Gait stability in stroke survivors

The assessment and training of gait stability in chronic stroke survivors

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door

Michiel Punt

geboren te Neede

promotor:	prof.dr. J.H. van Dieën
copromotoren:	dr. S.M. Bruijn
	dr. H. Wittink

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CHAPTER 1

GENERAL INTRODUCTION

Introduction

Stroke or cerebrovascular accident (CVA) is a central neurological deficit with an abrupt onset that lasts over 24 hours [1]. Stroke is common and the incidence increases with age [2]. Based on demographic characteristics in Europe, incidence of stroke is expected to rise [2]. A stroke can lead to long term disability [3], depression [4], reduction in quality of life [5] and death [6]. Moreover a large proportion of all stroke survivors report falls [7]. These falls can have devastating results such as hip fractures [8], which result even more often in long term disability in stroke survivors than in older adults and death rate three months post hip fracture is doubled in stroke survivors [9]. Adequate identification of fall-prone stroke survivors and preventing falls is of paramount importance and therefore the central goal in this thesis.

A promising area of fall risk assessment is the study of gait analysis. Gait can be assessed in a laboratory setting, but novel techniques allow us to analyze gait in daily life and in (standardized) challenging conditions (i.e. after perturbations). This thesis aims to explore a variety of gait assessments for fall risk in stroke survivors, and explores the potential for improving gait stability using perturbation based gait training. Ultimately, this work could give guidance on how to identify individuals at elevated risk for falls and on how to improve their gait stability and prevent falls.

Gait in stroke survivors

In order to achieve a level of community involvement and physical independence, being able to walk is the primary aim of many stroke survivors [10]. It is therefore one of the most important goals during rehabilitation. Lord et al. (2004) reported that around 75% of the stroke survivors found it very important or even essential “to get out and about” [11]. Unfortunately, after having a stroke only 60% of survivors reach some level of community walking again [11]. Those who managed to start walking again, still suffer from the consequences of a stroke, as gait deficits are still present. Common gait deficits are a more asymmetrical gait pattern [12] and a slower gait speed [13]. Also trunk–pelvis coordination in gait is often impaired, generally with more in-phase rather than anti-phase transverse plane rotations [14] and the amplitude of the center of mass in vertical direction is increased up to three times relative to normal gait, probably as a consequence of a compensatory strategy to lift the paretic limb into swing [15, 16]. These gait deficits explain to some extent the increased energy cost of locomotion in stroke survivors [16, 17]. Moreover, considering the high fall rates in stroke survivors [7], stability of gait is affected. Here, we define stable gait as gait that does not result into a fall [18]. Finally, the quantity of gait in stroke survivors is reduced and below physical activity recommendations [19], which may result in further deconditioning and cause a further decline in functioning and increased risk of falls in the long term.

Falls

In this thesis, we defined a fall as ‘any unanticipated event that results in participants coming to the ground, floor or lower level’ [20]. We excluded falls that had a clearly different cause than a loss of balance, such as fainting or an epileptic seizure.

Falls are common in all stages after stroke [7]. Reported fall rates in the chronic stage after stroke range from 43 to 70% during one year follow up. Moreover, stroke survivors are more likely to become repeated fallers as compared to healthy older adults [7]. Consequences of a fall can be devastating, including serious injuries such as hip fractures [8] and even death [9]. In addition, hip fractures as a result of a fall more often lead to immobility in stroke survivors [8], as compared to age matched controls. Other consequences of falls are loss of independence, social isolation [8] and as a consequence a further decline in physical functioning.

Falls in stroke survivors occur during different activities, such as gait, transferring, reaching and bending [21]. However, the literature consistently states that most falls occur during gait followed by transferring [21–23]. Stroke survivors report that they fall during walking due to a trip or a slip [23] but also due to a loss of balance, a misjudgment of the environment, a lack of concentration and foot dragging [22]. Finally, the direction of falls is more often towards the paretic side [21] indicating a reduced ability to maintain balance or restore balance after a perturbation to the paretic side. This suggests that falls in stroke survivors have multiple causes, which suggests that multiple types of assessments are required to indicate fall risk.

Fall risk assessments

Considering the devastating effects of falls in stroke survivors, adequate fall risk assessment is of paramount importance, as it is a first step in targeted fall prevention. Accurate identification of fall risk helps to assign the actual fallers to fall prevention programs, comprising exercise and or other interventions, which may reduce the risk of falls. Moreover, with accurate identification of fallers, time and money can be spent on those who could actually benefit from a fall prevention program, and thereby enhance the cost-effectiveness of such a program. Finally, discovering differences between fallers and non-fallers could potentially function as a starting point for tailored fall prevention programs.

Previous attempts to assess fall risk have focused on balance and transfer related tasks such as the Berg Balance score (BBS) [24], Time Up and Go Test (TUGT) [25] or Performance Oriented Mobility Assessment (POMA) [26]. Other studies focused on psychological factors such as the fear of falling [27] or depression [28, 29] to determine risk of falls. Although it seems that those assessments have some ability to indicate fall risk, results are often inconsistent with other studies [24] which renders the use of these assessments questionable.

Assessment of gait

As the majority of all falls occur during dynamic activities such as walking [21–23] fall risk could be assessed using gait analysis. To this end several gait assessment methods are available.

First, gait can be assessed in a controlled set up, thereby minimizing the influence of disturbing factors that could affect gait characteristics. Usually a treadmill or an over ground pathway is used, while motion capture cameras or accelerometers and force plates are used to collect kinematics and kinetics.

Gait characteristics collected using such a set up will be further referred to as steady-state gait characteristics.

Second, gait can be assessed in a daily life setting using wearable technology like for instance accelerometers. An advantage is that gait is captured at the location were the actual falls occur. Therefore, this approach is more ecologically valid. Gait characteristics captured using such a set up will be further referred to as daily-life gait characteristics.

The third and final gait assessment method applied in this dissertation is the assessment of perturbed gait. After gait is perturbed, ultimately, the type and quality of the responses will be decisive in whether someone will fall or not. As fallers frequently report that they fell due to misjudgment of a situation, slips and trips, [22] it intuitively makes sense to measure the responses of stroke survivors to gait perturbations. Assessing responses to gait perturbations requires a set up to perturb gait, preferably at a fixed moment in the gait cycle and with a fixed perturbation magnitude.

Steady-state gait and fall risk

Steady-state gait characteristics describe 'how' people walk. Steady-state gait characteristics are often collected while walking on a treadmill at preferred gait speed. To obtain reliable estimates of someone's gait quality, it is important to collect and analyze a sufficient number of strides [30]. Some examples of gait characteristics are: gait speed, step length, swing time, gait variability, local dynamic stability and sample entropy.

Interestingly, previous studies have indicated that gait characteristics can predict fall risk [31–37]. Most of these studies are based on data derived from older adults [31–35] but people with Parkinson's disease have been studied as well [36, 37].

Steady-state gait characteristics in stroke survivors are different from older adults. For instance, variability of gait in stroke survivors appears to be higher than in age matched controls[38]. Due to differences in gait, it is questionable if similar, and to what extent gait characteristics predict fall risk in stroke survivors. Only one recent study found an association between gait characteristics and falls in stroke patients [39]. Therefore, chapter 4 of this dissertation examines if and how steady-state gait characteristics predict falls in stroke survivors.

Daily-life gait and fall risk

It is only recent that technology enables us to monitor gait over several consecutive days, thereby allowing us to assess quality of gait in daily life.

An essential step prior to studying the association between falls and daily-life gait characteristics is selecting episodes of gait activity, because only the selected gait episodes should be processed to determine the quality of daily-life gait. Misclassification of episodes could lead to random errors and potentially bias in estimates of quality of daily-life gait. Chapter 2 addresses the topic of selection of gait episodes in terms of validity and test-retest reliability.

In regard to daily-life gait characteristics, it is important to note that daily-life gait characteristics are derived from lower back acceleration signals alone rather than determining the location of each body segment as is the case in steady-state gait. Therefore, most gait characteristics that are determined in steady-state gait cannot be reliably estimated during daily-life gait. Thus, alternative measures have been applied to quantify 'how' people walk in daily life. Some measures, like the index of harmonicity [40] and harmonic ratio [41], are derived from the power spectrum [42]. Other measures based on time-domain analysis are stride regularity [43] and movement intensity, which is defined as the standard deviation of the acceleration signal [41].

An example of a three dimensional acceleration time series obtained from a trunk mounted accelerometer on a walking participant is given in the upper panel of figure 1.1. The red line represents the acceleration in the vertical (VT) direction, the blue line the anterior-posterior (AP) acceleration and the green line the medio-lateral (ML) acceleration. The lower panel of figure 1.1 illustrates the power spectrum of an acceleration time series of multiple walking episodes and indicates the location of the dominant and subsequent harmonics used to calculate the index of harmonicity [40] and harmonic ratio [41].

Recent studies explored daily-life gait characteristics and found that indeed quality of gait contains valuable information regarding fall risk in older adults [44–47]. Additionally, by estimating the number of strides taken and or the total minutes walked during a day, accelerometry can be used to determine the amount of physical activity. Interestingly, it was recently found that after correcting for the quality of gait, increased quantity of gait increased the risk of falls [47]. This highlights the potential of accelerometry to gain information about which factors contribute to falls. Nevertheless this research area is in its infancy, and the currently available prediction models require further validation [48].

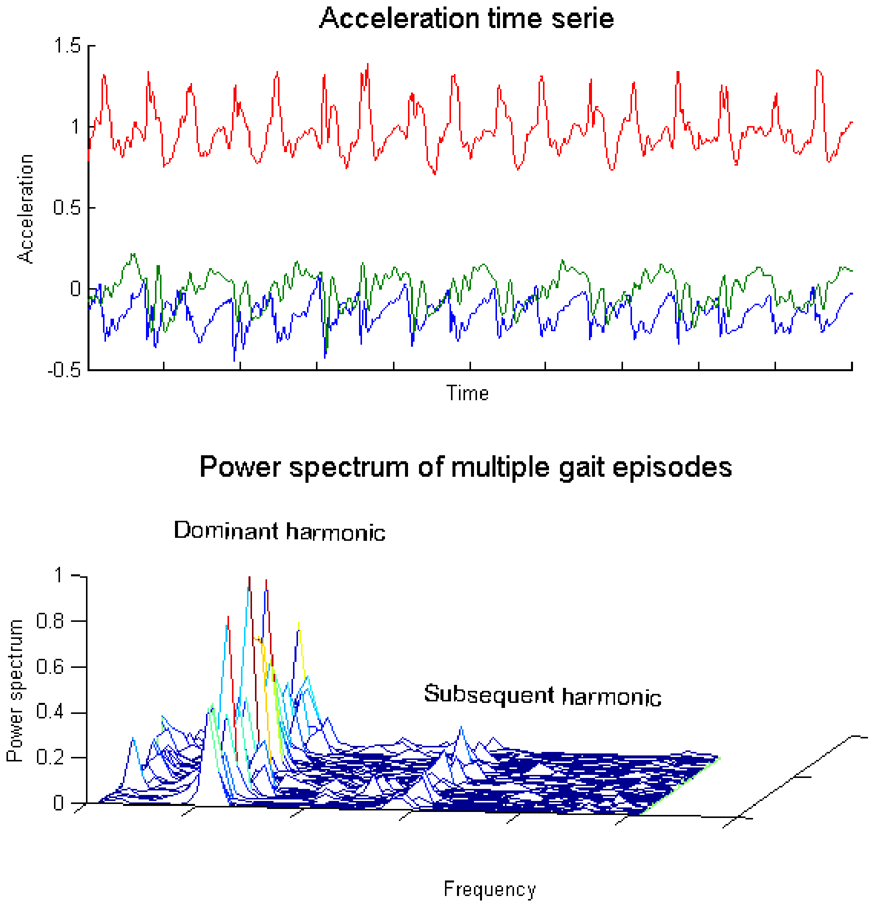

Figure 1.1: The upper panel illustrates a three-dimensional acceleration time series of a walking participant. The lower panel illustrates the power spectra of the AP acceleration time series of multiple gait episodes and indicates the dominant and subsequent harmonics.

Finally, similar to steady-state gait and it's associations with falls, it is unknown whether daily-life gait characteristics reveal valuable information regarding fall risk in stroke survivors. The presented results at this point are based on healthy older adults. Chapters 3 and 4 determine whether daily-life gait characteristics predict falls in stroke survivors and how this is different from a general, healthy older population.

Perturbed gait and fall risk

Gait perturbations can be separated into two types. The first type are unexpected perturbations such as trips and slips. The second type of perturbations are expected perturbations like stepping over a curb, or avoiding a puddle. Both perturbation types require partly different skills which are affected in stroke survivors [49–51]. The work performed in this research area is limited, probably due to the expensive instrumentation needed to systematically perturb gait and measure responses. Moreover, performing such a perturbation experiment is labor-intensive, because measurement of kinematic responses requires placement of many markers, data collection often requires repeated trials and data analysis is not yet standardized and consequently time consuming.

Responses to gait perturbations are usually explored by simulating trips or slips [52, 53] or by pulls applied to the upper body [54]. There is a large number of measures that aim to characterize the responses after a perturbation [55]. Most commonly used measures are Base of Support (BoS) measures: step length and width and measures that relate the Center of Mass (CoM) to the BOS, such as the Margin of Stability (MoS) [56, 57].

