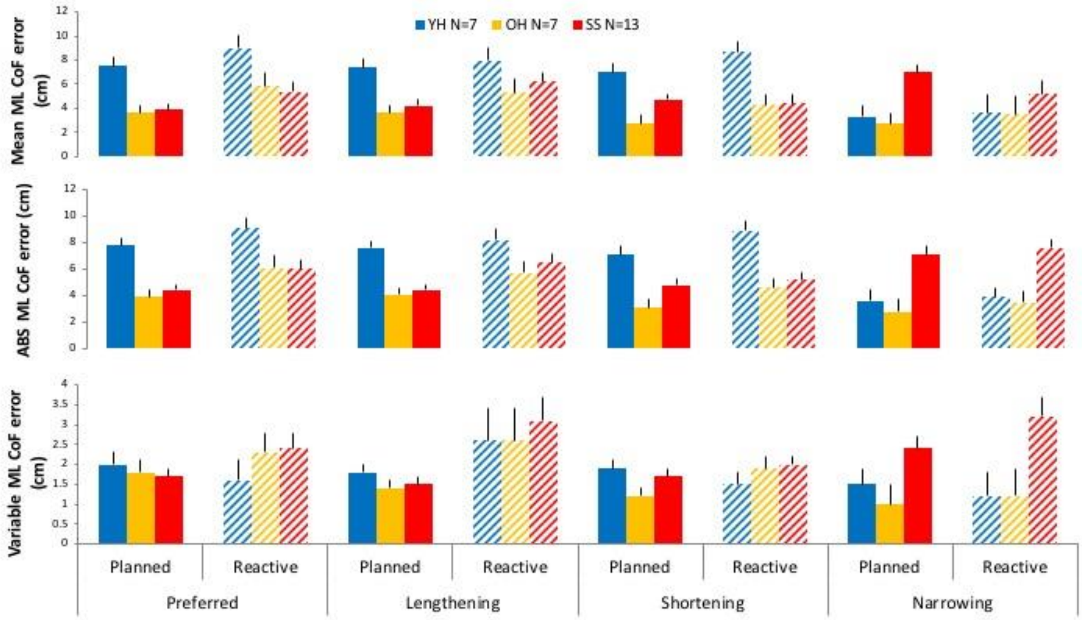

Figure 4.5 *Medio-lateral (ML) Centre of Foot (CoF) mean error (A), absolute error (B) and variable error (C) for young healthy adults (YH), older healthy (OH) and stroke survivors (SS), for each type of step adjustment (preferred, lengthening, shortening, narrowing) in both planned and reactive conditions. Error bars represent standard deviation.*

4.3.4 Power calculation

The average absolute error means of the 13 participating stroke survivors (8.5cm in AP direction) and 7 participating young healthy adults (5.1cm in AP direction) with a combined standard deviation of 2.2cm results in an effects size of 1.5 and a power of 0.86.

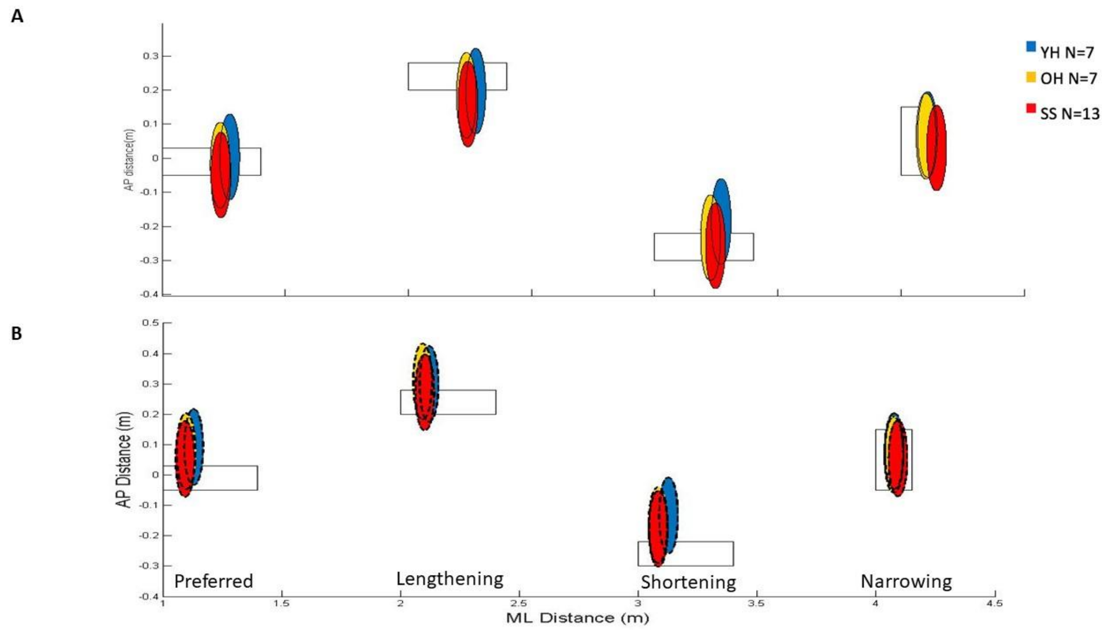

Figure 4.6 *Schematic representatation of A) planned, and B) reactive foot positioning (mean CoF position and average size of the feet) for stroke survivors, young , and older healthy adults for preferred, lengthening, shortening, and narrowing steps AP, anterio-posterior; ML, medio-lateral.*

4.4 Discussion

The main aim of this study was to determine the feasibility and robustness of a target stepping paradigm, to confirm methods for the experiments following in this thesis. This is necessary because variability in methods of target stepping paradigms across studies in the current literature prevents definitive understanding of the type and nature of stroke survivors impairments in foot placement control and gait adaptability. Secondary, investigation of hits and misses and foot placement accuracy will be determined, the percentage of misses is set by scoring the unsuccessful foot placements as a percentage and foot placement accuracy is measured by the direction (mean), magnitude (absolute) and variability of foot placement error.

A pilot study can determine whether it is feasible to perform a full-scale study. This is traditionally determined by recruitments rates, completion of the protocol and adherence to treatment to allow for sample size calculations. In this pilot only the recruitment and completeness of outcomes can be taken into account. Firstly, enough participants were recruited to have enough power to reach significant differences between groups. Secondly, the target stepping paradigm has shown to be feasible in young, older healthy participants and stroke survivors, all participants finished the testing day.

Generally, participants missed more reactive than planned targets (see percentage of misses in figures 4.2 and 4.3); stroke survivors missed more targets than young and older healthy adults in both planned and reactive conditions. The tendency for stroke survivors to miss significantly more targets than healthy counterparts is perhaps not surprising and coincides with previous studies of obstacle avoidance (Den Otter et al., 2005; van Swigchem et al., 2013) and target stepping from standing (Nonnekes et al., 2010). These studies, along with the present study, indicate that stroke survivors have poorer control of foot placement that healthy participants. With additional time pressure the performance decreases for stroke survivors when stepping to targets and crossing obstacles under time pressure. This indicates that response time is an important factor in gait adaptations more so in stroke survivors than in healthy young and older adults.

We found that the percentage of missed targets increased more in stroke survivors than healthy participants generally. In particular narrowing steps were missed more often in stroke survivors. Also, stroke survivors showed to have more difficulty hitting the target when they were reactive than planned. These results show that stroke survivors have impaired ability to adapt foot placement compared to young and older healthy adults, which is particularly visible in error on the narrowing and reactive steps. This is in line with previous literature where stroke survivors were worse in narrowing steps from standing (Nonnekes et al., 2010), and were less successful avoiding obstacles with less available response time (Den Otter et al., 2005; van Swigchem et al., 2013). This high number of misses for medial targets implies that balance is challenged during step narrowing.

There was no difference between paretic and non-paretic foot placement, so in this pilot study we chose to combine the sides to exploit the differences for further development of the target stepping task. However, the fact that both paretic and non-paretic legs had a similar number of misses does not provide evidence both sides are affected by the same impairments. Loss of neuro-motor control in the affected limb, could affect targeting with the paretic limb. Alternatively, instability in paretic limb support could present due to loss of strength and control, which would affect targeting with the non-paretic limb because balancing on the paretic limb is necessary. Or impairments could contribute to the difficulties seen. Likely the limitation of the base of support affects both legs and challenges balance more than other foot placement adaptations. In conclusion, it is likely that balance and response time are important factors in foot placement control that may be affected by stroke. Therefore, the paretic and non-paretic limb will be analysed separately in the following chapters.

In addition to the overall performance measure of percentage targets missed, measuring foot placement error when adjusting footfall in particular directions may help identify why some step adjustments are problematic for stroke survivors. Stroke survivors (AP 8.5cm, 5.7ML cm) do show to have more magnitude (absolute) error that young healthy adults (AP 5.1cm, ML 0.1cm) (both AP and ML direction). In anterio-posterior direction stroke survivors (AP -7.4cm) show to undershoot (mean error) targets more than healthy young (AP -3.2cm) and be more variable than older healthy adults (AP, SS 3.3cm and OH 2.1cm). The medio-lateral direction shows especially narrowing steps have increased medial error in stroke over healthy adults, which is in line with the high number of missed medial targets as shown in (Nonnekes et al., 2010). The reactive targets show to be more variable in anterio-posterior direction and have increased magnitude of error in medio-lateral direction. This is surprising, because of the increased number of missed targets in the reactive condition. This apparent discrepancy between percentage of misses and the bias might be partially explained by the size of the targets, 40cm wide and 8 deep for normal, shortening and lengthening targets and 10cm wide and 20cm deep for medial steps. The size of the target is designed to elicit lengthening/shortening or medial stepping however, however does not fit the foot. We propose that our results indicate that participants aim with the toe (figure 4.6) instead of the CoF, as on average CoF error is negative for all participant groups. This toe targeting results in a negative mean error (undershoot of the CoF relative to the centre of target) of about -5.6cm. The negative mean error is because the CoF was behind the centre of target and therefore the part of the foot people can see, the toes, aimed to reach the furthest edge of the target. In this way, the number of misses may not be reflected in the outcome measure of mean error. Indeed, variable error in reactive target stepping is greater than planned target stepping, implying that small errors resulting in undershoot misses may have been averaged out by equal or larger overshoot errors which do not yield a miss. High variability represents an inconsistent foot placement (R. A. Schmidt & Lee, 1999). Variable foot placement was previously associated with higher attentional costs (Mazaheri et al., 2014) and occluded visual feedback (Reynolds & Day, 2005b). Therefore, an increased variable error could either mean there was not sufficient time to use the visual feedback in the reactive condition, or the attentional costs were too high [relative to available cognitive capacity which has been shown to be reduced in stroke survivors (Zinn et al., 2007)] to process the visual information, both resulting in a more variable placement of the foot. Indicating that as well as the available response time, the executive function and cognitive capacity might be indicative for the accuracy of gait adaptations.

Stroke survivors had significantly greater mean and absolute CoF error in all directions and conditions of step adjustments compared to young and older healthy adults, in accordance with the percentage of misses and previous literature on obstacle avoidance (Den Otter et al., 2005; van Swigchem et al., 2013). The present study showed that mean CoF errors of shortening steps were significantly smaller than preferred steps and lengthening steps (figure 4.4a). However, the apparent smaller error in step shortening compared to lengthening could be due to the size of the targets and/or the target stepping strategy. In preferred/lengthening steps the negative mean error was because the CoF was behind the centre of target and therefore the part of the foot people can see, the toes, were aimed to reach the furthest edge of the target. In shortening steps the mean CoF error showed that the CoF was placed closer to the middle of the target, which would result in an overshoot of the toes. This is in accordance with the findings by Bank et al. (2011) that a degree of adaptations are made, but not completely. A smaller error in step shortening than in step lengthening would imply that step shortening is more accurately controlled than other step adjustments and contradicts current suggestions in the literature that step shortening is more difficult than lengthening in healthy young adults (Hoogkamer et al., 2015; van Swigchem et al., 2013). However, the differences in target sizes between the recent study and previous study (Hoogkamer et al., 2015) the explanation might be we need to investigate target stepping and foot placement further with better representation of how errors are actually made. In order to do this foot sized targets will be used in future.

4.5 Limitations

Although this target stepping paradigm might not be representative of gait adaptations in real life, as typically the adaption is to avoid obstacles e.g. dog faeces, puddles and loose paving slabs, which gives a range of options as to where the foot can be placed around the obstacle. However, how people avoid obstacles, and the preferred strategy for avoidance strategies, are known (Den Otter et al., 2005; van Swigchem et al., 2013). Therefore, the focus in this study is how these adaptations are actually made, i.e. how foot placement is controlled, and where the difficulty in adapting gait lies.

In future studies, foot-sized targets should be used to give a true representation of the percentage of misses and error rate. Although the size of the targets in this study was chosen to allow for the normal variability of foot placement in stroke survivors and only elicit adaptation of foot placement in the anterio-posterior or medio-lateral direction, comparisons to previous literature are difficult and the association between percentage of misses and the magnitude (absolute) of bias (mean error) are complex. Using foot-sized targets will help to avoid results that give the appearance that there is more error in lengthening steps than shortening steps due to the part of the foot participants aim with and the position of the CoF in relation to the centre of target. With foot-sized targets the error measure will be a truer representation of how well a target has been hit by the participant.

4.6. Conclusion

For the context of this thesis, this pilot gives a good rationale to study gait adaptability in young and older healthy adults and stroke survivors. Reactive target stepping during walking has shown to be different than planned target stepping; however, the cause of this difference could be due to different factors affecting foot placement. Reactive target stepping has been shown to be a sensitive measure for the differences in gait adaptability between stroke survivors and healthy people. Also, step narrowing seems to be limited in stroke survivors, which could be due to the balance problems stroke survivors' experience. In addition, the pilot study revealed that narrowing steps are missed most frequently, and shortening steps differ from preferred step length more than lengthening steps. Follow up studies, focussed on balance and reaction time and executive function will be carried out taking the limitations into account and considering foot-sized targets to make error interpretations more straightforward.

5 General methods

5.1 Introduction

Based on our findings from gait event detection validation experiments explained in chapter 3 and the pilot study in chapter 4 we altered our testing protocol to allow robust measurement of factors affecting gait adaptability after stroke. Three key changes to the methods used in the Pilot study are briefly explained here as well as the definitive methodology used to assess factors affecting gait adaptability in stroke survivors. The factors investigated are, the effect of balance on target stepping accuracy (Chapter 6), the effect of response time on target stepping accuracy (Chapter 7), and whether irregular visual target stepping paradigms require more executive function than regular target stepping and normal walking (Chapter 8). These factors are assumed to affect the adaptability of gait, specifically in stroke survivors, based on existing literature (Chapter 2), outcome measures validated in the validation studies (Chapter 3) and results from the pilot study (Chapter 4).

Firstly, based on comparisons of the centre of pressure and centre of foot error measures, explained in detail in Section 3.3 the error of the centre of foot to the centre of target (CoF-CoT) has been selected as the measure of foot placement accuracy for all future work. However, it should be noted that marker placement has been adapted to provide a more accurate centre of foot calculation. In the pilot study anterio-posterior CoF is based on the 2nd proximal phalanx head and the calcaneus, which gives a slight posterior representation of the CoF. In the experimental studies the 2nd distal phalanx head was used to calculate centre of foot with the heel marker, to give a true CoF location.

Secondly, the sizes of the targets have been altered from what was used in the pilot study. The size of targets in the pilot study were chosen to allow for the normal variability of foot placement in stroke survivors (i.e. such that targets would only be missed if error exceeded normal variability) and to only elicit adaptation of foot placement in one direction at a time i.e. anterio-posterior or medio-lateral directions (K. L. Hollands et al., 2016; K. L. Hollands et al., 2015). While, these target sizes proved valuable in measuring ‘hit-and-miss’ scores in a clinically applicable over-ground target stepping task in previous studies (K. L. Hollands et al., 2016; K. L. Hollands et al., 2015), CoF-CoT measures of accuracy of foot placement can be misleading if people aim to just hit a target with their toe/heel (as opposed to the CoF). So, in addition, to facilitating reliable measurement of hit and miss scores during treadmill walking, and for a more specific error measure in anterior-posterior and medial-lateral direction on the treadmill (C-Mill, Motekforcelink, The Netherlands, Culenborg), foot sized targets were used to give a true representation of how well foot placement was controlled (as stepping within a foot sized target demands CoF overlying the CoT).

Finally, lateral step adaptations or step widening was added. In the pilot study the original target locations were based on the target stepping task used previously by K. L. Hollands et al. (2016). The four step conditions (preferred foot-fall, shortening, lengthening, and medial stepping) allowed comparison between the preferred foot-fall, shortening and lengthening; however, because of the shape of the targets (8x40cm for preferred, shortening and lengthening, and 10x15cm for medial stepping), and the lack of lateral stepping, an accurate interpretation could not be made of the foot placement control during medial steps. This is important because medial targets were missed most often (Chapter 4). In a recently published paper by Hoogkamer et al. (2015) targets were placed to elicit shortening, lengthening, and lateral stepping. The lateral steps showed a success rate between that of the lengthening and shortening steps. Measuring both medial and lateral steps allowed us to compare how these adaptations were made, and the foot sized targets allow for a true comparison between preferred, shortened and lengthened steps in the anterio-posterior direction as well as between preferred, narrowing and widening steps in the medio-lateral direction.

The changes discussed above were implemented in the following finalised methods to be used in all subsequent chapters.

5.2 Methods

5.2.1 Participants

Young (18-40 years old), and older (age matched with stroke survivors) healthy adults were recruited by poster advertisement and email invitations circulated to University staff and students. Stroke survivors were recruited from community stroke support and exercise groups in Greater Manchester. Some of the participants taking part in the main study had taken part in the pilot study over a year prior to the main data collection, 8 of the stroke survivors, 3 of the age-matched older healthy adults and one of the young healthy participants took part in both data collections. Demographic and anthropometric data were taken from all participants (if applicable) including: date of birth, date of stroke, hemiparesis side, height, weight, and clinical assessments of cognition, executive function, balance, gait adaptability, motor recovery, falls history and visual field deficits. Exclusion criteria for both healthy participants and stroke survivors were neuro-musculoskeletal (apart from stroke) conditions that would affect walking ability, and receptive and/or language problems that could preclude informed consent.

For stroke survivors, inclusion criteria were: >6 months post-stroke, self-selected walking speed (SSWS) >0.4m/s, able to walk 10m independently without orthopaedic aids or personal assistance. Walking speeds >0.4m/s correspond with a limited ability of community ambulation (Perry et al, 1995). As such, these individuals may experience difficulties with adaptability of walking. However, recruiting only those participants with speeds >0.4m/s ensures that they have sufficient independent mobility to safely take part in the tasks. The University of Salford College of Health and Social Care Research Ethics Committee approved the study and all participants provided written informed consent.

5.1.2 Clinical assessment

A set of ten clinical assessments were carried out with stroke survivors in order to document clinical recovery and mobility status:

- Cognition: The Montreal Cognitive Assessment (MoCA) (Pendlebury, Cuthbertson, Welch, Mehta, & Rothwell, 2010))
- Executive function: trail making test (TMT) (Hester, Kinsella, Ong, & McGregor, 2005).
- Hemianopia and visual attention test: apple cancellation test (Bickerton, Samson, Williamson, & Humphreys, 2011)
- Walking ability: 10m walking test (Green et al., 2002), timed up and go(TUG) (Hiengkaew et al., 2012), dynamic gait index (DGI) (Jonsdottir & Cattaneo, 2007), falls in the past 12 months (C. Cooper & Barker, 1995)
- Balance: Berg Balance scale (BBS) (K. O. Berg, Wood-Dauphinee, Williams, & Maki, 1992).
- Motor control: Fugl-Meyer assessment, the lower limb and sensory intactness are assed (Gladstone, Danells, & Black, 2002).
- Tone: modified Ashworth scale (MAS) (Gregson et al., 1999).

The tests used to assess healthy older adults were: falls history, the Montreal cognitive assessment, and the trail making test. In young healthy adults only the trail making test was carried out. The selection of tests for healthy participants was based on the sensitivity and appropriateness for healthy adults.

5.1.3 Apparatus

A treadmill with a single embedded force platform (C-Mill, MotekForcelink, Culemburg, The Netherlands) was used allowing for online gait event detection (Chapter 3.1: Validation of Gait event detection) while projecting visual stepping targets that move at the speed of the treadmill belt (Chapter 3.2: Calibration of the visual targets), this calibration of the targets was re-done before the main study and the offset between systems was similar to the initial offset. Gait event detection was based on the CoP calculated from kinetic data and performed automatically by C-Mill software, CueFors1. A six-camera system (Qualisys, Gottenorg, Sweden) was used to track the trajectory of the foot synchronously with the CoP from the force platform. The centre of the foot was calculated from the four foot markers (calcaneus, $1^{st,}$ and 5^{th} metatarsal head and 2^{nd} distal phalanx head) at midstance (as detected by CueFors1 gait event detection validated in Chapter 3.1), and was used to define the error between the centre of foot and the centre of the target.

5.1.4 Familiarisation

Participants were familiarised with walking on the treadmill for about 3 minutes: for each participant, self-selected walking speed (SSWS) was determined by gradually increasing speed from 1 km/h with 0.1km/h increments until participants felt they were walking faster than preferred, speed was then reduced in 0.1km/h increments until participants reported that the speed was comfortable. This speed was used as their SSWS for the rest of the experiment. After participants reached their SSWS, they walked (without targets) for 1 minute. Targets were then projected on the treadmill positioned at participants' usual step lengths and widths to allow participants to become acquainted with target stepping. If participants felt uncomfortable with the SSWS during target stepping, a new SSWS was identified at which participants felt they could comfortably walk to the targets for a minute. After this minute of familiarisation with target stepping, participants walked without targets on their final SSWS for 30 seconds; in this period, step length and width were calculated for the left and right side to inform future target locations.

5.1.5 Experimental setup and protocol

Participants stepped to targets projected onto the C-Mill (see figure 5.1), at locations determined according to each individual's step length and width for both the left and the right leg, while walking at SSWS. Stroke survivors wore a safety harness to prevent falls, this harness did not provide any support for weight or balance.

All participants were asked to fulfil sixteen trials of 100 steps each (table 5.1) in one visit: one preferred stepping trial (all targets on preferred foot positioning), and three trials of each of the 6 conditions, 1.) Baseline walking, 2.) Preferred targets, 3.) Unsupported planned, 4.) Unsupported reactive, 5.) Supported planned, 6.) Supported reactive, see table 5.1. Only one trial of preferred target stepping was carried out as it would provide sufficient (100 subsequent foot falls) foot placement errors. The different conditions were selected to allow investigation of each factor thought to play a role in gait adaptability/foot placement control.

These 16 walking trials were presented in a randomised order and interspersed with the baseline trials as the 1st, 8th and 16th trial (figure 5.2). Baseline trials were performed on the 1st, 8th and 16th trial to allow for correction of global drift in the fNIRS data (in chapter 8). All trials together accounted for a total of 1600 steps, less than half of what has been shown to be manageable (Holleran et al, 2014) in a 1-hour session with stroke survivors of similar mobility (inclusion/exclusion criteria were the same). Rests were planned every 100 steps and could also be taken at any time should the participants or researchers deem them necessary. We therefore anticipated that the intensity of the protocol was well within the comfortable limits of both stroke survivors and healthy adults.

Table 5.1 *Description of trials*

Number of trials	*Condition*	*Steps required (total of 100 for every trial)*	*Data reporting per chapter*
3	Baseline	No targets (100 steps)	Executive function (chapter 8)
1	Preferred target stepping	• At preferred foot placement location (100 targets) • Visible for the length of the treadmill in front of the participant (2 metres).	Executive function (chapter 8)
3	Unsupported planned	• Adaptation targets (6 lengthening, 6 shortening, 6 narrowing, 6 widening), interspaced with 74 preferred targets • All visible for the length of the treadmill in front of the participant (2 metres). • No support.	Balance (chapter 6) Response time (chapter 7) Executive function (chapter 8)
3	Unsupported reactive	• Adaptation targets (6 lengthening, 6 shortening, 6 narrowing, 6 widening), interspaced with 74 preferred targets • All visible from contralateral midstance • No support.	Response time (Chapter 7)
3	Supported planned	• Adaptation targets (6 lengthening, 6 shortening, 6 narrowing, 6 widening), interspaced with 74 preferred targets • Visible for the length of the treatment in front of the participant • Support from elbow crutches.	Balance (Chapter 6)
3	Supported reactive	• Adaptation targets (6 lengthening, 6 shortening, 6 narrowing, 6 widening), interspaced with 74 preferred targets • Visible from contralateral midstance • Support from elbow crutches.	Balance Response time Executive function (not analysed within this thesis)

c

Figure 5.1 *Overview of the lab setup, the C-Mill with forearm crutches installed on the sides to stabilize participants and projections on the treadmill. fNIRS were positioned next to the treadmill.*

In total fourteen young, eleven older healthy adults and eleven stroke survivors took part in the experiment. For the balance chapter (chapter 6) data was complete of the supported and unsupported planned target stepping tasks for thirteen young, ten older healthy adults and eleven stroke survivors. The response time chapter (chapter 7) included complete planned and reactive target unsupported target stepping conditions for eleven young, ten older healthy adults and eleven stroke survivors. For the executive function chapter (chapter 8) included fNIRS data of the baseline walking, preferred target stepping and the unsupported planned trials of nine young, seven older healthy adults and nine stroke survivors.

In each target stepping condition trial consisted of 100 steps, 24 were adaptation steps (6 shortening, 6 lengthening, 6 narrowing, 6 widening) interspersed semi-randomly with 76 preferred foot landing targets (see figure 5.3). Adaptation targets were randomised between step 10 and step 100 of each trial and interspersed with at least two preferred target steps; this allowed participants to synchronise with the target stepping paradigm for the first 10 steps, and limit carry-over effect from one adaptation step/direction to the next. In the preferred target stepping trial, all targets were positioned at the preferred foot landing position; step length and width were on-line determined by the centre of pressure in CueFors1. For the narrowing and widening steps, step width was altered by -50%, resulting in narrowing steps on the midline of the treadmill, as in the pilot study (Chapter 4) and widening steps were adjusted with the same magnitude as narrowing steps (+50%). For lengthening and shortening steps, steps were either shortened or lengthened by 25%, remaining with the same adjustments as in the pilot study (Chapter 4).

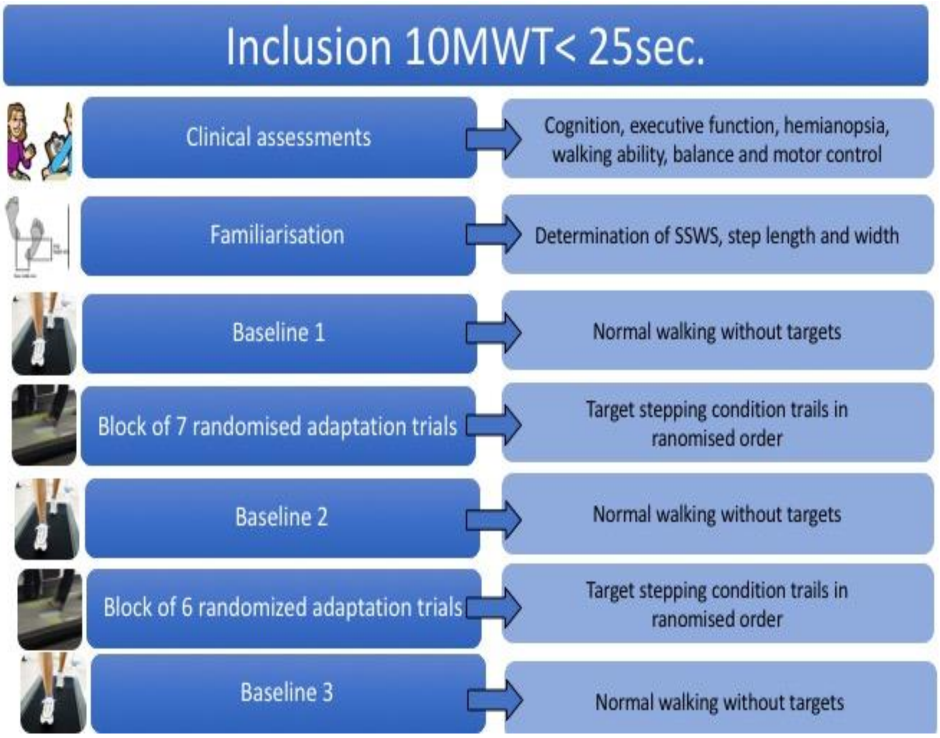

Figure 5.2 *Schematic representation of the protocol.10 MWT <25s (10meter walking test completed within 25 seconds as an inclusion criteria).*

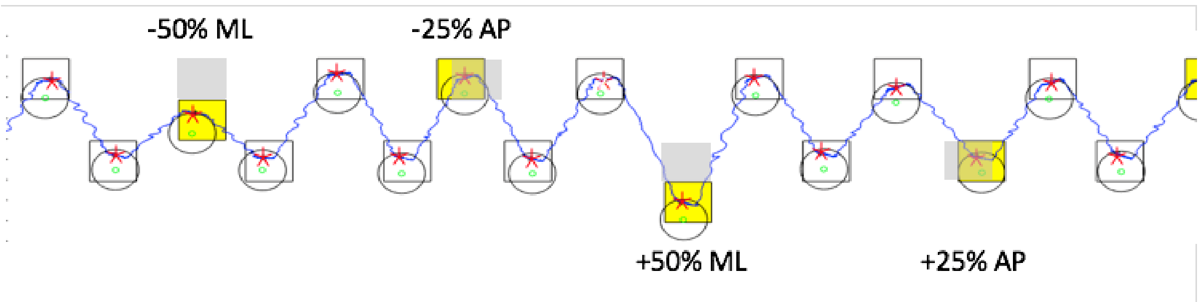

Figure 5.3 *A schematic representation of the target positioning on the treadmill, white squares are preferred target positions, yellow targets represent the targets requiring adaptations to foot placement (short/long, wide/narrow) with grey shadow of where the target would have been for preferred foot location. The Blue line represents the centre of pressure trajectory of one participant with the red asterisk representing centre of pressure at midstance. The green circle represents the centre of foot at time of midstance with the representation of the foot (larger circle around the centre of foot). AP, adjustments in anterior/posterior direction; ML, adjustments in medio-lateral direction.*

5.1.6 Measure of stepping performance

Firstly, the percentage of misses for a given condition was reported to get a general overview of how well participants were able to adjust foot placement to the targets. This percentage of misses was calculated as the number of misses divided by the total number of steps taken in that condition (i.e. if all three trials of every condition were carried out successfully, the de nominator for each condition would be 300 steps). Percentage of misses was based on centre of foot position; the size of the foot was projected around the centre of the foot and overlaid on the centre of target, a miss was recorded when no part of the foot was touching the target. Off-line kinematic analysis to calculate CoF was used (see apparatus) determine centre of the foot, foot length and width were taken in account to calculate hits-and-misses.

In addition to percentage of targets missed, stepping error was used to measure accuracy of foot placement control. This stepping error was defined as the distance of the centre of foot to the centre of target. As described previously in Chapter 3, centre of foot error gives insight into the level of accuracy participants can achieve given the task instruction: "step onto the targets with no part of the foot overhanging the target".

The error of foot placement was analysed separately in the medio-lateral and anterio-posterior directions for all steps. Mean error per participant was used to analyse the direction of error (average tendency to undershoot vs. overshoot targets medial vs. lateral deviation of narrowing steps). Absolute error was used to compare the magnitude of error between the different steps (preferred, narrowing, widening, lengthening and shortening); variable error was used as a measure of consistency, using the variability around the mean of a participant's foot placement: $\sqrt{\sum (x_i\text{-}M)^2/ n}$ (R. A. Schmidt & Lee, 1999), where the square root is taken as the sum of the squared differences between the mean (M) and the foot placements (xi) divided by the number of foot placement (n).

5.1.7 Statistics

Repeated measure analysis of covariance (ANCOVA) was conducted for the mean error measures (mean, absolute and variable). Within factors were the conditions of interest for the specific aahpter, the directions of target steps (preferred, shortening, lengthening, narrowing, widening), and side (left, right fot healthy and paretic, non-paretic for stroke). The between factor was group, and a covariance of SSWS was used. walking speed was used as a covariate in both ANCOVA analyses as speed differs between participant groups and is known to be related to balance control when target stepping (Hollands et al 2016).