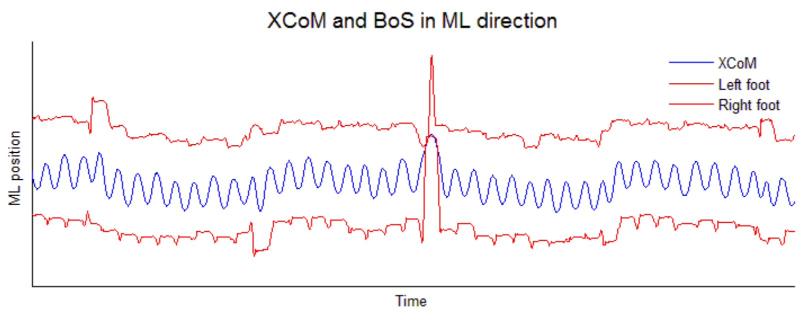

Figure 1.2: The extrapolated center of mass (XCoM) (blue line), a function of CoM position and velocity, and foot positioning (red lines) in medio-lateral direction. Halfway this time series the treadmill was translated, which resulted in deviating foot placements.

Figure 1.2 illustrates the BoS together with the extrapolated center of mass (XCoM), which equals the center of mass position plus its velocity times the square root of the center of mass height divided by the gravitational acceleration [56, 57] during a walking trail with medio-lateral perturbations. See chapter 5 for a more detailed explanation.

To our knowledge, no studies explored differences in gait responses after perturbations between fallers and non-fallers neither in healthy older adults nor in stroke survivors. Nevertheless, a few studies have compared responses after perturbations between older adults and stroke survivors [51, 53, 58]. While Krasovsky et al (2013) found a larger response in terms of timing of gait rhythm (i.e. larger deviations of gait events like heel strike as compared to steady-state) after perturbations in stroke survivors compared to healthy older adults [58], Kajrolkar et al (2014) concluded that stroke survivors have a preserved ability to adjust gait characteristics and maintain dynamic stability [51]. In chapter 5, we determined whether gait responses in unexpected gait perturbations are different between fallers and non-fallers among stroke survivors.

Expected gait perturbations are usually explored by setting up a pathway with an obstacle [49, 59–63]. Participants are asked to step over such an obstacle and obstacle crossing characteristics like: success rate, pre-crossing obstacle distance, toe clearance during crossing, crossing step length and post-crossing obstacle distance are examined. At present, interestingly, one study found that fall-prone stroke survivors were less successful in obstacle negotiation as compared to non-fall-prone stroke survivors[64]. In addition, stroke survivors had an impaired ability to cross obstacles compared to a general older adult population [62, 63, 65, 66]. Yet, whether expected gait perturbations have added value in identifying fall-prone stroke survivors remains largely unknown. Therefore, we studied in chapter 6 whether gait responses to expected perturbations are different between fallers and non-fallers.

Interventions to improve gait stability

Effective fall prevention programs exist for older adults [67] although frail elderly seem not to benefit from such programs [68]. According to a fairly recent Cochrane review, no effective programs are available for stroke survivors [69]. Fall prevention programs generally aim to improve physical activity, thereby improving physical functioning and reduce fall rates. Yet, falls are potentially influenced by many factors, such as for instance, the amount of gait activity [47]. Thus, although stroke survivors might improve their physical functioning to some extent, this could be outweighed by the increased exposure to fall hazards caused by the increased physical activity.

A recent review identified only unsuccessful intervention studies aiming to reduce fall rates in stroke survivors [69]. Thus, as most falls occur during gait, perhaps, we should first explore whether it is possible to improve gait stability in fall prone stroke survivors, which is at present unknown. An interesting novel intervention has emerged over the past several years [70]: Perturbation Based Training (PBT), which aims to increase the resistance against perturbations and thereby improve stability. There appears to be converging evidence that PBT can reduce fall rates in older adults and people with Parkinson's disease [70]. In chapter 7 of this thesis, we studied whether this intervention improves gait stability in stroke survivors.

Aims and Outline of this dissertation.

The aim of this thesis was twofold. First, this thesis studied a variety of gait assessments with respect to their ability to assess fall risk in ambulatory chronic stroke survivors. Second, this thesis explored whether stroke survivors can improve their gait stability through PBT.

In **chapter 2,** the validity and reliability of an accelerometry based gait recognition algorithm was examined by comparing quantitative gait characteristics against video observation in a repeated measures design. **Chapter 3** determined whether the same accelerometry-based fall prediction models used in older adults can be applied in stroke survivors, or whether modifications are needed either in the selection of gait characteristics or the coefficients of such a model. In **chapter 4,** a comparison between conventional, clinical assessments, daily-life gait characteristics and steady-state gait characteristics regarding their ability to predict fall risk was made. In

chapter 5, responses after unexpected gait perturbations were compared between fall-prone and non-fall-prone stroke survivors. **Chapter 6** explored whether negotiation of obstacles during gait, thus responses to expected perturbations, are affected in fall-prone stroke survivors in comparison to non-fall-prone stroke survivors. Additionally, test-retest reliability of obstacle crossing gait characteristics was examined. In **chapter 7,** a pilot PBT was designed and applied to explore whether gait characteristics improved and consequently predicted decreased fall risk in a group of fall-prone chronic stroke survivors. Finally, in chapter 8 overall conclusions are drawn regarding fall risk assessment and fall risk reduction in stroke survivors. Moreover, a general discussion addresses the applied methods, clinical implications and future work.

CHAPTER 2

QUANTIFYING GAIT BY ACCELEROMETRY

Clinimetric properties of a novel feedback device for assessing gait parameters in stroke survivors Michiel Punt, Belinda van Alphen, Ingrid G van de Port, Jaap H van Dieën, Kathleen Michael, Jacqueline Outermans, Harriet Wittink, Journal of NeuroEngineering and Rehabilitation,2014.

Abstract

Background. Community-dwelling stroke survivors tend to become less physically active over time. There is no 'gold standard' to measure walking activity in this population. Assessment of walking activity generally involves subjective or observer-rated instruments. Objective measuring with an activity monitor, however, gives more insight into the actual walking activity. Although several activity monitors have been used in stroke patients, none of these include feedback about the actual walking activity. FESTA (FEedback to Stimulate Activity) determines number of steps, number of walking bouts, covered distance and ambulatory activity profiles over time and also provides feedback about the walking activity to the user and the therapist.

Objective. To examine the criterion validity and test-retest-reliability of the FESTA as a measure of walking activity in chronic stroke patients. To target the properties of the measurement device itself and thus exclude effects of behavioral variability as much as possible evaluation was performed in standardized activities.

Methods. Community-dwelling individuals with chronic stroke were tested twice with a test-retest interval varying from two days to two weeks. They performed a six-minute walk test and a standardized treadmill test at different speeds on both testing days. Walking activity was expressed in gait parameters: steps, mean-step-length and walking distance. Output data of the FESTA was compared with video analysis as the criterion measurement. Intraclass Correlations Coefficients (ICCs) and Mean Relative Root Squared Error (MRRSE) were calculated.

Results. Thirty-three patients were tested to determine criterion validity, 27 patients of this group were tested twice for test-retest reliability. ICC values for validity and reliability were high, ranging from .841 to .972.

Conclusion. This study demonstrated good criterion validity and test-retest-reliability of FESTA for measuring specific gait parameters in chronic stroke patients. FESTA is a valid and reliable tool for capturing walking activity measurements in stroke, and has applicability to both clinical practice and research.

Introduction

In many Western nations, stroke is a leading cause of death and serious long-term disability [71].

A frequent consequence of stroke is unilateral loss or limitation of muscle function, leading to a loss of mobility, movement and functional ability [72, 73]. Van de Port et al.(2006) showed that a substantial proportion of community-dwelling stroke survivors becomes less physically active over time[74]. Post-stroke physical inactivity may produce physical deconditioning, and as a consequence a decline in function[75]. A decline in function reduces participation in the community and quality of life[76] and decreases independence of the stroke survivor[75]. Furthermore, physical inactivity increases the risk of developing co-morbidities and having a recurrent stroke[75]. Accurate measurement of real life walking activity could be beneficial in tailoring rehabilitation. Using actual performance data and providing feedback might support self-management strategies to prevent physical and functional decline and subsequent consequences.

Currently assessment of walking activity generally involves subjective or observer-rated instruments[77]. These instruments have disadvantages such as the risk of recall bias, social desirability of answers, and poor generalisation[77]. Objective assessment of the number of steps can be done with pedometers. Roos et.al.(2012) demonstrated the disadvantage of measuring only the total number of steps taken.[78]. They found differences in walking bouts and time between older adults and stroke survivors and that it varied based on functional ability. This relevant variation could not have been identified when measuring only steps per day [78]. Measuring gait parameters with accelerometers overcomes the limitation of measuring only the number of steps. To measure gait parameters by accelerometry in this population specific algorithms are required since stroke survivors are slow walkers[79] and accuracy of detecting steps decreases when gait speed and step frequency decrease [80].To date, several motion sensors have been used [81, 82], such as the accelerometer based StepWatch Activity Monitor (SAM) which had good validity in measuring gait parameters in stroke survivors. However, current devices are not capable of providing feedback to the stroke survivor about their walking activity. Providing feedback about their walking activity might prevent physical inactivity, and as a consequence a decline in function [75]. To monitor walking and to investigate potential beneficial effects of feedback in stroke survivors we developed FESTA.

FESTA (FEedback to STimulate Activity) is a telemetric system that includes a tri-axial piezo capacitive accelerometer which can be coupled to a docking station. The station is capable of; calculating gait parameters, evaluating whether the amount of walking activity during the day was sufficient according to the goal set by the physical therapist, providing the feedback at a screen visible for the stroke patient, sending an email towards the physical therapist with the calculated gait parameters and recharging the battery of the accelerometer to continue monitoring the next day.

As measuring gait parameters is more challenging in stroke survivors, the first step in this developing process was to examine the criterion validity and test-retest reliability of FESTA at gait parameter recognition in chronic stroke survivors using a stroke specific developed algorithm. We examined gait parameters; steps, mean-step-length with a standardized treadmill test and walking distance with an over ground 6 minute walk test. Furthermore FESTA calculates walking time and walking bouts as a derivative from steps[83].

Methods

Participants

A convenience sample of community-dwelling, chronic stroke survivors was recruited from ten private physical therapy practices, the daycare center of 'Zorgspectrum' and the patients' association 'Samen verder' in the Netherlands and the University of Maryland in the United States of America. Stroke was defined according to the World Health Organization definition. Participants were able to walk independently without physical assistance (Functional Ambulation Categories score ≥ 3) [84] and were at least three months post stroke.Participants were excluded if they had severe cognitive disorders (Mini-Mental State Examination <24)[85], severe communicative disorders (Utrechts Communicatie Onderzoek <4) [86]or acute disorders impairing gait. All participants gave written informed consent prior to participation in the study. The research protocol and all informational material were approved by the Medical Ethical Committee (MEC) of the University Medical Center Utrecht and the Institutional Review Board of the University of Maryland, Baltimore.Treatment of the participants was according to the Helsinki declaration [87].

Equipment & experimental protocol

procedure

Participants were tested twice with a test-retest interval of a minimum of two days and a maximum of two weeks using the six-minute walk test (6MWT) and a standardized treadmill test. At baseline, inclusion measurements and collection of personal and anthropometric data were performed prior to the physical tests.

FESTA monitor

During both tests the FESTA was worn around the back site of the waist, between the spina iliaca posterior superiors. The FESTA contains one tri-axial, piezo-capacitive accelerometer (70*80*25mm, 150 grams, range ± 2.5g). Based on sensor alignment, acceleration signals were identified as anterior-posterior (AP), medio-lateral (ML) and vertical (VT). Output is in mV, a change of 1mV corresponded to a change of 0.08 m/s^2 (resolution). Acceleration signals were digitally stored on a memory card with a sampling rate of 25 samples/s.

6MWT

The 6MWT was performed to assess over ground walking distance. The 6MWT was performed according to the American Thoracic Society Guidelines[88]. Walked distance was determined by counting the number of walked laps (20 meters) and adding any final fraction of laps, measured by a measuring wheel. Results were used to calculate the comfortable walking speeds for the treadmill test (CWT) and to assess the over ground walking distance validity and reliability of the FESTA.

Standardized treadmill test

Gait parameters, number of steps and mean-step-length were determined using a standardized treadmill test. Because accuracy of the gait parameter; steps recognition depends on gait speed and gait speed may vary during a day and is low in this population [79] we executed a treadmill test at three different gait speeds within each subject. Gait speeds were established at 15% below, equally to and 15% above comfortable gait speed. Each speed condition lasted for two minutes. The mean walking speed measured by the 6MWT -10% was used to define the comfortable walking speed. Fingertip handrail support was allowed during testing. The treadmills (En Mill treadmill, Enraf Nonius, the Netherlands and Gait Trainer 3™, Biodex, USA) was calibrated prior to the study. A camera was placed 1.2 meter behind the treadmill (Panasonic type HC-V70, 50 samples/s)

Data processing and algorithms

From every block of two minutes at different speeds, only the last 90 seconds were analysed. The researcher counted the number of steps during these blocks of 90 seconds from the video afterwards and was blinded from the results of FESTA. Distances from the treadmill test were determined by using the treadmill speed and the testing time of the treadmill test. The average step length for both legs, the mean-step-length was derived from the distance and divided by the steps taken by both legs.

From the same blocks of 90 seconds, the gait parameters (number of steps and mean-step-length) from FESTA were analysed using Matlab (Matlab 7.10.1, The MathWorks Inc, USA).For the step detection we used spectral analysis derived from the AP acceleration signal. Taking the individual variety of the distance-acceleration relationship into account, we used an individual calibration procedure for distance measures to determine the acceleration-distance relation[89]. Firstly we calculated the root mean square of the AP acceleration signal, secondly conducted a linear fit (first order polynomial) between the different gait speeds and the different root mean square values thirdly we used the polynomial function to predict the walking speed and subsequently walking distance in the treadmill test and 6MWT.This distance prediction derived from a single acceleration signal and the individual calibration procedure is descripted by Schutz et al. (2002) [89] in more detail.

To assess the validity and reliability of FESTA, we compared the gait parameters derived from FESTA with the golden standard. Comparisons for the gait parameters steps and mean-step-length were performed by using the data from the treadmill test. The comparison of the gait parameter walking distance was performed using the data derived from the 6MWT. The steps counted from the video analysis and the actual distance walked calculated by multiplying speed and time. This procedure is consistent with procedures from similar validation studies[90, 91], [92, 93] and video analysis seems to be the most appropriate criterion standard for the assessment of physical activity[93].

Statistics

Descriptive statistics were performed for all variables and normality was assessed by visual inspection of histograms and quantile-quantile plots. An $ICC_{3,1}$ of ≥ .75 was defined as high as suggested by Burdock et al.(1963) [94].

All calculations were performed using SPSS (IBM Software, SPSS Statistics 20, USA) or Matlab (Matlab 7.10.1, The MathWorks Inc, USA).

Validity

To assess the level of agreement between FESTA and the golden standard, and thus the criterion validity, single measures intraclass correlation coefficients$_{agreement}$ ($ICC_{3,1}$, Two-way mixed model) were calculated for the different gait parameters; number of steps and mean-step-length obtained from the treadmill test and over ground walked distance in the 6MWT. Furthermore the Mean Relative Root Square Error (MRRSE) was calculated for each parameter. The MRRSE is a measure of the differences between the values of FESTA and the observed values, relative to the unit of measurement (see Formula). The MRRSE gives an indication of the mean error of FESTA per step or number of steps as a percentage of the measurement unit.

$$MRRSE = \frac{\sqrt{\sum_{i=1}^{n}(Xobs,i - X\,model,i)^2}}{\overline{X}_{obs}} * 100$$

$\overline{X}_{obs}$ *= mean of the observed values, criterion measurement, video analysis*

$X_{model,i}$ *= values obtained by FESTA*

Reliability

Single measures intraclass correlation coefficients$_{consistency}$ ($ICC_{3,1}$, Two-way mixed model) was calculated to analyse the test-retest reliability of FESTA. Additionally, the Minimal Detectable Change (MDC_{95}) was calculated from the Standard Error of Measurement (SEM) as MDC_{95} = [1.96*$SEM_{consistency}$ *√2] and

SEM = [sd * $\sqrt{[1-r]}$], where r is the test-retest reliability coefficient $ICC_{agreement\ 3,1}$ and sd is the standard deviation of the scores at the first test occasion (T0). The SEM is multiplied by 1.96 to determine the 95% confidence interval and multiplied by the square root of 2 to account for the additional error associated with repeated measurements[95]. The MDC_{95} is the minimal amount of change that must be observed before the change can be considered to exceed the variation and measurement error at the 95% confidence level.

Results

A total of 33 participants (17 men and 16 women) were tested and their data were used to determine the criterion validity of FESTA. Twenty-seven participants were tested twice. The other six participants did not perform a second test, due to motivational problems to perform a second test or being unable to perform a second test within the set time limit of two weeks after the first test. The mean age of the 33 participants was 61.8 ± 8.8 years, time since stroke was 5.6 years ± 3.8 years and the functional ambulation category (FAC) scores ranged from 3 to 5 (mean 4.4 ± 0.7). The average distance walked in the 6MWT was 317.3 meters, which is 0.88 m/s, ranging from 36 to 580 meters. For the treadmill testing, the different walking speeds varied from 0.08 to 1.5 m/s.

Validity

For steps and mean-step-length at the three different gait speeds, $ICC_{agreement\ 3,1}$ varied between 0.841 and 0.971 ($p \leq 0.001$ for all values). Mean Relative

Root Squared Errors (MRRSE) ranged between 3.4 and 9.1%. All agreement parameters are presented in table 2.1.

Table 2.1: Criterion validity results FESTA

Speed	Parameter	Video Analysis	FESTA	MRRSE (%)	ICC
Speed 1 = CWT - 15%		*Mean ±SD*	*Mean ±SD*		
Mean ± SD: 2.4 ± 1.1 km/h	Step Count	129 ±25	135 ± 21	5.8	.841
Range: 0.3 - 4.4 km/h	Mean step length (m)	0.45 ± 0.14	0.43 ± 0.16	9.1	.910
Speed 2 = CWT					
Mean ± SD: 2.8 ± 1.2 km/h	Step Count	138 ± 27	141 ± 23	3.5	.964
Range: 0.4 - 5.2 km/h	Mean step length (m)	0.50 ± 0.15	0.48 ± 0.16	6.2	.964
Speed 3 = CWT + 15%					
Mean ± SD: 3.2 ± 1.4 km/h	Step Count	145 ± 28	146 ± 25	3.4	.964
Range: 0.5 - 5.6 km/h	Mean step length (m)	0.54 ± 0.17	0.52 ± 0.18	5.3	.971

MRRSE = Mean Relative Root Squared Error; percentage mean absolute deviation, ICC = Intraclass Correlation Coefficient, CWT = Comfortable Walking Speed for Treadmill.

Figures 2.1 illustrates the differences between the golden standard and FESTA for the gait parameters steps and mean-step-length, with the difference in steps (top panel) and mean-step-length (bottom panel).

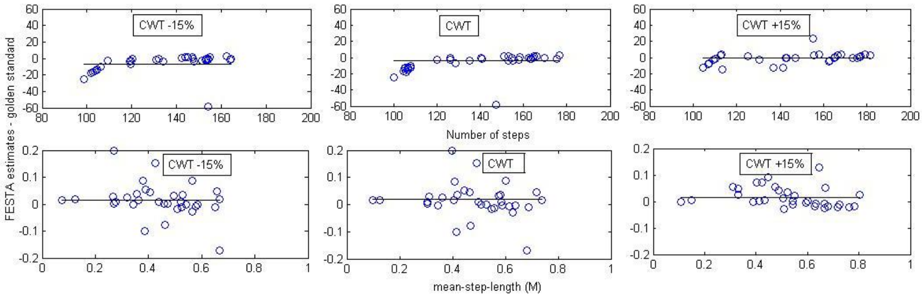

Figure 2.1: FESTA estimates of steps minus golden standard (top panel). FESTA estimates of mean-step-length minus golden standard (bottom panel). At 15% below comfortable walking speed (CWT −15%) equal to (CWT) and 15% above.

Criterion validity for over ground walking distance during the 6MWT is presented in table 2.2. Difference between measured and estimated over ground walking distance in meters averaged -20.1 meters see figure 2.2.

Table 2.2: Criterion validity of distance measure for over ground walking: 6MWT

	6MWT (m) measured	**6MWT (m) FESTA**	**MRRSE (%)**	**ICC**
Mean ± SD	317.3 ± 134.7	337.4±136.3	12.1	.937
Range	36.0 -580.0	44-581.5		

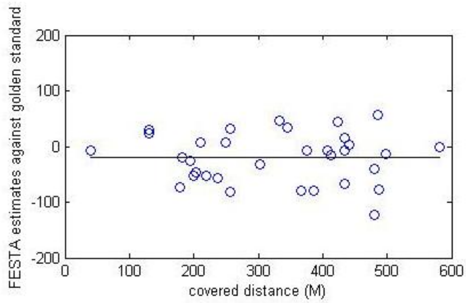

Figure 2.2: FESTA estimates of covered distance (M) minus golden standard at the 6MWT.

Reliability

Table 2.3 presents the test-retest reliability for the gait parameters steps and mean-step-length, including ICC values and MDC. $ICC_{consistency\ 3,1}$ scores ranged from 0.876 to 0.972 and were all significant at p≤ 0.001.

Table 2.3: Test-retest reliability of gait parameters obtained by FESTA

Speed	Parameter	T0 (*Mean ± SD)*	T1 (*Mean ± SD)*	ICC	MDC_{95}
Speed 1 = CWT - 15%	Step Count (steps)	136 ± 21.0	135 ± 20.4	.938	14.3
	Mean step length (m)	0.44 ± 0.15	0.42 ± 0.14	.876	0.14
Speed 2 = CWT	Step Count (steps)	141 ± 22.5	140 ± 22.6	.949	14.1
	Mean step length (m)	0.48 ± 0.14	0.48 ± 0.15	.942	0.10
Speed 3 = CWT + 15%	Step Count (steps)	145 ± 23.9	144. ± 25.6	.972	11.4
	Mean step length (m)	0.52 ± 0.16	0.53 ± 0.16	.944	0.10

Figure 2.3 illustrates the differences between the first and second test occasion, reliability of the gait parameters; steps (top panel) and mean-step-length (bottom panel).

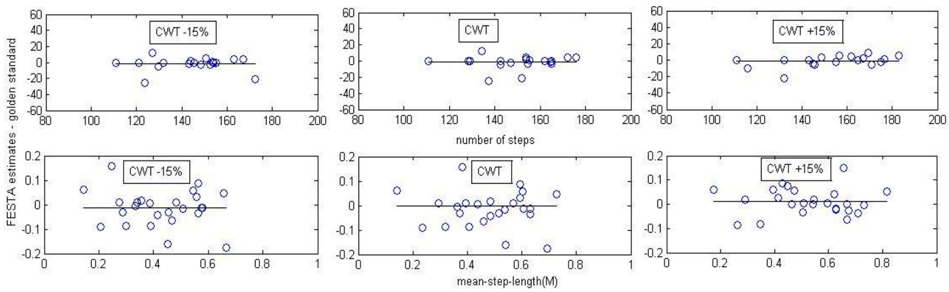

Figure 2.3: FESTA estimates, difference between steps at the first and second test occasion (top panel). FESTA estimates, difference between mean-step-length at the first and second test occasion (bottom panel).

Test-retest reliability for over ground distance covered during the 6MWT for $ICC_{agreement\ 3,1}$,is .97. Mean difference in meters was 8.1 meter, see figure 2.4.

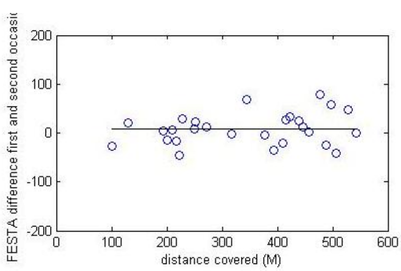

Figure2. 4: FESTA estimates difference in covered walking distance (M) between the first and second test occasion.

Discussion

The objective of this study was to examine the criterion validity and test-retest reliability of the novel telemetric system, FESTA, in measuring walking activity in stroke survivors. To this end, we tested gait parameters; steps, mean-step-length and walking distance in chronic stroke survivors. Results of criterion validity and test-retest reliability indicate good validity and reliability as all ICC values were between .841 and .972. These results are similar to the most commonly used accelerometer in the stroke population [80] [82] [96]. Moreover the results present higher accuracy in comparison algorithms not specifically developed for the stroke population [96].

No clear trend can be seen between ICC values and MRRSE and the three gait speed conditions. This indicates that the validity of the FESTA is not affected by gait speed. Although the latter finding demonstrates the possible robustness of the FESTA for real-life use, we have to take into account that gait parameters differ for treadmill walking and over ground walking[97]. When walking on a treadmill, the gait patterns of chronic stroke survivors are more symmetrical and stable compared to over ground walking. Furthermore in real-life gait speed may vary during a day and even within a walking bout. Therefore the gait parameters steps and mean-step-length have to be interpreted with caution since these parameters were only tested at the treadmill and might not be generalizable to walking over ground. Further research is needed to determine these outcomes in over ground walking. Another limitation of the study was the test-retest reliability design. Although all conditions were similar in the first and second test occasion, subjects did perform slightly different in the first and second test. In example subjects took slightly fewer steps at the treadmill test or walked a few meters further in the second 6MWT compared to the first test occasion. This affected the reliability results of FESTA.

For specific measurement devices, measurement errors should be smaller than the Minimal Clinically Important Difference (MCID) to detect a valuable effect for individuals. For the treadmill tests, no MCIDs have been defined. The MDC_{95} score of the FESTA for over ground walked distance at the 6MWT was 62.2 meters. Although we used for the distance parameter an individual calibration, which appears to be more accurate than a general estimation [89], MDC of 62.2 meters is still slightly greater than the MDC of 54.1 meters [98] for the 6MWT. Herein we assumed that 54.1 was the optimum MDC value, as we used the same 6MWT with similar subjects. Therefore distance measures still have to be interpreted with caution.

Statistical considerations

Previous studies with a similar design and aim as we had [81, 82] [99–101] expressed accuracy performance in ICC values and Limits of Agreement. In this study, we added a new measure for validity; the Mean Relative Root Squared Error (MRRSE). It is known that ICC values are strongly influenced by the magnitude of the variance within the study sample. Furthermore, other than the name $ICC_{agreement}$ suggests, the ratio of variances is calculated, rather than the absolute agreement score [102]. When taking a closer look at the ICC formula, it is clear that a large variance in subject scores, as is the case in this study, will lead to a higher ICC [102]. Studies with different variances in their study populations can therefore not be compared directly. To get a better insight in the true agreement between the output of the FESTA and 'gold standard', and to eliminate the effect of the high variance in our study population, we calculated the MRRSE for each gait parameter. The MRRSE represents the mean absolute percentage difference between the two measurement devices, expressed in the percentage of unit of the parameter. This score is easy to use in daily practice, easy to interpret and not dependent of variance between patients. Therefore, we hereby suggest using the MRRSE in future research, as it provides a more direct comparison between studies and between measurement devices.