Percentage of misses were angular transformed to stabilise the variance, similar to previous foot placement studies (Hoogkamer et al., 2015; van Swigchem et al., 2013). After this transformation, repeated measures analysis of variance (ANOVA) was conducted for the difference conditions (preferred, unsupported planned, unsupported reactive, supported planned). For details on specific statistical analyses, see the specific Chapter. Post hoc comparisons were assessed using Bonferroni test adjusting for multiple comparisons. The software package SPSS (version 24.0) was used. A $p< 0.05$ was used for statistical significance.

6 The effect of balance on target stepping accuracy.

6.1 Introduction

Understanding how foot placement is controlled and adaptations to steps during walking are achieved, is important because altering foot placement is the most effective means of balance control when walking (Winter, 1987, 1995). Balance impairments are common after stroke and balance deficits are known to be related to poor mobility, reduced functions of daily living and increased number of falls (Au-Yeung, Ng, & Lo, 2003; Garland, Willems, Ivanova, & Miller, 2003; Morgan, 1994). These balance impairments may contribute to a reduced foot placement control (or vice-versa i.e. balance impairments may be due to poor foot placement control) which might be one of the causes of increased risk of falling and generally poorer independent mobility for stroke survivors (Blennerhassett et al., 2012; Hyndman et al., 2002; Smith et al., 2006).

Balance traditionally is specified by the position of the centre of mass within the base of support (BoS) and so, is intrinsically linked with foot placement which defines the BoS. The larger the BoS the larger the area over which the CoM can travel without approaching the limits of stability. Consequently, foot adaptations that limit the size of the base of support (e.g. step shortening and narrowing) might be the most difficult to achieve accurately compared to adjustments which enlarge the BoS (e.g. lengthening and widening). When making individual steps from standing, it has been shown narrowing steps are less accurately achieved than widening steps in healthy adults (Nonnekes et al., 2010; Reynolds & Day, 2005a). When adapting foot placement while walking, Hoogkamer et al. (2015) showed that shortening steps were missed the more than widening and lengthening steps. These findings support the idea that limiting the size of the base of support, either narrowing or shortening, increases stepping error even in healthy adults. However, this does not explain why widening steps are missed more often than lengthening steps. The different magnitudes of error reported by studies for the different directions of adaptation might be explained by the throw and catch model (Bancroft & Day, 2016). The throw and catch model, stipulates that the direction and momentum of the body during push-off are specific to the intended landing position of the foot. So, the BoS (foot placement) is planned according to the direction and size of the momentum of the centre of mass (the body) and accurate foot placement control is therefore intrinsically important for balance control.

During forward walking the centre of mass naturally has forward momentum so to make medio-lateral steps adjustments this momentum would need to be redirected sideways. Directing body momentum sideways to step more widely or narrowly might be expected to be more challenging than slowing or speeding up already existing anterior momentum to reach shortening and lengthening targets. Indeed, greater difficulty changing lateral momentum has been described in studies of passive walkers (2 legs with a hinge joint) in which small step adjustments in the anterior-posterior direction (shortening and lengthening) were able to be made passively where-as medio-lateral (narrowing and widening) step adjustments required active stabilization (Kuo, 1999). Other studies have also shown step widening requires higher peak hip abduction moments (Hurt & Grabiner, 2015). These findings indicate the required direction of foot placement adjustment is a factor affecting both the accuracy of foot placement control and the consequences on balance (direction and magnitude of the momentum of the body within the base of support) in healthy adults.

Balance deficits are common after stroke, but we know very little about how these impairments affect foot placement control and adaptability of foot placement when walking. Our pilot study (chapter 4) showed stroke survivors missed more narrowing targets than more than any other directions of stepping adjustments. This finding is in line with those of Nonnekes et al. (2010) who showed, stroke survivors had larger errors narrowing their step from standing than widening. However, when balance was supported by crutches similar amounts of error were seen for both widening and narrowing steps. The fact that balance support reduces foot placement error and that medial step adjustments, which narrow the base of support, are missed more often by stroke survivors highlights that balance control is an important factor limiting foot placement accuracy/ability in stroke survivors. Further support for the idea that balance control and ability to adjust steps are intrinsically linked comes from the observation that clinical measures of balance after stroke are significantly correlated with the speed at which stroke survivors can walk when adapting foot placement to targets (K. L. Hollands et al., 2016). However, none of these studies have yet tested how balance affects foot placement accuracy while walking in stroke survivors, and whether impaired foot placement control could be aided with walking aids providing balance support. Establishing the role of balance deficits and the effects of crutch support on control of foot placement for stroke survivors is particularly important as crutches/walking aides are often prescribed but, sometimes linked with increased falls risk in neurological patients (Stolze et al., 2004).
In addition to the potential role balance deficits play in limiting foot placement control in stroke survivors, motor control deficits of the lower limb may also affect accuracy of foot

aiming differentially across paretic and non-paretic limbs. K. L. Hollands et al. (2016) found that the number of targets missed with the paretic leg was related with clinical measures of lower limb motor recovery after stroke. However, in the few existing studies of stroke survivors' abilities to alter foot placement, no differences in stepping errors between paretic and non-paretic limbs were found (Nonnekes et al., 2010). However, in a study of obstacle avoidance (Said et al., 2008) an increased separation between centre of pressure and centre of mass (a reflection of balance control) in paretic limb stance, compared to the non-paretic was found. Good balance control on the paretic leg is important to endure a stance phase while aiming with the non-paretic leg. If there is no stable base on the paretic stance limb, control of non-paretic foot placement might be affected. Given theoretical reasons for foot placement control to be deleteriously affected in both paretic and non-paretic limbs and for the confounding role of balance in supporting lower limb aiming, it remains to be seen if foot placement accuracy is different in paretic and non-paretic limbs when stepping with and without balance support.

Given the overall paucity of research examining the role of balance in the control of foot placement accuracy and the need to understand how balance may contribute differently to the accuracy of step adaptations in different directions and when stepping with the paretic and non-paretic leg. The aim in this chapter is to measure the influence of balance on stepping accuracy, which will be achieved by the following questions: 1) Does balance support affect stepping accuracy? 2) Do stroke survivors benefit more from support than healthy counterparts? 3) Does balance support improve accuracy of step adaptations in some directions more than other directions? 4) Does balance support influence accuracy of foot placement differently for the paretic and non-paretic legs?

6.2 Methods

The general methods of participant recruitment, clinical assessments, apparatus, familiarization, and stepping performances are as explained in the methods chapter (Chapter 5: General Methods). In this specific chapter the percentage of misses and the three error measures are used to compare foot placement accuracy when stepping to targets without balance support (walking to an adaptability target stepping paradigm without the support of crutches) and with balance support (walking to an adaptability target stepping paradigm with the support of crutches, see fig 6.1.

6.2.1 Protocol

The main protocol is the same as discussed in the general methods (Chapter 5: General methods). However, to study the effect of balance during target stepping while walking, two forearm gutter crutches where installed next to the treadmill to provide comparable stabilization to the study by Nonnekes et al. (2010). In some studies participants have been stabilised by elastic bands (Bruijn, Van Dieen, & Daffertshofer, 2015; Donelan, Shipman, Kram, & Kuo, 2004) however, in the study here is chosen to stabilise participants with similar to the study done on target stepping from during standing (Nonnekes et al., 2010). In addition, using crutches to stabilise participants employs a method that is similar to that being used in practice (i.e. walking aids as crutches and rollators). Arguably stabilizing people with either elastic bands, handle bars, or forearm crutches could be comparable to walking with a walking frame or rollator. The armrests are adjustable to the individual's height, and the paretic arm can be fixated with a strap.

6.1.2 Statistics

Statistical analysis was done similar to previous foot placement studies, percentage of missed targets was angular transformed to stabilize the variance and reach normal distribution (Hoogkamer et al., 2015; van Swigchem et al., 2013), and compared between different conditions (unsupported and supported) with a repeated measures ANOVA.

A repeated measure ANCOVA and ANOVA were conducted for the three measures of stepping error (absolute, mean and variable) in anterio-posterior stepping direction however, no significant effects were found for variable error so results for this measure will be reported in supplementary tables. In general, the ANCOVA will be reported, except when significant differences were only found in the ANOVA, this will be specified in the results. The within subject factors were condition (unsupported, supported), steps (shortening, preferred and lengthening) and side for stroke survivors (paretic and non-paretic and healthy left and right), groups are between subject factor. No differences between left and right legs in the healthy participants were expected or found, no separate reportage will be made for left and right leg in healthy participants. The same within and between factors were used for medio-lateral stepping adjustments, only the step factor different steps were used (narrowing, preferred and widening). When comparing groups results were covaried for walking speed as speed differs between participant groups and is known to be related to balance control (Hollands et al 2016). Post hoc comparisons were assessed using Bonferroni test with adjustment for multiple comparisons. The software package SPSS (version 24.0) was used. A $p < 0.05$ was used for statistical significance.

6.3 Results

6.3.1 Participants

13 young adults, 10 older adults and 11 stroke survivors (participant demographics see table 6.1) took part in the study. According to suggested thresholds for SSWS of stroke survivors (H. Schmidt, Werner, Bernhardt, Hesse, & Kruger, 2007), two participants were non-functional walkers (<0.4m/s), seven limited outdoor walkers (0.4-0.8m/s) and two healthy walkers (>0.8m/s). Three healthy older and one young adult were healthy walkers (0.4-0.8m/s) and the rest of the healthy adults walked at SSWS exceeding the 0.8m/s limit. According to the suggested thresholds for Berg balance scores, one stroke survivor should be walking with assistant device (score <40) (K. O. Berg et al., 1992), two had higher risk of falls (score <45) (K. Berg, Wood-Dauphinee, Williams, & Maki, 1988).

Table 6.1 *Participant demographics and clinical characteristics represented in mean± SD unless specified differently.*

	Young adults	Older adults	Stroke Survivors
N(F)	13(8)	10(4)	11(2)
Age (years)	30.2± 6.3	64.3± 8.3	66.7±9.4
SSWS (m/s)	1.09± 0.17	0.91± 0.21	0.54± 0.21
Trial making test A (s)	25± 11	28± 13	56± 36
Trial making test B (s)	50± 26	57± 28	406± 919
Montreal cognitive assessment	-	27.8± 1.8	26.6± 2.9
Falls (in last 12 months) (N)	-		
0 fall		9	5
1 fall		1	1
1< falls		0	2
Time since stroke (months)	-	-	87.5± 13436
Paretic (Right)	-	-	5
Berg balance	-	-	50.4± 5.4

Fugl-Meyer (lower limb)	-	-	26± 5.6
Dynamic gait index	-	-	24.8± 4.6
10m-walking speed (s)	-	-	12.8± 4.3
Timed up and go (s)	-	-	16.7± 5.9
Apples test	-	-	46.4± 10.1

6.1.2 Does balance support affect stepping accuracy?

6.3.2.1 Hits and misses:

When investigating the percentage of misses no significant differences were found between the supported (Mean± SEM 3.5± 1.4%) and unsupported (3.4± 1.2%) walking conditions (figure 6.1).

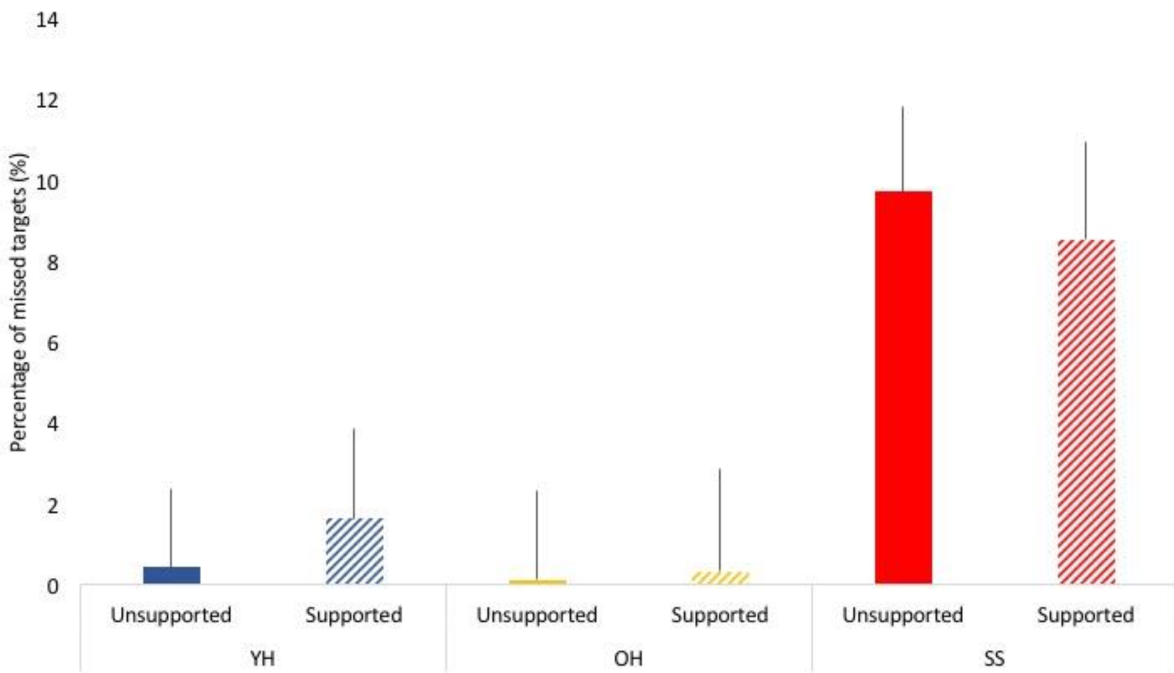

Figure 6.1 *Bars represent the mean percentage of target misses for young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red, for each type unsupported (solid) and supported (striped) conditions. Error bars represent standard error of the mean.*

6.1.2.1 Size of error (Absolute error):

For absolute error, a main effect for condition is found in anterio-posterior direction (F (1, 30) =13.518, p=0.001); the magnitude of error was significantly greater in the unsupported (5.2± 0.5cm) than in the supported condition (4.1± 0.4cm), see figure 6.2.

Medio-lateral adaptations show a main effect of condition (F (1, 30) =18.141 p<0.001), in the supported condition error (1.9± 0.2cm) has significantly less magnitude than the unsupported condition (2.3± 0.2cm). See figure 6.5.

6.1.2.2 Direction of error (Mean error):

A main effect of condition was found for mean error as well (F (1, 30) = 5.199, p=0.021). The unsupported condition (-2.0± 0.7cm) was undershot more than the supported condition (-1.0± 0.6cm) in anterio-posterior direction, see figure 6.4. Medio-lateral mean error did not show a main effect of condition. The supported condition (-0.5± 0.1cm) did not have a different direction of error than the unsupported condition (-0.4± 0.1cm), see figure 6.6.

6.1.3 Do stroke survivors benefit more from support than healthy counterparts?

6.1.3.1 Hits and misses:

A main effect of group was found for the percentage of misses (F (2, 31) =11.091 p=0.001). Stroke survivors in general missed (9.13 ± 2.07%) significantly more targets than healthy young (1.03± 1.91 %,) and older adults (0.22± 2.18 %,) in both supported and unsupported target stepping conditions. No interaction effect was found for group and condition (F (4, 62) =3.756) such that support was not seen to reduce targets missed for stroke survivors more than healthy young or older adults. See figure 6.2.

6.1.3.2 Size of error (absolute error)

No main effect of group was found (AP F (2,30) =0.427,), young (AP 4.2± 0.7cm, ML 1.3± 0.3cm), older (3.8± 0.8cm, ML 1.6± 0.3cm) healthy adults, and stroke survivors (AP 5.8± 0.8cm, ML3.3± 0.3cm) had similar magnitude of error when covaried for speed. We investigated whether balance support affected the absolute error differently for stroke survivors (AP unsupported 7.0± 0.9cm and supported 4.7± 0.7cm, ML unsupported 3.6± 0.3cm and supported 3.0± 0.3cm) compared to healthy young (AP unsupported 4.2± 0.8cm and supported 4.2± 0.6cm, ML unsupported 1.5± 0.3cm and supported 1.2± 0.3cm) and older (AP unsupported 4.3± 0.9cm and supported 3.4± 0.7cm, ML unsupported 1.7± 0.3cm and supported1.4± 0.3cm) adults. No interaction of condition and group (F (2,30) =0.656) was found due to covariation for SSWS. See figure 6.3 for anterio-posterior and 6.5 for medio-lateral.

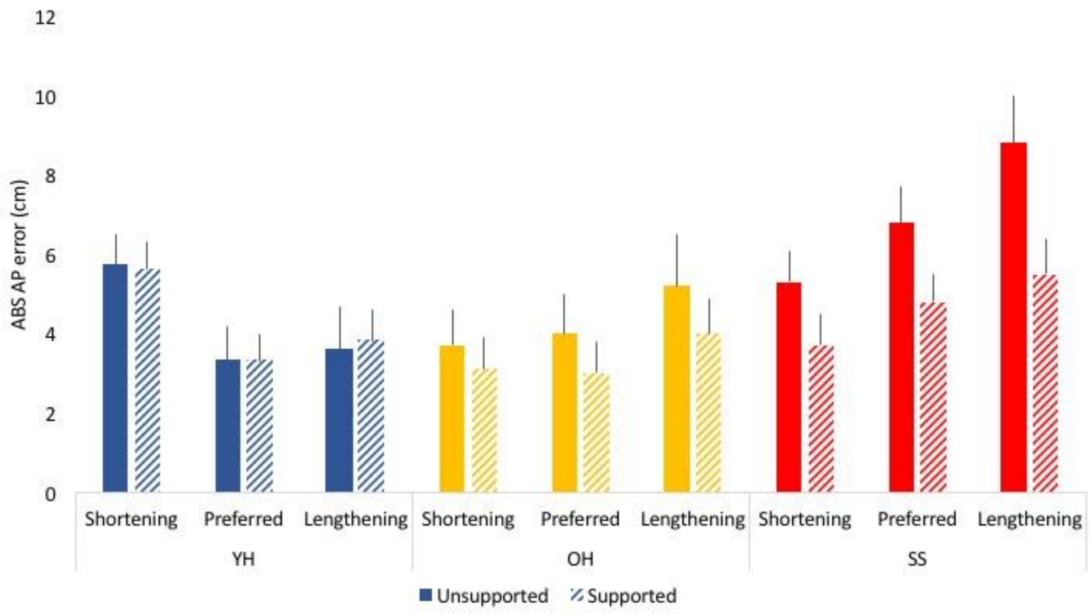

Figure 6.2 *Bars represent the absolute error in anterio-posterior direction of foot placement for young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red, for each type both unsupported (solid) and supported (striped) conditions in anterio-posterior (AP) stepping error for shortening, preferred and lengthening steps.*

6.1.3.3 Direction of error (mean error)

No main effect of group (F (2,30) =0.713) or interaction for group and condition (F (2,30) =0.204) was found for mean error in anterio-posterior direction when covaried for SSWS. This was despite large differences in mean error for stroke survivors between supported and unsupported conditions (unsupported -5.4± 1.3cm, supported -2.6± 1.0cm). A lack of significant interaction between supported and unsupported conditions across stroke survivors, young (unsupported 1.5± 1.2cm, supported 1.2± 0.9cm) and older (unsupported -2.1± 1.3cm, supported -1.5± 1.1cm) healthy adults, is due to the covariance for walking speed as a main effect of group (F (2,31)= 6.805, p=0.004) and condition (F(1.31)= 6.159, p=0.019). See figure 6.3.

No main effect of group (F (2,30) =0.002) or interaction for group and condition (F(2,30)= 0.496) was found for mean error in medio-lateral direction, stroke survivors (unsupported -0.5± 0.2cm, supported -0.4± 0.3cm) had no significant error reduction due to support as young (unsupported 0.3± 0.2cm, supported 0.4± 0.2cm) and older (unsupported -0.3± 0.2cm, supported -0.5± 0.3cm) healthy adults, see figure 6.5.

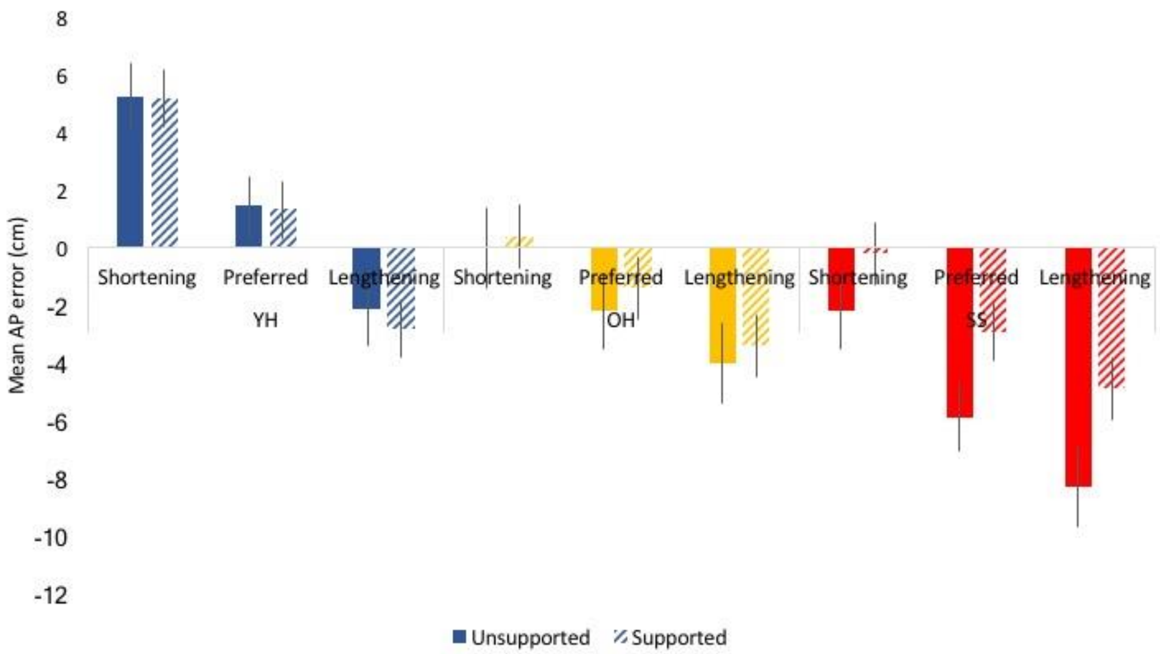

Figure 6.3 *Bars represent the mean error of foot placement for young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red, for each type both unsupported (solid) and supported (striped) conditions in anterio-posterior (AP) stepping error for shortening, preferred and lengthening steps.*

6.1.4 Does balance support improve accuracy of step adaptations in some directions more than other directions?

6.1.4.1 Size of error (absolute error)

A main effect of step direction was found for the anterio-posterior direction such that absolute error when lengthening (5.2± 0.6cm) steps (covaried for SSWS: F (2, 29) =14.423, p=0.005, without covariation: F(2,30)= 15.025, p<0.001) was significantly greater than preferred steps (4.2± 0.5cm), but not significantly different from shortening (4.5± 0.4cm). No interaction effect for condition and direction of step was found (F (1,30)= 2.528). Unsupported steps in all directions (short (4.9± 0.5cm), preferred (4.7± 0.5cm), lengthening (5.9± 0.7cm)) had similar magnitude of error as supported steps (short (4.1± 0.4cm), preferred (3.7±0.4cm), lengthening (4.4± 0.5cm)). An interaction effect of group and step direction was found (F (4, 60) = 2.848, p=0.031). Young healthy adults have higher magnitude of error when shortening (5.6± 0.7cm) their steps then older healthy adults (3.4± 0.8cm) and stroke survivors (4.5± 0.7cm). For preferred and lengthening steps young healthy (preferred 3.3± 0.8cm, lengthening 3.7± 0.9cm) have less magnitude than older healthy adults (preferred 3.5± 0.9, lengthening 4.6± 0.1cm) and stroke survivors (preferred 5.8± 0.8cm, lengthening 7.2± 1.0cm), see figure 6.2.

For medio-lateral step adjustments, preferred widening and narrowing steps, a main effect is found (F (2, 29) =10.183, p<0.001), where both widening (2.5± 0.4cm) and narrowing (2.3± 0.2cm) had increased absolute error over preferred (1.4± 0.1cm), target stepping. No interaction effect for condition and direction of steps was found (F (1,30)= 0.571), meaning that no particular step had significantly more decreased stepping error while supported for balance than other steps. However, without the covariation for SSWS an interaction of condition and direction was found (F(1,31)= 11.616, p<0.001) with narrowing steps showing a decline in foot placement when supported (unsupported 2.8± 0.2cm, supported 1.8±0.1cm). Nor an interaction effect of step direction and group has been found (F (2,30)= 0.123, F(1,31)= 2.376), young (narrowing 1.8± 0.3cm, preferred 1.1± 0.2cm, widening 1.1± 0.6cm) older (narrowing 1.7± 0.3cm, preferred 1.2± 0.2cm, widening 1.9± 0.7cm) healthy adults and stroke survivors (narrowing 3.4± 0.3cm, preferred 1.9± 0.2cm, widening 4.6± 0.7cm) have similar magnitudes of error when covaried for SSWS, see figure 6.4.

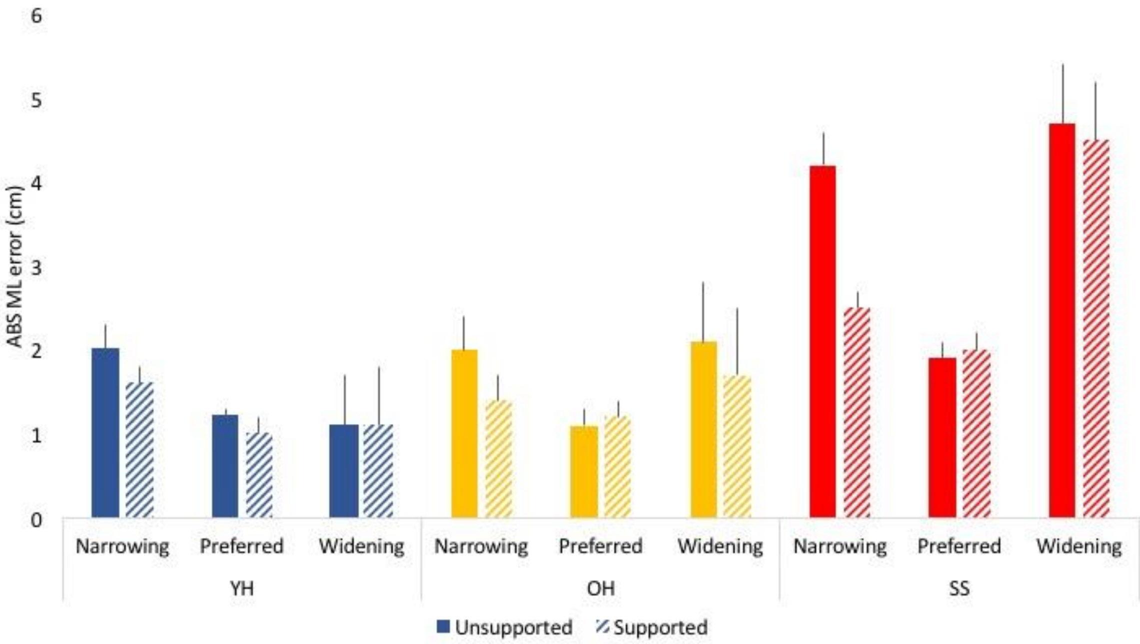

Figure 6.4 *Bars represent the absolute error in medio-lateral direction of foot placement for young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red, for each type both unsupported (solid) and supported (striped) conditions in anterio-posterior (AP) stepping error for shortening, preferred and lengthening steps.*

6.1.4.2 Direction of error (mean error)

A main effect of direction of step was found for mean foot placement error in anterio-posterior direction (F (2, 29) =117.313, p<0.001). All steps had significantly different mean error with shortening steps (1.0± 0.7cm) over-shot, and preferred (-2.4± 0.7cm) and lengthening (-5.1± 0.8cm) steps under-shot. See figure 6.1a. No interaction effect is found for the direction of error for condition and step in anterio-posterior direction (F (1,30)= 1.118). Shortening (unsupported 1.0± 0.7cm, supported 1.8± 0.6cm), preferred (unsupported -2.2± 0.7cm, supported -1.0± 0.6cm) and lengthening (unsupported -4.8± 0.8cm, supported -3.7± 0.6cm) steps all have similar change in direction of error du to support. An interaction effect for the mean error in anterio-posterior stepping directions was found for group and direction of steps (F (4, 60) = 3.720, p=0.009). Young overshot shortening (5.2± 0.1cm) and preferred (1.2± 0.9cm) steps and undershot lengthening steps (-2.4± 0.1cm), Older healthy adults just overshot shortening (0.2± 1.2cm) steps and undershot preferred (-1.8± 1.2cm) and lengthening (-3.7± 1.2cm) steps. Stroke survivors undershot all steps; shortening (-1.2± 1.1cm), preferred (-4.4± 1.2cm) and lengthening (-6.6± 1.2cm) steps. See figure 6.3.

No main effect is found for the direction of error in medio-lateral stepping directions (F (2,29) =1.465). Narrowing (-0.2± 0.2cm), preferred (-0.4± 0.1cm) and widening (-0.6± 0.2cm) had similar directions or error. Neither an interaction effect for condition and step was found (F (2,60) =0.157), narrowing (unsupported -0.2± 0.2cm, supported -0.3± 0.2cm), preferred (unsupported -0.3± 0.1cm, supported -0.5± 0.2cm) and widening (unsupported -0.7± 0.2cm, supported -0.6± 0.2cm) steps all have similar change in direction of error du to support. Nor an interaction effect is found for group and steps (F (4,60)= 0.585), young (narrowing -0.3± 0.3cm, preferred -0.4± 0.2, widening -0.4± 0.3cm), older (narrowing -0.3± 0.3cm, preferred -0.4± 0.2, widening -0.5± 0.3cm) and stroke survivors (narrowing -0.1± 0.3cm, preferred -0.4± 0.2, widening -1.0± 0.3cm) have similar errors per step adaptation in medio-lateral direction. See figure 6.5.

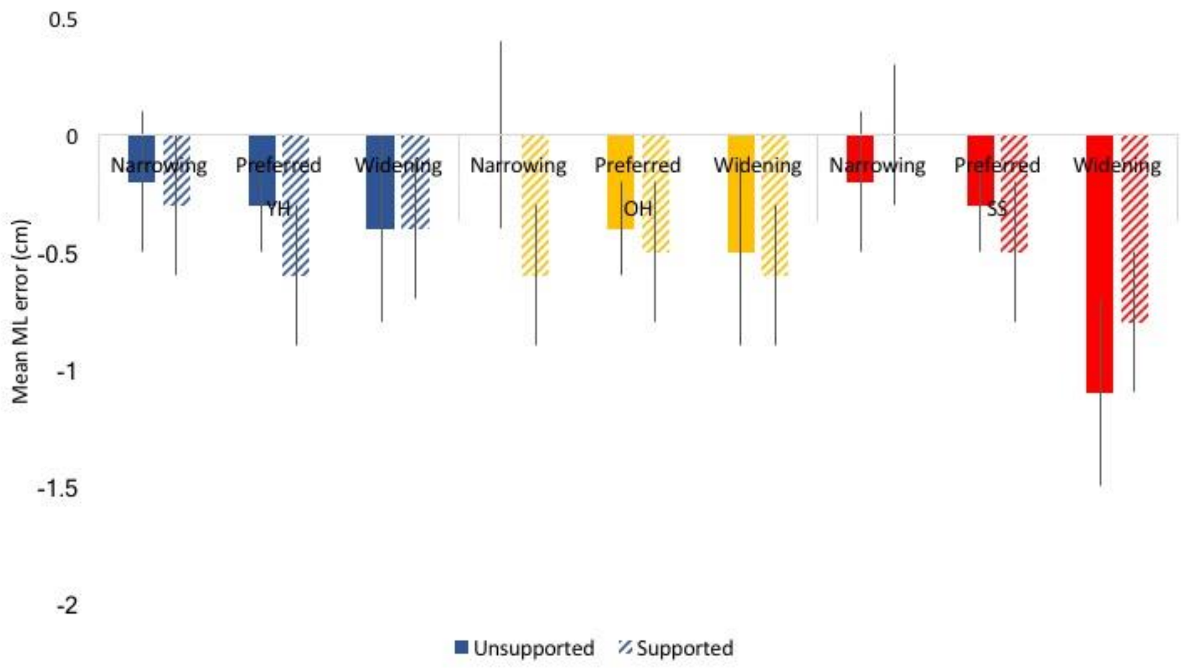

Figure 6.5 *Bars represent the mean error in medio-lateral direction of foot placement for young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red, for each type both unsupported (solid) and supported (striped) conditions in anterio-posterior (AP) stepping error for shortening, preferred and lengthening steps.*

6.1.5 Does balance support influence accuracy of foot placement differently for the paretic and non-paretic legs?

6.1.5.1 Size of error (absolute error)

No main effect of side (paretic and non-paretic) is found within stroke survivors when adapting gait in anterio-posterior direction (F (1,10=1.753). The paretic (anterior-posterior 5.6± 1.1cm and medio-lateral 3.8± 0.6cm) and non-paretic (anterior-posterior 6.1± 1.3cm and medio-lateral 2.9± 0.5cm) did not differ. Nor interaction effects of condition and side (F (1, 10)= 0.002) or direction and side (F (1,10)= 0.050) were found. In anterio-posterior direction the paretic leg (unsupported (6.8± 1.5cm) and supported (4.4± 0.9cm)) had a similar decline in error when supports as the non-paretic leg (unsupported (7.2± 1.5cm) and supported (4.9± 1.2cm)). Similar for medio-lateral step directions the paretic leg (unsupported (4.2± 0.7cm) and supported (3.3± 0.5cm)) and non-paretic leg (unsupported (3.0± 0.5cm) and supported (2.7± 0.5cm)) had a similar decline when supported.

6.1.5.2 *Direction of error (mean error)*

No main effect of side is found for the direction of error ($F(1,10) = 2.678$). The paretic leg (AP (-3.4± 1.4cm) and ML (-0.4± 0.7cm)) has similar direction of error as the non-paretic leg (AP (-4.7± 1.6cm) and ML (-0.6± 0.7cm). An interaction effect is found for condition and side in anterio-posterior direction ($F(1, 10) = 16.176$, $p=0.002$), the direction of error of the paretic (unsupported (-5.3± 1.7cm) and supported (1.5± 1.3cm)) leg decreased in the amount of under-shot when supported more than the non-paretic leg (unsupported (-5.6± 1.9cm) and supported (3.8± 1.4cm)). However, no interaction effect is found for condition and side in medio-lateral direction ($F(1,10) = 0.889$), steps with the paretic leg (unsupported (-0.6± 0.6cm) and supported (0.1± 0.5cm)) have similar direction of error as the steps on the non-paretic side (unsupported (-0.5± 0.6cm) and supported (0.8± 0.6cm)).

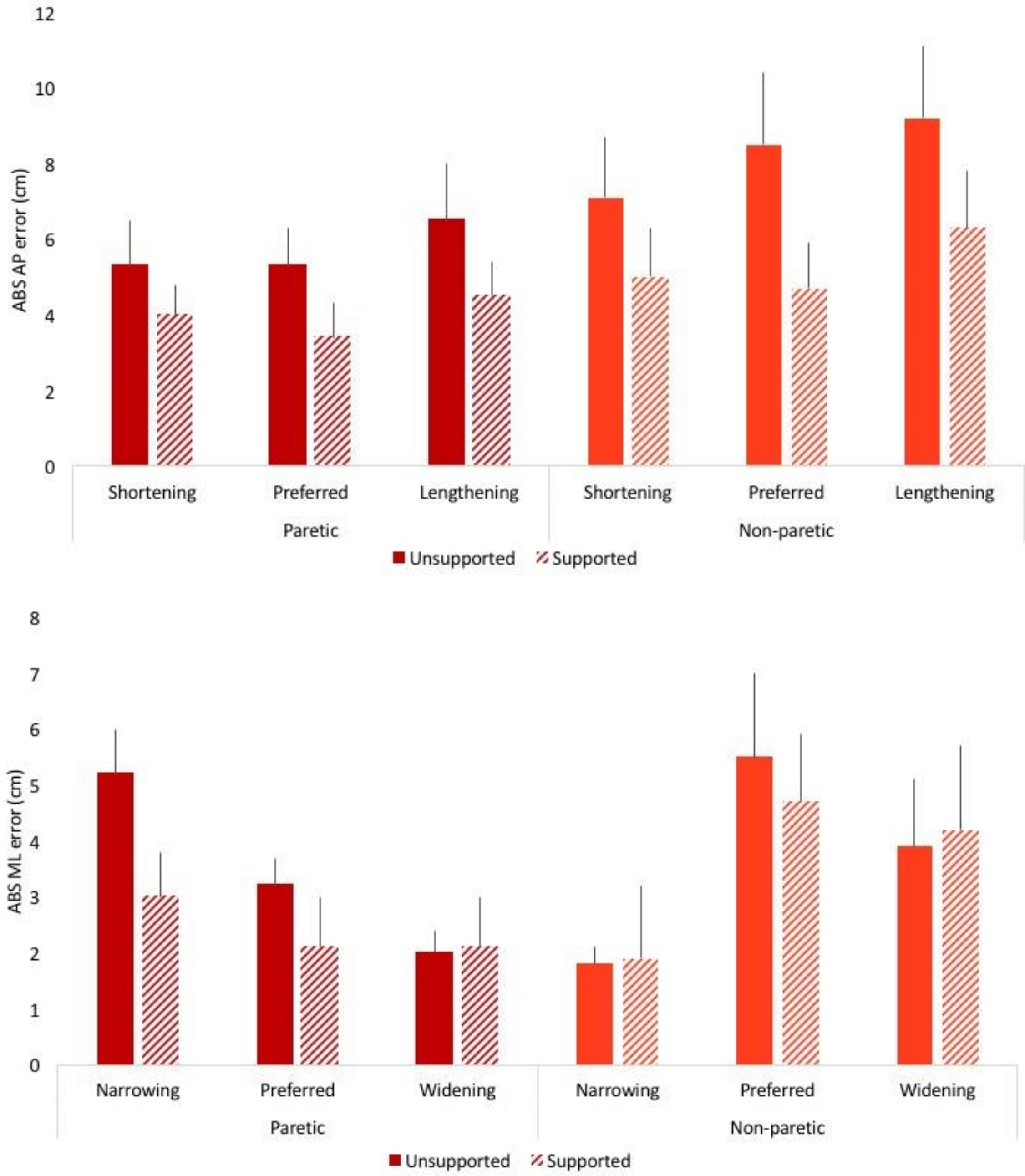

Figure 6.6 *Bars represent the mean absolute error of foot placement for the paretic (red) and non-paretic (bordeaux) side in stroke survivors a) anterio-posterior (AP) error combined for shortening, preferred and lengthening steps, b) medio-lateral (ML) error combined for narrowing, preferred and widening step for both, unsupported (solid) and supported (striped) conditions. Error bars represent standard error of the mean.*

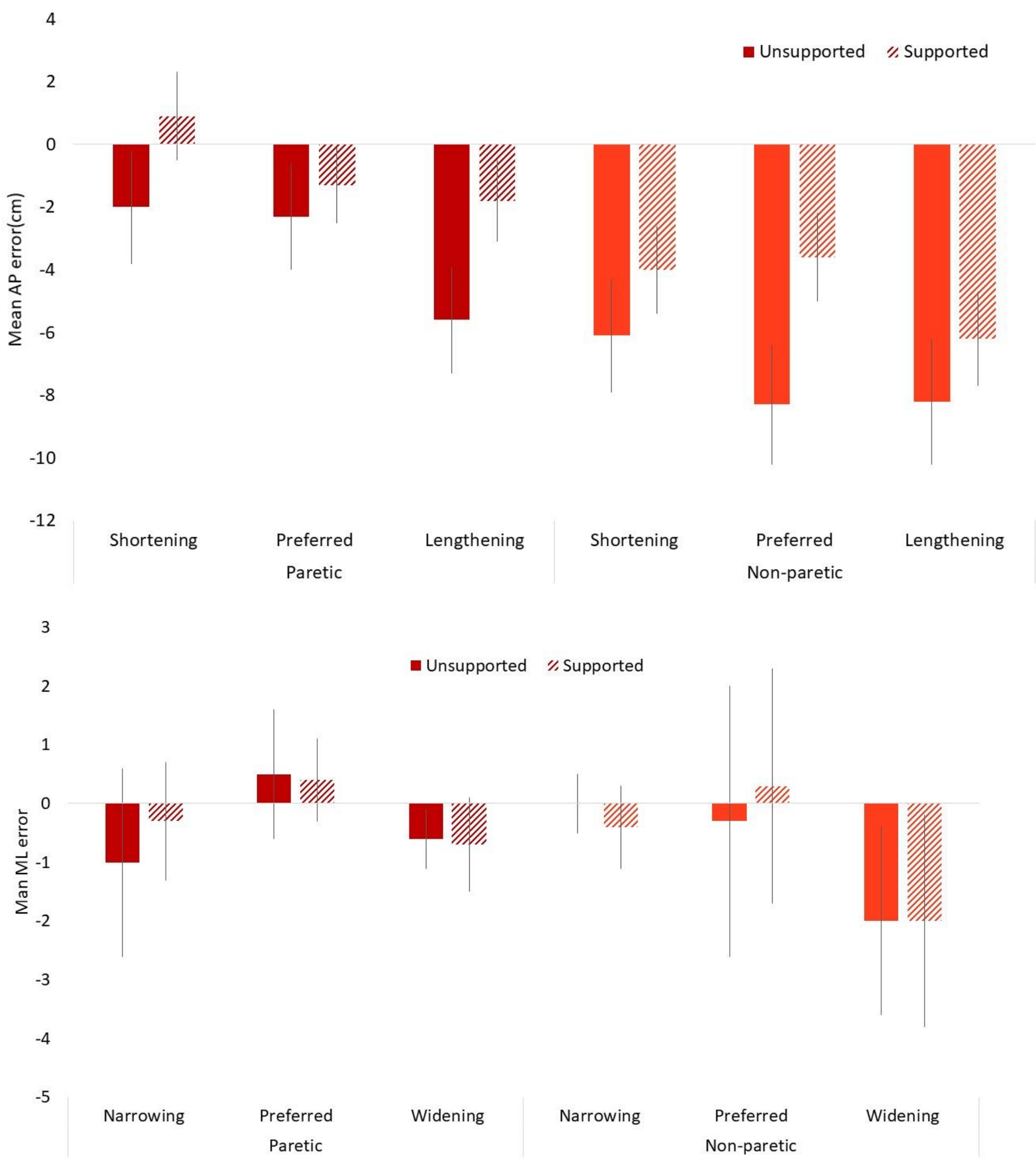

Figure 6.7 *Bars represent the mean error of foot placement for the paretic (red) and non-paretic (bordeaux) side in stroke survivors a) anterio-posterior (AP) error combined for shortening, preferred and lengthening steps, b) medio-lateral (ML) error combined for narrowing, preferred and widening step for both, unsupported (solid) and supported (striped) conditions. Error bars represent standard error of the mean.*

6.4 Discussion

This is the first study to examine the effects of balance on foot placement control during walking in healthy young adults, older adults and stroke survivors. The method used to evaluate balance (support with crutches), mimics clinical approaches to treatment and therefore allows insight into not only the mechanisms of balance control of stroke survivors, but also potential benefits of typical treatments. The results of this study show balance support increases foot placement accuracy for any direction of step adjustment in all participant groups during walking. There were no significant differences in foot placement accuracy between the paretic side and the non-paretic side for stroke survivors and balance support did not improve accuracy more when changing foot placement location in one direction over another. These results suggest balance is important for foot placement accuracy in all directions and that balance support may help stroke survivors, in a general way, when needing to alter foot placement.

6.4.1 Does balance support affect stepping accuracy?

Magnitude of stepping error (absolute error) decreases in both anterio-posterior and medio-lateral directions when support for balance is offered in comparison to when no support is offered, indicating foot placement accuracy benefits from support. However, the number of targets missed and the direction of stepping error (mean error) is not significantly reduced with support for balance for any group. Five stroke survivors missed fewer targets in the supported condition than unsupported, actually missing less targets when supported for balance and indicating some stroke survivors do benefit from support. These five stroke survivors did not show differences in walking speed, balance or coordination based on clinical measures of the 10meter walking test, Berg balance scale and Fugl-Meyer test. While error measures in both anterio-posterior direction and medio-lateral direction did reduce significantly with balance support, compared to unsupported walking, the magnitude of reduction in absolute error was too small to reflect an overall significant increase in the success of target stepping. This is mainly due to the low average percentage of misses and therefore an already low average magnitude of absolute error. The percentage of misses reported, 9% in stroke survivors, is comparable to the percentages of obstacles contacted with the longest response time, around 10%, (first 20% of the gait cycle) found by Den Otter et al. (2005) and slightly higher than the number of missed targets reported by K. L. Hollands et al. (2016) (2.8 of 60 steps). The fact that stroke survivors do miss significantly more targets than healthy adults, even when targets are visible at least two steps ahead, indicates that the target stepping task is challenging enough to reveal impairments and their potential causes. Additionally, if a missed target represents a faulty foot placement adjustment in daily life, the difference between 1% of missed targets in healthy adults and 9% in stroke survivors is likely to increase falls risk. This is especially true if misplaced steps result in a trip or slip and force and foot placement control are declined in stroke survivors making them less able to make a sufficient trip recovery (Pijnappels, Reeves, Maganaris, & van Dieen, 2008). The fact that, support does not significantly decrease the percentage of missed targets, might mean that support does not adequately aid the limitations in foot placement control due to stroke during walking. However, reduction in foot placement error does not need to be big enough to make a difference between target hit and missed to be functionally meaningful. Targets were foot sized for each participant (average 30cm), which means an average error of 30cm has to be made to miss targets in the antrio-posterior direction. When walking unsupported, the average error in anterio-posterior direction was 5.2cm. In the medio-lateral direction margins are smaller (11cm wide on average), requiring errors >11cm to result in a miss. When walking unsupported, errors in the medio-lateral direction were much smaller than this with an average of 2.3cm. The average reduction in absolute error with balance support compared to unsupported was 1.1cm in antero-posterior and 0.4cm in medio-lateral direction.

In a previous study balance support was shown to decrease foot placement error to a greater extent (about 7cm) in stroke survivors than seen in this study (by 9.8cm) in both stroke survivors and healthy controls (Nonnekes et al., 2010). The two main differences between this study and that of Nonnekes et al. (2010) is the difference in target stepping from standing, under time pressure compared to during walking with at least two steps to plan the step adjustment. Support seems to decrease error more when adapting foot placement from standing than during walking. The smaller reduction in stepping error with balance support in walking (compared to standing) may be caused by the dynamic stability afforded by the forward momentum of the centre of mass during walking. Adjusting steps (particularly medially) from a single standing step demands initiation of momentum, followed by termination of momentum and then maintenance of balance in the new, narrowed, stance position. Additionally, larger forces and moments are necessary to make the foot placement adjustments during single stance (Winter, 1995; Winter et al., 1993). In stroke survivors these increased forces and moments necessary to adjust foot placement during single stance, as opposed to foot placement adjustments that can be achieved by altering already existing momentum, might not be feasible due to stroke related compromised force generation (Arene & Hidler, 2009). The second main difference between this study and that of Nonnekes et al. (2010) is that in in this study participants are provided with visibility of the target at least two steps ahead, allowing time to plan the foot placement, whereas in the Nonnekes et al. (2010) study in 40% of the trials the target jumped to elicit narrowing or widening the step at the moment of foot off. The difference in the size of error seen in this study and that of Nonnekes et al. (2010) might mean that balance is more effected when limited time is available to adjust a step. In conclusion, support for balance does generally reduce foot placement error for all participants an in all directions of step adjustment. While, the effect is small when targets are visible two steps ahead during walking, further consideration of interaction effects will help identify if small reductions in error are functionally meaningful and the potential causes of impairment for stroke survivors.

6.4.2 Do stroke survivors benefit more from support than healthy counterparts?

Stroke survivors in general missed more targets than healthy young and older adults. However, they did not have significantly more magnitude (absolute error), or a different direction of foot placement error (mean error) or benefited more from support than young and older healthy adults while walking when the confound of walking speed was covaried for. These results suggest that foot placement accuracy in stroke survivors benefits the same as in young and older healthy adults when being supported for balance while walking. However, when you look at the observed mean absolute error (as opposed to the mean absolute error adjusted for statistical covariance of walking speed), reductions in error due to support for the different participant groups, there certainly is a bigger decrease among stroke survivors (AP 2.3cm, ML 0.6cm) than for young (AP 0.0cm, ML 0.3cm) and older (AP 0.9cm, ML 0.3cm). In fact, stroke survivors do benefit from support whereas for young healthy adults the benefit is negligible. Similarly, in the study by Nonnekes et al. (2010) stroke survivors (7cm) were shown to have greater decline in stepping errors than controls (2cm) when narrowing steps with support than without. The difference of improvement in stepping accuracy du to support shown in the recent study and Nonnekes et al. (2010) and the recent study is big. These differences could be due to differences in study protocols. First, in Nonnekes et al. (2010) shifts in targets were shown during swing phase, only short time was available to plan for the adapted foot placement, while in the recent study at least two steps were available to plan foot placement ahead. The difference in error reduction due to support may be a result of the balance difficulties of making foot placement adaptations during single stance phase, while BoS is small and thus on is more unstable. Secondly, the experiment by Nonnekes et al (2010) was executed from standing and not during walking as in the recent study however, stepping errors were covaried for speed in the recent study foot placement adaptations during walking may be different than from standing. Given the differences seen between errors in the recent study and that of Nonnekes et al (2010), the effects of time pressure and that statistical covariance for speed has eliminated the otherwise statistically significant effects and that previous studies (K. L. Hollands et al., 2016) have shown target stepping speed is correlated with walking speed – these all indicate the potential importance of walking speed/time to respond in accuracy of foot placement.

6.4.2.1 Speed accuracy

Stroke survivors in this study walked more slowly (0.54± 0.21ms) than healthy people (young (1.09± 0.17ms) and older healthy adults (0.91± 0.21ms)) as a direct result of the stroke. The cause of the decreased walking speed in stroke survivors could be due to decreased strength of the lower limb (Arene & Hidler, 2009). Participants in this study had Fugl-Meyer assessment scores of the lower extremity (26± 5.6 out of 34, corresponding with 76.5%) corresponding with a moderate impairment of motor function (P. W. Duncan et al., 1994). A secondary reason stroke survivors walk slower could be because of speed accuracy trade-offs. Reduced accuracy of movement at greater speeds is a well investigated phenomenon (Fitts, 1954). It may be that stroke survivors generally walk slower to compensate for difficulties in controlling accuracy of foot placement that they would otherwise experience at faster speeds. This idea is supported by the study of K. L. Hollands et al. (2016) who showed that Berg Balance Scale scores are related with target stepping speed; so stroke survivors with more stability are able to fulfil a target stepping task at higher speeds. Further, the fact that even healthy young adults have been shown to slow down (compared to SSWS with no targets) when stepping to targets, even when target locations coincide with where participants would normally step (Peper et al., 2015) also supports the idea that speed accuracy trade-offs play a crucial role in foot placement control. Healthy older adults further reduced their walking speed (compared to young healthy adults) when target stepping and, while not significant, older adults tended to slow even more when walking to targets demanding greater step adjustments; indicating that people do alter walking speed to afford themselves the necessary time (in accordance with ability) to accurately control foot placement. In this study SSWS was determined after a minute of target stepping on the treadmill. It is likely therefore that the speed at which target stepping was completed was slower than the SSWS participants would have normally chosen to walk over clear level ground. However, once the SSWS during target stepping was determined this was held for all tasks, so no further decline in walking speed was allowed for more complicated target stepping tasks. If healthy young adults have sufficient control to be accurate, even with complex targets, at faster paces then the consistency of speed on a treadmill may have made the target stepping more challenging for stroke survivors. Given this, covarying for speed will equalize the performance of the groups. However, decreased walking speed and balance (Krasovsky, Lamontagne, Feldman, & Levin, 2013) are direct results of stroke and therefore, covarying for speed accounts for effects we know to be the direct result of stroke. In some ways therefore, comparisons at SSWS without covariance for speed would allow identification of significant results that are due to stroke; but, lack of significant differences when speed is accounted for isolate the importance of walking speed as a characteristic impairment following stroke. Therefore, it can be argued the higher amounts of error in stroke survivors is a result of the foot placement deficits in stroke and not a result of the lower walking speed, as a faster walking speed would theoretically make people less balanced during walking and able to accurately target in general.

6.4.3 Is foot placement accuracy affected more in some directions more than other directions?

In addition to the effect of crutch support for balance on target stepping, the direction of the required foot placement adaptation is likely to affect balance in different ways. Limiting the BoS (narrowing or shortening) is likely to be more threatening for balance than adaptations that enlarge the BoS (widening and lengthening). Additionally, changes to foot placement in the medio-lateral direction could require more force (Hurt & Grabiner, 2015). Therefore, narrowing and shortening steps were expected to be more challenging with higher errors expected in the unsupported condition and potentially larger reductions in error seen when support is offered than for widening and lengthening steps.

6.1.5.3 Does limiting the BoS affect foot placement accuracy?

BoS limiting steps (narrowing and shortening) did not have increased magnitude of error in comparison to BoS enlarging steps (widening and lengthening). Lengthening (AP ABS 5.2cm, Mean -5.1cm), narrowing (ML ABS 2.3cm, Mean -0.2cm) and widening (ML ABS 2.5cm, Mean -0.6cm) had increased error magnitude (absolute error) and different directions of error (mean error) compared to preferred stepping (AP ABS 4.2cm, Mean -2.4, ML ABS 1.4cm, Mean -0.4cm); while step shortening had similar error magnitudes and direction of error as preferred steps. Surprisingly, despite that narrowing steps is known to be a direct challenge to balance when making a single step from a stationary standing position, narrowing and widening steps were seen to have similar error magnitudes, which indicate both step adjustments are equally challenging. The higher peak hip abductor moments during widening steps (Hurt & Grabiner, 2015) shows to be as limiting as the reduction of the base of support. The fact that narrowing and shortening steps does not actually increase error more than widening and lengthening steps indicates the balance challenge thought to be different according to different directions of step is not the only factor affecting accurate foot placement control.

The result that widening has similar errors to narrowing is in contradiction with the results of Nonnekes et al. (2010) that showed medial steps adjustments from standing have higher stepping errors than lateral step adjustments and that of Moraes, Allard, and Patla (2007) who showed shortening and narrowing step adjustments to avoid a sudden obstacle were less successful than widening and lengthening obstacle avoidance steps. So, previous studies demonstrated step narrowing is more challenging that widening both from standing and during walking. The differences between these findings and that of the current study could possibly be explained by differences between studies in the amount of time participants were afforded to adjust their foot placement. In both the study by Nonnekes et al. (2010) and Moraes et al. (2007) the time to adjust foot placement was limited; the target and obstacles were only shown during swing phase of the aiming leg. This could, again, indicate that limited time available to respond (adjustments made during swing phase of the aiming leg) to foot placement adjustments threatens more than foot placement adjustments that can be planned for (targets visible at least two steps ahead), which will be investigated in chapter 7.

6.1.5.4 *Are shortening steps more difficult step adjustments than lengthening steps?*

Surprisingly older healthy adults and stroke survivors had greater magnitude of error (absolute error) in lengthening than shortening steps. The mean error provides an indication of the direction of error and therefore could be used to explain the difference in absolute magnitude of error between young healthy adults and older healthy adults and stroke survivors. Mean error indicates young healthy adults overshoot shortening and preferred steps while they undershoot lengthening steps; this is in agreement with the findings of Hoogkamer et al. (2015). The authors give three possible reasons for the difference in success for shortening and lengthening steps; 1) lengthening steps allow more time to adapt, 2) lengthening is biomechanically more similar to steady state walking than shortening steps and 3) shortening steps reduces margin of stability by reducing the BoS while the centre of mass has forward momentum. However, older healthy adults, and stroke survivors in this study were seen to undershoot all targets; including preferred steps. Undershooting is seen as a negative offset (or mean error) and may account for different magnitudes of error with different step adjustments; preferred and shortened steps are undershot to a small extent (i.e. small magnitudes of absolute error), and lengthening steps who would be expected to be undershot is no attention was payed to the targets (preferred footfall location) are now even undershot more, represented by larger error magnitudes of error. This tendency to fall behind the targets could be due to difficulty synchronising to the targets, similar to the lagging of foot falls to auditory beats seen in other studies (Roerdink et al., 2009). Young healthy adults anticipate foot falls with the beats, so timing of foot falls actually occur just before the beat is perceived (Bank et al., 2011; McIntosh et al., 1997; Roerdink et al., 2011; Roerdink et al., 2007; Roerdink et al., 2009). Stroke survivors are known to lag the beat, with timing of foot falls just after the perceived beat (Roerdink et al., 2009). The fact that this phenomenon is present in both stepping to beats and visual target stepping indicates that stroke survivors have difficulty anticipating and synchronising their steps in time as well as space. This might mean that the anticipation and planning of a foot placement is reduced due to stroke and they need more time to synchronise foot placement and have greater difficulty adjusting with less time to respond.

6.1.5.5 Does balance support improve accuracy of step adaptations in some directions more than other directions?

Previously we discussed shortening and narrowing steps were not associated with increased magnitudes of error and support for balance did not decrease error measures more in shortening and narrowing steps than for lengthening and widening steps. Stroke survivors however, do show a decline in magnitude of error of 1.7cm in narrowing steps and only 0.2cm in widening steps between the supported and unsupported condition, indicating support for balance does help foot placement accuracy when step narrowing is needed. Healthy participants do not show a difference in error with balance support in a specific direction (difference between supported and unsupported: YH AP 0.0cm, ML0.3cm and OH AP 0.8cm, ML 0.3cm), which indicates they are not limited in adjusting their foot placement by balance. It does appear as stroke survivors do benefit from support when narrowing there steps more than stepping laterally. The reduction of foot placement error by 1.7cm is not the difference between a successful and an unsuccessful foot placement on a two-dimensional target. In daily living however, a situation that needs foot placement adaptation is rarely just two dimensional; avoiding a loose tile, reaching a curb etc. It could be imagined in a three-dimensional situation the difference between an error magnitude of 7.0cm and 4.7cm in anterio-posterior direction and 3.6cm and 3.0cm in medio-lateral direction in stroke survivors could be the difference between keeping and losing balance. These differences in overhang (AP 2.3cm and ML 0.6cm) are effectively the reduction in BoS size within which the CoP can travel before exceeding margins of stability. While, error measures based on CoP and CoF location cannot be used interchangeably to measure foot placement accuracy (see chapter 3.3), the position of CoP under the foot might be more reflective of balance, especially when part of the foot overhangs support (i.e. only part of the foot is placed on a curb). As seen in Chapter 3.3, when adapting foot placement (CoF), the CoP lands more anteriorly when shortening and more posteriorly when lengthening, this indicates naturally the adaptation is kept biomechanically as similar to steady state walking as possible. However, this means that CoP would be expected to approach the margins of the BoS (which are reduced by the extent of CoF error/overhang), thereby challenging balance. Therefore, although smaller than seen in other studies, the differences between supported and unsupported target stepping are likely clinically meaningful differences that could reflect the difference between a successful and unsuccessful foot placement adaptation.

6.4.4 Does balance support influence accuracy of foot placement differently for the paretic and non-paretic legs?

Balance control may be expected to affect the aim of the paretic leg differently than the non-paretic leg; an increased separation between centre of pressure and centre of mass (a reflection of balance control) in paretic limb stance, compared to the non-paretic has been previously observed (Said et al., 2008). However, foot placement error on the paretic (means: AP 5.6cm ML 3.8cm) and the non-paretic (means: AP 6.1cm ML 2.9cm) legs in stroke survivors were similar across different directions of stepping adjustments and reduced by similar amounts when balance was supported (mean reduction by support, paretic AP 2.4cm, ML 0.9cm and non-paretic AP 2.3cm, ML 0.3cm). Which indicates the paretic and non-paretic leg are affected similarly by balance control.

It was expected that balance support would increase accuracy when aiming with the non-paretic leg more than with the paretic, as maintaining paretic stance has shown to be the most challenging for balance (Said et al., 2008). However, the results seen here (showing no differences according to side of paresis) are in line with the results by Nonnekes et al. (2010) who also show a bilateral increase of stepping accuracy with balance support in stroke survivors. This indicates control of foot placement relies on bilateral organisation to maintain balance and, adjustments have to be made in both the stance and swing legs when aiming with the lower limb (Reynolds & Day, 2005a)..

6.5 Implications

This chapter implicates that balance affects all directions of foot placement adaptation in both anterio-posterior and medio-lateral direction. Balance rehabilitation be needed in people with high foot placement errors, or walking aids as a stick, crutches, or a rollator might be a solution as foot placement errors are reduced in all directions when using the stabilizing crutches in the target stepping task in this study. However, walking speed seems to be a major factor in how well step adjustments are made, which could indicate the time participants have to plan their stepping adjustment is important for successful step adaptations as previously shown by Bancroft and Day (2016).

6.6 Limitations

The limitation in this chapter is that no biomechanics of the centre of mass is included. It would be very interesting to see how anterio-posterior gait adaptations are affected by balance and how step widening is affected similarly as narrowing. It was expected that mainly narrowing steps would be limited by balance, however all steps became more accurate during the supported condition, which even increases the importance of balance during walking.

6.7 Conclusion

Balance support does help to bring stepping error down, therefore, it might help foot placement coordination and safety of walking. However, support did not affect stepping accuracy enough to bring the percentage of misses down, so gait adaptations exceeding 25% lengthening or shortening a step or 50% narrowing or widening may exceed stroke survivor's ability during gait. Also, stroke survivors do not seem to benefit more from support than their healthy counterparts. The effect of response time on target stepping accuracy.

7 The effect of response time on target stepping accuracy.

7.1 Introduction

People need time to a plan to step to a safe foot-fall location. In the previous study, we saw that stroke survivors appear to undershoot all targets; preferred and even shortening steps were undershot (negative foot placement errors). The fact that stroke survivors undershot even preferred steps may have led to greatest magnitudes of error (again, undershooting) in lengthening steps which followed (because error on preferred steps would increase the challenge of a subsequent step lengthening). Healthy young adults also undershot lengthening steps. However, in contrast to stroke survivors they overshot shortening steps. The fact that stroke survivors “fall behind” targets (undershoot all targets) and healthy young adults do not (undershoot lengthening targets but overshoot shortening targets), indicates stroke survivors may need more time to plan or may have a compromised ability to adjust steps in sufficient time as discussed in the balance chapter (chapter 6). Further support for the idea that stroke survivors need more time to adapt foot-placement when walking is found when considering the difference in findings between those of chapter 4 and previous literature.

Previous studies by Moraes et al. (2007) and Nonnekes et al. (2010) found errors when step narrowing and shortening were larger than those observed when step lengthening and widening. This finding was not replicated in the work presented in the previous chapter and this may be because, participants had to sufficient time (at least two steps ahead) to plan their steps in our study (chapter 6) in comparison to the restricted time participants got to respond in previous literature (Moraes et al., 2007; Nonnekes et al., 2010). Collectively, these findings indicate accuracy of stepping to targets requiring step lengthening, narrowing, shortening and widening may be significantly influenced by the available response time to plan and execute foot placement adjustment.

Previous literature has provided evidence for the time needed for healthy adults to plan and execute a foot placement adjustment in response to the environment. Specifically, in uncluttered terrain/walking over clear level paths, young healthy adults normally look about two steps ahead (M. A. Hollands & Marple-Horvat, 2001). With more cluttered terrain, they shift their attention closer (M. A. Hollands & Marple-Horvat, 2001; Matthis & Fajen, 2014), affording less time to plan to adjust steps as required to navigate terrain. This reduced time to plan however does not appear to compromise the ability of healthy young adults to adjust foot placement as they have been shown to be able to adjust foot placement up until late swing (M. A. Hollands & Marple-Horvat, 2001; Young & Hollands, 2012). However, healthy young adults do slow down when targeting foot placements regardless of the irregularity of the target positioning (Peper et al., 2012). Collectively, these observations indicate that while it is possible to execute adjustments to foot placement in a very short time frame, healthy young adults prefer to afford themselves time to plan steps either by way of looking ahead and/or slowing down. Indeed, accuracy of foot placement is reduced when time to respond is limited (Hoogkamer et al., 2015).