FESTA

FESTA (FEedback to STimulate Activity) is a newly developed telemetric system and validity and reliability were shown to be good in the present analysis. It is designed to monitor and stimulate stroke survivors with respect to their daily walking activity. The physical therapist is able to interact by setting walking activity goals based on walking time and walking bouts. FESTA has several advantages over other methods for assessing walking activity; it can measure different gait parameters such as number of steps, mean-step-length, distance and as derivatives walking time and the number of walking bouts[83], whereas a step-counter can only determine the number of steps. Roos et. al.(2012) clearly stated that steps alone is not sufficient to characterize physical inactivity in stroke survivors[78].Due to the docking station FESTA is not limited by battery life and data capacity. Therefore it is able to monitor for a long time period without recharging or removing data. Furthermore FESTA provides the researcher and physical therapist and stroke survivor with real-life walking activity information. Future research will involve studying the effect of giving feedback using this device. The aim will be to increase walking activity by providing feedback to the user and providing information of actual walking activity and the daily pattern of walking activity to the physical therapist. Using FESTA provides new possibilities to measure walking activity of chronic stroke survivors in a valid and reliable way and thereby offers a variety of perspectives for research and treatment in this population.

Conclusion

Based on ICC values and MRRSE, this study demonstrated good criterion validity and test-retest reliability of the telemetric system FESTA for measuring gait parameters in chronic stroke survivors. FESTA provides the possibility to measure gait parameters in a valid and reliable manner and can be used, in both clinical practice and academic research.

CHAPTER 3

STROKE SURVIVORS VS OLDER ADULTS

Characteristics of daily life gait in fall and non fall-prone stroke survivors and controls Michiel Punt, Sjoerd M. Bruijn, Kimberley S. van Schooten, Mirjam Pijnappels, Ingrid G. van de Port , Harriet Wittink , Jaap H. van Dieën. Journal of NeuroEngineering and Rehabilitation, 2016.

Abstract

Background. Falls in stroke survivors can lead to serious injuries and medical costs. Fall risk in older adults can be predicted based on gait characteristics measured in daily life. Given the different gait patterns that stroke survivors exhibit it is unclear whether a similar fall-prediction model could be used in this group.

Objective. Therefore the main purpose of this study was to examine whether fall-prediction models that have been used in older adults can also be used in a population of stroke survivors, or if modifications are needed, either in the cut-off values of such models, or in the gait characteristics of interest.

Methods. This study investigated gait characteristics by assessing accelerations of the lower back measured during seven consecutive days in 31 non fall-prone stroke survivors, 25 fall-prone stroke survivors,20 neurologically intact fall-prone older adults and 30 non fall-prone older adults. We created a binary logistic regression model to assess the ability of predicting falls for each gait characteristic. We included health status and the interaction between health status (stroke survivors versus older adults) and gait characteristic in the model.

Results. We found four significant interactions between gait characteristics and health status. Furthermore we found another four gait characteristics that had similar predictive capacity in both stroke survivors and older adults.

Conclusion. The interactions between gait characteristics and health status indicate that gait characteristics are differently associated with fall history between stroke survivors and older adults. Thus specific models are needed to predict fall risk in stroke survivors.

Introduction

Falls are a major problem in the growing older population. Falls can result in serious injuries leading to considerable medical costs[103]. In stroke survivors, fall rates are higher in comparison to healthy older adults[7, 104]. Falls may increase the fear of falling and may subsequently reduce physical activity[105],which can result in physical deconditioning and may further increase fall risk in the long term.

Objective fall risk assessment often involves assessment of balance control, for example with the Berg Balance Scale [24]. However, the relation between deficits in balance control and fall rates in stroke survivors is inconsistent[7, 24]. It has been suggested that this might be due to fact that most balance tests are static in nature[106],while most falls occur during dynamic tasks such as walking and transfers[7]. Interestingly, several characteristics of gait quality have been shown to differentiate fallers from non-fallers among older adults[44, 46, 47]. These characteristics can be measured in daily life by accelerometry, and reflect aspects such as stability, symmetry, smoothness and variability. van Schooten et.al.[47] demonstrated the added value of such gait characteristics to conventional clinical predictors of fall risk.

A similar approach may be useful for stroke survivors, and could add value to existing clinical tests. However, quantity and quality of gait are different in stroke survivors[12, 38, 78] than in healthy individuals, and it is therefore unclear whether a fall risk prediction model as used by van Schooten et al[47] can be used in stroke survivors. For example, stroke survivors have a more asymmetrical[12] and unstable gait[38] compared to age matched controls. Furthermore stroke survivors are physically less active[78] and physical activity has been associated to falls as well[47]. Thus, even if the same gait quality characteristics predict falling in stroke survivors and in healthy controls, it may be that regression coefficients for these characteristics are markedly different in a prediction model for stroke survivors compared to models developed for healthy older adults.

To this date, exploring the potential of fall prediction models based on gait characteristics has been limited to older adults; however, gait in stroke survivors is remarkably different and fall incidences are a frequent problem in stroke survivors. To explore the potential of using daily life gait assessment to predict falls in stroke survivors, the main purpose of the current study was to examine whether fall-prediction models that have been used in healthy older adults[44, 46, 47] can also be used in a population of stroke survivors, or if modifications are needed, either in the regression coefficients of such models, or in the gait characteristics of interest.

Methods

Participants

We tested community-dwelling stroke survivors as well as healthy older adults. Stroke survivors were recruited via local physical therapy centers and through national peer group meetings. Stroke survivors were above the age of 18, at least one year post stroke and were living in the community independently. Stroke survivors were excluded from the study if they had a functional ambulation category of two or less. Data for the healthy older adults group were derived from a data set of a larger study on 'fall risk assessment in older adults'(FARAO)[46, 47]. We only included participants from who we were certain that they were free of any neurological damage, such as a history of stroke or Parkinson's disease. Control participants for this study were recruited via general practitioners, pharmacies and residential care facilities in the area of Amsterdam, The Netherlands. Participants were excluded from the study if they had severe cognitive disorders, as indicated by a minimal mental state examination score of 24 or less[85]. All participants were able to walk independently for at least 20 meters, if necessary with a walking aid. The research protocol was approved by the medical ethical committees of the University Medical Center Utrecht and the VU medical center Amsterdam, The Netherlands. All participants signed informed consent and treatment of the participants was according to Good Clinical Practice.

Data collection

Fall status was determined using a self-reported questionnaire asking about falls in the last twelve months prior to determining gait characteristics. A fall was defined as; 'any unanticipated event that results in participant coming to the ground, floor or lower level' [20]. To estimate quantitative and qualitative gait characteristics, participants were asked to wear a tri-axial accelerometer (55 grams), (McRoberts, Den Haag, The Netherlands) at the middle of the lower back using an elastic belt[107]. The accelerometer was aligned to coincide with the anterior-posterior (AP), medio-lateral (ML) and vertical (VT) body-axis. Participants were instructed to realign the accelerometer during the monitoring period if necessary. Data were sampled at 100 samples/s with a range ± 6g and digitally stored on a mini SD card. Participants were instructed to wear the accelerometer for seven consecutive days, preferably during day and night, but were allowed to take it off when going to bed. The accelerometer was removed during showering and other water-related activities to prevent damage.

Data analysis

Based on health status and fall history of at least one fall in the previous year, we classified participants into four groups: non fall-prone stroke survivors (NF-SS), fall-prone stroke survivors (F-SS) and a control (CON) group of older adults thus fall-prone older adults (F-CON) and non fall-prone older adults (NF-CON) and used these groups for further analyses.

Gait activity was identified from the weekly time series using a validated algorithm for gait detection and gait quantification[108]. The algorithm searches for gait activity based on the spectral content of the AP acceleration and discards periods of activity shorter than eight seconds. Total monitoring time was defined as the time between the first and last gait episode of each participant over the seven days. Prior to estimating gait characteristics, potential accelerometer misalignment was corrected according to the method described by Rispens et al [107].

Gait quantity was expressed as the duration of gait activity per 24 hours and the number of walking bouts per 24 hours. We classified walking bouts of 24 seconds or shorter as short walking bouts. Short walking bouts are likely to be executed predominantly in at-home settings, which might affect gait characteristics (for instance, turning affects step length symmetry, and usually in-home walking coincides with more turning as compared to walking outdoors). All walking bouts were divided into eight-seconds epochs for further analysis. We calculated the number of eight seconds epochs that were part of the short walking bouts and divided this by the total number of epochs. Thus we were able to determine whether the characteristics of gait quality were derived under similar circumstances between groups.

We estimated gait quality characteristics that have shown promise in differentiating between fallers and non-fallers among older adults[46]. Specifically, we calculated gait speed [109], gait symmetry determined by the harmonic ratio (HR) [41]. This HR measure divides the sum of the first ten even harmonics through the sum of the first ten odd harmonics. Symmetrical gait in the VT and AP direction will predominantly contain even harmonics which will result in a higher HR. The smoothness of gait was determined by dividing the ground frequency (first harmonic) of the time series by the first six harmonics of the time series, the index of harmonicity (IH) [40]. A complete smooth gait can be described by one sinusoidal function and no higher harmonics would be necessary to describe the signal. Subsequently this would result in a higher IH value. Several indicators of gait variability were determined. Firstly the amplitude of the dominant peak which represents the 'strength' of the dominant peak relative to the rest of the signal [42], and hence a high value represents a low variability. Secondly the width of peak of the power spectrum reflects the dispersion of the dominant peak [42] and hence a higher value represents a higher variability. Thirdly stride frequency variability, and fourthly local dynamic stability expressed as the local divergence exponent (LDE), which quantifies the exponential rate of divergence from initially nearby kinematics states as a function of stride time[46]. A higher LDE indicates a faster diverging acceleration signal and indicates a more unstable gait pattern. Except for gait speed and stride time all these characteristics were determined in three directions using algorithms previously described by Rispens et al.[46]. Estimation of gait quality characteristics was performed on each epoch of 8-seconds length, which was sufficient long for estimating spectral features [110]. For each characteristic, the median value over all gait epochs of a participant was used for statistical evaluation. We took the median value as the median is less sensitive in comparison to the mean for outliers in the estimated gait characteristic.

Statistics

For each group, means and standard deviations are reported. Participant characteristics and monitoring duration were compared between groups using health status (stroke survivor or healthy older adult) and fall history as two categorical factors in an analysis of variance (ANOVA).When these analyses revealed differences between groups, the variable concerned was used as a covariate to control for its effects in subsequent analyses. To facilitate objective comparison between independent variables we z transformed continues variables prior to performing the logistic regression. We developed a fall prediction model per gait characteristic using binary logistic regression. Fall history was used as dependent variable, while the gait characteristic and the categorical variable health status (stroke survivors versus healthy older adults, coded as 1 and 0 respectively) were the independent variables. The interaction between health status and the gait characteristic was also included in the model, but if the interaction did not reach a p-value of ≤ 0.05 it was removed from the model and a new model with health status and the gait characteristic only was created. The odds ratio (OR)is a number indicating the amount of increased fall risk per unit increase of the independent variable. If a significant OR is found for a specific gait characteristic only, this implies that it is associated with fall history and that this association does not depend on health status (controls, older adults and stroke survivors). If in addition a significant OR is found for health status, but no interaction, this implies that fall risk is dependent on health status, but that the change in risk with a unit change in the gait characteristic is independent of health status. If an interaction effect is found, this implies that the relation of the gait characteristic with fall history is different between health status groups, suggesting that a specific model is needed for stroke survivors. All statistical analyses were performed using SPSS software version 20.0,and a p-value of ≤ 0.05 was considered statistically significant.

Results

A total of 106 participants volunteered for the study. Of the 56 participating stroke survivors 25 (45%) had experienced at least one fall in the previous year. A total of 50 control older adults participated of whom 20 (40%) had experienced at least one fall in the previous year. Participant characteristics and monitoring duration results for each group are presented in table 3.1. Tables 3.2 and 3.3 provide an overview of which gait characteristics show promise in regard to predicting fall risk in stroke survivors and older adults. More precise, table 3.2 provides an overview of quantitative and qualitative gait characteristic values between stroke survivors and older adults and is as well subdivided in fallers and non fallers. An overview of the corresponding Odds ratios (OR) between all four groups and p-values derived from the binary logistic regression models are presented in table 3.3.

Table 3.1:Participant characteristics for the four groups.

	NF-SS Mean ± SD	F-SS Mean ± SD	NF-CON Mean ± SD	F-CON Mean ± SD
Female/male	15/16	15/10	13/17	14/6
Age (years)	64.1 ± 11.6	69.0 ± 9.2	71.9 ± 4.1	74.9 ± 8
Height (m)	171.4 ± 8.8	172.3 ± 9.3	169.4 ± 9.2	170.4 ± 7.7
Weight (kg)	79.7 ± 14.7	82.9 ± 16.5	75.1 ± 10.5	75.3 ± 13.7
BMI (kg/m2)	27.0 ± 3.8	28.1 ± 6.5	25.8 ± 2.5	26.1 ± 3.7
Monitoring(days)	6.5 ± 0.5	6.5 ± 0.4	6.4 ± 0.7	6.5 ± 0.6

	Health status		Fall history		Health * Fall history	
F-Value / P-Value	F	P	F	P	F	P
Age (years)	14.98	**<0.001**	0.29	0.59	5.21	**0.024**
Height (m)	1.37	0.244	0.01	0.99	0.33	0.564
Weight (kg)	3.87	0.051	3.89	0.534	0.34	0.561
BMI (kg/m2)	3.52	0.063	0.71	0.400	0.21	0.645
Monitoring(days)	0.85	0.771	0.48	0.827	0.945	0.333

Main effects for health status and fall history and their interaction are presented. Significant p-values are printed in bold. non-fallers, stroke survivors (NF-SS), faller, stroke survivor (F-SS) non-faller control group of older adults (NF-CON), faller control group of older adult (F-CON).