Previous studies have shown, a non-step specific braking impulse is required i.e. all foot placement adjustments induced a breaking impulse (Moraes et al., 2007). This braking impulse possibly allows more time to adjust foot placement (Moraes et al., 2007), and might be why participants slow down walking speed during target stepping (Peper et al. (2012)). But what is this extra time needed for? Time might be needed to physically orient gaze to the right place in the terrain (Nonnekes et al., 2010; Young & Hollands, 2012), process visual information to base a foot placement plan /change on (which needs to be transmitted to the cortex as opposed to short-latency spinal reflex loops as shown in animal studies (Amos, Armstrong, & Marple-Horvat, 1990; Armstrong, Edgley, & Lidierth, 1988; Beloozerova & Sirota, 1993; Drew, 1993; Drew et al., 2004; Jiang & Drew, 1996) and then shape the plan for precise limb trajectory and activate muscles to execute the movement (Takakusaki, 2017). Within this process, firstly, visual attention has to be brought to the specific target footfall location to be reached for or avoided (and other irrelevant ques in the environment ignored). When, in the gait cycle, we look at a target, and for how long, has been shown to be important for the accuracy of the foot placement (M. A. Hollands & Marple-Horvat, 2001). Specifically, looking at a target too early and then looking away too soon have been shown to be causally linked with an increase in stepping error and foot placement variability (Chapman & Hollands, 2006a, 2006b, 2007, 2010) and fear of falling (Young et al., 2012). This indicates that we may need time to physically scan and then orient our gaze to the right place in the environment to effectively guide the foot placement adjustment required. Secondly, the visual information acquired about the terrain and target foot fall location is processed, perceived and integrated to make a feed-forward plan to place the foot. Based on the theory of Grillner and Wallen (1985), steady state walking can be maintained subcortically. However, when adaptations have to be made cortical control is likely to be needed needed. Evidence for cortical control has been shown in adaptive walking in decerebrate animal studies, where in visually guided walking the partial posterior cortex is involved in planning and the motor cortex in execution of walking and, in humans, in delayed response times on a probe-reaction time dual task during target stepping (Mazaheri et al., 2015). Any sensory motor transformation processes which are supraspinal are known to be of longer latency than spinal reflex pathways (Rossignol, Dubuc, & Gossard, 2006) and so require additional neural transmission time to cross multiple synapses across multiple networks. Lastly, execution of the foot placement adaptation has to be achieved. To adjust the foot placement the direction of the foot and body momentum (Bancroft & Day, 2016) has to be changed. To accomplish these changes, muscles have to be activated and time allowed to generate force (electromechanical delay) and overcome moments of inertia to achieve physical change in ongoing movement (Arene & Hidler, 2009). These changes can be made biomechanically on low cost when the foot placement position is known for at least two steps ahead, both the feet positioning and the velocity can be adjusted gradually (Matthis & Fajen, 2013). However, when the position of foot placement is known later than two steps ahead muscular changes have to be made to either adjust push off or midswing CoM trajectory (Matthis & Fajen, 2013).

A stroke is associated with visual impairments, including hemi-neglect and oculomotor deficits (affecting ability to physically orient gaze to the right location in space and to take-in good quality visual information)(Rowe & Group, 2017), an increase in visual response time (visuomotor transformation processing times) (Kaizer, Korner-Bitensky, Mayo, Becker, & Coopersmith, 1988) and delayed and diminished muscle activation (Arene & Hidler, 2009). All of these impairments will inevitably affect stroke survivors' success in adapting foot placement with limited available time to respond. In young healthy adults we know normally foot placement is planned about two steps ahead, and corrections can be made up until swing phase of the targeting foot (M. A. Hollands & Marple-Horvat, 2001; Matthis et al., 2015; Reynolds & Day, 2005b), or in means of time up until 114-121ms prior to foot contact (Reynolds & Day, 2005a). In stroke survivors however, the onset of motor-related cortical potential to the onset of electromyography shows to be delayed, when reaching with the upper body (Daly, Fang, Perepezko, Siemionow, & Yue, 2006). This prolonged time needed to plan movements is likely to affect adjustments of foot placement during walking as well as movements of the upper extremity (Peters, Handy, Lakhani, Boyd, & Garland, 2015). However, how much time stroke survivors need to plan or adjust their foot placement is largely unknown.

Investigations of how stroke survivors adjust stepping in response to the environment have only been carried out in standing (Nonnekes et al., 2010) or induced by obstacle avoidance (Den Otter et al., 2005; van Swigchem et al., 2013). During these obstacle avoidance studies stroke survivors have been shown to hit the obstacle more often when less response time is given (Den Otter et al., 2005; van Swigchem et al., 2013). Sorter available response time was also associated with a preference for lengthening steps on approach to the obstacle more often than in healthy adults under the same response time conditions (Den Otter et al., 2005). Lengthening a step provides more time to respond (literally prolonging the ongoing movement) which allows for more propulsion than shortening a step (Moraes et al., 2007). Stroke survivors' reported preference for step lengthening strategies and difficulty shortening steps could be partly explained by the fact that shortening steps requires a termination of an ongoing movement (literally shortening time to respond). In stroke survivors shortening steps might be impaired due to delayed muscle onset when adjusting foot placement to targets (Nonnekes et al., 2010) and avoiding obstacles (van Swigchem et al., 2013). This delayed muscle onset in foot placement adjustments in stroke survivors could either be due to slower cognitive visuo-motor transformations and/or delayed muscle activations related with individual joint coordination (Daly, Roenigk, Cheng, & Ruff, 2011) and the effects of the hemiplegia affecting descending activation from the motor cortex (Arene & Hidler, 2009). These deficits in planning and execution, due to stroke, are likely to affect stepping accuracy more when response time is reduced.

Differences in the ability to reactively adapt foot placement between paretic and non-paretic limb could additionally be expected owing to the fact that stroke related impairments (at visual, cognitive and muscular levels) tend to affect one side of the body more than the other. Nonnekes et al. (2010) showed response latencies were delayed in the paretic leg, which can be explained by the affected descending activation from the motor cortex to the spinal tracts. However, both the paretic and non-paretic leg showed similar error magnitudes in target stepping (chapter 4 (pilot) and 6 (balance) and success rates (Den Otter et al., 2005) and response times (van Swigchem et al., 2013) in obstacle avoidance. A comparison between the accuracy of the paretic and non-paretic limb could indicate what the impact of hemiparesis is in foot placement control. The hemiparesis would merely affect the paretic aim, while a deficit in visuo-motor response and planning could bilaterally affect foot placement accuracy.

In stroke survivors the exacerbation of error when adjusting foot placement is expected to be larger than in healthy adults as deficits in visual response time, motor-planning, and movement executions are known impairments following stroke. These deficits are likely to affect different directions of movement and the paretic and non-paretic limb differently, therefore the aims in this chapter are to address the following questions: 1) Does accuracy of foot placement diminish with diminished response time? 2) Are there differences between stroke survivors and healthy control participants on the accuracy of stepping to reactive targets? 3) Are performance deficit characteristics dependent on direction of adaptation? 4) What is the influence of hemiparesis on foot placement adaptability?

7.2 Methods

The general methods of participant recruitment, clinical assessments, apparatus, familiarization, and stepping performances are as explained in the methods chapter (Chapter 5: General Methods). In this specific chapter the percentage of misses and absolute, mean and variable error are used to compare planned (walking to an adaptability target stepping paradigm with targets visible for at least 2 steps ahead) and reactive (walking to an adaptability target stepping paradigm with the targets appearing at contralateral midstance) adaptations of foot placement during walking, and the planned condition is this chapter is the same condition as the unsupported condition in the previous chapter. Based on previous literature young healthy adults can adjust foot placement up until late stance (M. A. Hollands & Marple-Horvat, 2001; Matthis & Fajen, 2014) however, as well young (Hoogkamer et al., 2015) as older healthy adults and stroke survivors showed a decline with available response time (Den Otter et al., 2005; van Swigchem et al., 2013). Additionally, target presentation at midstance has shown to be challenging in the pilot study (Chapter 4).

7.2.1 Statistics

Similar to previous foot placement studies (Hoogkamer et al., 2015; van Swigchem et al., 2013), the percentage of missed targets data were subjected to angular transformation to stabilize the variance and normalize distribution and compared between different conditions (planned and reactive) with a repeated measures ANOVA. The between subjects' factor was group (stroke, healthy young and older adults). The within subjects' factor was timing condition (supported and unsupported).

A repeated measure ANCOVA was conducted for three stepping errors (absolute, mean and variable) in anterio-posterior stepping direction No significant effects were found for variable error so results for this measure will be reported in supplementary tables. The within subject factors were condition (planned, reactive), steps (shortening and lengthening) and side (left and right for healthy and paretic and non-paretic for stroke survivors). Left and right foot placement error in healthy adults were not expected to be different and did not show any significant main or interaction effects, and therefore, are not reported in this chapter. Between subject factor was groups (Healthy young, older adults and stroke survivors). The same ANCOVA model was repeated for analysis of medio-lateral stepping adjustments. For medial-lateral steps the within subject factor of steps was narrowing and widening.

7.3 Results

In the following results section mainly, main results will be presented as no interaction effects were found.

Participants (11 young adults, 9 older adults, and 12 stroke survivors) (participant demographics see table 7.1) took part in the study. According to suggested thresholds for SSWS of stroke survivors (H. Schmidt et al., 2007), two participants were non-functional walkers (<0.4m/s), seven limited outdoor walkers (0.4-0.8m/s) and two healthy walkers (>0.8m/s). Two healthy older and one young adult were limited outdoor walkers (0.4-0.8m/s) and the rest of the healthy adults walked at SSWS exceeding the 0.8m/s limit.

Table 7.1 *Participant demographics and clinical characteristics represented in mean± SD unless specified differently.*

	Young adults	Older adults	Stroke Survivors
N (F)	11(7)	10(3)	11(2)
Age (years)	29.5± 6.2	63.8± 7.9	66.7±9.4
SSWS (m/s)	1.09± 0.18	0.88± 0.19	0.54± 0.21
Trial making test A (s)	24± 12	31± 14	56± 36
Trial making test B (s)	50± 28	69± 42	406± 919
Apples test	-	27.4± 1.9	26.6± 2.9
Falls in the last 12 months	-		
No fall (N)	-	9	8
1 fall		1	1
1< fall		0	2
Apples test	-	-	46.4± 10.1
Time since stroke (months)	-	-	87.5± 134.3
Paretic (Right)	-	-	5
Berg balance	-	-	50.4± 5.4
Fugl-Meyer (lower limb)	-	-	26± 5.6
Dynamic gait index	-	-	24.8± 4.6
10m-walking speed (s)	-	-	12.9± 4.3
Timed up and go (s)	-	-	16.7± 5.9

7.3.2 Does the response time limitation affect stepping accuracy?

7.1.1.1 Hits and misses

When investigating the percentage of misses a main effect of condition was found ($F(1, 29) = 4.183$, $p=0.05$). Targets in the planned target stepping condition (3.4± 1.3%) were missed less than in the reactive condition (4.7±1.3%). See figure 7.1.

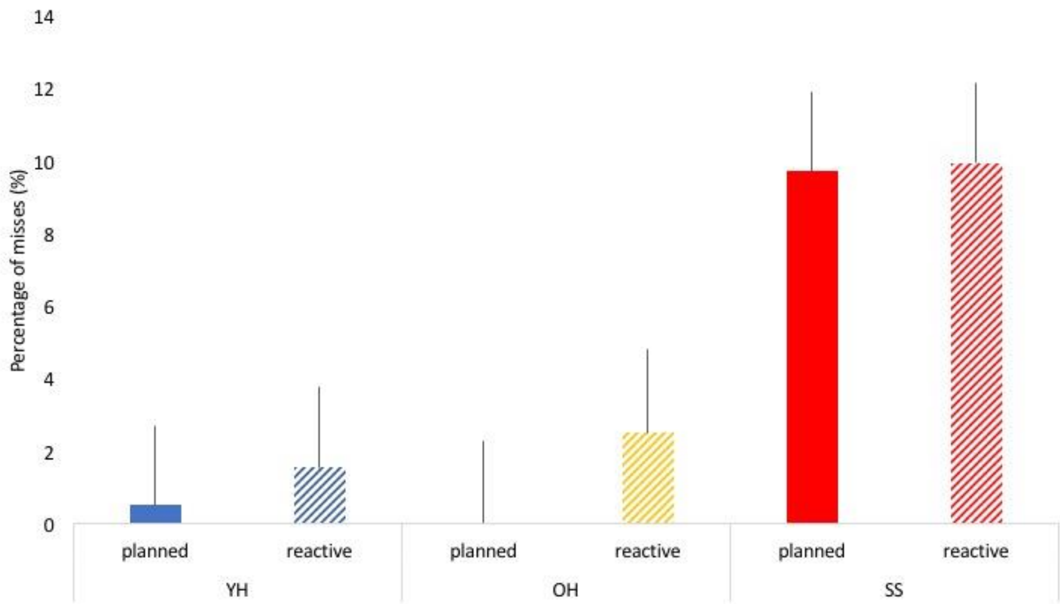

Figure 7.1 *Bars represent the mean percentage of target misses for young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red, for each type planned (solid) and reactive (striped) conditions. Error bars represent standard error of the mean.*

7.1.1.2 Size of error (Absolute error)

For absolute error, in anterio-posterior direction, a main effect for condition was found (F (1, 28) =5.932, p=0.021). The magnitude of error was significantly greater in the planned (5.5± 0.5cm) than in the reactive condition (4.6± 0.5cm,), see figure 7.2.

The absolute error in medio-lateral direction showed a main effect of condition (F (1, 28) =6.013, p=0.021). The magnitude of error was significantly smaller narrowing and widening steps in the planned (2.7± 0.3cm) condition than the reactive condition (3.7± 0.5cm,), see figure 7.4.

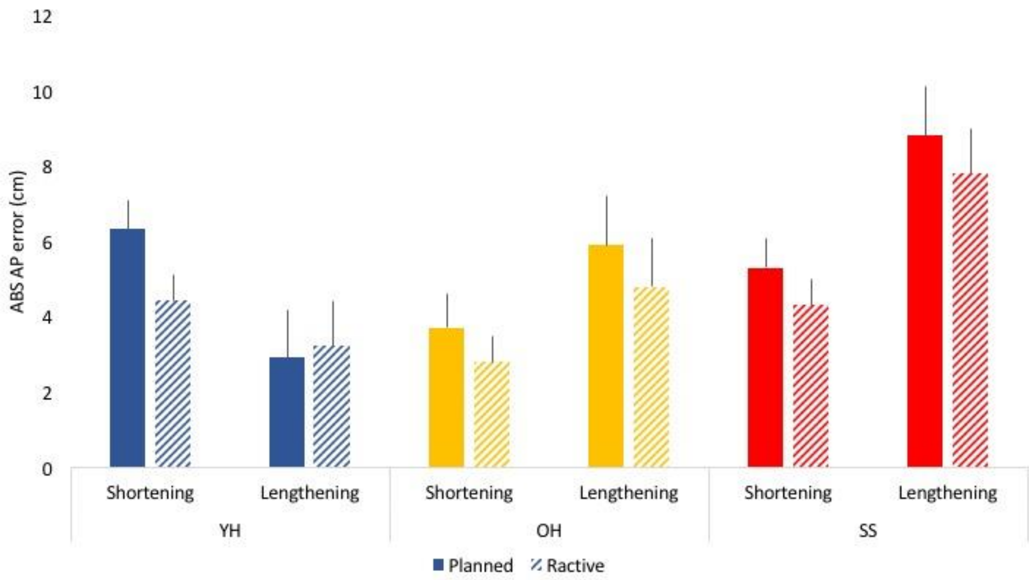

Figure 7.2 *Bars represent the mean anterio-posterior absolute error of foot placement for young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red, for each type both planned (solid) and reactive (striped) conditions. Error bars represent standard error of the mean.*

7.1.1.3 Direction of error (Mean error)

For mean error, no main effect for condition in anterio-posterior (covaried for SSWS: $F(1,28)= 0.032$, without covariation $F(1,29)= 0.025$) was found. The direction of error was similar for the planned (AP -1.8± 0.7cm,) and the reactive condition (AP -1.6± 0.6cm), see figure 7.3.

For mean error in medio-lateral direction a main effect for condition (covaried for SSWS: $F(1,28)= 6.373$, $p=0.018$, without covariation $F(1,29)= 6.408$, $p=0.017$) was found. The direction of error for the planned steps was more under shot (-0.4±0.1cm) compared to reactively (-0.1±0.1cm), see figure 7.4.

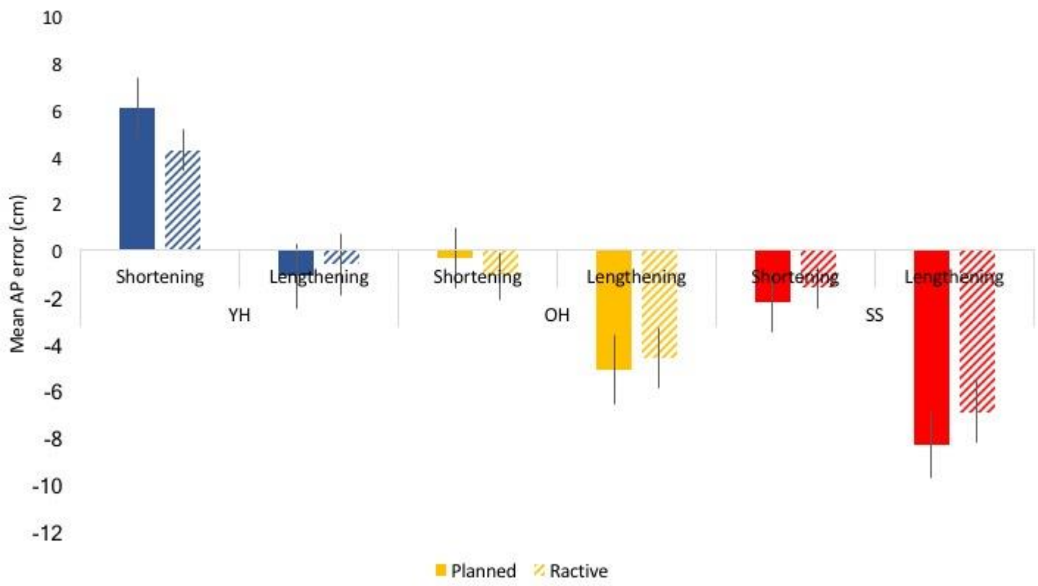

Figure 7.3 *Bars represent the anterio-posterior mean error of foot placement for young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red, for each type both planned (solid) and reactive (striped) conditions. Error bars represent standard error of the mean.*

7.3.3 Do stroke patients have a reduced ability to make reactive corrections vs planned adjustments?

7.1.1.4 Hits and misses

A main effect of group was found for the percentage of misses ($F(2, 29) = 11.419$); stroke survivors (9.8± 2.1%) missed significantly more targets than older (1.3±2.2%, p=0.001) and young (1.0± 2.1%, p=0.001) adults in both planned and reactive target stepping condition. No interaction effect was found for group and condition such that response time reduction was not seen to induce targets missed for stroke survivors' more than healthy young or older adults. See figure 7.1.

7.1.1.5 Size of error (Absolute error)

We investigated whether the absolute error altered differently for stroke survivors (AP 6.6± 0.9cm, ML 4.8± 0.6cm) than healthy young (AP 4.2± 0.9cm, ML 2.0± 0.6cm) and older (AP 4.3±0.9cm, ML 2.9± 0.6cm) adults for planned and reactive target stepping condition. No main effect of group (covaried for SSWS: AP $F(2,28)=0.711$, ML $F(2,28)= 1.332$, without covariation: AP $F(2,29)=2.279$) except when no covariation of SSWS was used for medio-lateral adaptations ($F(2,29)= 5.977$, p=0.007) stroke survivors had greater foot placement error (4.8±0.6cm instead of 2.0±0.6cm and 2.9±0.6cm in healthy young and older adults, respectively). No interaction of condition and group was found (covaried for SSWS: AP F(2,29)=0.390 ML F(2,29)=0.403 , without covariation: AP F(2,30)= 0.058, ML F(2,30)=0.428). See figure 7.2 and 7.4.

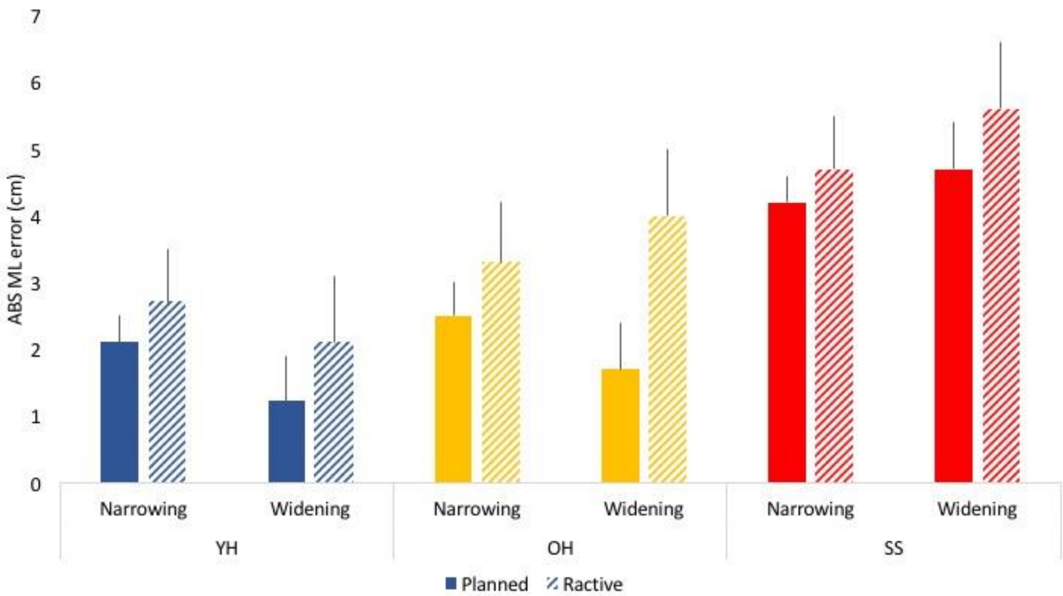

Figure 7.4 *Bars represent the mean medio-lateral absolute error of foot placement for young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red, for each type both planned (solid) and reactive (striped) conditions. Error bars represent standard error of the mean.*

7.1.1.6 Direction of error (Mean error)

No main or interaction effect was found for the mean error in anterio-posterior direction. Due to the covariation for walking speed stroke survivors (-4.7± 1.1cm) did not have a different direction of error than young (2.2± 1.1cm) and older (-2.8± 1.1cm) healthy adults. Without the covariation for SSWS stroke survivors did show to significantly (F(2,29)=10.565, p<0.001) undershoot targets more than healthy young and older adults. All participant groups were affected similarly in the planned (SS -5.2± 1.3cm, YH 2.5± 1.3cm, OH -2.7± 1.3cm) as reactive targets (SS -4.2± 1.0cm, YH 1.9± 1.0cm, OH -2.8± 1.1cm).

No main (F(2,28)= 0.052) or interaction effect was found for the mean error in medio-lateral direction. When the influence of walking speed is covaried for, stroke survivors (-0.3± 0.3cm) did not have a different direction of error than young (-0.2± 0.3cm) and older (-0.2± 0.3cm) healthy adults. All participant groups were affected similarly in the planned (SS -0.7± 0.3cm, YH 0.3± 0.3cm, OH -0.2± 0.3cm) as reactive targets (SS 0.0± 0.3cm, YH -0.2± 0.3cm, OH -0.2± 0.3cm).

7.3.4 Are performance deficit characteristics dependent on direction

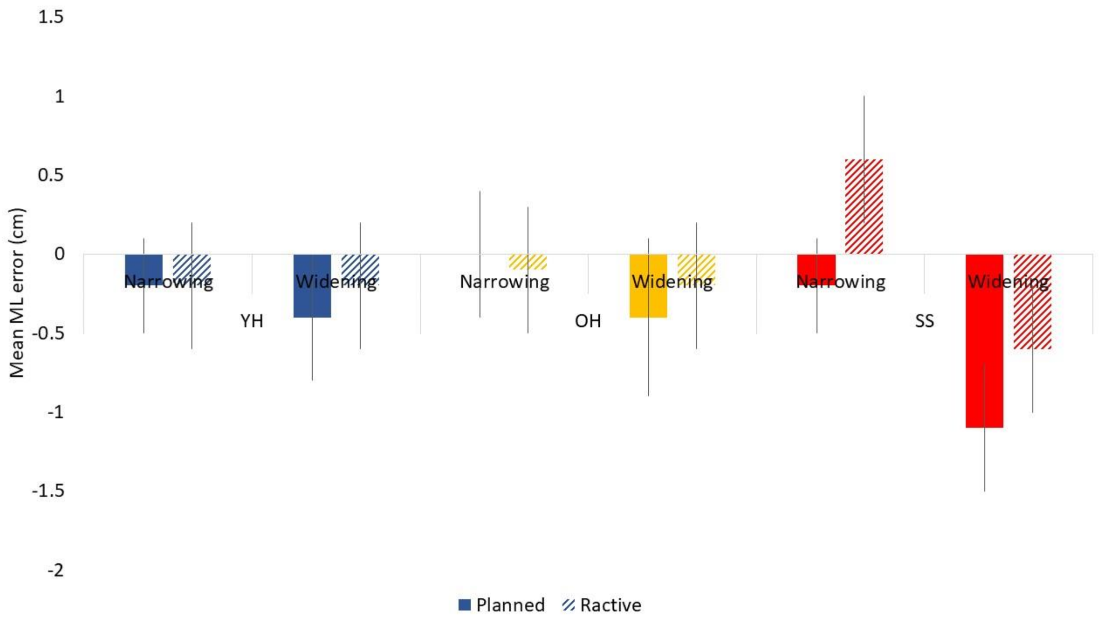

Figure 7.5 *Bars represent the medio-lateral mean error of foot placement for young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red, for each type both planned (solid) and reactive (striped) conditions. Error bars represent standard error of the mean.*

of adaptation?

7.3.4.1 Size of error (Absolute error)

A main effect of direction of steps was found in anterio-posterior stepping direction (F (1, 28) = 5.641, p=0.025). Shortening steps (4.5±0.4cm) had significantly less error than lengthening steps (5.6± 0.7cm,). An interaction effect of group and step was found (F (2, 28) =3.478, p=0.045); stroke survivors had greater magnitude of error in lengthening (8.3± 1.2cm) steps than shortening steps (4.8± 0.7cm) while young and older healthy adults had similar error magnitudes for lengthening (YH (3.0± 1.2cm), OH (5.4± 1.2cm)) and shortening (YH (5.3± 0.7cm), OH (3.3± 0.7cm)). No interaction effect for condition and step was found. Planned steps (shortening (5.1± 0.5cm) and lengthening (5.9± 0.7cm)) had similar magnitude of error as reactive steps (shortening (5.9± 0.7cm) and lengthening (5.3± 0.7cm)). See figure 7.2.

For medio-lateral step adjustments, narrowing (3.2± 0.3cm) and widening (3.2± 0.4cm) steps, condition no main effect of steps ($F(1,28)=0.005$) or interaction effect of step and condition was found when covaried for SSWS ($F(1,28)=0.010$), however without a covariation an interaction effect was found ($F(1,29)= 4.942$, $p=0.034$) where widening steps got less accurate reactive (3.6±0.5cm error) than planned (2.5±0.2cm error). Planned steps (narrowing (2.9± 0.3cm) and widening (2.5± 0.4cm)) had similar magnitude of error as reactive steps (narrowing (3.6± 0.5cm) and widening (3.9± 0.6cm)). Nor an interaction effect for group and step was found, narrowing (YH (2.4± 0.6cm), OH (2.9± 0.6cm) and SS (4.5± 0.6cm)) had similar magnitude of error as widening (YH (1.7± 0.7cm), OH (2.9± 0.7cm) and SS (5.1± 0.7cm)). See figure 7.4.

7.3.4.2 Direction of error (Mean error)

A main effect of steps was found in anterio-posterior stepping direction ($F(1, 28) = 9.078$, $p=0.005$). Shortening steps (0.9± 0.6cm) were generally overshot and lengthening steps (-4.4± 0.7cm) were undershot. No interaction effect for condition and step was found. Planned steps (shortening (1.2± 0.7cm) and lengthening (-4.8± 0.8cm)) had similar magnitude of error as reactive steps (shortening (-0.5± 0.5cm) and lengthening (-4.0± 0.8cm)). Nor an interaction of step and group was found, shortening (YH (5.2± 1.0cm), OH (-0.7± 1.1cm) and SS (-1.9± 1.0cm)) had similar magnitude of error as lengthening (YH (-0.8± 1.3cm), OH (-4.9± 1.3cm) and SS (-7.6± 1.3cm)). See figure 7.3.

For medio-lateral step adjustments, narrowing (0.0± 0.2cm) and widening (-0.5± 0.2cm) steps, condition no main effect of steps ($F(1,28)=2.273$) or interaction effect of step and condition is found. Planned steps (narrowing (-0.1± 0.2cm) and widening (-0.6± 0.3cm)) had similar magnitude of error as reactive steps (narrowing (0.1± 0.2cm) and widening (-0.3± 0.2cm)). Nor an interaction of step and group was found, narrowing (YH (-0.2± 0.3cm), OH (0.0± 0.4cm) and SS (0.2± 0.3cm)) had similar magnitude of error as widening (YH (-0.3± 0.4cm), OH (-0.3± 0.4cm) and SS (-0.8± 0.4cm)). See figure 7.5.

7.3.5 What is the influence of hemiparesis on foot placement adaptability?

7.3.5.1 Size of error (Absolute error)

No main effect of side in paretic (AP 6.5± 0.9cm, ML 5.5± 0.7cm) and non-paretic (AP 6.6± 0.9cm, ML 4.1± 0.6cm) side in stroke survivor was found. No interaction effects were found for the adaptations either in anterio-posterior direction as medio-lateral direction, see figure 7.6 a and b.

7.3.5.2 Direction of error (Mean error)

No main effect was found for the paretic (-4.9± 1.5cm) and non-paretic (-4.6± 1.5cm) side in anterio-posterior direction, nor an interaction effect of condition and side is found. Planned (paretic (-5.1± 1.8cm), non-paretic (-5.3± 1.9cm)) and reactive (paretic (-4.6± 1.4cm), non-paretic (-3.8± 1.1cm)) steps are similar for both sides, see figure 7.7.

No main effect was found for the paretic (0.0± 0.6cm) and non-paretic (-0.7± 0.7cm) side medio-lateral direction, nor an interaction effect of condition and side was found. Planned (paretic (-0.6± 0.7cm), non-paretic (-0.7± 0.8cm)) and reactive (paretic (0.7± 0.5cm), non-paretic (-0.7± 0.7cm)) steps are similar for both sides, see figure 7.7.

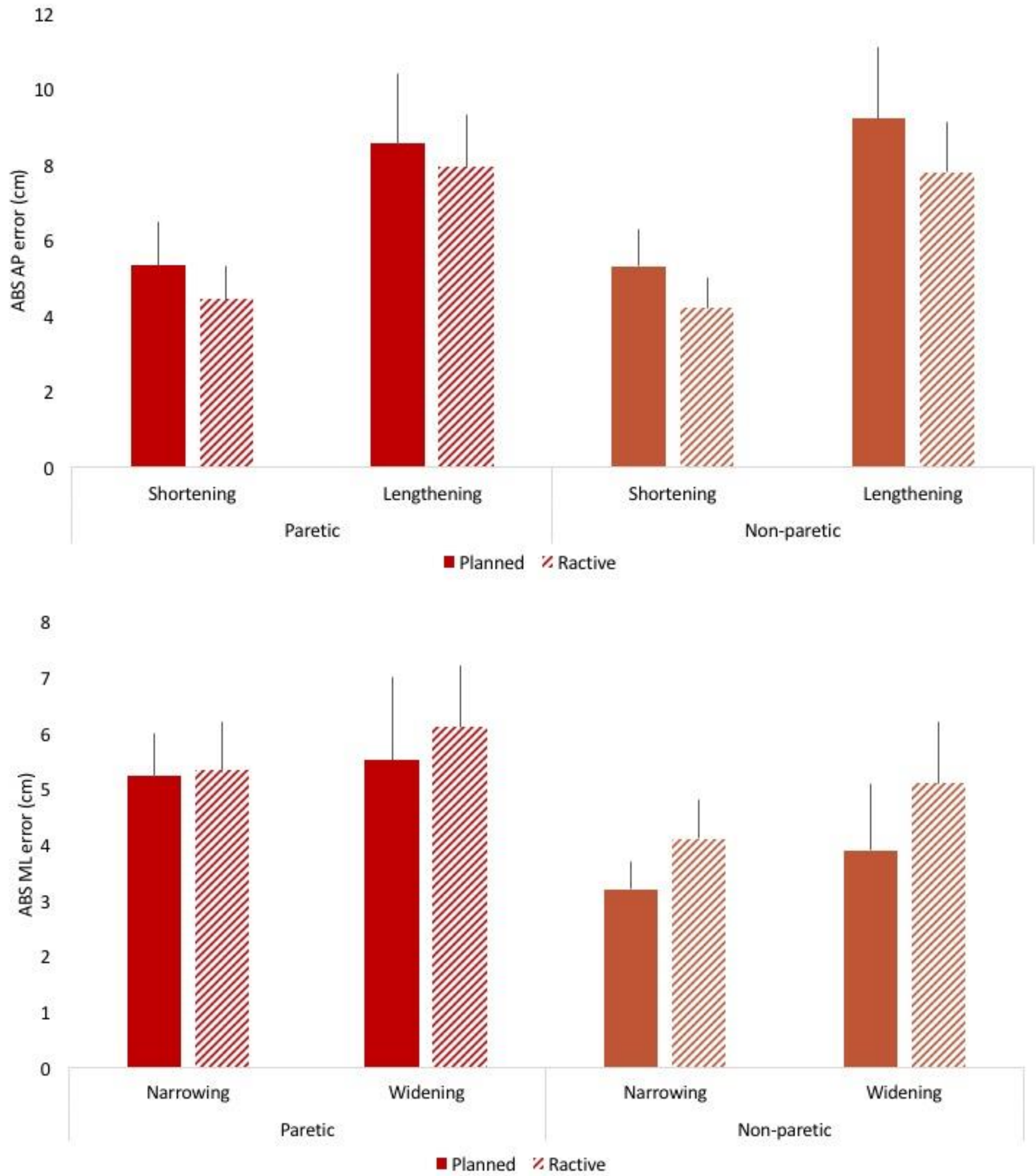

Figure 7.6 *Bars represent the mean absolute error of foot placement for the paretic (red) and non-paretic (bordeaux) side in stroke survivors a) anterio-posterior (AP) error combined for shortening, preferred and lengthening steps, b) medio-lateral (ML) error combined for narrowing, preferred and widening step for both, unsupported (solid) and supported (striped) conditions. Error bars represent standard error of the mean.*

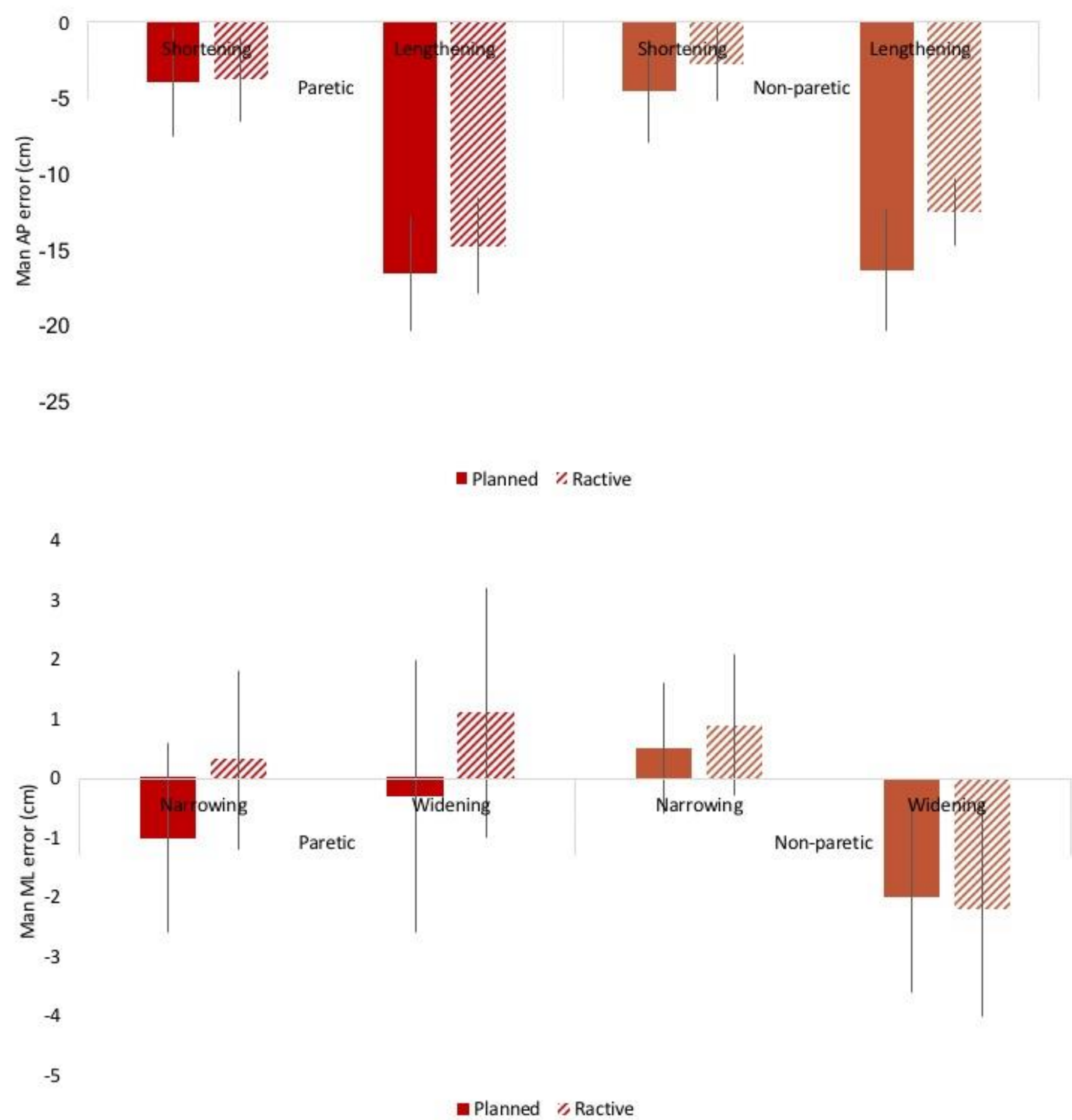

Figure 7.7 *Bars represent the mean error of foot placement for the paretic (red) and non-paretic (bordeaux) side in stroke survivors a) anterio-posterior (AP) error combined for shortening, preferred and lengthening steps, b) medio-lateral (ML) error combined for narrowing, preferred and widening step for both, unsupported (solid) and supported (striped) conditions. Error bars represent standard error of the mean.*

7.4 Discussion

This is the first study to compare foot placement accuracy during walking for planned and reactive targets in four adaptation directions (shortening, lengthening, narrowing and widening) between young and older adults and stroke survivors. The results from this study show more targets are missed in the reactive condition than in the planned condition. However, only narrowing and widening steps showed an increase in magnitude of medio-lateral error when targets were reactive, and shortening and lengthening actually showed a decrease of anterior-posterior error magnitude when response time was limited. Although stroke survivors generally do miss more targets, they are not affected more by the reduced response time than healthy young and older counterparts i.e. stroke survivors miss targets even in the planned condition and this does not worsen with reduced time to respond. In contrast young and healthy older adults have high rates of success and a high degree of accuracy in both planned and reactive target stepping.

7.4.1 Is foot placement accuracy affected by reactive targets?

In general, for all participants, reactive targets are missed more often (4.7%) than planned targets (3.4%). However, this difference in success only translates to a higher magnitude of medio-lateral error in reactive narrowing and widening step adjustments, anterio-posterior magnitude of error of shortening and lengthening steps actually declined. The increased number of misses and magnitude of ML error under time pressure indicate the time available to adjust foot placement is important for the accuracy of the foot placement- especially narrowing steps. This is in agreement with previous literature, reporting that target stepping success, in young healthy adults, declines with less response distance (Hoogkamer et al., 2015) and declined success avoiding obstacles in stroke survivors (Den Otter et al., 2005; van Swigchem et al., 2013). However, failure rates reported in the recent study are low in comparison with the target stepping study by Hoogkamer et al. (2015); who reported failure rates of 33% when participant had more than on step length time to plan the step adjustment (target would show 70cm before you would place the foot on the target and participants had an average step lengths of 55cm) increasing to a failure rate of 93% when time to plan was just shorter than one step length (40cm). The methodology used to determine a successful step was slightly different in this thesis than in the study by Hoogkamer et al. (2015). In this thesis a miss was determined when no part of the foot (the width and length of the foot was projected over the CoF) was overlapping the target. Hoogkamer et al. (2015) determined a miss when the corrected CoP (the average error to preferred steps was subtracted from the error made to adaptation steps) was placed outside the borders of the target, which effectively neglects the size of the foot leading to a higher number of missed targets. While, conditions might have been slightly more challenging in the study by Hoogkamer et al. (2015) than in this current study, it is surprising healthy young adults have such high failure rates as they are known to be able to adjust foot placement up until late stance of the targeting leg (M. A. Hollands & Marple-Horvat, 2001; Matthis & Fajen, 2014). The difference between the study by Hoogkamer et al. (2015) and the two other studies (M. A. Hollands & Marple-Horvat, 2001; Matthis & Fajen, 2014) might be due to the paradigms used, and how visual information was provided. Hoogkamer et al. (2015) used a so called dual-step paradigm in which targets are shown, but sometimes the target shifts position. At this switching time it is likely the visual information of the original position has been used to provide a feed forward plan that suddenly had to be revised with the new, accurate, information of the shifted target location. In the studies of M. A. Hollands and Marple-Horvat (2001) and Matthis and Fajen (2014) target location does not change. Instead, sight of the targets is made unavailable at certain points during the gait cycle. Occluding visual information during the gait cycle challenges making a feed forward model rather than revising the ongoing step. This could explain the relatively low failure rates in the recent study; participants did not get information up until midstance of the contralateral leg, so no foot placement plan would have been based on previous visual information as in the double-step task, but merely information was just not available early enough to make and pre-existing foot placement plan.

The results found in this chapter differ from the results found in the pilot study (chapter 3). In the pilot chapter a greater increase of missed steps was shown in the reactive condition, especially in stroke survivors, whereas in the recent chapter a (just) significant difference was found between conditions, mostly driven by healthy adults. The difference between these two studies could lie in the different shapes of the targets used in the two studies. The pilot study used targets 40cm x 8cm deep for AP adjustments and 10cm x 15cm for ML adjustments, whereas this chapter used foot sized targets. This means the pilot chapter allowed 4cm error from the middle of the target plus half of the length of the foot (14.5cm as the average foot length was 29cm in this study) in AP direction, whereas this chapter allowed the error to be half the foot sized target (14.5cm) + half of the foot length (14.5cm), allowing people 10.5 cm more deviation in AP direction.

7.4.2 Are stroke survivors affected more severely by limiting the response time than healthy adults?

While all participants missed more targets in the reactive condition compared to planned condition, stroke survivors in this study missed 9.7% of planned steps and 10.0% of reactive steps. This is a higher failure rate overall for stroke survivors, compared to healthy counterparts, but a relatively smaller difference in failure rate between planned and reactive conditions than for healthy individuals (difference in failure rate for stroke survivors 0.22%, older 2.48% and young healthy adults 1.04%). Failure rates of obstacle avoidance in stroke survivors are known to be higher than healthy adults (Den Otter et al., 2005; van Swigchem et al., 2013) declining with less available response time. However, both these studies report very different success rates to one another in stroke survivors. The failure rates reported by Den Otter et al. (2005) are around 10% when the obstacle is released early in the gait cycle (1-60%, which corresponds with a release/visibility of about 2 to1.2 steps ahead to early swing phase of the avoiding leg) – which coincides with the rates of targets missed in this study when targets are seen in advance. In the den Otter study failure rates increase to about 25% when the obstacle is released with only little time to respond (61-100% of the gait cycle, corresponding with mid/late swing). The failure rates reported by van Swigchem et al. (2013) are much higher; 50% for the longest available response time (450-600ms) and 90% for the shortest available response time (150-300ms). The response times used by van Swigchem et al. (2013) (150-600ms) are all relatively short, with a walking speed of 0.56ms and an average stride length of 81cm a stride would take about 1450ms, the longest available response time would effectively leave about 41% of the gait cycle to adjust foot placement. These adjustments in the study by van Swigchem et al. (2013) would be comparable with adjustments made from mid to late swing which allows less response time than that by Den Otter et al. (2005), accounting for higher failure rates in van (van Swigchem et al., 2013). It could be argued the timing of target presentation in the reactive condition of this study (at mid swing) were less challenging than the obstacle avoidance studies. However, it is more likely that differences in severity of the stroke accounts for the difference in success rates. In the study van Swigchem et al. (2013) stroke survivors with drop foot were selected, whereas none of the participants of this study had severe footdrop. The pilot study (chapter 3) revealed step adjustments made in mid-swing were challenging enough to illuminate significant differences between planned and reactive failure rates and in magnitudes of stepping error (see sample size calculation in pilot chapter). Further consideration of magnitudes of foot placement error and interaction effects between direction of step adjustment and available response time in the sections below will help identify if size of foot placement errors are functionally meaningful and the potential causes of impairment for stroke survivors.

However, statistical analyses did not identify significantly increased magnitudes of error for stroke survivors compared to healthy young and older adults. The lack of statistical significance is due to covariance for SSWS as explained in the balance chapter (chapter 6). Direct interpretation of the statistical analyses indicates the reduction of response time did not harm foot placement accuracy of stroke survivors more than healthy participants when differences in walking speed are accounted for. Slower walking speed of stroke survivors, compared to healthy younger and older counterparts, could result in them having more time to plan their foot placement. However, whether the absolute response time available is important or the gait phase within which the information is processed is more important is yet unknown. Although, more time might be available to adjust foot placement when walking slower, the gait phase (mid stance) in which adjustments are required is the same for all participants groups in the present study.

The fact that reactive targets are delivered at the same phase in the gait cycle for all, normalizes the challenge of the task with respect to individual abilities (or gait speeds). Given this, additional controls (covariance for speed) for the possible confound of the groups performing the task at different speeds may be unnecessary.

Examination of the observed means (i.e. unadjusted by statistical covariance for walking speed) of absolute and mean error indicates stroke survivors do generally have larger errors than healthy adults. The increased percentage of misses in stroke survivors in both planned and reactive target stepping over the percentages of misses in healthy adults could indicate that stroke survivors had more difficulty target stepping in general. This difficulty adjusting foot placement in stroke survivors might be because they gather visual information differently that healthy adults. People at low risk of falling look at a target up until the foot has landed on the target and only switch to the next targets when they have finished this target movement. Whereas people with high risk of falling shift their gaze to the next target before the foot has landed on the target (Chapman & Hollands, 2007). The difference between this and the recent study is that Chapman and Hollands (2007) only had two targets two steps apart, so enough time was given to plan the next step. In the recent study, every foot placement was required to land on a target and therefore, a more cluttered environment approach (M. A. Hollands & Marple-Horvat, 2001; Matthis & Fajen, 2014) of directing gaze closer to foot placement, may be used. This may mean participants of this study only start planning the new step when the previous step is completed instead of planning two steps ahead as may be preferred in uncluttered situations. So, the small difference between success of planned and reactive target stepping tasks for stroke survivors may lie in the fact that target stepping is so compelling/challenging for stroke survivors that they only look at the next target when the previous foot is placed (mid swing), exactly the time the target shown in reactive target steps. Therefore, target stepping or walking in cluttered terrain may as well be seen as reactive in stroke survivors. This mean that when stroke survivors walk in cluttered terrain (cobble stones, cluttered streets etc.) continuous monitoring and aiming for foot-fall location is needed. This will cause stroke survivors to use the cluttered terrain planning strategy, which only allows them little time to adjust their foot placement to a safe foot-fall and about one out of ten steps will be missed. Even if they could – in theory- plan ahead for steps. They go into "reactive" mode, multiple studies have shown results in poorer accuracy (den otter, van swichem, kaizer, mayo). In contrast your healthy adults do have an increase in misses when in reactive compared to in planned stepping. This indicates healthy people can deal with cluttered environments by planning ahead and then only 4-6% are missed even when reactive – so the frequency in which healthy folks are forced to deal with a "misfired" step is reduced. This reduces percentage of misplaced steps will reduce the risk of a fall directly, without taking in account healthy adults will be more robust against a misplaced step than stroke survivors as balance, force and motor control are intact.

7.4.3 Does foot placement accuracy worsen more in steps that limit the BoS with reduced response time?

In the chapter on the effect of balance on target stepping accuracy (chapter 6) lower failure rates and magnitudes of error have been reported than in previous studies respectively (Moraes et al., 2007) and (Nonnekes et al., 2010). The higher success rates of achieving BoS limiting steps (narrowing and shortening) in our study (compared to previous studies) may be attributed to the additional time participants got to plan foot placement adjustment (about two steps ahead in the recent study (Chapter 7) compared to during swing phase of the aiming leg (Moraes et al., 2007; Nonnekes et al., 2010)). Therefore, in this study, we limited time to adapt steps to investigate the control of step adjustments further. We found that lengthening steps on average had greater magnitude of error than shortening steps and no difference was seen between errors for step narrowing and lengthening. Further, no particular direction of step adaptation became worse under time pressure. We did not find BoS limiting steps to have higher magnitudes of error, overall, which is in similar to the findings of previous studies. Hoogkamer et al. (2015) found that shortening steps were less accurate than widening or lengthening, and all directions of adaptation declined similarly under time pressure. Although the time to plan in reactive stepping condition (targets became visible at contralateral midstance) was similar to Hoogkamer et al. (2015) (who shifted targets (0.7, comparable with 37% in to stride phase or early swing 1.6 step before foot placement on the target and 0.4m comparable with 74% or late swing phase 0.4 steps), our results were not comparable to those of (Hoogkamer et al., 2015). Differences might be due to the differences in paradigms; dual-step paradigms allow you to make a plan in time but make you change this plan, whereas just little time allowed to plan foot placement , in which case a new foot placement plan with the given direction had to be made, or selected from multiple trajectory plans and others inhibited (Duque, Lew, Mazzocchio, Olivier, & Ivry, 2010). However, participants were only required to adjust their steps in 20% of the walks. This means participants probably walked at steady state without targets and, when targets appeared, adjustments were sudden. In contrast, this study required continuous foot placements to targets and, in the reactive condition, the position of the target was unknown up until midswing. If the target was not yet visible participants would suspect one coming up, just not knowing the position. This may have caused participants to have full attention and, while the task was challenging (evident in the higher rate of targets missed for stroke survivors than healthy), the visual cues of the targets may have actually improved performance on the reactive task for stroke survivors over what it may have been in situations where required adjustments are wholly unanticipated. This improvement in performance in reactive situations has also been seen for stroke survivors when turning reactively (Hollands et al 2010).

In the situation where participants are walking in contexts in which they anticipate changes to be required several plans for limb trajectories may be primed in advance and those that are inappropriate inhibited (Duque et al., 2010). The difference in dual-step targets (Hoogkamer et al., 2015; Moraes et al., 2007) might be only one movement plan is planned, as initial foot location is present. Whereas, when no foot location is known yet, the possibility exists multiple foot placement options are prepared for, as in the two target tasks (Coallier, Michelet, & Kalaska, 2015; Pastor-Bernier & Cisek, 2011).

7.4.4 Does foot placement accuracy worsen more in medio-lateral vs. anterio-posterior steps adjustments with reduced response time?

Our results show that medio-lateral step adjustments (narrowing and widening) have increased error when adjusted reactively while anterio-posterior step adjustments (shortening and lengthening), surprisingly, become more accurate when reactive. The difference between anterio-posterior and medio-lateral step adjustments may be that anterio-posterior adjustments are made in line with the existing direction the momentum of the body (forward). In contrast, adjusting foot placement in the medio-lateral direction, may require that forward momentum of the body has to be redirected. This notion is supported by the work of Bancroft and Day (2016) who showed that specific foot placements are planned in accordance with the direction of the body momentum. Our results therefore indicate redirecting the limb trajectory, at mid swing in a medio-lateral direction, is more challenging than prolonging or terminating the anterio-posterior limb movement. This is in contradiction with both Moraes et al. (2007) and Hoogkamer et al. (2015) who show shortening and narrowing are more challenging than widening and lengthening step. In the recent study neither the BoS limiting adjustments declined more in accuracy as shown in Moraes et al. (2007) nor all adjustments declined similarly in stepping accuracy when limiting the available response time as shown by Hoogkamer et al. (2015). The fact that all adjustments steps show different errors might be explained by Bancroft and Day (2016), who describe the direction and the moment the body has, has to be specific to reach the specific foot placement target. This momentum and direction the body has is specified before the targeting foot leaves the floor when stepping from standing (Bancroft & Day, 2016). During steady state walking the body already has a forward momentum, this momentum will only have to be speed up or slow down to reach lengthening and shortening steps. However, when narrowing or widening steps the momentum has to be redirected sideways. When this redirecting of the momentum is done before the foot leaves the floor (planned condition) less force is needed than when made during swing (reactive condition) which may be the cause of the increased errors when adjusting foot placement medio-laterally reactively.

7.4.5 Is foot placement accuracy of the paretic limb affected more severely than the non-paretic limb when response time is limited?

No differences in error have been shown between the paretic and non-paretic leg in stroke survivors when stepping under time pressure. This could be explained in one of two ways: 1) both limbs are affected to a similar extent by different impairments; impaired motor control of the paretic limb in aiming and impaired strength/balance during paretic stance and non-paretic aiming, or 2) the stroke affects the bi-lateral control affecting both legs in a similar way. Both theories have been argued in previous literature. Said et al. (2008) found obstacle crossing during paretic stance was more balance threatening (greater separation between CoP and CoM) than when standing on the non-paretic leg, which indicates stroke survivors are less stable during paretic stance. In addition, Nonnekes et al. (2010) found delayed responses in adaptations during paretic swing, which led to slower reactions to the sudden appearance of a target. Both these impairments directly affect the ability to aim with the paretic leg. However, difficulty keeping balance during paretic stance affects aim of the non-paretic limb. Finally, it has been suggested that walking is requires bilateral organisation. Specifically, planning and execution of a successful foot placement adjustment requires adjustment to both the aiming and stance legs (Reynolds & Day, 2005a). Moreover, because the paretic side may show the most obvious impairments bilateral effects of stroke are often overlooked. For example, Debaere, Van Assche, Kiekens, Verschueren, and Swinnen (2001) found evidence for coordination deficits on the non-paretic side. In the present study paretic and non-paretic aim are affected similarly in both absolute and mean error. The previous chapter, investigating the role of balance in control of foot placement, also did not show differences in paretic and non-paretic foot placement when balance was supported. Taken together these results suggest bilateral affects of stroke and the fact that aiming foot placement requires adjustments to both the stance and aiming limbs are the key factors affecting foot placement accuracy in stroke survivors and account for the lack of difference in aiming ability between paretic and non-paretic limbs.

7.5 Implications

The increased percentage of misses during target stepping in both planned and reactive condition in stroke survivors indicates a lack of anticipation on upcoming steps in stroke survivors. The fact that they do not seem to plan foot placement about two steps ahead- even when it is possible- may indicate they only have time to plan the next foot placement to moment resulting in last minute foot placement adaptation in both planned and reactive target stepping conditions. Whereas, healthy adults showed an increase in percentage of missed targets indicates they did plan their steps ahead when information was available. The fact that any walking context which requires stroke survivors to continuously plan, monitor and adjust steps results in them missing one in every ten steps may account for some of the reasons for falls during trips slips and misplaced steps. This finding implies 1) Future investigations of reactive foot placement control need to use paradigms in which reactive steps are totally unanticipated rather than paradigms in which people may be primed to anticipate adjustments will be needed. 2) Cognitive processes are involved in controlling ongoing foot placement adaptations, which might indicate the prefrontal cortex (PFC) is involved in monitoring, processing, inhibiting and planning accurate foot placement.

7.6 Limitations

Although, more time might be available to adjust foot placement for stroke survivors who walked more slowly than healthy young and older adults, the gait phase (mid stance) in which adjustments are required is the same for all participants groups in the present study. The fact that reactive targets are delivered at the same phase in the gait cycle for all, normalizes the challenge of the task with respect to individual abilities (or gait speeds).

The main limitation of this study lies in the use of continuous target stepping paradigms which reduced the intended challenge of the reactive targets which were shown only at mid-stance. Instead, the fact that participants were walking in a context which primed them to anticipate continuous demands to adjust steps (regardless of whether they could see the step in advance or not) allowed us to examine how stroke survivors deal with cluttered environments rather than unanticipated change. The results of this work suggest that stroke survivors deal with cluttered environments in a reactive or online mode while healthy young and older adults appear to be able to plan ahead even within the context of needing to adapt most steps (this is seen in the fact that there was an increase in missed targets in the reactive condition compared to the planned condition for healthy young and older adults while stroke survivors showed no differences in planned and reactive conditions). Further, the use of visual cues to specify targets may have served to draw and maintain attention to the task and in so doing actually improved the performance of stroke survivors on the reactive condition (compared to the rates of hits and misses other studies have shown in more unanticipated conditions). This indicates that future studies and indeed treatment should focus on the interplay of attention/cognition and gait adaptability.

7.8 Conclusion

Instead of measuring the differences between planned and reactive foot placement, the continuous target stepping in the recent chapter allowed us to examine how stroke survivors deal with cluttered environments rather than unanticipated change. The results of this work suggest that stroke survivors deal with cluttered environments in a reactive or online mode while healthy young and older adults appear to be able to plan ahead even within the context of needing to adapt most steps (this is seen in the fact that there was an increase in missed targets in the reactive condition compared to the planned condition for healthy young and older adults while stroke survivors showed no differences in planned and reactive conditions). However, this chapter does not answer the question whether stroke survivors need more time to adjust their foot placement, it does implicate stroke survivors have difficulty with cluttered terrain. The likelihood of misplacing a step in cluttered terrain is large, as one out of ten steps is likely to be misplaced, and could possibly lead to a fall. Therefore, further investigation is needed to understand why stroke survivors do not use information available in cluttered situation.

8 Can we use fNIRS to measure executive function during target stepping?

8.1 Introduction

In previous chapters (6 and 7) we saw that stroke survivors undershot all targets, implying they experienced difficulty planning steps in response to the task/environmental demands. Indeed, adapting walking in response to the environment requires processing of visual information to plan and execute changes to foot-placement. It has been proposed that adjusting foot placement in response to the environment may be more cognitively demanding than steady state walking (Malouin, Richards, Jackson, Dumas, & Doyon, 2003; Mazaheri et al., 2015; Mazaheri et al., 2014; Takei, Grasso, Amorim, & Berthoz, 1997; Takei, Grasso, & Berthoz, 1996) and that the reported impaired executive function of both older adults and stroke survivors may be a cause for impaired ability to adapt gait (Yogev-Seligmann, Hausdorff, & Giladi, 2008). Specifically, the pre-frontal cortex (PFC) is involved in cognitive processing to plan and execute foot placement adaptations:

1) The dorsolateral pre-frontal cortex, is responsible for on-line integration and inhibition of visual information (Miller & Cohen, 2001) about the environment and motor planning of the limb trajectory (Miller & Cohen, 2001; Miyake et al., 2000). The dorsolateral cortex is therefore involved in, inhibiting visual information that is not of any meaning for the movement and solve the problems of planning the new foot trajectory based on the relevant visual information as about the changing environment (Gentili, Shewokis, Ayaz, & Contreras-Vidal, 2013).

2) The orbitofrontal cortex monitors ongoing behaviour and is responsible for impulse control by selecting the relevant visual information used in the dorsolateral cortex to make the motor plan (Lezak, Howieson, & Loring, 2004).

3) The anterior cingulate cortex is involved in emotional drives, experience and integration. Part of that means that this particular part of the brain is involved in fear inhibition (Giustino & Maren, 2015). But is also able to flag up when the movement plan is in conflict with abilities in the past (Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999), Like when a certain step-movement has fall in a like situation previously.

Lesions in these particular regions of the PFC, which are common after stroke and can occur irrespective of the location and severity of the lesion (Zinn et al., 2007), are associated with a decline in all the above cognitive or “executive” functions (Alvarez & Emory, 2006; G. M. S. Nys et al., 2007; Vataja et al., 2003; Zinn et al., 2007). Further, impaired executive function has been associated with reduced performance on balance and mobility tests (Liu-Ambrose, Pang, & Eng, 2007) and could be the reason stroke survivors stop walking while talking- a key indicator of falls risk (Hyndman & Ashburn, 2004; Lundin-Olsson, Nyberg, & Gustafson, 1997; Weerdesteyn et al., 2007).

Evidence from previous studies in this body of work indicates that stroke survivors have a surprising ability to achieve the movements necessary to reach foot fall landing locations with relatively good accuracy. This implies that impaired ability to adapt walking in response to the environment is not due to an inability to achieve the required movements but may, instead, be due to cognitive/motor planning impairments. Specific support for this idea stems from the fact that a previous study (Nonnekes et al., 2010) saw no differences between stroke survivors and healthy counterparts in aiming to a foot placement target when balance was supported, and the previous chapters in this body of work show stroke survivors’ errors in foot placement, although larger than healthy controls are relatively small. So, achieving a degree of accuracy in foot placement is feasible even for stroke survivors with balance and motor control impairments. Instead we hypothesize that impaired gait adaptation after stroke may not be due to an inability to produce movement patterns necessary to achieve a safe foot placement, but due to cognitive-motor interference (Plummer-D'Amato et al., 2008; Yogev-Seligmann et al., 2008). Cognitive motor interference (an inappropriate utilization of limited cognitive resources) causes an exacerbation of motor impairments when additional cognitive demands are made during a motor task. Therefore, the tendency for stroke survivors to fall behind targets, as seen in previous chapters (see chapter 6 and 7), might be due to impairments in processes of motor planning mediated by the PFC.

Multiple studies have investigate the role of executive function in control of foot placement in healthy individuals either by adding a dual task (e.g. counting backwards, stroop etc.) to the initial target stepping task (Mazaheri et al., 2015; Mazaheri et al., 2014), or by making the target positions in the stepping task more complex (Peper et al., 2012). These studies demonstrate that more complicated walking tasks require additional cognitive resources compared to steady state walking (Mazaheri et al., 2015; Mazaheri et al., 2014; Peper et al., 2012). Specifically, more complicated walking tasks have been shown to decrease walking speed in healthy older adults (Peper et al., 2015). This observed decrease in speed may allow additional time to process visual information and align the motor plan of foot placement positon to the position of the target. Variability and magnitude of foot placement error have also been shown to increase with more complex tasks, like target stepping in combination with a response time dual-task where participants had to respond to a vibratory stimulus by pressing a response button (Mazaheri et al., 2015; Mazaheri et al., 2014). However, measuring dual-task decrement (that is the reduction in motor performance caused by a concurrent cognitive task) is only an indirect indication of cognitive load or movement automaticity (McFadyen, Gagne, Cossette, & Ouellet, 2015). Arguably, a more direct measure is that of cortical activation. However, measures of cortical activation during walking are limited to functional near-infrared spectrometry (fNIRS) or electroencephalography (EEG). Both of which are in their infancy in being applied during walking and have limitations in spatial resolution (reflecting which areas of the brain are involved in the task), temporal resolution (reflecting when in the gait cycle a given network is involved) and are vulnerable to motion artefact and heamonamic responses due to activity (Scholkmann, Spichtig, Muehlemann, & Wolf, 2010).

Only two studies to-date have used (fNIRS) to measure activation of the frontal lobe during gait (Koenraadt, Roelofsen, Duysens, & Keijsers, 2014; Mihara, Miyai, Hatakenaka, Kubota, & Sakoda, 2007). One study showed increased activation of the PFC before the start of the target stepping task in comparison to steady state walking (Koenraadt et al., 2014); which authors interpreted as an increased requirement for cognitive preparation/planning for target stepping than normal walking. In a study comparing involvement of the PFC in healthy participants and stroke survivors while accelerating their walking speed (Mihara et al., 2007), there was a trend for increased (PFC) activation when altering speed of gait in healthy adults. Stroke survivors, on the other hand, showed a significantly higher PFC activation in both walking tasks compared to the healthy participants. Additionally, control participants showed a decrease of activation in the PFC during the steady state phase which was not seen in stroke survivors. This generally increased PFC activation might indicate that stroke survivors require more attention to control walking than healthy adults and that this creates a ceiling effect where requirements for further increases in cognitive resources to control more difficult tasks are not possible.