Two-way ANOVAs for participant characteristics revealed no differences in monitoring duration and anthropometrics between groups, but showed a significant interaction effect on age, with the NF-SS group being significantly younger than the other three groups. Further results were corrected for this difference by using age as covariate.

No associations with a history of falls were found for gait quantity characteristics (see table 3.3). Four gait quality characteristics were found to be associated with a history of falls independent of health status (see table 3.3). A reduced gait symmetry (HR) in the VT and AP direction and decreased gait smoothness (IH) in the VT direction were associated with a history of falls in both groups. Moreover an increase in the dominant amplitude of the power spectrum in the ML direction was associated with an increased fall risk in both groups. Increased stride time and reduced gait speed showed a trend of increased fall risk in both groups, respectively (p=.06 and p=.07). In addition for four gait quality characteristics a significant interaction term between health status and gait characteristic, was predictive for fall history (see table 3.3). For gait smoothness (IH) in the ML direction, this indicated that a higher IH increased fall risk, but less so in stroke patients, although stroke increased the fall risk. Moreover an larger width of the dominant peak of the power spectrum in VT direction higher fall risk in stroke survivors but lower in older adults. A higher amplitude of the dominant peak in VT was associated with a lower fall risk in stroke survivors but not in older adults, with stroke increasing fall risk as well. Finally, an increase in the local divergence exponent (decrease in local dynamic stability) in the ML direction, increased fall risk in stroke survivors, but not in healthy older adults.

Table 3.2: Quantitative and qualitative gait characteristics for the four groups.

	NF-SS	F-SS	NF-CON	F-CON
Quantitative measures	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Gait activity (min/day)	35.9 ± 20.1	34.4 ± 24	47.5 ± 21.8	50 ± 19.8
WB/day	127 ± 64.5	125 ± 77.3	158 ± 54.4	152 ± 49.9
Short WB (%)	91.6 ± 4.8	92.4 ± 6.2	89.7 ± 6	90.2 ± 3.9
Short WB epochs(%)	27.8 ± 18.4	43.3 ± 28.5	25.5 ± 15.9	23.8 ± 10.1
Qualitative measures				
Gait speed (m/s)	0.74 ± 0.14	0.67 ± 0.17	0.93 ± 0.30	0.90 ± 0.21
Stride time (seconds)	1.26 ± 0.20	1.44 ± 0.40	1.14 ± 0.13	1.15 ± 0.08
Harmonic Ratio VT	1.31 ± 0.20	1.20 ± 0.20	1.92 ± 0.31	1.67 ± 0.32
Harmonic Ratio ML	1.33 ± 0.13	1.35 ± 0.22	1.45 ± 0.15	1.51 ± 0.26
Harmonic Ratio AP	1.17 ± 0.20	1.07 ± 0.20	1.71 ± 0.19	1.39 ± 0.24
Freq. Variability VT	0.15 ± 0.05	0.14 ± 0.03	0.14 ± 0.20	0.14 ± 0.02
Freq. Variability ML	0.18 ± 0.04	0.21 ± 0.05	0.16 ± 0.40	0.17 ± 0.04
Freq. Variability AP	0.17 ± 0.04	0.19 ± 0.05	0.14 ± 0.30	0.15 ± 0.04
IH VT	0.48 ± 0.18	0.39 ± 0.16	0.64 ± 0.12	0.56 ± 0.13
IH ML	0.38 ± 0.21	0.50 ± 0.25	0.34 ± 0.13	0.25 ± 0.15
IH AP	0.51 ± 0.15	0.52 ± 0.15	0.57 ± 0.11	0.52 ± 0.09
Amplitude (psd) VT	0.47 ± 0.12	0.40 ± 0.09	0.56 ± 0.09	0.58 ± 0.11
Amplitude (psd) ML	0.40 ± 0.15	0.50 ± 0.19	0.36 ± 0.08	0.36 ± 0.08
Amplitude (psd) AP	0.42 ± 0.11	0.46 ± 0.17	0.42 ± 0.09	0.41 ± 0.08
Width (psd) VT	0.98 ± 0.01	0.99 ± 0.02	0.95 ± 0.01	0.94 ± 0.01
Width (psd) ML	0.95 ± 0.02	0.95 ± 0.03	0.95 ± 0.01	0.95 ± 0.01
Width (psd) AP	0.95 ± 0.02	0.95 ± 0.01	0.94 ± 0.01	0.93 ± 0.01
LDE/stride VT	0.98 ± 0.19	1.02 ± 0.19	0.92 ± 0.15	0.94 ± 0.16
LDE/stride ML	0.89 ± 0.18	0.90 ± 0.20	0.71 ± 0.08	0.78 ± 0.11
LDE/stride AP	0.87 ± 0.19	0.90 ± 0.21	0.72 ± 0.10	0.78 ± 0.11

Table 3.2, Quantitative and qualitative gait characteristics for all four groups expressed as means and standard deviations. Abbreviations: WB is walking bouts, Freq. Variability is the stride frequency variability, IH is the Index of Harmonicity, Amplitude (psd) is the amplitude of the dominant peak in the power spectral density, Width (psd) is the width of the dominant peak in the power spectral density, LDE/stride is the local divergence exponent per stride. VT is the vertical direction, ML is the medio-lateral direction and AP is the anterior-posterior direction. Significant associations derived from logic regression (table 3.3) are printed in bold.

Table 3.3: Binary logistic regression.

	Gait characteristic	Health status	Interaction
Quantitative measures	OR (p)	OR (p)	OR (p)
Gait activity (min/day)	1.01 (.94)	0.82 (.63)	
WB/day	0.94 (.74)	0.85 (.69)	
Short WB (%)	1.17 (.43)	0.88 (.76)	
Short WB epochs(%)	1.48 (.06)	0.99 (.99)	
Qualitative measures			
Gait speed (m/s)	0.64 (.06)	1.17 (.71)	
Stride time (seconds)	1.71 (.07)	1.19 (.68)	
Harmonic Ratio VT	**0.54 (.02)**	1.61 (.33)	
Harmonic Ratio ML	1.23 (.31)	0.71 (.41)	
Harmonic Ratio AP	**0.34 (<.01)**	2.72 (.06)	
Freq. Variability VT	0.81 (.34)	0.81 (.59)	
Freq. Variability ML	1.45 (.08)	1.01 (.94)	
Freq. Variability AP	1.41 (.12)	1.08 (.86)	
IH VT	**0.46 (<.01)**	1.81 (.23)	
IH ML	**1.64 (.05)**	0.65 (.37)	**0.22(<.01)**
IH AP	0.84 (.40)	0.87 (.73)	
Amplitude (psd) VT	**0.44 (.02)**	1.21 (.70)	**2.76 (.04)**
Amplitude (psd) ML	**1.54 (.04)**	1.05 (.91)	
Amplitude (psd) AP	1.04 (.83)	0.90 (.81)	
Width (psd) VT	1.11 (.63)	**0.09 (.04)**	**0.01 (.02)**
Width (psd) ML	0.98 (.94)	0.82 (.62)	
Width (psd) AP	0.87 (.51)	0.81 (.61)	
LDE/stride VT	1.31 (.21)	1.02 (.97)	
LDE/stride ML	1.16 (.54)	2.23 (.13)	**4.86 (.03)**
LDE/stride AP	1.54 (.06)	1.31 (.55)	

Quantitative and qualitative gait characteristics association with a history of falls. Health status includes stroke survivors versus older adults. Data was z-transformed prior to logistic regression. Significant associations are printed in bold.

Discussion

The main purpose of the study was to test whether fall-prediction models that have been used in healthy older adults can also be used in a population of stroke survivors, or if modifications are needed, either in the regression coefficients, or in the gait characteristics of interest.

Previous studies assessing gait in older adults have shown that gait speed[111], gait variability[32], local dynamic stability [35, 46, 47] and symmetry[45] provide valuable information concerning fall risk in older adults. Our results are partly in line with these findings as we found several similar gait characteristics that were able to predict falls in both groups. However the limited number of participants in our study reduced statistical power in comparison to previous work [46, 47], which could explain that not all findings are reproduced in this study. For instance gait speed and stride time showed only a trend of predictive ability in both groups, respectively (p=.06 and p=.07).

Interestingly, we found four interactions indicating a different relation between gait quality and fall history in stroke survivors compared to the group of healthy older adults. In addition gait symmetry in the AP direction was predictive for falls in both groups, but health status showed a trend (p=.06) indicating a different cut off value in the regression. Thus, since we found gait characteristics that were predictive for falls in both groups but we also found gait characteristics with a interaction or different cut off value the overall results indicate that predicting falls in stroke survivors based on daily-life gait characteristics is possible but requires a stroke specific fall-prediction model.

Surprising results were found for the index of harmonicity, which is calculated by dividing the power of the fundamental frequency by the power of the first six harmonics. This measure is thought to reflect the smoothness of gait. Interestingly, based on mean and standard deviations between groups the F-SS group had the highest index of harmonicity in the ML direction but the lowest in the AP and VT directions. This different relation between ML and AP, VT direction for the index of harmonicity can possibly be explained by a more pronounced and rapid shift of the center of mass between both legs in this group, to reduce the time standing on the paretic leg. Such fast movement results in a high peak in the acceleration signal at the stride frequency. Therefore the index of harmonicity in the ML direction, measured at the pelvis might reflect more a rigid gait pattern and loss of control in the paretic leg rather than smoothness of gait. Considering the present differences between groups, it is a gait characteristic of interest in the stroke population. Moreover, this opposite relation between ML and AP, VT direction for the index of harmonicity was confirmed by our findings on the amplitude of the dominant peak in the power spectrum. The amplitude of the dominant peak was highest for the F-SS group in the ML direction but lowest in the VT direction, which is in line with the findings by Weiss et al [44].

Although none of the gait quantity characteristics were associated with a history of falls, gait activity and the number of walking bouts seems to be reduced in stroke survivors, see also table 3.2. Since most falls occur during gait[21], this reduced gait activity could be a fall risk avoidance strategy. However reduced gait activity may cause further deconditioning and subsequently increased fall risk in the long-term.

Study limitations

To divide our groups of interest into fallers and non-fallers we have used self-reported retrospective fall incidents. Retrospective fall reports can be influenced by recall bias and their relation with gait quality may slightly differ from prospective fall reports[47]. These differences may have influenced our classification. Second, the identification of gait epochs for estimating gait characteristics was accomplished by a gait detection algorithm[108]. Although validity and reliability was good for slow and fast walking, it still remains unknown to what extent the algorithm identified other forms of cyclic movements such as biking. Misclassifications of gait activity or for instance wearing the accelerometer away from the midline of the lower back will result in deviating estimations of gait characteristics for those epochs. Yet the error in our final estimating gait characteristics is limited by taking the median value over all epochs rather than the mean. Third, the results showed differences in percentages of short walking bouts between groups. This suggests that the median value for the qualitative gait characteristics were estimated based on slightly different environmental circumstances. This is an important finding, because for example gait symmetry may be affected by bends and shorter walking bouts are probably performed in a more complex setting, which contains more bends. To examine whether this finding influenced our results we compared gait characteristics between groups including only walking bouts lasting 16 seconds or more. Mean values were somewhat different but no consistent changes were found and the main findings would have been the same as presented here. In addition we reanalyzed our statistical models taking weight and BMI as covariates, since both variables were nearly significant different between groups. OR were slightly different yet the same interactions were still present.

Conclusion

In conclusion, due to the present interactions found, several gait characteristics are differently associated with a history of falls in stroke survivors as in older adults. This suggests that specific models are needed to predict fall risk in stroke survivors.

CHAPTER 4

PREDICTING FALLS

Do clinical assessments, steady-state or daily-life gait characteristics predict falls in ambulatory chronic stroke survivors? Michiel Punt, Sjoerd M. Bruijn, Harriet Wittink, Ingrid G. van de Port, Jaap H. van Dieën, Journal of Rehabilitation Medicine, 2017

Abstract

Background. At present it remains unknown if gait characteristics predict falls in stroke survivors and whether they perform better than existing, current used fall risk assessments.

Objective. This exploratory study investigated to what extent gait characteristics and clinical physical therapy assessments predict falls in chronic stroke survivors.

Methods. Gait characteristics were collected from 40 participants. Participants walked on a treadmill with motion capture, to collect steady state gait characteristics, such as spatio-temporal, variability, and stability measures. Moreover, we used an accelerometer to collect daily-life gait characteristics during seven days. Six physical and psychological assessments were administered. Fall events were determined using a 'fall calendar' and monthly phone calls over a six-months period. After data reduction through principal component analysis, the predictive capacity of each method was determined by a logistic regression.

Results. 38% of the participants were classified as fallers. Laboratory based and daily-life gait characteristics predicted falls acceptable well, with an area under the curve (AUC) of respectively 0.73 and 0.72, while fall predictions from clinical assessments were limited (0.64).

Conclusion. Independent of the type of gait assessment, qualitative gait characteristics are better fall predictors than clinical assessments. Therefore clinicians should consider gait analyses as a alternative to identify fall prone stroke survivors.

Introduction

Falls are common among chronic stroke survivors [22, 28] and can lead to injuries [112, 113]. Predicting falls may help in assigning stroke survivors to fall prevention interventions, and may aid in the development of tailored fall prevention. Clinically, physical performance tests have been used to assess fall risk in stroke survivors [29, 97, 114, 115]. While some studies reported that these tests were associated with falls [114, 115] other studies did not confirm such an association [29, 116]. In addition, several studies attempted to predict falls based on psychological factors such as depression [28, 29]. Again, some studies did [28], while others did not [29] find an association between depression and falls in stroke survivors. Since most falls occur during dynamic activities such as walking or transfers [22, 29] and current used fall risk assessments lack in consistency, it has been suggested to explore gait characteristics in relation to fall risk in stroke survivors [7].