However, as mentioned previously, use of fNIRS during walking is still in its infancy. Since these initial studies using fNIRS a recent systematic review (Vitorio, Stuart, Rochester, Alcock, & Pantall, 2017) has been published which gives clearer guidelines on use and provides suggested protocols for processing of fNIRS. All of the aforementioned studies fall foul of one or more of these recent guidelines for protocolling and/or processing. For example, Koenraadt et al. (2014) measured only 2 optodes on the PFC and only found differences between tasks in one of them. - this emerging guidance provides an opportunity to assess the feasibility and utility of using this measurement tool to gain insight into the role of the PFC in control of foot placement after stroke.

The aim of this chapter is to explore if executive function can be measured using fNIRS when walking by asking: 1) does fNIRS show systematic changes in PFC activation when stepping to targets in preferred stepping locations compared to irregular targets. 2) Does fNIRs show systematic differences in PFC activation between stroke survivors and healthy young and older adults in different walking conditions?

8.2 Methods

The general methods of participant recruitment, clinical assessments, apparatus, familiarization, and stepping performances are as explained in the methods chapter (Chapter 5: General Methods).

8.2.1 Protocol

Participants walked a baseline; the baseline was started the moment the treadmill reached self-selected walking speed and lasted until the first tasks started. The 7 seconds before the start of the task were taken as baseline. The three walking conditions: steady state walking: walking without targets at self-selected walking speed, regular stepping: stepping to targets located in preferred foot locations and irregular stepping: targets eliciting lengthening or shortening of steps (±25% of baseline step lengths) and narrowing or widening (±50% of baseline step widths) when targets could be seen at least 2 steps in advance.

8.2.2 Executive function

In order to measure cognitive involvement in the control of foot placement we measured cerebral blood flow using fNIRS. fNIRS is a non-invasive way to measure cortical activity (Power, Falk, & Chau, 2010) through the haemodynamic response associated with neuron behaviour validated against functional magnetic resonance imaging (fMRI) (Cui, Bray, Bryant, Glover, & Reiss, 2011). The technique involves placing a flexible rubber headband on the participants' forehead. Sensors within the headband measure changes in reflections of infrared light absorption, which corresponds to changes in levels of blood oxygenation in the area of the brain below (Pre-frontal cortex). Differences in the oxygenated haemoglobin

(HbO_2) and deoxygenated haemoglobin (HbR) allow measurement of relative changes haemoglobin concentration through the use of light attenuation (A. Duncan et al., 1996). Any changes in blood flow and blood oxygenation that are detected during a given task (or during a task compared to baseline/usual walking without targets) can be used to infer the recruitment of those underlying brain structures during the task. These assumptions are the same principles that fMRI is based upon (Cui et al., 2011). However, fNIRS offers some unique advantages when compared to fMRI. One such benefit is that the procedure is non-invasive whereby a flexible rubber headband is strapped to an individual's forehead in a natural environment, removing the need for an individual to enter the restrictive fMRI scanner. All proposed fNIRS procedures are standard and have been used in previously approved projects (HSCR14/12).

To asses executive function clinically, the Trail making test is used. The time it takes to fulfil a trial making test connecting subsequent numbers is taken (1-2-3-4 etc., Trial making test A) and the time it takes to connect a number to the corresponding letter in the alphabet (1-A-2-B etc., Trial making test B). The Trail Making Test is a neuropsychological test to evaluate visual attention and task switching. The time difference between section A and B provides information about the speed of visual searching, scanning, processing, and mental flexibility (Arbuthnott & Frank, 2000; Kortte, Horner, & Windham, 2002; Moll, de Oliveira-Souza, Moll, Bramati, & Andreiuolo, 2002) which are part of executive function and relevant to the task of adapting steps to step on a trail of targets. To interpret relative performance, the B-A difference and the B/A ratio are often derived; however, the B/A ratio has shown to be a better indicator for difficulty switching attention between tasks than the B-A difference (Arbuthnott & Frank, 2000). This test has been validated (Arbuthnott & Frank, 2000) and normative data has been provided (Hester et al., 2005). In addition, the Trail Making Test is previously used to base groups on with low and high level of executive function (low executive function= B/A ratio> 2.78 and high executive function= B/A ration< 1.91) in a target stepping study (Mazaheri et al., 2014). This separation of low and high executive function showed differences on the available response time in the dual task during target stepping and walking on a treadmill between groups (Mazaheri et al., 2014). Therefore, the Trail Making Test is used to get an idea of the level of cognitive functioning of participants that took part in this study.

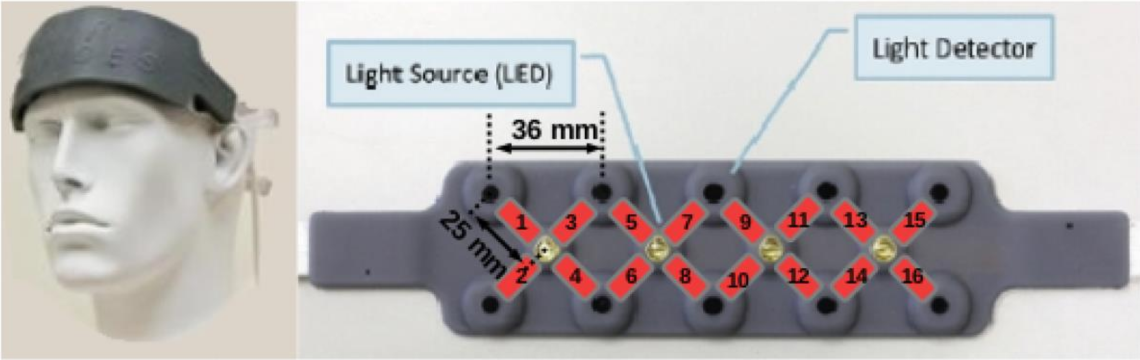

Figure 8.1 *Schematical representation of a) placement of the fNIRS on the head and b) positioning of probes (light detectors) and light sources within the fNIRS head band used.*

8.2.3 Data processing

In this study a 16-probe functional near infrared spectrum (Biopac, Goleta, United States) 2Hz, wavelength 730 and 850nm is used to measure percentage of change of oxygenated haemoglobin (HbO_2) and reduced haemoglobin (HbR) in the frontal lobe. All fNIRS data processing was done using HOMER2 (an open-source MATLAB program). The optical density was calculated from raw data, motion artifacts were detected using the motion artifact by channel tool in HOMER2 (Huppert, Diamond, Franceschini, & Boas, 2009), these motion artifacts were corrected with a cubic spline interpolation. A bandpass filter was applied to correct for physiological and systemic noise like respiratory, blood pressure and cardiac signals (1.14-0.5Hz). Changes in optical density was transferred in to HbO and HbR concentration using the modified Beer-Lambert law and the age dependent path length factor (A. Duncan et al., 1996). Lastly, block average of HbO_2 and HbR was calculated over the 3 trials of all 3 conditions (steady state walking, regular and irregular target stepping). Data was averaged over probes with most complete data, least variability of signal and which were located over the dorsolateral PFC region of interest for more complex walking (located on the top half, centrally on the forehead) (Gentili et al., 2013). To determine which probes would contribute to the block means of HbO_2 and HbR concentrations for each condition of walking, all 16 probe activations per participant were checked visually to determine the extent to which data from any given probe was missing, variability of signal and the location of probes. (see appendix 3). Visual inspection of the response of HbO_2 and HbR concentration of all participants, showed probes 5,7,9 and 11 seemed most responsive to the visual target stepping tasks and were those which corresponded with the dorsolateral PFC region of interest. Mean of HbO_2 and HbR concentrations over the duration of each walking condition were normalised with respect to the level of HbO_2/HbR during the 7s of walking preceding the appearance of the targets Given that neither HBO2 or HBR show trends for change, and HBO_2 has been reported previously as the most reliable and sensitive measure for cerebral oxygenation changes during walking (Holtzer et al., 2015) for simplicity, only HBO_2 results will be reported. The blocks are divided into an early and late stage of the tasks, as done by Koenraadt et al. (2014). For the early task, a block average of the first 20s of data was taken and the late task was a block average of the last 20s of the task. All three walking tasks (steady state walking, regular and irregular target stepping) were split in an early and late task average, resulting in six averages. For process specifics see table 8.1.

Table 8.1 Processing details fNIRS data.

Filter/ Proces	Input	Study specifick	Reason	Described by
Motion artefact	SDTHResh=12 (12-20) AMPTresh=0.5 tMotion= 2.0s tMask= 0.5s	Review time-series analysis for fNIRS	Identifies motion artefacts based on changes in signal amplitude and/or standard deviation	Huppert et al. (2009)
Cubic spline correction	P=0.99 (Parameter for accuracy of the spline interpolation)	Validation of motion artefact reduction method. Comparison of motion arifact correction techniques.	Defined motion artefacts are modelled one by one, throughout each NIRS time-course using cubic spline interpolation.	Scholkmann et al. (2010) R. J. Cooper et al. (2012)
Band pass filter	0.14- 0.5Hz	Review time-series analysis for fNIRS	Reducing physiological systemic noise as cardiac cycle, blood pressure	Huppert et al. (2009) Boas 2004 (physiological changes)
HbO_2 and HbR calculation	Beer-Lambert law	Discription of the Beer-and lambert law in fNIRS	Concentration of Hbo more reliable and sensitive to locomotion-related cerebral blood flow	A. Duncan et al. (1996) Miyai et al. (2001)
Block analysis	t=-7 50 1-20s=early 31-50s= late	Found difference early in the task between normal walking and precision stepping	Calculates block average over a given time range (t<0) corrected for baseline (t0)	Koenraadt et al. (2014)

8.2.4 Statistics

Statistical analysis was done using SPSS 20. Repeated measure ANOVA was conducted for the average change of HbO_2 and HBR a comparison was made between the within subject factor, there walking conditions (steady state walking, regular and irregular target stepping) and time averages (early and late) were tested. The between subject factor was the different groups, stroke survivors, healthy older adults and healthy young adults. Only HbO_2 will be reported by lack of a trend in both HbO_2 and HbR changes, with HbO_2 being reported previously as the most reliable and sensitive measure for cerebral oxygenation changes during walking (Holtzer et al., 2015).

8.3 Results

No differences were found between early and late blocks, data of these blocks were merged again in further analysis.

8.3.1 Participants

9 young adults, 7 older adults and 9 stroke survivors (participant demographics see table 9.2) took part in the study. Stroke survivors have shown to have more difficulty switching attention in the trail making test (B/A ratio of 21± 49), whereas healthy young and older adults do not have much difficulty (B/A ratio of 2± 0). The results of the trial making test (TMT) are explained by the ratio (TMT-B divided by TMT-B) and threshold based on the high (<1.91s) and low (>2.78s) functioning executive function by Mazaheri et al. (2014). Only one young healthy adult and one stroke survivor had a low functioning executive function and six young, four older healthy adults and three stroke survivors had high functioning executive function. The Montreal cognitive assessment (MoCa) (Pendlebury et al., 2010) showed two healthy older adults and two stroke survivors had mild cognitive impairments based on the MoCa score (score ≤26) (Ada et al., 1998). However, all participants understood the meaning, and were competent to give informed consent. According to this data the population taking part in this study was cognitively high functioning.

Table 8.2 *Participant demographics and clinical characteristics represented in mean ± SD unless specified differently.*

	Young adults	Older adults	Stroke Survivors
N (F)	8 (5)	7 (3)	8 (2)
Age (years)	30.3± 5.8	65.7± 9.3	66.1±9.3
SSWS (m/s)	1.01± 0.16	0.94± 0.23	0.52± 0.26
Trial making test A (s)	29± 12	30± 15	46± 28
Trial making test B (s)	52± 32	59± 33	531± 1089
TMT B/A ratio	2± 0	2± 0	21± 49
Montreal cognitive assessment	-	27.7± 1.9	26.5± 4.3
Falls (last 12 months)	-		
No fall (N)		6	6
1 fall (N)		1	1
1< fall (N)		0	1
Time since stroke (months)	-	-	100.6± 158.2
Paretic (Right)	-	-	5
Berg balance	-	-	49.6± 5.8
Fugl-Meyer (lower limb)	-	-	24.5± 6.1
Dynamic gait index	-	-	24.0± 5.4
10m-walking speed (s)	-	-	14.3± 6.2
Timed up and go (s)	-	-	17.7± 6.8

8.3.2 Are there systematically changes between steady state walking, regular or, and irregular target stepping?

No main effect of walking condition was found (Mean ±SEM HbO_2 concentrations for steady state walking 0.002± 0.074Mm, regular -0.058± 0.075Mm and irregular target stepping requiring step adaptation 0.035± 0.029Mm). All tasks induce similar HbO_2 concentration changes in the PFC relative to baselines taken during steady state walking in between trials (see figure 9.2). Basically, you would expect steady state walking to have no change in HbO_2 compared to a baseline taken while walking steady state. However, in 12 of 23 participants the HbO_2 change was smaller in the steady state walking condition than at least one of the target stepping conditions, these 12 participants did not show lower or higher TMT A/B ratios. The lack of systematic results make it difficult to identify participants who might have followed the hypothesized increase in HbO_2 during target stepping in comparison to steady state walking.

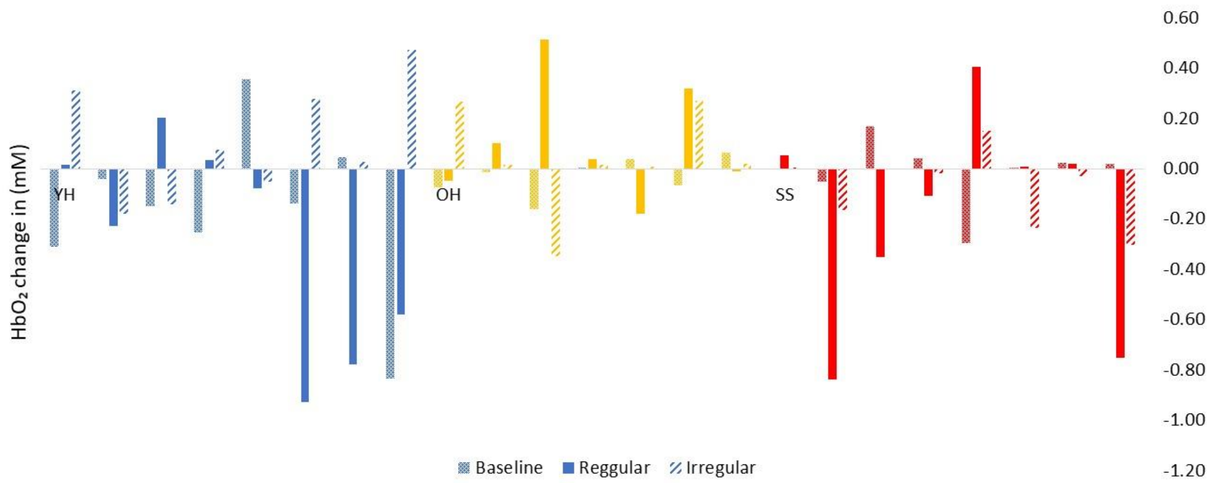

Figure 8.2 *Data represent the mean change of HbO_2 for each individual participant in the three walking conditions (steady state walking, regular and irregular target stepping in relation to the 7s baseline taken before each walking task. Young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red, for each condition steady state walking (dotted bars), regular (filled bars) and irregular (striped bars) target stepping.*

8.3.3 Is this the change in concentration for the different conditions different for the different groups?

No interaction effect of group and condition is found. Young (steady state walking (0.028± 0.120Mm), regular (-0.091± 0.122Mm), irregular (0.062± 0.048μm)) older healthy adults (steady state walking (-0.013± 0.136Mm), regular (0.101± 0.139Mm), irregular (0.115± 0.054Mm)) and stroke survivors (steady state walking (-0.010± 0.127Mm), regular (-0.186± 0.30Mm), irregular (-0.073± 0.051Mm)) have similar HbO_2 concentrations in the PFC.

8.3.4 Can we measure Executive function using fNIRS?

The observed power for the different conditions for all groups was for a combined sample of 24 participants (9 young, 7 older healthy adults and 8 stroke survivors) with and average difference of 0.091mM between steady state walking and regular target stepping and an average standard deviation of 0.84 lead to a power of 0.08. The main difference between groups had an observed power of 0.23. The comparison between conditions had an observed power of 0.16.

8.4 Discussion

Difficulties with anticipating upcoming targets seen in stroke survivors in previous chapters may be due to difficulties with cognitive/executive functions sub serving adaptations to foot placement in response to the environment. To date only two studies have investigated a direct measure of executive function during target stepping (Koenraadt et al., 2014; Mihara et al., 2007). However methodology is questionable (in light of recent guidelines (Vitorio et al., 2017) and PFC activation during gait adaptability is tested either in young healthy adults (Koenraadt et al., 2014) or stroke survivors altering speed rather than foot placement (which has higher demands for precision and planning) (Mihara et al., 2007). Although, we know stroke survivors are impaired in walking adaptability, the cause of the impairment could be at a number of levels. Impairments in processing speed, inhibition, cognitive planning and peripheral motor execution could all cause difficulties of foot placement adaptations for stroke survivors. How and if activation of the PFC and executive function is a part of the limitations in gait adaptability in stroke survivors could be answered with robustly measuring PFC activation during gait adaptation tasks. Testing PFC oxygenation in stroke survivors as well as young and older healthy adults can give us insight if stroke survivors cope differently with gait adaptation tasks and use full capacity during steady state walking. However, the methodology of measuring cortical activation directly during walking still needs development. This study therefore sought to determine if changes in PFC activation measured by fNIRS changed systematically in response to walking conditions which could be expected to progressively increase requirements for movement planning and adjustment involving the networks of the PFC. Our results indicate that: 1) fNIRS measurement of PFC activation did not vary systematically with increasingly challenging walking conditions. 2) fNIRS measurement of PFC activation did not detect differences between stroke survivors and healthy counterparts.

8.4.1 Implications for cortical networks sub-serving gait adaptations

Ultimately the results indicate there is no significant difference between steady state walking and target stepping in PFC activation. If we take confidence that the fNIRS measures reflect the real cortical demands of this task, this could be interpreted as stroke survivors use their full capacity of their PFC during steady state walking, not allowing and increase for more complicated walking tasks. Although, in this study, no difference between steady state walking and regular or irregular target stepping was found in any of the participant groups. Which would mean all participants, including young healthy adults, would be reaching their limit of executive function/ activation of the PFC during steady state walking. Taking into account, hits and misses and foot placement errors in previous chapters were very small for healthy young, it would be very unlikely they would be reaching PFC limits during just steady state walking. Therefore, it is more likely either the different walking tasks do not require increasing degrees of cognitive processing or measuring tools lacked specificity. However, previous studies were able to find differences in fNIRS measures of cortical activation between steady state walking and target stepping in healthy adults (Koenraadt et al., 2014) or acceleration of walking speed in both healthy adults and stroke survivors (Mihara et al., 2007) there was also a study showing online/reactive adjustment could might be done subcortically (Corporaal et al., 2018).

Koenraadt et al. (2014) showed, in the beginning of a target stepping task, more activation is registered in the PFC than during steady state walking and this effect washes out when people were walking for longer than 12.5 sec. Assuming targets were placed at preferred foot positions, which is not actually specified in the methodology, the increase within the first 12.5 seconds of a task could indicate people activate the PFC more during the synchronisation period than when walking at steady state. However, limitations of this study are that differences are only found in one out of two optodes and increased metabolic response might be due to the start of walking (as time is needed to reach steady state walking speed).

Mihara et al. (2007) showed, both ataxic stroke survivors and healthy controls had increase PFC oxygenation during acceleration and steady walking over the rest period (standing still) in between walking tasks. Control subjects showed higher oxygenation of the PFC during the acceleration phase than during steady state walking (Mihara et al., 2007). Stroke survivors showed to have increased steady state PFC oxygenation, however the oxygenation during the acceleration phase was actually lower than during the steady state walking (Mihara et al., 2007). This indicated stroke survivors do have increased PFC activation during steady state walking over that seen in healthy counterparts. However, acceleration, which can be considered an adaptation, did require more activation in control subjects but, in stroke survivors' acceleration actually required less PFC activation than steady state walking. This is somewhat surprising as the adaptation, the acceleration phase, would be expected to need more or at least similar amount of cortical activation to steady state walking (which is confirmed in healthy subjects). Limitations of this study were that they compared stroke survivors with a control group that had a mean difference of 10 years in respect to the stroke survivors. It is known that oxygenation levels increase with age (Beurskens, Helmich, Rein, & Bock, 2014), so the observed increase in level of oxygenation in stroke survivors could be due to the average age of 53years and only 43years in control participants. Additionally, participants walked at different speeds (controls average 3.5km/h and stroke 1.19km/h) which could have induced different levels of metabolic costs as well as motion artefacts and noise.

8.5 Limitations

There may be several reasons for not finding significant differences between walking tasks and groups. Generally, the main issue is the high inter-subject variability which could be caused by 1) The limited used sample sizes 2) Data exclusion because of motion artefacts. 3) The baseline measure that was used as the reference for normalizing data from different conditions.

The number of participants in the current study is limited (12 young healthy adults, 8 older healthy adults and 9 stroke survivors). However, 12 young healthy adults in Koenraadt et al. (2014) was sufficient to show significant differences between target stepping and steady state walking. The groups used by Mihara et al. (2007) were slightly bigger (12 stroke survivors and 11 controls). Vitorio et al. (2017) suggest a sample size of at least be 15 participants. However, taking the results of the previous literature, we at least should have been able to identify trends of systematic responses of PFC activation in increasingly complex target stepping conditions compared to steady state walking and group differences between stroke survivors over healthy participants. The fact that intersubject variability was high and no differences in activation are apparent between steady state walking and target stepping highlights the importance of rigorous methodology for using fNIRS.

Due to motion artefacts, high number of channels were excluded from analysis. Originally data of 29 participants was collected (12 young, 8 older healthy adults and 9 stroke survivors), data of 6 participant was lost due to motion artefacts (see appendix 5). Some of these motion artefacts might be due to the fact a tethered system is used in the recent study, when Vitorio et al. (2017) suggest to use wireless systems for use of fNIRS during walking. While, wires were handled with caution and secured at the back of the participants to reduce the noise induced from movements of the wires, they might still be accountable for an increase in noise and motion artefacts. If this is the case it could be anticipated that the noise could readily be filtered out. We attempted to treat the data for noise artefact in two ways 1) filtering and 2) use of an appropriate baseline/normalisation reference.

The baseline we used was, as suggested by Vitorio et al. (2017), taken in between every walking condition (block). However, in the recent study the baseline was taken during steady state walking, while traditionally it has been taken during rest in stance as used in Koenraadt et al. (2014). The rational for taking the baseline during steady state walking was that it would correct for the noise induced by the walking itself, and therefore the comparison of steady state walking to steady state walking would be zero (e.g. common mode rejection), and any differences seen in other walking conditions would reflect the real change due to increased cognitive demands/cortical activation. However, the walking itself induced a high amplitude oscillation around 0.2Hz (see appendix 4), which was not corrected by motion artefact correction or bandpass filtering. In this study a baseline of 7 seconds was taken. In theory, this time would allow the haemodynamic response to react, but no specific guidelines on duration of the baseline are given in previous literature (Cui, Bray, & Reiss, 2010; Tong & Frederick, 2010). The 7s baseline under sampled this 0.2Hz high amplitude oscillation. This greatly affected the average of the baseline, and therefore the comparison of the walking tasks (steady state, regular and irregular target stepping). However, a longer baseline duration was not possible as 7s was the longest possible time all patients walked prior to the start of targets being presented in each block of walking conditions. The 0.2Hz oscillation would have been accounted for with a baseline of about 10s, however a multitude of 10, providing a longer baseline for about 60s, an even longer baseline duration would be better. In previous literature of fNIRS during walking, baselines during standing ranged from 1s-35s (Atsumori et al., 2010; Koenraadt et al., 2014; Mirelman et al., 2014). However, a more robust solution would be to address the cause of the oscillation and try and exclude it from the analysed data (either by adjusting the protocol so the oscillation is not present of by developing a way to filter it out).

8.6 Implications/ Recommendations

The difficulty reaching significant differences and the number of limitations in this study call for a standardization of protocols and data processing of the use of fNIRS during walking. While, Vitorio et al. (2017) just published a list of recommendations, the following additions/adjustments to some of their recommendations are suggested:

8.6.1 Protocol

- Sample sizes should be sufficient, future work should identify a minimum clinical important difference.
- When comparing different participants groups, match participants by age, as PFC activity changes are related to age (Beurskens et al., 2014).
- Baselines should be taken in between al trials (Vitorio et al., 2017). However, it should be added that baseline should be done during walking (if that is the task carried out during the study) so that the baseline reference is subject to the same sources of noise and metabolic requirements of the task (Kline, Huang, Snyder, & Ferris, 2015), and of a sufficient duration (as shown in this study walking might induce high oscillation noise). Further a baseline test of cognitive tasks only should be done alongside any walking tests to establish that the fNIRS in non-walking tasks is indeed responsive to cognitive demands so that null results in walking can be taken with confidence.
- Different walking speeds may account for different levels of metabolic cost (Passmore & Durnin, 1955). This must be accounted for when comparing different groups with different self-selected walking speed, and/or walking tasks that might also affect walking speed, such as visually guided walking tasks have been shown to do (Peper et al., 2015). The different metabolic costs of walking should be considered when designing a test protocol and sufficient duration, to allow participants to reach metabolic steady state, of each walking condition be carried out so that blood flow changes due to cortical activation can be separated from those associated with the metabolic demands of the task alone.
- Differences between over ground and treadmill walking need to be kept in mind when generalizing findings. Treadmill walking has shown to have higher activation of the PFC measures with fNIRS (Clark, Christou, Ring, Williamson, & Doty, 2014) however, this might be due to the higher metabolic costs that come with treadmill walking compared to over ground walking (Beurskens et al., 2014; Fraser, Dupuy, Pouliot, Lesage, & Bherer, 2016).

8.6.2 Processing

- Atomized motion artefact algorithms are proposed as opposed to visually checking the data for motion artefacts. Atomizing artefact detection makes it objective and reproducible and therefore is preferred (Huppert et al., 2009).
- Correction of motion artefacts should be done by using a cubic spline correction, as this method produced the most significant improvement of data representation over all (mean-squared error, Pierson's correlation coefficient, contrast to noise ratio) (R. J. Cooper et al., 2012).
- Filtering for systemic noises should be done with a band-pass filer 0.14-0.5Hz to account for physiological changed due to the task, which might account for two times the changes of the cognitive task (Boas, Dale, & Franceschini, 2004).

8.7 Conclusion

This study showed that use of fNIRS during walking tasks requires careful consideration of methodology and data processing to be considered robust. Our results indicate that fNIRS does not systematically detect differences between tasks of increasing cognitive challenge. Recent studies suggest that reactive adjustments to walking are related to subcortical matter so it is possible that gait adaptation is indeed mediated by subcortical networks and therefore no additional PFC activation is required over steady state gait (Corporaal et al., 2018). However, this notion is very new and contrary to results of the limited previous literature. Albeit, evidence for the role of PFC activation in walking adaptation tasks and in stroke survivors provided by current literature should be taken with caution as these studies have methodological flaws. Further development of fNIRS processing and methodology is required in order to apply this potentially powerful measurement tool towards addressing key questions regarding which neural networks are involved in supporting cognitive processes required to adapt walking. Identifying which networks are involved in control of gait adaptations will help enable predictions of patients' ability to benefit from therapy using knowledge of functions served by viable neural control networks.

9 Discussion

Stroke survivors are known to have a high falls risk (Hyndman et al., 2002; Jorgensen et al., 2002; Lamb et al., 2003; Smith et al., 2006; Yates et al., 2002). These falls mostly are due to a trip, slip or misplaced step (W. P. Berg et al., 1997; Blennerhassett et al., 2012; Weerdesteyn et al., 2008). The circumstances of falls imply that impaired ability to control and alter foot placement in response to environmental, task and body constraints may be a cause of falls for stroke survivors. Stroke survivors are known to have reduced gait adaptability, indicated by impairments avoiding obstacles (Den Otter et al., 2005; van Swigchem et al., 2013), turning (K. L. Hollands et al., 2010), and adjusting foot placement medially (Nonnekes et al., 2010). Therefore, the ability to adapt foot placement may be the key to understanding why falls risk is increased in stroke survivors. However, research is only just beginning to look at the control of foot placement as an underlying factor in supporting overall adaptability of walking. As a result, much work is needed to determine the best way to measure adaptability of walking and foot placement control in order to then identify the role of balance, response time and executive function in the control of foot placement.

9.1 Methodological development of target stepping

Gait adaptability is multi-dimensional and encompasses a wide scope of possible manoeuvres including turning, obstacle avoidance, avoidance/recovery from trips and slips, etc. (Balasubramanian et al., 2014). Given the breadth of traits which speak to the functional skill of gait adaptability (Balasubramanian et al., 2014) there are few standardised clinical or research measures which accurately capture all aspects of gait adaptability. As a result, research reports everything from toe clearance, foot placement error, percentage of targets/obstacles hit and missed, and time and steps taken to turn as outcome measures reflecting ability to adapt walking. Even within the same gait adaptability paradigm, e.g., target stepping, different outcome measures are used including crude measures of percentage of targets hit and missed (K. L. Hollands et al., 2015; Hoogkamer et al., 2015; Mazaheri et al., 2015; Mazaheri et al., 2014) and more specific measures of foot placement error either based on the centre of pressure (CoP) (Hoogkamer et al., 2015; Mazaheri et al., 2015; Mazaheri et al., 2014; Potocanac, Smulders, Pijnappels, Verschueren, & Duysens, 2015) or Centre of foot (CoF) (Nonnekes et al., 2010; Reynolds & Day, 2005a, 2005b). Whether or not these different measures relate to one another or if they are interchangeable remains unknown. Ultimately, the plethora of measures and paradigms for assessing gait adaptability precludes a synthesis of the existing evidence to create a better understanding of the underlying causes of impaired gait adaptability for stroke survivors. Therefore, this thesis first sought to validate and standardise measures to robustly evaluate foot placement accuracy, as control of foot placement is hypothesized to form the basis of all manoeuvres of gait adaptability (obstacle avoidance, turning, etc.).

Firstly, a comparison of CoP based gait event detection against kinematic gait event detection (Pijnappels et al., 2001; Zeni et al., 2008), confirmed that mid-stance (the time point at which foot placement accuracy is ideally measured) could be validly determined for hemi-paretic gait using CoP. Previously, CoP based gait event detection had been validated for young healthy participants (Roerdink et al., 2008). However, the characteristics of the CoP cyclogram is known to change after stroke (Wong et al., 2004), so a validation of CoP based gait event detection for hemiparetic gait was needed. Our comparison showed CoP gait event detection is likely more robust than kinematic gait event detection methods during gait adaptations, as loading and unloading of the feet is likely more directly related to gait events than the changing trajectories. This may be especially true when people are asked to adapt their gait during walking when changes to acceleration (and third derivative jerk) of feet trajectories are expected and could lead to false positive gait event detections.

Lastly, foot placement error, based on CoP and CoF position relative to the centre of the target, were compared. These two forms of foot placement error measurement have both been used in previous literature to reflect different aspects of foot placement control (i.e. success of foot aiming/fulfilment of target stepping task objectives vs control of balance when altering the BoS). This comparison showed CoP position on the foot changes when adjusting step lengths/widths. When lengthening a step, CoP lies more posteriorly on the foot than when shortening a step (where CoP is more anterior on the foot). The fact that CoP and CoF foot placement error measures did not respond to changes in foot placement systematically and consistently compared to one another indicates that these measures are not interchangeable and do indeed reflect different aspects of foot placement control. Because CoF error most directly reflects fulfilment of target stepping task objectives, CoF error was selected as the most appropriate measure for subsequent studies of foot placement control.

9.2 Control of foot placement and stroke related impairments

The overarching aim of this thesis was to gain insight into the causes of impairments of gait adaptability in stroke survivors by examining control of foot placement. A pilot study was done to determine how best to measure foot placement, and it highlighted impairments in balance and ability to adjust foot placement with limited time available as key factors which may affect foot placement accuracy during walking. The subsequent experimental investigations of these factors (balance, response time and executive function) provide insights into possible mechanisms of control of foot placement and indications for future research to increase the understanding of foot placement control in stroke survivors.

9.2.1 Balance

The first experimental study in this body of work examined the role of balance in foot placement control during target stepping. The role of balance in foot placement control was examined in two ways: 1) by systematically enlarging/limiting the BoS through lengthening/widening and shortening/narrowing foot placements, and 2) by comparing accuracy of foot placement when support for balance was provided (through crutches) and when participants were unsupported.

The main results from this experiment showed that limiting the BoS during walking did not increase foot placement error in either healthy adults or stroke survivors. In comparison to previous literature of stroke survivors who performed step adaptations from standing (Nonnekes et al., 2010) and healthy young subjects who performed target stepping while walking (Hoogkamer et al., 2015), foot placement errors in this study were small and, accordingly, the reductions in errors with balance support were also small. Further, contrary to the results of (Hoogkamer et al., 2015), BoS limiting steps (shortening/narrowing) were not less accurate than steps which were not expected to challenge balance (lengthening/widening). Collectively, the results of this work and that of previous literature indicate that **dynamic balance control during walking affects foot placement control differently than when taking a step from standing**.

Support for balance deficits however, were shown to benefit foot placement accuracy. The fact that balance support did elicit general (not direction or limb specific) improvements in accuracy of foot placement for stroke survivors indicates that impaired balance does affect accurate foot placement control and confirms the relationship between these factors. **Balance**

is important for accurate foot placement, especially in stroke survivors, who seem to benefit from balance support when target stepping during walking.

This experiment also provided insight into the negative speed accuracy correlation, due to the slower self-selected walking speed in stroke. However, stroke survivors taking part in the balance study were moderately impaired for walking (seven out of eleven were moderately impaired walkers, two were non-functional walkers and two were functional walkers). Three of the stroke survivors reported one or more falls six months prior to the data collection. Not surprisingly, stroke survivors on average walk slower than healthy young and older adults. When the self-selected walking speed was accounted for (when covariation was included) no significant differences between healthy participants and stroke survivors were seen. This shows that impairments of foot placement control due to stroke affect both aiming and stance limbs equally and that speed accuracy trade off may be an important factor for control of foot placement. Given the latter, the fact that stroke survivors walk at slower speeds may allow them sufficient time to plan and adjust foot placement. Given that increasing walking speed a key priority for rehabilitation (Dickstein, 2008), future studies need to examine the effects of increasing speed on foot placement accuracy. In other words, we may be aiming to help patients to walk at faster speeds and putting them at risk of not being able to alter foot placement in response to the environment. **Stroke survivors walk at different speeds and have greater magnitudes of error, indicating that impaired walking speed is a feature of stroke.**

Lastly, although errors were relatively small, stroke survivors were generally poorer at making accurate foot placements and undershot all directions of step adjustment, whereas healthy young adults overshot shortening targets. This is somewhat surprising given that undershooting a step means making a step even shorter than required and healthy young adults did not behave this way. One interpretation of this is that stroke survivors 'fall behind' the targets and, subsequently, have difficulty catching up during a constant stream of targets. This occurred even when adjusted steps were separated by a number of targets appearing at the preferred step location in attempt to limit cumulative effects of errors in adjusted steps. Similar results have been found among stroke survivors during walking to auditory cues. These studies found the paretic leg lagged behind the auditory cues and the healthy leg and healthy adults actually anticipated the foot placement just before the audio cues (Roerdink et al., 2011). This suggests that the time stroke survivors need to anticipate the target is important for the accuracy of the foot placement.

9.2.2 Response time

The second study was done to investigate how limiting time to anticipate to a target would affect foot placement accuracy during walking. A reactive condition of target stepping, where targets were only visible at contralateral midstance, was compared to the planned target stepping condition in which the target was visible for at least two steps ahead.

Stroke survivors generally missed more targets than healthy counterparts in both conditions, but did not miss more targets in reactive conditions compared to planned conditions. Healthy older adults do miss more targets during reactive target stepping task, in agreement with a previous study on limiting the available response time (Hoogkamer et al., 2015), indicating healthy older adults may deal with the two walking conditions differently. Healthy older adults may be able to use information to pre-plan steps when targets are visible in advance (planned target stepping), but when the targets only become visible at mid-stance, they miss more targets. In contrast, stroke survivors had similar failure rates in both planned and reactive target stepping. The fact that stroke survivors perform similarly in both tasks shows a ceiling effect in their target stepping performance and may imply that they deal with both conditions with the same strategy. When taken together with the knowledge that stroke survivors 'fell behind' target (had negative stepping error in AP direction on shortening, lengthening and preferred stepping tasks), this indicates that stroke survivors may use a cluttered terrain strategy when continuously stepping to targets, only bringing attention to the next step when the previous step is finished. This only allows one step to plan for a foot placement, which likely is the cause of the similar failure rates in the planned and the reactive target stepping task. **Stroke survivors miss more targets during ongoing target stepping because they tend to use a 'cluttered terrain' strategy, and only allow themselves a short time to plan for the upcoming foot placement.**

Surprisingly, placement errors were relatively small in both experiments, even for stroke survivors who missed 10% of all targets (reactive/planned). The fact that time pressure did not exacerbate foot placement errors more in stroke survivors is surprising, but may be explained by how people tend to direct attention in cluttered terrains. Matthis and Fajen (2014) and M. A. Hollands and Marple-Horvat (2001) found that when walking in more cluttered environments, people shift their gaze closer to their body. This could mean stroke survivors use a "cluttered terrain strategy" and, effectively, make reactive step-by-step adjustments to ALL targets (even those they *could* look at to plan in advance) when they are walking to continuous targets. This "cluttered terrain strategy" has been seen in previous studies and is characteristic of older adults with high risk of falls and/or fear of falling (M. A. Hollands & Marple-Horvat, 2001; Matthis & Fajen, 2014). **This highlights that absolute time to plan the next foot placement may not be as crucial as the actual processes of directing attention and planning foot placement adjustments.**

9.2.3 Executive function

The last experiment was done in order to better understand which neural networks might be involved in the planning of step adjustments. The PFC activation (by oxygenation changes) during steady state walking, regular target stepping and irregular target stepping was measured. The PFC activation was expected to increase with the increase of cognitive demands that was done by adding visual-spatial information on foot placement and more challenging foot placement. Most studies attempt to measure the role of cognition in controlling movement using dual task paradigms. Dual task decrement, however, is only an indirect indication of how much and what kind of attention is required to control the movement, complimenting fNIRS as a more direct measure of cortical activation. Only two studies have yet directly measured cortical activation during walking using fNIRS (Koenraadt et al., 2014; Mihara et al., 2007), and both showed an increased PFC activation during more complex walking tasks. However, these studies involved healthy young participants or stroke survivors adjusting speed, therefore, we currently have no understanding of which cortical networks may be involved in planning precise foot placement.

In the recent experiment the sample sizes used were small (group sizes of 7-8 where Vitorio et al. (2017) advised sample sizes of 15); however, no trend of increased PFC activation was seen for targeted walking over steady state walking in any group. The lack of any trend in the data demonstrates that measuring PFC activation with fNIRS is less straight forward than it seems. Measures of oxygenated blood flow had high inter-rater variability, possibly due to the data collection and processing methods used in this specific study. To guide future work attempting to measure cortical activation during walking, a detailed description of the used protocol and processing methodology is provided alongside a discussion providing the rationales, limitations and recommendations for future work. However, measuring with fNIRS is still in its infancy. Understanding how the cortex is involved in gait adaptability is a very important question, as cognitive processing speed recently has been identified as a strong predictor of injurious falls (Davis et al., 2017), and suggestions have been made that cognitive processes are cortical for planned and subcortical for reactive foot placement adjustments (Corporaal et al., 2018). Future research is therefore needed to establish if and how fNIRS can be used to achieve these aims during walking tasks. **It is likely that cognition is involved in gait adaptability; however, measuring systems that have enough specificity to measure spatial and temporal changes in specific areas of the brain are needed to confirm this hypothesis.**

9.3 Implications and Recommendations for Methodology of future research

As discussed above, this body of thesis work, in combination with current literature, indicates key problems in gait adaptability in stroke survivors as well as key features of foot placement control in healthy adults. In addition to the key problem/features explored, critical next steps to improve current understanding will be suggested by exploring the answers to the following questions: 1) What does CoP tell us about the control of foot placement adaptation? 2) What is the amount of foot placement error that will make someone fall prone? 3) How do we best determine how much time is required to adapt our foot placement (i.e., how do we test reactive responses and unanticipated responses)? 4) What is the best way to provide evidence for the use of a 'cluttered terrain strategy' in stroke survivors? 5)How should we be measuring cortical activation during walking?

Firstly, in this thesis, CoF error is recommended for use as the most valid measure for foot placement accuracy. However, CoP position relative to the margins of the BoS (margins of stability) might be a more indicative measure of how foot placement and balance are affected by the gait adjustment. In this thesis, CoP was seen to be located more posteriorly on the foot (at mid-stance) when lengthening a step and more anterior on the foot when shortening a step. This indicates the location of the CoP in relation to the foot placement change that is made differs with where the CoF lands. Arguably, the position of the CoP under the foot is more important for keeping balance that the position of the foot. For example, if the CoF overhangs the curb when the CoP is still located on the part of the foot that is supported by the curb, this does not present a problem. Therefore, balance problems when adjusting foot placement might not be caused by the location of the foot, but by the location of the CoP. In addition to this, it may be that while the task requires participants to place their feet such that the CoF overlies the CoT, people may not aim the foot using the CoF, but rather may aim with the border of their foot or some other point that affords visibility of the foot and target for the longest possible time in the limb trajectory. In this way, CoF may reflect task demands but not necessarily control processes. Future research should therefore determine what CoP location relative to the CoT indicates about control.

One pressing issue remaining is how much error would indicate whether or not someone is fall prone when measuring foot placement error with the CoF. Currently there is no indication of a functionally relevant size error in foot placement. It has been shown that greater time is taken to walk over and hit targets and is correlated with poorer balance scores (K. L. Hollands et al., 2016). Poor balance scores have been associated with a higher risk of falling. Hence this shows, albeit indirectly, that control of foot placement and the ability to alter foot placement may be related to falls risk. But as yet, there is no evidence that the size of foot placement error discriminates sensitivity between groups of fallers and non-fallers (or high and low falls risk).

A common-sense argument could be made for how big the error needs to be before the foot is in a position which is likely to be difficult to recover from. Stroke survivors miss about 1 in every 10 steps which reinforces that stroke survivors have difficulty in making step adjustments. This would affect falls risk when one in every 10 steps could possibly be an unsafe step. In addition, stroke survivors have an average foot placement error of 7.0±0.9cm when unsupported and only 4.7±0.7cm when supported for balance, reiterating the importance of balance in foot placement control. This decrease of foot placement error in stroke survivors when supported for balance is closer to the error healthy participants make when walking to targets; a 95% CI for YH 3.0±6.3cm and OH 2.5-6.3cm when not supported for balance. It could be argued that healthy young adults have 'healthy' foot placement control and therefore the range of errors made in young healthy adults is simply 'normal' range of error. The error made in young healthy adults ranged from 5.1 to 9.0cm. It would be expected that stroke survivors within this range of error would have enough control of their foot placement to safely walk in their community. Looking at the foot placement errors made in stroke survivors, 3 stroke survivors were within the 'normal' range of foot placement error, 4 stroke survivors had smaller magnitudes of foot placement errors, and 4 stroke survivors had increased foot placement magnitudes of error and therefore would be considered at risk to fall prone. Further, the amount of foot placement error was not related to the self-selected walking speed. The fact that as many stroke survivors had increased foot placement errors as those who had decreased foot placement errors may indicate that foot placement error alone is not an informative measure to indicate individual falls risk. Both healthy older adults and stroke survivors had similar number of falls in the past 12 months making it difficult to differentiate between high and low fall risk though. The fact that balance support reduced average foot placement error in stroke survivors to be within the same range as healthy adults indicates that foot placement error is an indicative measure for balance, which is known to be associated with high risk of falling. Additionally, in previous work by Nonnekes et al. (2010) similar foot placement error was found in healthy controls (about 4cm for medial and 2cm for lateral steps) while in stroke survivors larger foot placement errors were measured (about 11cm for medial targets and 5cm for lateral targets). In this study stroke survivors showed that, with support for balance, foot placement errors decreased to comparable errors made in healthy controls. However the magnitude in the study by Nonnekes et al. (2010) is larger than measured in this body of work and showed a decrease in foot placement error indicating a similar normalising effect on foot placement errors in stroke survivors. The difference in error magnitudes may be caused by the difference in study design considering Nonnekes et al. (2010) used a one step paradigm (static balance, where the recent work was during walking (dynamic balance). This difference in foot placement error between walking and taking one step indicates static balance and dynamic balance are affected differently due to stroke, while both are likely to affect safe ambulation in daily life.

In this body of work the difference between foot placement error made in unsupported stroke survivors (7cm) and supported stroke survivors (4.5cm), and older (3.8cm) and younger (4.2cm) healthy adults, shows balance support decreases foot placement error to an almost ‘normal’ level. However, when no support is offered stroke survivors show to have an increased foot placement error of 7cm, which is about 24% of their foot length (29cm on average). For example, this could mean a stroke survivor aims for a curb with the centre of the foot, but only lands on the curb with about a quarter of the foot. In this case, to direct the CoP on the curb hip and ankle strategies must be used; a large plantar flexion movement is needed to direct the CoP to the front of the foot followed by a hip extension moment to raise the torso above the lower limb and maintain an upright position. Stroke survivors are known to have slower force production and might not even be able to recruit enough force to redirect the CoP using these ankle and hip strategies. When the ankle and hip strategies are not available for stroke survivors, the other option to maintain stability would be to take a quick step forward with the contralateral leg, bringing the CoP to the new stance leg on the curb. However, reaction times as well as force recruitment are known to decline in stroke survivors. Therefore, this attempt to step up a curb leads to imbalance, and when one has not enough recourses to recover with either force of the aiming leg or the response to recover with the contra lateral leg, it is likely to lead to a fall. Therefore, this 7cm/24% of foot length foot placement error is likely to be meaningful for the position of the CoP and therefore balance. Future investigations of how foot placement adjustments in real life are made (i.e. 3D targets or obstacles) and how foot placement error correlates with fall incidence, coordination, lower limb strength and the berg balance scale might be helpful to determine more evidence.

When limiting time to respond to targets, medio-lateral foot placement adjustments were affected negatively (greater magnitudes foot placement error) by limiting time to plan foot placement while anterior-posterior foot placement adaptations were actually improved (smaller magnitudes of foot placement error). Further insight into how and when adjustments to limb trajectories are made might tell us more about what has caused this somewhat curious difference in the effect of time limitation on the accuracy of different directions of foot placement adaptations. Specifically, previous studies have shown that trajectories of the foot are planned. The moment the foot leaves the floor, the direction and body momentum are set (Bancroft & Day, 2016; Reynolds & Day, 2005b). Besides that, the trajectory of the foot does not change according to the time at which the information about the position is given, but in respect to the foot placement time (Reynolds & Day, 2005b). Studying the time adaptation of the trajectory of the foot and how these trajectories change might tell us more about how different foot placement adaptations are affected.

The theory used in this body of work explaining why foot placement error did not increase with less time to respond, 'the cluttered terrain strategy', is a way to explain why stroke survivors have negative foot placement error. The idea behind this theory is that stroke survivors do not have the ability to pre-plan foot placement. This could be tested by showing a target and making it disappear the moment the previous foot is placed. If foot placement gets worse (with greater magnitude than in healthy age matched participants) when targets disappear in comparison to when the target stays visible, it might tell us whether stroke survivors do not plan foot placements ahead. Two factors that are also likely to be involved in the planning of foot placement are where participants look, as the sequence of acquiring visual information and turning has shown to be important (K.L. Hollands et al., 2013), and executive function, which is needed to process visual-spatial information and act on it.

Executive function during walking has shown to be measurable with fNIRS in some cases (Koenraadt et al., 2014; Mihara et al., 2007). However, the protocols and processing methodology are poorly described, making it hard to actually reproduce a robust study. Other flaws in methods of existing literature are: 1) Allowing limited room for the actual haemodynamic response in a block analysis of 12.5s when the haemodynamic response can be delayed up to 7s (Koenraadt et al., 2014), 2) Reporting arbitrary units without discussing how these units are defined (Koenraadt et al., 2014), 3) Comparing between groups with an age difference of ten years (Mihara et al., 2007), as oxygenation levels are shown be related with age (Beurskens et al., 2014), and 4) Differences in walking speeds between groups (Mihara et al., 2007) , which could lead to different levels of movement artifacts and systemic noise, such as heart rate and respiratory noise. Vitorio et al. (2017) suggest some guidelines for collecting data with fNIRS during walking, highlighting the attention that needs to be paid to processing options and noise and movement artifact cancellation. For example, the cause of the high amplitude/low frequency noise introduced when walking, as shown in appendix 4, should be investigated; it could either be caused by the tethered system we used or be a direct result of walking. In both cases neither the bandpass filter (0.14-0.5Hz), nor the cubic spline correction to correct for movement artifacts adequately corrected for this (assuming it is indeed physiological systemic or movement related noise).

Aside from the previously described limitations of the fNIRS, some limitations of the resolution of the fNIRS also warrant consideration. Firstly, spatial resolution of the headband is limited; rough guidelines are considered for the placement on the forehead: two arrows to align with the nose and the middle of the top of the forehead for medio-lateral localization and two arrows to place over the temporal areas for distal-proximal localization are provided. However, the precise position of the probes is hard to control. Besides the global positioning of the headband, the differences in head sizes will affect the positioning of the probes over their forehead. Additionally, standardization or at least capturing of the positioning of the fNIRS on the head is hard accomplish. Spatial resolution of the fNIRS therefore is limited to the broad area to be captured, which in this study was the PFC. For more specific areas, different systems of hardware might be necessary, for instance, to measure specific areas involved of visually guided walking on inhibiting actions.

Secondly, temporal resolution is limited. The haemodynamic response is known to have a delay of 4-7 seconds (Grice, Brunt, Kushner, & Morrow, 1974; Mihara, Miyai, Hatakenaka, Kubota, & Sakoda, 2008). Capturing heamodynamic response to one adaptation step during walking is therefore not feasible. Therefore, the use of blocks of specific walking tasks are encouraged to allow averages over blocks of different tasks to be compared. Unless the research question is carefully derived according to the spatial and temporal resolutions afforded by fNIRS, an in depth understanding of the involvement of different cortical areas in gait adaptation won’t be achievable.

9.4 Future research questions

Ultimately, this work indicates that future research should attempt to isolate which of the different processing stages needed for visually guided foot placement stroke survivors have the most difficulty with, in order to inform treatments targeted at the cause of stroke related impairments. Determining whether patients' problems lay in scanning the environment (through gaze monitoring), directing attention to the appropriate place in the environment (inhibiting attention to irrelevant cues (- thought to be mediated by PFC networks and measured through both appropriate use of fNIRS and attention probe tasks) at the appropriate time in the gait cycle (manipulating available response time), perceiving and using visual information, or executing an adjustment to the limb trajectory will allow us to indicate what step in this chain of executive functions are problematic for patients and to guide targeted treatment.

9.5 Limitations

In this thesis, the focus was measuring foot placement accuracy, and the factors that affect the foot placement accuracy, of stroke survivors. While an attempt was made to measure this accuracy as robustly as possible, the following limiting factors should be considered. 1) Although CoF is considered a robust measure of foot placement accuracy, the meaning of the position of the CoP on the foot/ in the BoS might be an informative measure for balance control. 2) Percentage of missed targets and the different error measures (mean, absolute and variable error) do not give information about the time point and the direction of the change in trajectory of the foot. 3) The continuous target stepping paradigms in this study did not allow us to study sudden adjustments to one's gait and might have induced attention on the participants. 4) The fNIRS study had limitations in the execution and the power of the study.

Firstly, CoF is considered the reliable measure of foot placement accuracy in this thesis. However, the meaning of the position of the CoP on the foot or in the BoS might be an informative measure for balance control. Stroke survivors positioned their CoP similarly on the foot during the different foot placement adaptations while healthy adults shifted CoP further backward on the foot in lengthening steps and further forward on the foot in shortening steps. This difference between stroke survivors and healthy adults implies stroke survivors can change their foot placement, however the position of the CoP on the foot does not shift to land in the position it naturally would (i.e. further forward when shortening and further backward when lengthening). This considerably static position of the CoP on the foot in stroke survivors may mean they can adjust their foot placement, but cannot control the CoP. This could mean adapting foot placement actually increases risk for balance loss in stroke survivors, and therefore increases risk of falling. Besides the difference in CoP positioning on the foot, CoP position within the BoS might be more important for stability than the accuracy of the placement of the foot. Therefore, it might be that people do not naturally control the position of the foot to maintain stability during a foot placement adjustment, but merely the positioning of the CoP. If CoP is the factor we control to maintain stability during gait adaptation, this might mean CoP (in relation to the foot or BoS) is the measure to manipulate and measure to further understand limitations of gait adaptability.

Secondly, analysis of the percentage of miss and the different error measures (mean, absolute and variable error) was used in this thesis to indicate limitation of gait adaptability in stroke survivors. However, by focusing on the endpoint of the movement, we might have ignored differences in how participants generally place and adapt their foot placement. The time at which participants change the trajectory of the foot according to targets is associated with when they step on the target more than when they get the visual information (Reynolds & Day, 2005b). Besides that, body direction and moments are preferably specified before the targeting foot leaves the floor (Bancroft & Day, 2016). Both of these studies imply that trajectory of the foot and the direction and the momentum of the body can tell us how well people planned or anticipated the upcoming steps. Studying the kinetics and kinematics of the full stride for an upcoming step adjustment may provide more in-depth information about how and when participants change trajectories, momentum and direction while walking, and more importantly might give us insight in what limits stroke survivors.

In addition, in the recent study no differences were found in the variability of foot placement error. As treadmill walking is known to stabilize variability of spatial and temporal gait parameters (Langhammer & Stanghelle, 2010), the lack of variability in this study was raised as a concern. The fact that Mazaheri et al. (2014) did observe differences in variability shows that the temporal and spatial stabilizing effect of the treadmill does not necessary limit the variability of foot placement error. However, in that specific paper CoP foot placement error was used to calculate the variability on where in this thesis CoF is used and these measures do represent different aspects of foot placement coordination and as is discussed in chapter 3 (validation studies).While walking on a treadmill enforces consistent walking speed, the size of the belt allows variability of foot placement so, philosophically it is not expected that variability of foot placement would be affected by the treadmill context.

Thirdly, the continuous target stepping paradigm used in this study did not allow us to study sudden adjustments to one's gait, as it might have induced attention for the upcoming targets on the participants. The fact that participants were walking in a context which primed them to anticipate continuous demands to adjust steps (regardless of whether they could see the step in advance or not), might have limited the study of planned versus reactive foot placement in stroke survivors. However, it allowed us to examine how stroke survivors deal with cluttered environments rather than unanticipated change. The use of continuous visual cues to specify targets may have served to draw and maintain attention to the task and in so doing actually improved the performance of stroke survivors on the reactive condition (compared to the rates of hits and misses other studies have shown in more unanticipated conditions). This indicates that future studies and indeed treatments should focus on the interplay of attention/cognition and gait adaptability.

Lastly, measuring activation of the PFC with fNIRS was less robust than expected. A number of limitations on this technique have been discussed in the implications of this thesis; however, the limitation of the sample size we have used can also be considered a limitation of this thesis. Initially, data from 29 participants was collected, which, due to excessive movement artifacts in 4 young adults, 1 older healthy adult and 1 stroke survivor, resulted in a total of 23 participants. (Vitorio et al., 2017) recommended a sample size of at least 15 participants, which should be kept as a guideline. However, significant differences between tasks and groups have been shown in previous studies with groups of 11/12 (Koenraadt et al., 2014; Mihara et al., 2007), and at least a similar trend should have been visible in the data of our groups of 7/8 participants. Due to the high variability in the oxygenation levels (which might be due to several previously described factors (the tethered system, baseline during walking) no trend was found in the present study, stressing the need and importance of well powered studies with robust protocols and methodology.

9.6 Conclusion

This thesis provides a more in-depth understanding of how stroke survivors control their foot placement in response to ongoing visual information. A 'cluttered terrain' strategy is used to monitor foot placement up until it is placed on the target, to only redirect attention to the next foot placement at that time. This may have caused the 'falling behind' of stroke survivors, as stroke survivors could not keep up with their previously self-selected walking speed and had difficulty reaching the targets. This might also clarify why foot placement errors and percentage of misses did not increase when targets were shown reactively. Healthy adults anticipated foot placement when information was available (planned target stepping) as demonstrated by the increased percentage of misses when targets were shown reactively. Also, stroke survivors benefited from support when adjusting foot placement during walking; foot placement errors did decline when support for balance was used. This indicates walking aides, such as a walking stick, crutches or walking frames might help stroke survivors with poor foot placement control and/or balance to walk more safely in the community. Although we have not been able to measure attention and PFC activation during steady state and visually guided walking, the fact that stroke survivors do seem to use a ‘cluttered terrain’ strategy is a strong indication that attention and processing speed do affect the ability of stroke survivors to anticipate and safely execute gait adaptations.

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Appendices

Appendix Chapter 5:

Methods 5.1: HSR1617-27 Approval letter

Methods 5.2: Participant information sheet

Methods 5.3: Consent form

Methods 5.4: Participant details form

Methods 5.5: Assessment Form

Methods 5.6: Protocol

Appendix Chapter 6:

Results 6.1: Variable foot placement with balance

Appendix Chapter 7:

Results 7.1: Variable foot placement with response time

Appendix Chapter 9:

Methods 9.1: Probe selection

Results 9.2: Oscillation in HbO_2 While walking

Methods 6.1: Automised motion artefact detection

5.1 HSR1617-27 Approval letter

University of Salford MANCHESTER

Research, Innovation and Academic Engagement Ethical Approval Panel

Research Centres Support Team
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20 December 2016

Dear Susanne Van Der Veen,

RE: ETHICS APPLICATION – HSR1617-27 - The role of balance and cognitive function in adaptive walking ability following stroke

Based on the information you provided, I am pleased to inform you that application HSR1617-27 has been approved.

If there are any changes to the project and/ or its methodology, please inform the Panel as soon as possible by contacting Health-ResearchEthics@salford.ac.uk

Yours sincerely,

Sue McAndrew
Chair of the Research Ethics Panel

5.2 Participant information sheet

University of Salford MANCHESTER

Participant Information sheet

How limiting are balance and cognition in gait adaptations of stroke survivors.

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish.

Ask us if there is anything that is not clear or if you would like more information.
Take time to decide whether or not you wish to take part.

Why is this study being carried out?

Walking safely and independently in the community requires the ability to step to safe footfall locations (e.g. level or stable ground, over puddles etc). Some studies have shown that stroke survivors may have difficulty controlling foot placement and that this may be a factor in the high number of falls experienced by people after a stroke. Studies have also shown that ability to adjust steps when walking may be related to problems with balance and/or cognition.

Why are we inviting you to take part?

Everyone in your community group who is more than 18 years old **OR** had a stroke and is able to walk 10 metres in 25 seconds (or less), safely, without any help from someone else or a walking aid, is being invited to participate.

Do you have to take part?

No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form, you are free to withdraw at any time without giving a reason and your participation in your normal community support groups, or the University of Salford will not be affected in anyway.

What will happen to me if I take part?

If you decide to take part, the researchers will arrange an appointment for you to attend the University of Salford at your convenience. **If you are a stroke survivor** who needs help arranging transportation, the researcher will help you do this and your **travel will be reimbursed**.

5.3 Consent form

University of Salford
MANCHESTER

Study Title: **The role of balance and cognitive function in adaptive walking ability following stroke**

CONSENT FORM

Name of Researcher: Susanne van der Veen

Please initial box to indicate agreement

1. I confirm that I have read and understand the information sheet dated 19 December 2017, version 2.0 for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I agree that video images of my legs and feet, from which I won't be identifiable can be taken during the study, and might be used for presentations in future. ☐
4. I agree to take part in the above study. ☐
5. I agree that the data collected from my participation in this study may be used for analyses in other studies. ☐

Name of Participant	Date	Signature
Name of person taking consent	Date	Signature

Participant consent form; version 2.0 19 Dec 2016

5.3 Participant details

Balance and cognition in walking

Participant ID ……………………………
Name of assessor ……………………………
Date ……………………………

Participant Details

Personal information

Participant ID	
Name:	
Date of birth:	.. / .. / ....
Gender:	

Contact information

Phone number:	
Address:	
Email address:	

Participation in Future studies

Can we contact you for future studies?

(There would be no obligation, you can tell us at any time to take your name off our list; we will not give your name or contact information to any other research team)

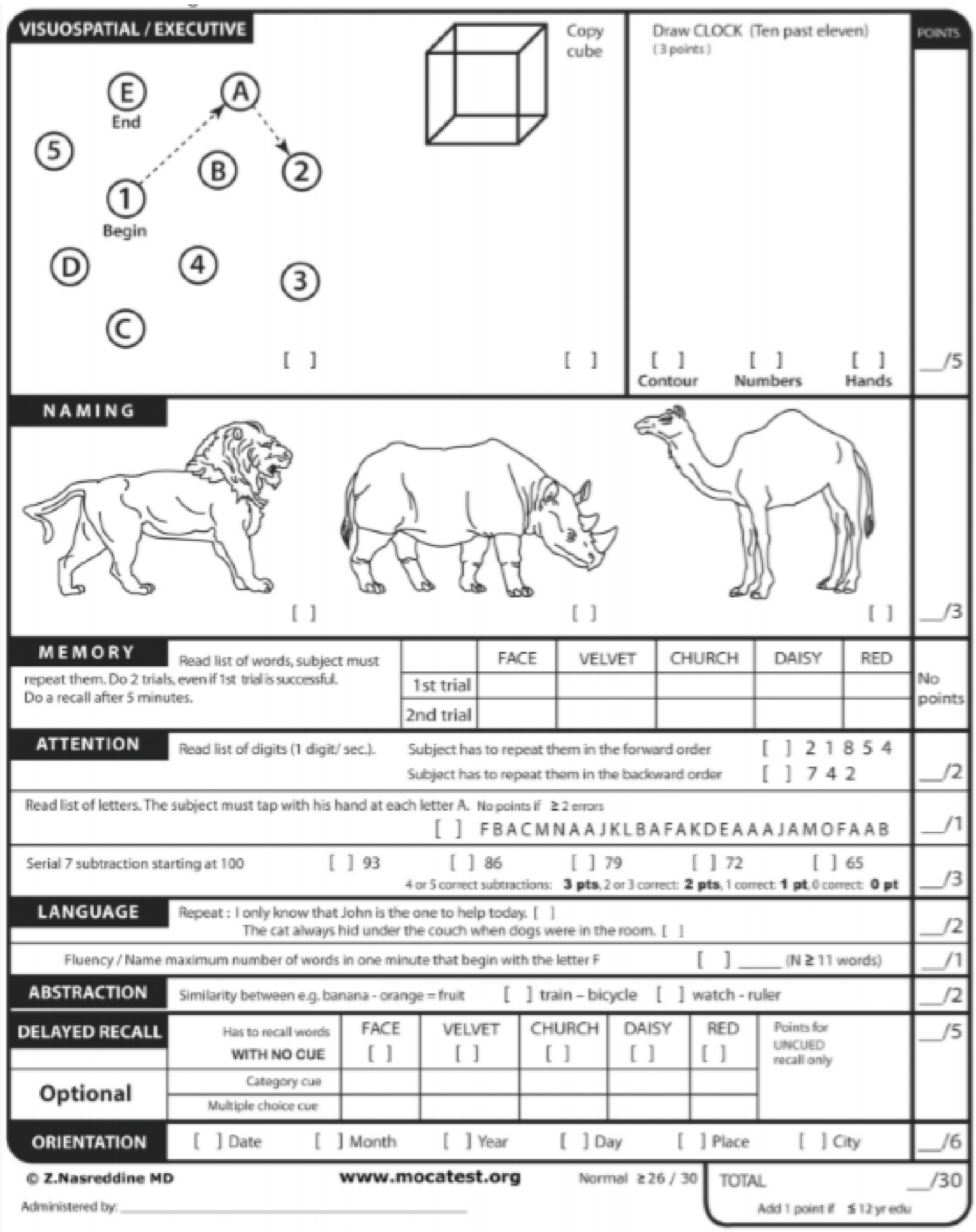
5.4 Assessment form

Balance and cognition in walking

Participant ID ....
Name of assessor ....
Date ....