Interestingly, in healthy older adults several studies were successful in predicting falls by estimating gait characteristics in a laboratory setting [35, 117]. In addition, several studies were able to predict falls based on gait characteristics determined from daily-life accelerometry [44, 47]. Despite the different approaches in estimating gait characteristics, both methods demonstrated that gait characteristics like gait speed [117], variability of gait [35, 47] and local divergence exponents (LDE)[35, 47] of gait kinematics predict falls in healthy older adults.

Gait characteristics in stroke survivors differ from those in healthy older adults. For instance, gait speed is reduced, and gait is more asymmetrical [118] in stroke survivors. Nevertheless, gait characteristics of stroke survivors have also been shown to predict falls [39]. Moreover, with regard to gait stability, it has been shown that the local divergence exponent (LDE) was larger in stroke survivors than in age matched healthy peers [38], indicating less stable gait. Still, stroke survivors had equal Margins of Stability (MoS) [38] probably accomplished by a larger step width [15]. Although there are profound differences in gait between stroke survivors and healthy older adults, a recent study indicated that the same gait characteristics measured in daily-life are related with fall history in stroke survivors [119]. However, this study also found that several gait characteristics had different associations with fall history than in healthy older adults [119].

It is currently unknown whether gait characteristics yield better fall predictions than current clinical assessments in stroke survivors. It is also not known which method of gait characteristic estimation, i.e., from daily-life or laboratory measurements, yields the most meaningful information regarding fall predictions, or whether these two methods are even complementary in this regard. Therefore, the aim of this exploratory study was two-fold. Firstly, we examined whether gait characteristics predict fall incidences in chronic stroke survivors better than current clinical assessments. Secondly, we examined how well both gait characteristic estimation methods predict falls and if a combination of both gait characteristic estimations yield better predictions of falls.

Methods

Participants

Stroke survivors were recruited via flyers in hospitals, general practitioners and physical therapy practices and through various national peer group meetings in the Netherlands. We included participants with a self reported stroke who were at least six months post-stroke, were living independently in the community and were older than 18 years of age. Stroke survivors were excluded from the study if they were institutionalized in, for instance, a nursing home, if they had a functional ambulation category (FAC) of 2 or less [84], a mini mental state examination (MMSE) of 24 or lower [85] and or severe cardiovascular, respiratory, musculoskeletal or neurologic disorder other than stroke that affected gait performance. The research protocol (NL49126.028.14) was approved by the medical ethical committees of “Noord Brabant”, The Netherlands. All participants signed informed consent prior to testing and treatment of the participants was according to Good Clinical Practice.

Measurement protocol

Twenty-four hours prior to clinical and laboratory testing, participants were asked not to drink any alcoholic beverages and to avoid any other activities that could affect physical and psychological performance during testing. All measurements were performed during a single visit at the rehabilitation center Revant, Breda, The Netherlands. Depending on the number and length of the breaks that a participant needed, the measurement protocol took from two up to three and a half hours. Demographic and stroke specific characteristics were obtained including; sex, age, body length and weight, time since stroke, hemiparetic side, daily use of a walking aid for inside and or outside use and use of prescribed medication.

Clinical assessments

Participants were asked to perform several physical performance assessments and questionnaires commonly used in rehabilitation practice. First, over ground preferred gait speed was assessed with a 10 meter walk test (10MWT, performed twice and mean was calculated) [120]. Second the ability to make a transfer was measured in seconds by the Time Up and Go Test (TUGT) [121], the test was repeated three times and mean was calculated. Third, static and dynamic balance was measured with the 14-item Berg Balance Scale (BBS) [122]. In addition, the 30-item Yesavage Geriatric Depression Scale (GDS) [123] , the Fall Efficacy Scale (FES) [124] and the Longitudinal Aging Study Amsterdam questionnaire (LASA, a questionnaire aimed to identify subgroups with highest fall risk) [125] were administered. See table 4.2 for an overview of all physical and psychological assessments.

Laboratory gait assessment

Laboratory-based gait analysis was conducted using a Gait Real-time Analysis Interactive Lab (GRAIL, Motekforce Link bv, Amsterdam). The GRAIL consists of a dual-belt treadmill with two embedded force platforms (Motekforce Link bv, the Netherlands), a motion-capture system (Vicon, Vicon Motion Systems, Oxford, UK) with ten infrared cameras (Bonita B10, Vicon Motion Systems, Oxford, UK) and synchronized virtual environments. Time series of ground reaction forces were sampled at 1000 samples/s and the infrared cameras were sampled, synchronized at a frame rate of 100 samples/s, both using

Vicon Nexus Software 1.8.5. The GRAIL was controlled by a custom designed application in D-flow (Motekforce Link b.v. the Netherlands).

Each participant wore black tight fitting clothes provided by the researcher and any jewelry was removed. We used 47 reflective passive markers (15 mm) [126] placed on anatomical points. Markers were placed by the same investigator to maximize consistency between participants.

During treadmill testing, participants wore a safety harness at all times. This harness was attached to the ceiling and prevented falls, while participants were still able to move freely on the treadmill. Participants walked without the use of a walking aid, except for an ankle-foot orthosis or orthopedic shoes. After familiarization to the treadmill steady state, gait characteristics were obtained at preferred gait speed. Preferred gait speed was determined by slowly increasing the treadmill speed until the participant reported a comfortable gait speed. If necessary, participants were allowed to hold on to the handrail for the first minute. As soon as handrail support was no longer needed and participants were familiarized with the treadmill, data recording started. A minimum of 60 consecutive strides was recorded and used for further analysis.

The gait data were recorded in Vicon Nexus and transferred to Matlab 2013B (The MathWorks Inc., Natick, MA) to extract gait characteristics. The gait events foot contact (FC) and foot off (FO) were determined using the Center of Pressure (CoP) [127]. Briefly, force plate data were first converted to center-of-pressure data i.e. time series of the point of application of the resultant ground reaction force, which shows a characteristic butterfly pattern over time. Then FC and FO were detected from this profile using peak detection. The left and right upper angles of the butterfly corresponded with right and left FO respectively and the left and right lower angles of the butterfly corresponded with the left and right FC.

All steady state gait characteristics during preferred gait speed were determined over 60 consecutive strides. Spatio-temporal gait characteristics included gait speed, stride time, step width, paretic and non-paretic step length, and step time.

Spatio-temporal gait symmetry index (SI) was determined based on difference in step length and step time between paretic and non paretic limb using equation 1.

$$1)\ Symmetry\ Index\ (SI) = 1 - 1/n \sum_{i=0}^{n} \left(\frac{PLi - NPLi}{PLi + NPLi}\right)$$

Where PL is the step length / time of the paretic limb and NPL is the step length / time of the non paretic limb, determined and averaged over *i* till *n* strides. An SI deviating from 1 reflects a more asymmetrical gait.

Gait smoothness was based on the velocity time series of the three averaged sacrum markers. Subsequently the index of harmonicity (IH) was determined by dividing the power of the spectral analysis of the ground frequency by the power of the sum of the first six harmonics [40]. Variability of gait was determined by calculating the standard deviation of stride time and of step time and step length for the paretic and non-paretic limb separately.

Two types of gait stability characteristics were determined. First, local dynamic stability, expressed as the local divergence exponent (LDE) was calculated from the velocity time series of the averaged three sacrum markers. Time series were time normalized towards, on average, 100 samples per stride, so that time-normalized time-series had a length of 6000 samples. Each time-normalized time series was reconstructed in a 5 dimensional state space by using a fixed delay of 10 samples. See for a more detailed explanation Bruijn et al. [18]. Finally, the maximum local divergence exponent was determined for the rate of divergence from 0-1 step [18]. Second Margins of Stability (MoS) were estimated by estimating the Center of Mass (CoM) using a 14 body segment model [128]. In short, CoM location and mass of each segment were estimated based on gender and body segment circumferences as well as length of the segments [128]. The extrapolated center of mass (XCoM) was determined by the CoM plus the velocity of the center of mass times the Eigenfrequency of a pendulum with limb length as length [56]. To determine the MoS in both medio-lateral (ML) and anterior-posterior (AP) directions, the marker position of the lateral malleolus in ML and the toe marker in AP direction at FC were subtracted from the XCoM in ML and AP direction respectively. See table 4.3 for an overview of steady state gait characteristics.

Daily life gait characteristics

The day after the laboratory tests, all participants started wearing a tri-axial accelerometer (McRoberts, The Hague, The Netherlands) during seven consecutive days. The accelerometer was located at the lower back so as to collect information of both limbs. Previous studies have clearly indicated that this location provides valuable information regarding fall risk [44, 47]. The accelerometer measured at a sample rate of 100 samples/s and was aligned in the vertical (VT), ML and AP direction. The data were analyzed with a gait recognition algorithm [108]. The algorithm searched each second for gait activity with a minimum length of eight seconds or a multiple of eight seconds. Gait characteristics were estimated for each eight second walking bout, longer walking bouts were subdivided in multiple eight second parts. Subsequently for each characteristic the median of all bouts value was taken to reduce the influence of outliers, further data analysis was similar to earlier studies by our research group [47]. We determined daily life gait characteristics that have been shown to be promising in regard to predicting falls in healthy older adults [47] and or in stroke survivors [119]. See table 4.4 for an overview of the daily-life gait characteristics.

Fall status

Falls were determined prospectively using a 'fall calendar' and monthly telephone calls over a six-month period, which is sufficiently long to identify recurrent fallers [114]. Participants were asked to report any falls and related (medical) consequences and circumstances on the calendar. During the monthly telephone calls the researcher decided whether reported falls matched the following definition: 'any unanticipated event that results in participants coming to the ground, floor or lower level' [20]. We excluded falls that had a clearly different cause than a loss of balance such as fainting or an epileptic seizure.

Statistics

Participants that experienced no falls during the six month follow up were classified as not fall prone stroke survivors (NF), the participants who experienced at least one fall were classified as fall prone stroke survivors (F). For each variable in both groups mean and standard deviations were determined. We used an independent sample t-test or Mann-Whitney or chi square test to examine differences in participant demographics.

Fall status (NF/F) was used as independent variable in our logistic regression models, gait characteristics and clinical measures were used as independent variables. To facilitate comparison of the results of univariate logistic regressions between variables, we first z-transformed all continuous variables. Subsequently, to determine the predictive capacity of clinical assessments and gait characteristics, we performed univariate logistic regression for each potential predictor variable. The resulting odd ratios (OR) for each independent variable represent the increased fall risk per unit standard deviation increase. OR higher than one indicate an increased fall risk.

Predicting falls

We created four fall prediction models, which were based on; (1) clinical physical and psychological assessments, (2) laboratory derived steady-state gait characteristics (3) accelerometry derived daily-life gait characteristics (4) accelerometry and laboratory derived gait characteristics.

To reduce the number of independent variables and avoid the risk of multicollinearity we created new latent variables by performing a principal component analyses (PCA). PCA reduces high dimensional data to new uncorrelated latent variables (PC's) such that variance explained by the PC's is maximized [129]. PC's were entered in the logistic regression if the PC discriminated between both groups with a p-value ≤.05 based on an independent sample t-test. All independent variables that were significantly associated with fall risk were per prediction model entered into the PCA and loading factors per independent variable and per model for PC1 are reported. We conducted the PCA and the logistic regression modeling within a 10-fold cross validation method, thereby taking into account the variability caused by performing the component analysis on different training sets on the robustness of the final model. The loading factor of each independent variable on the first principal component was averaged over the 10 folds. Validated model performances are reflected by the error rate (1- accuracy), sensitivity, specificity and the area under the receiver operating curve (AUC). Prediction models were compared by determining the confidence intervals (CI) off the AUC using a previous described method [130].

All statistical analyses were performed using Matlab 2013B (The MathWorks Inc., Natick, MA). Statistical significance was established a priori at a level of p-value ≤ .05. As this is an explorative study aimed at discovering the most promising fall prediction models, we did not correct for multiple comparisons.

Results

A total of 47 stroke survivors participated in the study. After testing we excluded five participants due to their inability to walk without the use of the handrail during the laboratory gait assessment.

Table 4.1: Demographic and stroke specific characteristics.NF is non fallers, F is fallers.

	NF (N=25)	F (N=15)	P-value
Age(y)	58.4 (±14.3)	64.6 (±8.5)	.09
Gender (female/male)	14 / 11	10 / 5	.33
Time since stroke (months)	71.8 (±65)	113(±109)	.11
Hemiparetic side (right/left)	16 / 9	10 / 5	.98
Number of strokes>1	3	0	.49
Weight (kg)	88.0 (±17.4)	79.2 (±17.2)	.13
Length (cm)	173.8 (±10.8)	171.8 (±9.9)	.55
BMI (kg/m^2)	29.1 (±5.5)	26.7 (±5.5)	.19
Use of walking aid (no / yes)	17 / 8	3 / 13	**<.01**
Use of medicines (no / yes)	2 / 23	2 / 13	1
MMSE (max 30)	27.7 (±2.8)	27.5 (±2.2)	.78

Mean ± standard deviation from demographic and stroke specific characteristics. P-values are based on independent sample t-test, Mann-Withney U test or chi-square tests. Significant differences are printed in bold.