MoCa

Years of education



VISUOSPATIAL / EXECUTIVE

E End

A

5

B

2

1 Begin

D

4

3

C

[ ]

Copy cube

[ ]

Draw CLOCK (Ten past eleven) (3 points)

[ ] Contour [ ] Numbers [ ] Hands

POINTS

__/5

NAMING

[ ] [ ] [ ]

__/3

MEMORY

Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION

Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

__/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] FBACMNAAJKLBAFAKDEAAAJAMOFAAB

__/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

__/3

LANGUAGE

Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

__/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] ____ (N ≥ 11 words)

__/1

ABSTRACTION

Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

__/2

DELAYED RECALL

Has to recall words	FACE	VELVET	CHURCH	DAISY	RED	
WITH NO CUE	[ ]	[ ]	[ ]	[ ]	[ ]	Points for UNCUED recall only
Optional: Category cue						
Optional: Multiple choice cue						

__/5

ORIENTATION

[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

__/6

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Normal ≥ 26 / 30

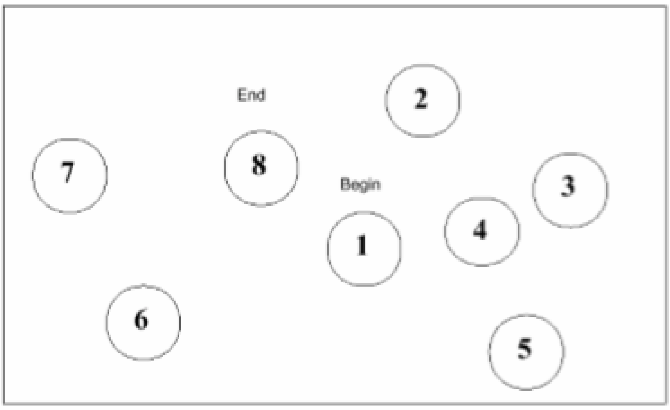
TOTAL __/30

Add 1 point if ≤ 12 yr edu

Administered by: ______________________

Participant ID ……………………………
Name of assessor ……………………………
Date ……………………………

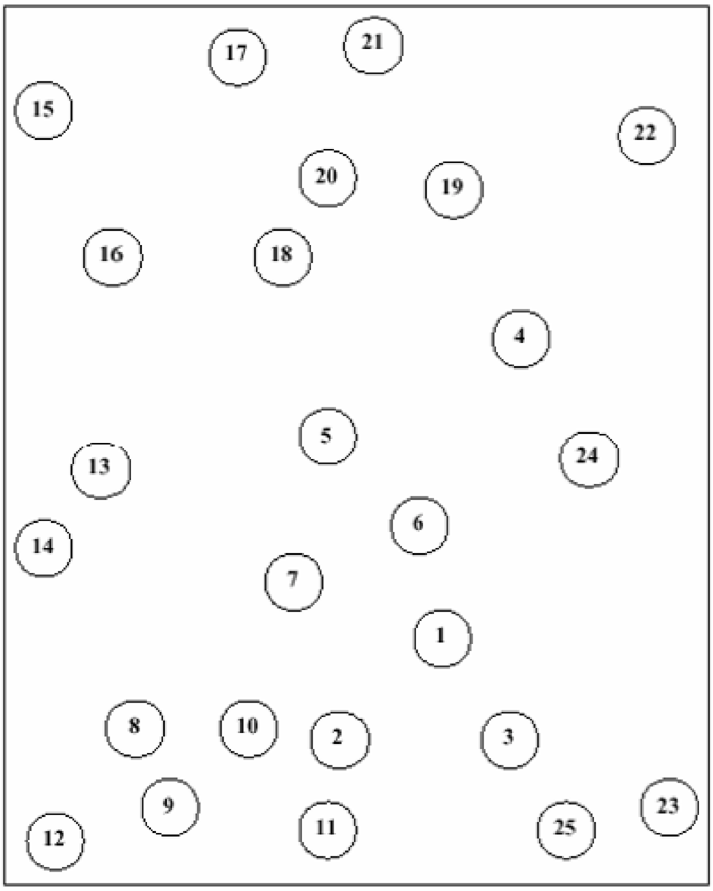
Trail Making Test Part A – *SAMPLE*



Participant ID ....
Name of assessor ....
Date ....

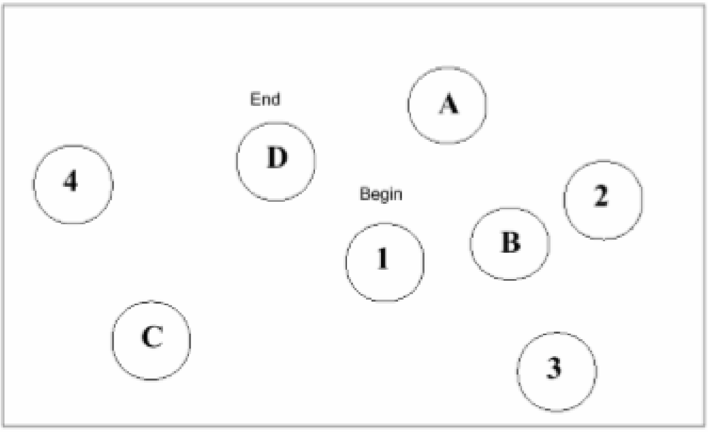
Trail Making Test Part A

Patient's Name: ______________________ Date: ________________



Participant ID ………………………………
Name of assessor ………………………………
Date ………………………………

Trail Making Test Part B – *SAMPLE*

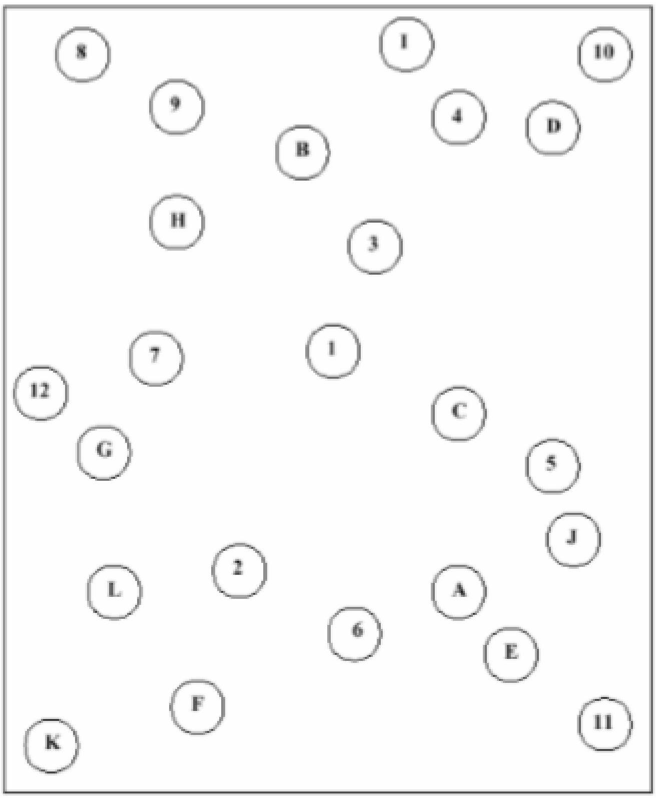


Balance and cognition in walking

Participant ID ……………………………
Name of assessor ……………………………
Date ……………………………

Trail Making Test Part B

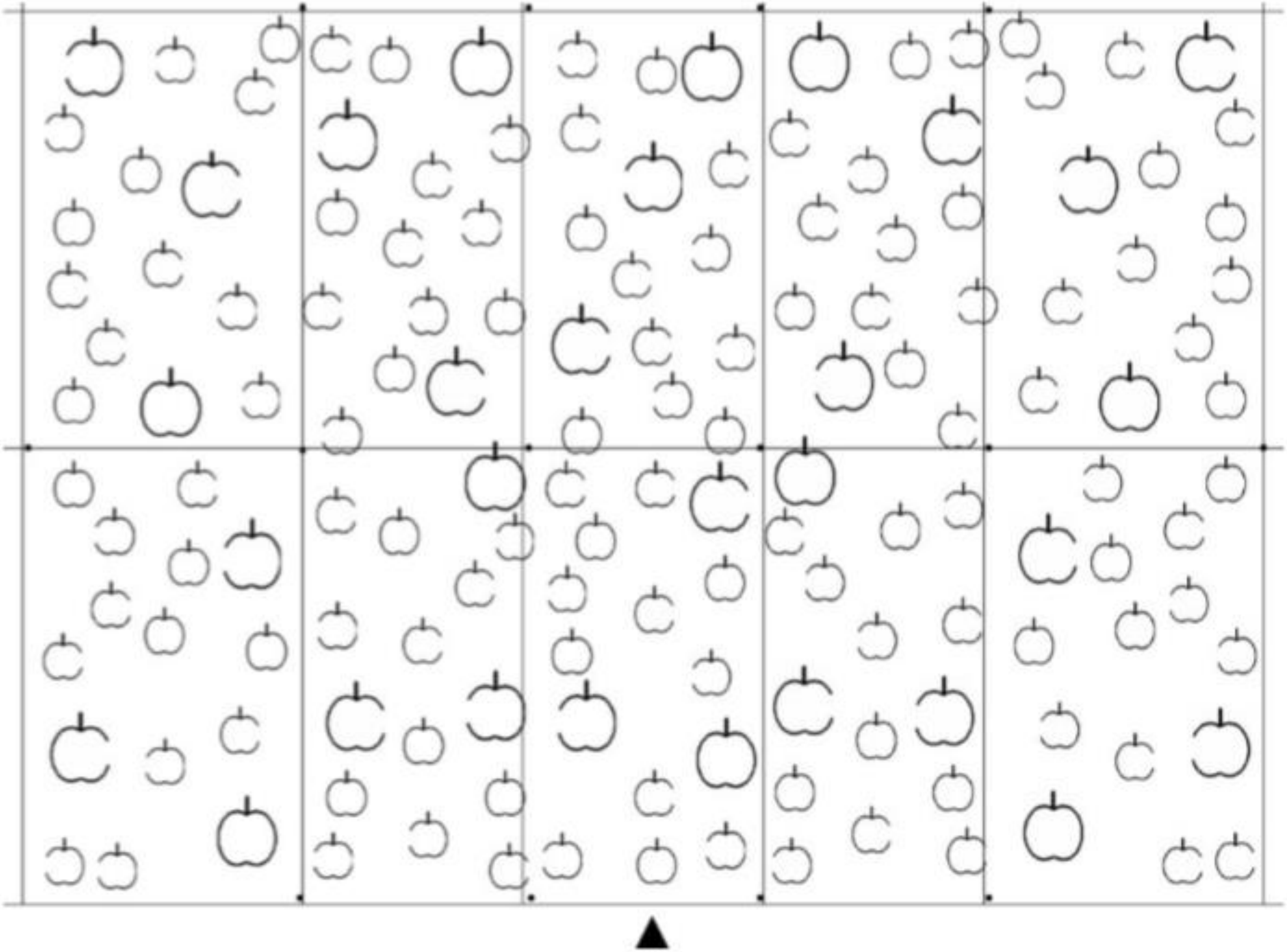
Patient's Name: ______________________ Date: ________________



Balance and cognition in walking

Participant ID ....

Name of assessor ....



Balance and cognition in walking

Participant ID ....
Name of assessor ....
Date ....

Apples Test

Maximum of 5 minutes
Positive values in asymmetry score indicate left neglect, and negative values right neglect
At least one practice trial (max 2) (show apples on midline only)

I. Accuracy score	Number of targets selected (full apples)	**.../50**
II. Egocentric asymmetry score	Number of targets selected on the right side minus number of targets selected on the left side, excluding the middle column (full apples)	...
III. Allocentric asymmetry score	Total left opening minus total right opening selected (distractor apples)	...

Berg Balance

1	Sitting to standing		**0**	**1**	**2**	**3**	**4**
2	Standing unsupported	2 min	**0**	**1**	**2**	**3**	**4**
3	Sitting with back unsupported but feet supported on floor or on a stool	2 min *Score 4 if able to stand unsupported in step 2*	**0**	**1**	**2**	**3**	**4**
4	Standing to sitting		**0**	**1**	**2**	**3**	**4**
5	Transfers		**0**	**1**	**2**	**3**	**4**
6	Standing unsupported with eyes closed	10 sec	**0**	**1**	**2**	**3**	**4**
7	Standing unsupported with feet together	1 min	**0**	**1**	**2**	**3**	**4**
8	Reaching forward with outstretched arm while standing		**0**	**1**	**2**	**3**	**4**
9	Pick up object from the floor from a standing position		**0**	**1**	**2**	**3**	**4**
10	Turning to look behind over left and right shoulders while standing		**0**	**1**	**2**	**3**	**4**
11	Turn 360 degrees	4 sec	**0**	**1**	**2**	**3**	**4**
12	Place alternate foot on step or stool while standing unsupported	20 sec	**0**	**1**	**2**	**3**	**4**
13	Standing unsupported one foot in front	30 sec	**0**	**1**	**2**	**3**	**4**
14	Standing on one leg	10 sec	**0**	**1**	**2**	**3**	**4**
TOTAL SCORE			**.../56**				

Balance and cognition in walking

Participant ID ....
Name of assessor ....
Date ....

Timed up and go

- Time to stand up from armchair, walk 3 metres (10 feet), turn and sit down (sit still)

Verbal instructions:
When I say go, I want you to walk to that tape on the floor, turn, walk back and sit down again. Walk at your normal pace.

Time 1	Time 2	Time 3	BEST

10-meter walk test

Stand at a line, walk to other side of the room (don't indicate other end of the 10meter track to prevent slowing down)

Time

Balance and cognition in walking

Participant ID ....
Name of assessor ....
Date ....

FUGL Meyer (Lower limb score)

- Movement with non-affected extremity first.
- Repeat each movement 3x on the affected side and score best performance. Only test Coordination/speed one time.

	IV. Movement out of synergy			Score		
4a	Standing	Knee flexion (90°)	*0=can't do, 1=part range, 2= full range*	**0**	**1**	**2**
4b		Ankle dorsiflexion		**0**	**1**	**2**
	III. Movement combining synergies					
3a	Sitting	Knee flexion (90°)	*0=can't do, 1=part range, 2= full range*	**0**	**1**	**2**
3b		Ankle dorsiflexion		**0**	**1**	**2**
	V. Normal Reflexes					
5	Sitting (or supine) ONLY DONE IF THE SUBJECT ATTAINS A SCORE OF 4 ON SECTION IV, OTHERWISE SCORE 0.	Patellar and Achilles phasic reflexes (reflex hammer) and knee flexors (quick stretch of the affected leg)	*0=both hyper, 1=one hyper, 2=normal*	**0**	**1**	**2**
	I. Reflex activity					
1a	Supine	Achilles reflex	*0=no reflex, 2=reflex exists*	**0**		**2**
1b		patellar reflex		**0**		**2**
	IIA. Flexor synergy					
2a	Supine	Hip flexion	*0=can't do, 1=part range, 2= full range*	**0**	**1**	**2**
2b		Knee flexion		**0**	**1**	**2**
2c		Ankle dorsiflexion		**0**	**1**	**2**
	IIB. Extensor synergy					
2d	Sidelying (or supine)	Hip extension	*0=can't do, 1=part resistance, 2= full resistance*	**0**	**1**	**2**
2e		Hip adduction		**0**	**1**	**2**
2f		Knee extension		**0**	**1**	**2**
2g		Ankle plantar flexion		**0**	**1**	**2**
	VI. Coordination/speed					
6a	Sitting (or supine)	Tremor	0=pronounced, 1=slight, 2=absent	**0**	**1**	**2**
6b		Dysmetria		**0**	**1**	**2**
6c	Heel to opposite knee repetitions in rapid succession (5 times)	Speed (compared to normal leg)	0= >6 s 1=2-5.9 s 2=<2 s	**0**	**1**	**2**
Total lower limb score				**... /34**		

Balance and cognition in walking

Participant ID	....
Name of assessor	....
Date	....

FUGL Meyer (Lower limb score) - sensory information

- Test first with eyes open, then repeat with eyes closed

	a. Light touch		Score		
1c	Test with eyes open (unaffected muscle belly) Eyes closed Unaffected followed by affected side If sensation ok, repeat and ask for differences	thigh	**0**	**1**	**2**
1d		Sole of foot	**0**	**1**	**2**
	b. Proprioception				
	Move the joint through a small range of motion (approximately 10 degrees for the limb joints and 5 degrees for the digit joints of the hand and foot) Move the limb at least 4 times in random directions. If the subject is wrong on any direction, then add several more to determine if the accuracy is great than 75% (score 2) or 75% or less (score 1). Examine differences in side	Hip (supine)	**0**	**1**	**2**
		Knee (supine)	**0**	**1**	**2**
		Ankle (supine or sitting)	**0**	**1**	**2**
		Toe (sitting or sitting)	**0**	**1**	**2**
Total lower limb score			**... /12**		

Modified Ashworth Scale

0	No increase in tone
1	Slight increase in tone with a catch and release or minimal resistance at end of range
1+	As 1 but with minimal resistance through range after the catch
2	More marked increase in tone but limb easily moved
3	Considerable increase in tone, passive movement difficult (*)
4	Limb rigid in flexion or extension

Muscle	**Affected side**
Achilles tendon	
Quadriceps	

Balance and cognition in walking

Participant ID ……………………………….
Name of assessor ……………………………….
Date ……………………………….

Dynamic Gait Index

		Observations				
1	Gait level surface		**0**	**1**	**2**	**3**
2	Change in gait speed		**0**	**1**	**2**	**3**
3	Gait with horizontal head turns		**0**	**1**	**2**	**3**
4	Gait with vertical head turns *(Do not perform when patient has vertigo/severe balance problems)*		**0**	**1**	**2**	**3**
5	Gait and pivot turn		**0**	**1**	**2**	**3**
6	Step over obstacle		**0**	**1**	**2**	**3**
7	Gait with narrow base of support		**0**	**1**	**2**	**3**
8	Gait with eyes closed		**0**	**1**	**2**	**3**
9	Ambulating backwards		**0**	**1**	**2**	**3**
10	Steps		**0**	**1**	**2**	**3**
TOTAL SCORE			**…/30**			

5.5 Protocol

Balance and Cognition affecting foot placement

Participant ID ………………………………
Name of assessor ………………………………
Date ………………………………

Balance/Cognition protocol

Health:

Falls:

Preferred leg

Date of birth

Anthropometrics:

Height:

Weight:

Foot length/width: /

Baseline f-Nirs (sitting)

Initial Gait Parameters

Baseline walking 5 Min with f-Nirs

SS speed

Step length Right/Left: /

Step width

	Condition	Trial	Additional info
1	Baseline1	1	
2	Cued walking		
3	Un-Supported Planned 1		
4	Un-Supported Planned 2		
5	Un-Supported Planned 3		
6	Un-Supported Reactive 1		
7	Un-Supported Reactive 2		
8	Baseline2	8	
9	Un-Supported Reactive 3		
10	Supported Planned 1		
11	Supported Planned 2		
12	Supported Planned 3		
13	Supported Reactive 1		
14	Supported Reactive 2		
15	Supported Reactive 3		
16	Baseline	16	

6.1 Variable foot placement for balance chapter.

Table.10.1 Mean± SEM variable foot placement error for supported and unsupported target stepping (chapter 6)

		Unsupported	Supported
Young healthy adults	Preferred (AP)	2.1± 0.3	2.2± 0.3
	Shortening(AP)	2.3± 0.2	2.1± 0.2
	Lengthening(AP)	2.1± 0.4	2.1± 0.1
	Preferred (ML)	0.7± 0.2	0.6± 0.2
	Narrowing (ML)	0.9± 0.1	0.6± 0.1
	Widening (ML)	0.9± 0.3	0.9± 0.2
Older healthy adults	Preferred (AP)	2.2± 0.3	2.0± 0.3
	Shortening(AP)	2.4± 0.3	1.9± 0.2
	Lengthening(AP)	2.5± 0.4	1.7± 0.1
	Preferred (ML)	1.1± 0.2	0.9± 0.2
	Narrowing (ML)	0.9± 0.1	0.9± 0.1
	Widening (ML)	1.2± 0.4	0.9± 0.3
Stroke survivors	Preferred (AP)	2.6± 0.3	2.3± 0.3
	Shortening(AP)	3.2± 0.3	2.9± 0.2
	Lengthening(AP)	2.9± 0.4	2.1± 0.1
	Preferred (ML)	1.9± 0.2	1.3± 0.2
	Narrowing (ML)	1.4± 0.1	1.1± 0.1
	Widening (ML)	2.1± 0.3	2.0± 0.3

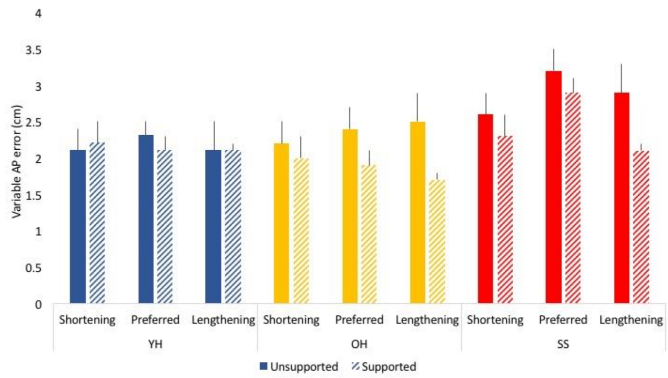


Figure 10.1: Bars represent the Variable error in anterio-posterior direction of foot placement for young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red,

for each type both unsupported (solid) and supported (striped) conditions in anterio-posterior (AP) stepping error for shortening, preferred and lengthening steps.

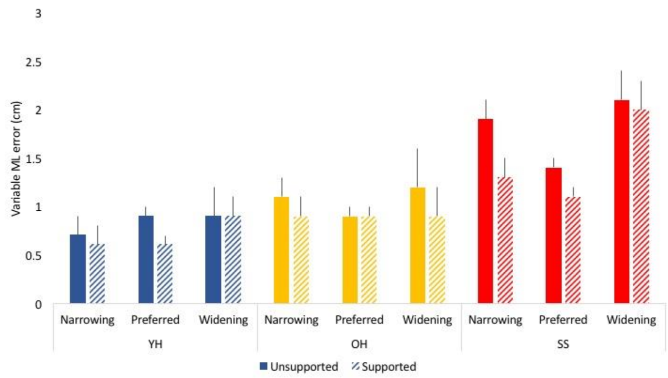


Figure 10.2 Bars represent the Variable error in medio-lateral direction of foot placement for young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red, for each type both unsupported (solid) and supported (striped) conditions in anterio-posterior (AP) stepping error for shortening, preferred and lengthening steps.

7.1 Variable foot placement error for response time chapter

Table.10.2 Mean± SEM variable foot placement error for supported and unsupported target stepping (chapter 6)

		Unsupported	Supported
Young healthy adults	Shortening	2.2± 0.3	2.8± 0.5
	Lengthening	2.2± 0.4	2.4± 0.5
	Narrowing	0.7± 0.2	1.7± 0.5
	Widening	0.9± 0.3	1.7± 0.6
Older healthy adults	Shortening	2.2± 0.3	1.5± 0.5
	Lengthening	2.0 ± 0.4	1.9± 0.6
	Narrowing	1.0± 0.2	1.1± 0.5
	Widening	0.9± 0.3	2.4± 0.7
Stroke survivors	Shortening	2.6± 0.3	2.6± 0.5
	Lengthening	2.9± 0.4	3.9± 0.5
	Narrowing	1.9± 0.2	2.7± 0.5
	Widening	2.1± 0.3	2.6± 0.6

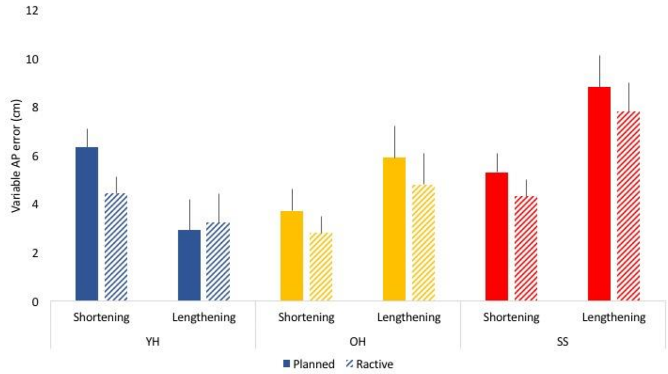


Figure 10.3: Bars represent the Variable error in anterio-posterior direction of foot placement for young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red, for each type both unsupported (solid) and supported (striped) conditions in anterio-posterior (AP) stepping error for shortening, preferred and lengthening steps.

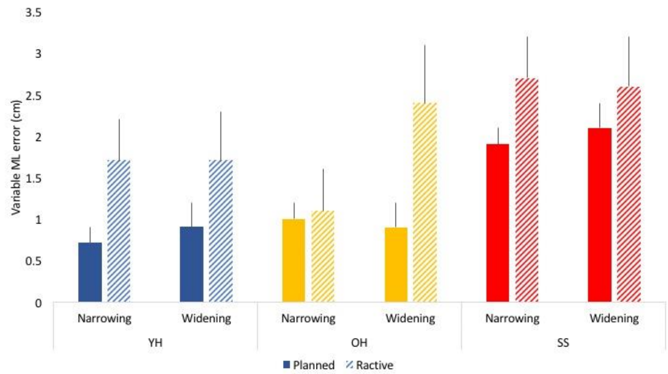


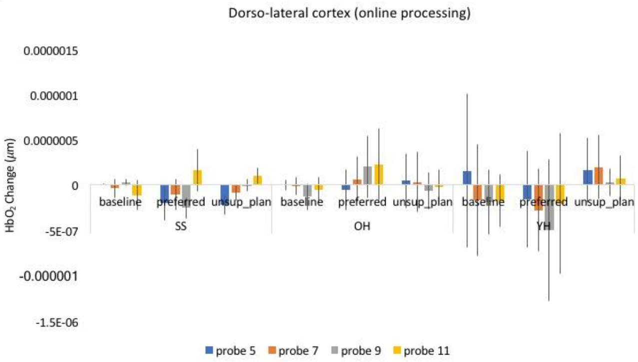
Figure 10.4: Bars represent the Variable error in medio-lateral direction of foot placement for young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red, for each type both unsupported (solid) and supported (striped) conditions in anterio-posterior (AP) stepping error for shortening, preferred and lengthening steps.

8.1 Probe selection

Table 10.3: Number of block averages per probe per walking tasks after correcting data for motion artifacts.

		Available for N number of participants								
		Walking trial			Preferred trial			Adaptation trial		
probe	total	Stroke (total 9)	Older (total 8)	Young (total 12)	Stroke	Older	young	Stroke	Older	young
1	53	6	5	7	5	5	7	6	5	7
2	71	8	7	9	8	6	9	8	7	9
3	48	4	3	9	4	3	9	4	3	9
4	63	6	4	11	6	4	11	6	4	11
5	63	7	6	8	7	6	8	7	6	8
6	72	7	7	10	7	7	10	7	7	10
7	57	7	4	8	7	4	8	7	4	8
8	69	7	6	10	7	6	10	7	6	10
9	51	8	3	6	8	3	6	8	3	6
10	60	6	6	6	6	6	9	6	6	9
11	53	5	6	7	4	6	7	5	6	7
12	69	5	7	11	5	7	11	5	7	11
13	57	8	5	6	8	5	6	8	5	6
14	59	4	5	10	5	5	10	5	5	10
15	45	4	4	7	4	4	7	4	4	7
16	72	7	7	10	7	7	10	7	7	10

A



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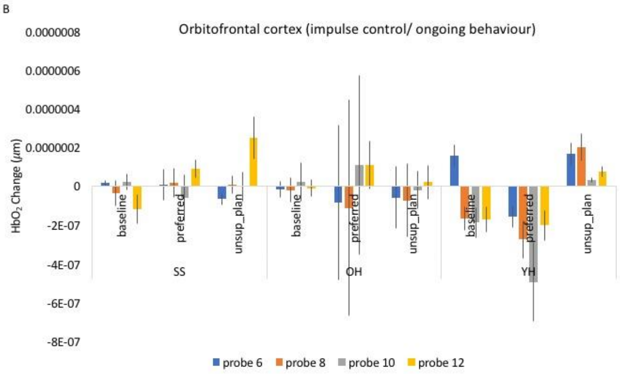

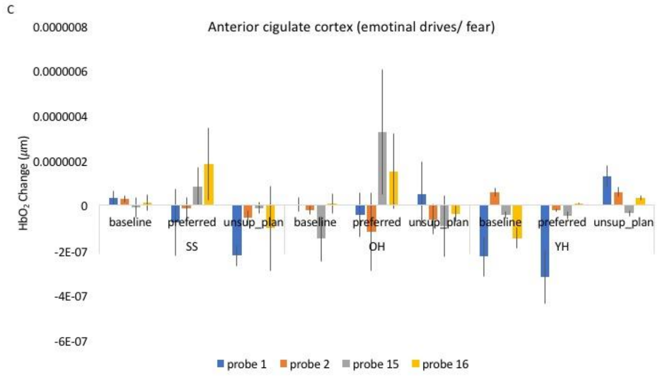

Figure 10.5: Bars represent the change of HbO_2 concentration change opposed to baseline measurement for young healthy adults (YH) in blue, older healthy (OH) in yellow and stroke survivors (SS) in red, for each condition walking, preferred and adaptation.

8.2 Oscillation in HbO_2 Due to walking

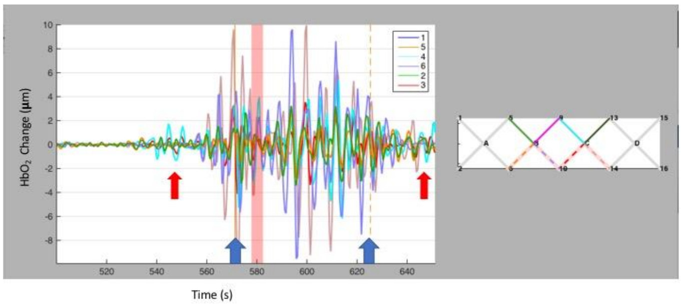

Figure 10.6: Representation of fNIRS data during steady state walking. Vertical orange line, marked with a blue arrow indicate the start of the task, red arrow indicates the start and the stop of walking. In-between red arrows all data shows about a 0.2Hz oscillation.

8.3 Sample data of fNIRS

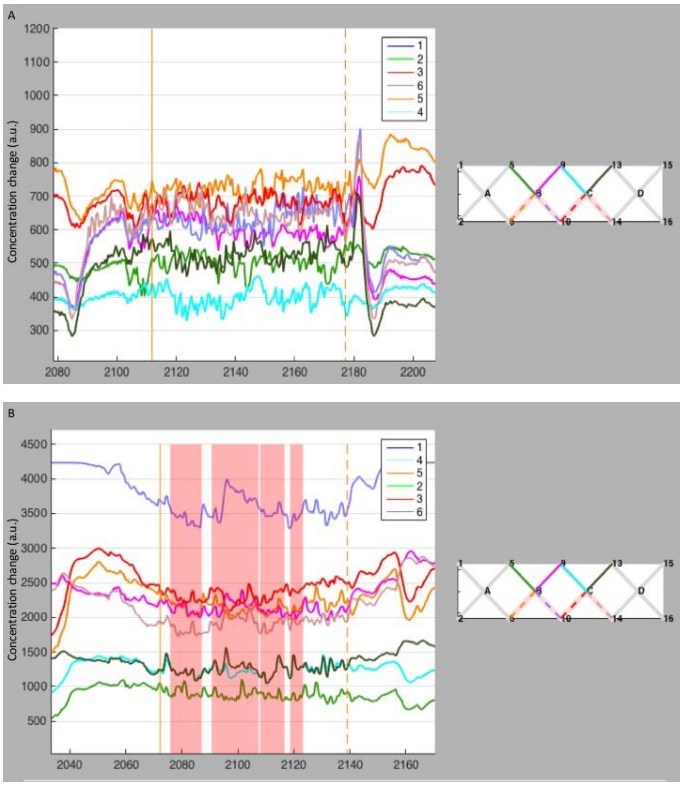

Figure 10.7: representation of unfiltered concentration data for A) a trial of a participant with little motion artefacts B) a trial of another participant with high number of motion artefacts (indicated by the red bars).