One participant was excluded from the analysis due to a technical failure of the accelerometer and one participant refused to wear the accelerometer. To avoid potential bias of having different participants for different independent variables, only the 40 stroke survivors that performed all tests were included in all further analyses. During six months follow-up, fifteen (38%) stroke survivors experienced at least one fall and were classified as fall-prone stroke survivors (F). All reported falls were due to a loss of balance, no falls were excluded. The remaining twenty-five (62%) stroke survivors were classified as not-fall-prone stroke survivors (NF). Between group demographics and stroke specific characteristics results are presented in table 4.1. Chi square test revealed a statistically significant difference in using a walking aid, where a greater percentage of the F used a walking aid.

For clinical assessments, laboratory based steady state gait characteristics and daily-life gait characteristics means and standard deviations are reported per group respectively in table 4.2, 4.3 and 4.4. In addition, predictive capacity of each independent variable, expressed as odds ratio (OR) determined by univariate logistic regression, is reported in the tables 4.2,4.3 and 4.4. Of the clinical assessments, LASA was able to predict falls as indicated by a significant OR, see table 4.2.

Table 4.2: Clinical assessments: physical performance and psychological tests. NF is none fallers, F is fallers, OR is odds ratio.

	NF (N=25)	F (N=15)	OR (CI)	P-value
BBS	50.2 (± 8.0)	47.5(±5.9)	0.69 (0.35 – 1.33)	.27
TUGT (sec)	10.9 (±6.9)	15.3 (±6.8)	1.92 (0.97 – 3.79)	.06
10MWT (sec)	10.4 (±4.8)	14.9 (±7.6)	2.28 (0.94 – 5.18)	.07
GDS	8.4 (±5.8)	10.1 (±7.4)	1.02 (0.93 – 1.12)	.56
LASA	4.4 (±3.6)	6.7 (±4.1)	**1.23 (1.03 – 1.46)**	**.02**
FES	29.6 (±10.8)	32.7 (±10.8)	1.02 (0.97 – 1.09)	.36

Mean ± standard deviation for physical performance and psychological tests. OR and p-values are based on univariate logistic regression. TUGT,10MWT and BBS variables are z-transformed. Significant differences are printed in bold.

Of the laboratory based steady state gait characteristics, smaller step length for the paretic and non paretic limb, lower preferred gait speed and lower gait smoothness (IH) in VT and AP direction increased the odds of becoming a faller, see also table 4.3. Furthermore, a larger stride time variability and step length variability of the paretic limb increased the odds of becoming a faller. A larger LDE, indicating a lower local dynamic stability, and smaller MoS in AP direction increased the odds of becoming a faller. Several daily-life gait characteristics were significantly associated with falls.

Table 4.3: Laboratory based steady state gait characteristics.
NF is none fallers, F is fallers, OR is odds ratio.

	NF (N=25)	F (N=15)	OR(CI)	P-value
Spatio temporal gait characteristics				
Step length PL (mm)	474 ± 116	369 ± 119	**0.30 (0.11-0.78)**	**.01**
Step length NPL (mm)	450 ± 127	316 ± 142	**0.27 (0.10-0.72)**	**<.01**
Step time PL (sec)	0.58 ± .08	0.58 ± .05	1.07 (0.53 - 2.16)	.85
Step time NPL (sec)	0.65 ± .12	0.72 ± .17	1.81 (0.87 - 3.81)	.11
Gait speed (m/s)	0.74 ± .27	0.58 ± .22	**0.37 (0.15 – 0.91)**	**.03**
Stride time (sec)	1.23 ± .19	1.29 ± .20	1.62 (0.79 – 3.30)	.18
Step width (mm)	155 ± 41	170 ± 55	1.41 (0.70 – 2.82)	.33
Symmetry gait characteristics				
Step length SI	0.91 ± .09	0.77 ± .25	0.28 (0.07 – 1.07)	.06
Step time SI	0.85 ± .16	0.76 ± .21	0.59 (0.29 – 1.22)	.15
Smoothness gait characteristics				
IH VT	0.78 ± .20	0.57 ± .31	**0.38 (0.17 – 0.85)**	**.02**
IH ML	0.93 ± .06	0.95 ± .02	1.89 (0.70 – 5.13)	.21
IH AP	0.84 ± .16	0.67 ± .29	**0.43 (0.19 – 0.97)**	**.04**
Variability gait characteristics				
Stride time	4.49 ± 2.56	7.46 ± 5.52	**3.08 (1.05 – 8.99)**	**.04**
Step length PL	32.4 ± 11.1	45.0 ± 22.4	**3.76 (1.14 – 12.41)**	**.03**
Step length NPL	35.1 ± 13.4	40.7 ± 18.4	1.52 (0.76 – 3.11)	.23
Step time PL	21.3 ± 7.94	23.7 ± 7.4	1.47 (0.74 – 2.94)	.27
Step time NPL	21.6 ± 7.2	23.1 ± 4.5	1.48 (0.73 – 2.99)	.28
Step-width	22.3 ± 7.6	23.7 ± 6.6	1.31 (0.66 – 2.58)	.44
Stability gait characteristics				
LDE VT	1.57 ± .25	1.61 ± .25	1.17 (0.58 – 2.37)	.65
LDE ML	1.62 ± .24	1.89 ± .32	**3.46 (1.31 – 9.12)**	**.01**
LDE AP	2.04 ± .30	2.21 ± .33	1.92 (0.93 – 3.98)	.07
MoS ML PL	0.18 ± .04	0.19 ± .04	1.94 (0.90 – 4.16)	.09
MoS AP PL	-0.44 ±.08	-0.38 ± .07	**2.56 (1.07 – 6.12)**	**.03**
MoS ML NPL	0.18 ± .02	0.19 ± .03	1.56 (0.76 – 3.23)	.22
MoS AP NPL	-0.44 ±.08	-0.37 ± .07	**2.74 (1.13 – 6.69)**	**.02**

Mean ± standard deviation for steady state gait characteristics. Odd ratio (OR) and p-values are based on univariate logistic regression. All variables are z-transformed. Significant differences are printed in bold. Abbreviations: (N) PL is (non) paretic limb, SI is symmetry index, IH is index of harmonicity, LDE is the local divergence exponent, VT is vertical, ML is medio-lateral and AP is anterior-posterior direction.

Table 4.4: Daily life gait characteristics. NF is none fallers, F is fallers, OR is odds ratio.

	NF (N=25)	F (N=15)	OR(CI)	P-value
Gait speed (m/s)	0.73 ± 0.16	0.62 ± 0.12	**0.32 (0.13 – 0.79)**	**.01**
Stride time (s)	1.34 ± 0.31	1.42 ± 0.45	1.27 (0.66 – 2.46)	.47
SD VT	1.63 ± 0.52	1.23 ± 0.39	**0.23 (0.08 – 0.69)**	**.01**
SD ML	1.37 ± 0.27	1.22 ± 0.27	0.49 (0.24 – 1.02)	.06
SD AP	1.38 ± 0.33	1.16 ± 0.23	**0.36 (0.16 – 0.84)**	**.02**
HR VT	1.25 ± 0.24	1.13 ± 0.26	0.53 (0.25 – 1.15)	.10
HR ML	1.33 ± 0.17	1.39 ± 0.21	1.41 (0.74 – 2.71)	.29
HR AP	1.13 ± 0.19	1.00 ± 0.19	**0.40 (0.18 – 0.90)**	**.02**
IH VT	0.44 ± 0.17	0.36 ± 0.17	0.55 (0.27 – 1.11)	.09
IH ML	0.42 ± 0.20	0.57 ± 0.26	**1.99 (1.02 – 3.92)**	**.04**
IH AP	0.51 ± 0.11	0.53 ± 0.17	1.16 (0.63 – 2.13)	.63
Amplitude (psd) VT	0.45 ± 0.12	0.41 ± 0.11	0.68 (0.36 – 1.29)	.24
Amplitude (psd) ML	0.44 ± 0.16	0.57 ± 0.24	**1.92 (1.01 – 3.75)**	**.05**
Amplitude (psd) AP	0.43 ± 0.14	0.52 ± 0.20	1.71 (0.88 – 3.34)	.11
Width (psd) VT	1.0 ± 0.13	1.07 ± 0.18	1.75 (0.82 – 3.75)	.15
Width (psd) ML	0.95 ± 0.02	0.95 ± 0.04	1.08 (0.57 – 2.05)	.84
Width (psd) AP	0.95 ± 0.02	0.95 ± 0.02	1.16 (0.61 – 2.21)	.66
LDE/stride VT	1.06 ± 0.38	1.11 ± 0.39	1.17 (0.62 – 2.20)	.62
LDE/stride ML	0.94 ± 0.31	1.01 ± 0.37	1.24 (0.65 – 2.35)	.51
LDE/stride AP	1.01 ± 0.65	1.02 ± 0.39	1.03 (0.55 – 1.93)	.91

Mean ± standard deviation for daily life gait characteristics. Odd ratio (OR) and p-values are based on univariate logistic regression. All continuous variables are z-transformed. Significant differences are printed in bold. Abbreviations: SD is the standard deviation, HR is the harmonic ratio, IH is index of harmonicity, VT is vertical, ML is medio-lateral and AP is anterior-posterior direction, PSD is the power spectral density and LDE is the local divergence exponent.

A lower gait speed, smaller standard deviation (SD) in VT and AP direction of the acceleration signal and lower harmonic ratio (HR) in AP direction increased the odds of becoming a faller. Furthermore, a larger IH in ML direction and a larger amplitude of the power of the dominant peak in the ML direction increased the odds of becoming a faller, see also table 4.4.

Independent sample t-tests revealed that for all four created fall prediction models only PC1 was significantly different between groups. The explained variance by PC1 ranged from 53.8% for model 4 up to 71.1% explained variance for model 2. The loading factors of all independent variables on PC1 for models 2,3 and 4 are presented in Figure 4.1. Fall predictions ability for all four models are presented in table 4.5. Model 1, based on clinical assessments, yielded a limited ability in predicting falls, with an AUC of 0.64 and a lower CI below 0.5. Prediction models 2, 3 and 4 based on respectively laboratory based steady-state gait characteristics, daily-life gait characteristics and a combination of both gait assessment methods, were able to predict falls, with AUC ranging between 0.72 and 0.73 and a lower CI above 0.5.

Table 4.5: Model performances

	Model 1	Model 2	Model 3	Model 4
Sensitivity	0.62	0.85	0.80	0.80
Specificity	0.66	0.65	0.65	0.66
AUC	0.64	0.73	0.72	0.73
AUC (CI)	(.46- .82)	(.57 - .89)	(.56 - .88)	(.57 - .89)
Error rate	0.32	0.28	0.28	0.28

Model 1 is based on clinical assessments, model 2 on laboratory based gait characteristics, Model 3 on daily-life gait characteristics and model 4 combines gait characteristics from model 2 and 3. CI are confidence intervals.

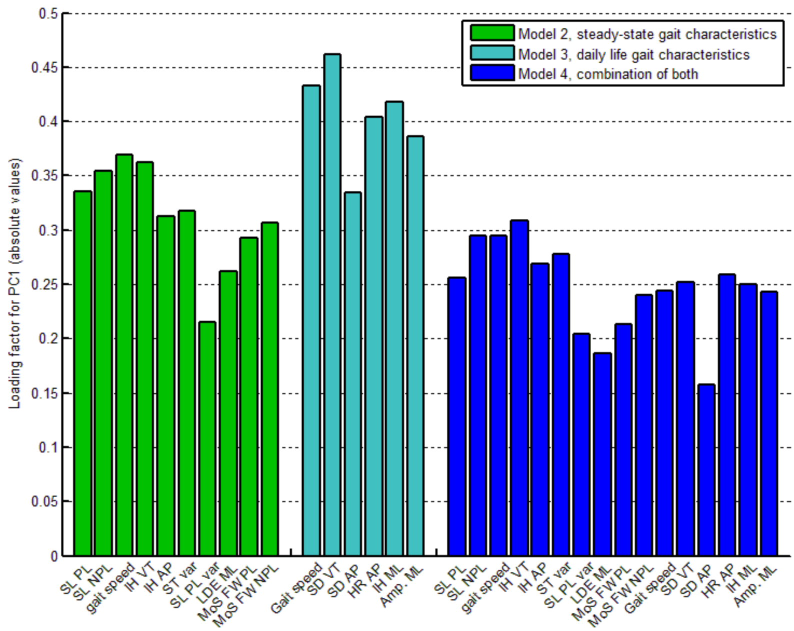

Fig. 4.1: Loading factors for prediction models 2, 3 and 4. SL: step length; PL: paretic limb; NPL: non-paretic limb; IH: index of harmonicity; ST:stride time; var: variability; LDE: local divergence exponent; MoS FW: forward margin of stability; SD: standard deviation; HR: harmonic ratio;

Discussion.

The main objective of the current study was to examine whether gait characteristics might improve fall predictions over current clinical assessments. We used two common methods of assessing gait characteristics, namely a standardized laboratory gait assessment and a daily-life gait assessment. In addition, we examined whether a combination of both methods yielded better predictions.

Of the clinical assessments tests, neither the physical performance tests nor the questionnaires were able to predict falls. The exception being the LASA questionnaire which did predict falls[125], which might be explained by the fact that LASA includes retrospective fall history in the final sum score while the other tests did not. Our results for the clinical assessments are in line with several other studies [29, 116] but not all [28, 114, 115].

Our results for model 2 show that laboratory based steady state gait characteristics can predict falls, as was expected based on studies in healthy older adults [35]. Daily-life gait characteristics (model 3) predicted prospective falls as well as lab-based characteristics, which is also in line with earlier results in healthy older adults[47] and stroke survivors[119].

Furthermore, despite a different methodological approach, both gait assessment methods (model 2 and model 3) were equally well able to discriminate between NF and F. Apparently, the disadvantages of daily-life gait assessment, such as more vulnerability to environmental circumstances and walking behavior, are compensated by a longer assessment time, and/or the more ecologically valid data. A combination of laboratory and daily-life gait assessments (model 4) did not result in a significantly more accurate fall prediction model. Therefore, to identify fall prone stroke survivors, one can choose between both gait assessment methods. Moreover, both gait assessments methods were able to predict prospective falls (lower CI above 0.5), while prediction performances by the conventional clinical assessments was limited in predicting falls, (lower CI below 0.5). Thus, gait assessment can be considered as a better alternative to identify stroke survivors at risk for falling. Additionally, to the best of our knowledge, this was the first study comparing clinical assessments and gait characteristics in the same sample of participants, which is the most objective comparison. For practical relevance, it is important to note that the gait characteristics significantly associated with falls are determined with just four markers located on the pelvic and one marker on each foot, rather than the 47 markers used in this experiment. Moreover, wearing the accelerometer was considered as a relatively easy task by the participants, making both methods applicable for practical use. Furthermore, considering the increasing availability of sensors in for instance smart phones and thereby relatively low costs of applying such analysis it is worth further investigation.

While we expected to find gait characteristics that were associated with falls [35, 44], at present it was unknown to what extent the Margins of Stability (MoS) in the ML direction were associated with falls in stroke survivors. Although maintaining MoS in ML direction is critical with respect to maintaining gait stability [56] and is therefore essential in fall prevention during gait, no differences were found between groups. This supports the finding that stroke survivors are able to maintain MoS in ML direction [38, 131], probably accomplished by increasing the step width [15, 131]. While MoS may not be an interesting gait characteristic for identifying F during steady state gait, perhaps this may be different when gait is perturbed and an adequate reaction is required in order to maintain the MoS.

Study limitations

Our inclusion and exclusion criteria were aimed at including all ambulatory walkers who suffered from a stroke. Of the participants that met our inclusion criteria, five participants were not able to perform the steady-state gait assessment without the use of the handrail and were excluded from our analysis. Therefore, our sample of stroke survivors is to some extent biased towards the higher functioning stroke survivors and will not reflect all ambulatory walking stroke survivors.

Fall incidences were captured over a six month period. Although six months appear to be sufficient to identify recurrent fallers [114], the extent to which seasonal influences have affected fall incidences is unknown, and could have affected our classification of groups.

Our sample of stroke survivors was relatively small, which may have affected the stability of our PCA, especially for model 4, containing 16 gait characteristics. On the other hand, PCA was part of our cross validation procedure and error rates between model 2,3 and 4 are similar, indicating similar stable PC determinations in model 4 as in model 2 and 3. Nevertheless, the present findings need replication in larger cohorts. Also due to the explorative nature of the study, we did not applied a correction for multiple comparison, which increases the chance of a type 1 error.

We explored the value of gait characteristics relative to clinical assessments with respect to fall predictions. Our method covered a range of different commonly used [24] assessments, however, not all commonly used clinical assessments were explored and thus our conclusion is restricted to the examined assessments. Several other assessments such as the: Barthel Index, the Postural Assessment Scale for Stroke Patients, Functional Reach Test and the balance subscale of Fugl-Meyer Assessment are highly correlated with the Berg Balance Scale that we used [24] and as such probably have limited added value over the BBS in regard to fall prediction. Finally, please note that LASA was developed on a general older population, not specifically for stroke survivors. Although having an stroke wasn’t an exclusion criteria of LASA either.

Conclusions

This explorative study indicates that both laboratory based, as well as daily-life gait characteristics, showed some ability to predict prospective falls in higher functioning chronic stroke survivors, whereas clinical assessments such as physical and psychological assessments were more limited in predicting falls. Therefore, further investigation of gait assessment over clinical tests is justifiable as clinicians might enhance currently used fall prediction assessments in ambulatory chronic stroke survivors by applying one of both tested gait assessments.

CHAPTER 5

UNEXPECTED GAIT PERTURBATIONS

Responses to gait perturbations in stroke survivors who prospectively experienced falls or no falls. Michiel Punt, Sjoerd M. Bruijn, Sanne Roeles, Ingrid G. van de Port, Harriet Wittink, Jaap H. van Dieën, Journal of Biomechanics, 2017.

Abstract

Background. Steady-state gait characteristics appear promising as predictors of falls in stroke survivors. However, assessing how stroke survivors respond to actual gait perturbations may result in better fall predictions. We hypothesize that stroke survivors who fall have a diminished ability to adequately adjust gait characteristics after gait is perturbed.

Objective. This study explored whether gait characteristics of perturbed gait differ between fallers and non fallers.

Methods. Chronic stroke survivors were recruited by clinical therapy practices. Prospective falls were monitored over a six months follow up period. We used the Gait Real-time Analysis Interactive Lab (GRAIL, Motekforce Link B.V., Amsterdam) to assess gait. First we assessed gait characteristics during steady-state gait and second we examined gait responses after six types of gait perturbations. We assessed base of support gait characteristics and margins of stability in the forward and medio-lateral direction.

Results. Thirty eight stroke survivors complete our gait protocol. Fifteen stroke survivors experienced falls. All six gait perturbations resulted in a significant gait deviation. Forward stability was reduced in the fall group during the second step after a ipsilateral perturbation.

Conclusion. Although stability was different between groups during a ipsilateral perturbation, it was caused by a secondary strategy to keep up with the belt speed, therefore, contrary to our hypothesis fallers group of stroke survivors have a preserved ability to cope with external gait perturbations as compared to non fallers. Yet, our sample size was limited and thereby, perhaps minor group differences were not revealed in the present study.

Introduction

Fall rates are high in the chronic stage after stroke [7] and higher than in healthy older adults [7]. Most falls occur during gait [112] and consequently assessment of gait could be useful in predicting fall risk. Assessing quality of steady-state gait may quantify how the system handles small, internal perturbations like neuromuscular noise [18, 132]. Interestingly, stroke survivors have a more variable gait pattern and a reduced quality of gait as compared to healthy controls [38, 119]. Moreover, quality of gait shows promise as a predictor of falls in stroke survivors [39, 119].

Other aspects than the quality of steady-state gait might contribute to the prediction of fall risks in stroke as well. Large, external gait perturbations experienced in everyday life, like trips and slips, may require a substantial change of the gait pattern to overcome the perturbation and prevent a fall [51, 53, 58]. Thus, measures of how subjects react to larger perturbations are interesting in relation to fall prevention. Stroke survivors appear to respond less effectively to external gait perturbations [58]. Thus external gait perturbations may provide additive information with respect to fall risk in stroke survivors.

It is currently unknown if, and how, gait recovery characteristics, after a gait perturbation are associated with falls in stroke survivors. This study attempts to discover the potential of using gait perturbations to predict falling in stroke survivors. Therefore, our aim was to explore whether differences exist in responses to external gait perturbations between a group of stroke survivors that experienced a fall in daily life, and a group that did not.

We focused on gait recovery characteristics that reflect how and to what extent stroke survivors are able to cope with external gait perturbations. Perturbations of gait require adequate base of support (BoS) adjustments through adapting foot placement. Dynamic stability quantified by the margins of stability (MoS) [56, 57] provides additional information by relating the kinematic state of the body center of mass (CoM) to the BoS. We prospectively studied the relation between gait adaptations after a perturbation and fall risk. We hypothesized that stroke survivors who fall during follow-up have less effective adaptations of foot placement after gait perturbations coinciding with smaller MoS than stroke survivors who do not fall during follow-up.

Method

We recruited stroke survivors through flyers in physical therapy practices and various national peer group meetings in the Netherlands. Stroke survivors were recruited if they were at least six months post-stroke, aged at least eighteen and lived independently in the community. We excluded stroke survivors with a functional ambulation category lower than 3 [84], a minimal mental state examination(MMSE) lower than 25 [85] and or other disorders such as neurologic, musculoskeletal, respiratory or severe cardiovascular disorders that affected gait performance. The medical ethics committee ‘Noord Brabant, The Netherlands’ approved the research protocol and treatment of the participants was according to good clinical practice. Prior to the gait analysis, demographic and stroke specific characteristics were collected such as; sex, age, body length and weight, time since stroke, hemiparetic side, use of a walking aid, use of medication.

Experimental set up

All participants walked on the Gait Real-time Analysis Interactive Lab (GRAIL, Motekforce Link B.V., The Netherlands). The GRAIL consists of: a motion-capture system (Vicon, Vicon Motion Systems, UK) with ten infrared cameras (Bonita B10, Vicon Motion Systems, UK), a dual-belt treadmill with two embedded force platforms and synchronized virtual environment (Motekforce Link b.v. The Netherlands). A custom written application in D-flow software (Motekforce Link b.v. The Netherlands) controlled the GRAIL.

Participants wore tight fitting black clothes. In order to collect full body kinematics we used a the human body model based on 47 passive markers [126] These were placed before the gait analysis by the same investigator throughout the study to maximize consistency between participants. Furthermore participants wore a safety harness which prevented actual falls.

Gait protocol

Twenty-four hours prior to clinical and laboratory testing participants were asked not to drink any alcoholic beverages and to avoid any other activities that could affect physical performances. All measurements were performed during a single visit at the rehabilitation center Revant, Breda, The Netherlands. After participants became familiarized to walking on the treadmill, we first assessed steady-state gait characteristics during sixty consecutive strides at a gait speed of 0.41m/s. Subsequently, all perturbations were executed at the same gait speed of 0.41m/s. In pilot experiments, this gait speed in combination with perturbations was found to be feasible for most community walking stroke survivors.

The perturbation protocol consisted of two separate trials; each trial comprised 16 perturbations; each perturbation was followed by a wash-out period of on average 15 seconds. Perturbations were triggered by foot contact (FC). The sequence of the perturbations was semi random as the perturbation type was fixed but the triggering at the left or right foot placement was random. Participants were allowed to hold the handrail during the first four perturbations, those perturbations were not included in the analysis. Each trial lasted for four minutes. Between trials breaks were taken to avoid fatigue as much as possible.

The first perturbation trial contained medio-lateral (ML) perturbations. More specifically, the walking surface of the treadmill moved either to the left or right side at FC of the participant (see figure 5.1 for an illustration and figure 5.2, ML Perturbation for the perturbation intensity). Depending on whether right or left FC was followed by a right or left walking surface translation, the perturbations were classified as “ipsilateral” or “contralateral” gait perturbations. From a static perspective we may expect that during ipsilateral perturbations participants respond quickly, because the supporting limb shifts away from the vertical projection of the CoM, (see figure 5.1 ipsilateral perturbation), which requires an immediate response to maintain stability. In contralateral perturbations (see figure5.1 contralateral perturbation), the supporting limb shifts towards the vertical projection of the CoM, which may not require an immediate response. However, it should be noted that this explanation holds for static situations while gait is a dynamic activity.

The second perturbation trial comprised anterior-posterior (AP) decelerating perturbations. At either right or left FC the belt speed on the side of the FC decelerated towards 0 m/s and subsequently accelerated towards 0.41m/s (see figure 5.2, AP Perturbation for an illustration).

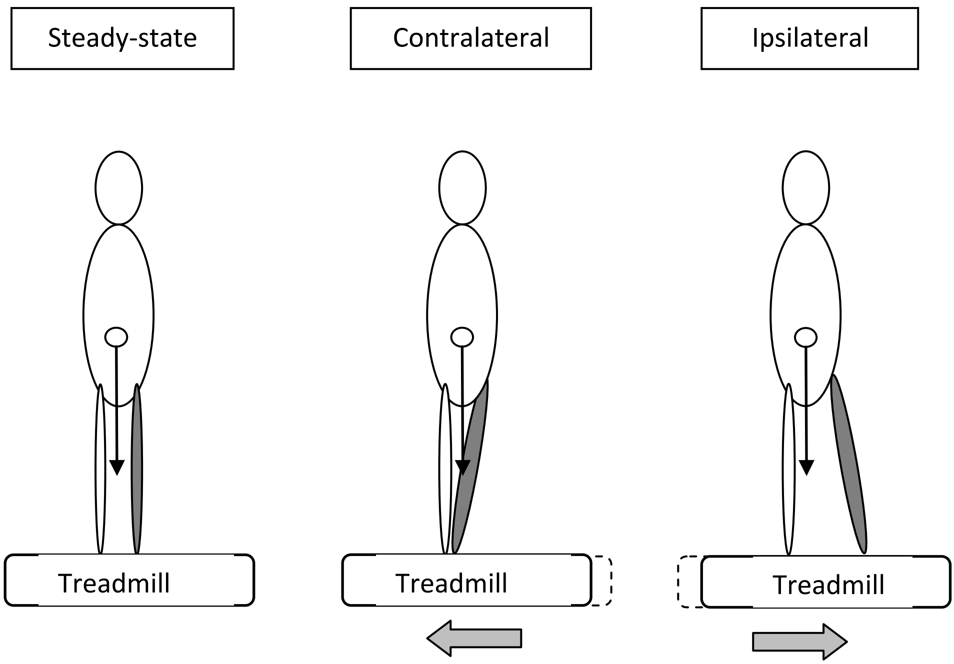

Figure 5.1: Backward perspective at right foot contact during medio-lateral treadmill displacements. Left panel represents steady state gait, mid panel represents a contralateral perturbation and the right panel represents an ipsilateral perturbation. Horizontal arrows show the direction of the treadmill displacement. Due to the medio-lateral treadmill displacement in the mid panel, the right foot shifts towards the projected CoM (vertical arrow).In the right panel the right foot shifts away from the projected CoM. The shaded limb represents the limb that was perturbed.

As a response with either the paretic leg or non-paretic leg could make a substantial difference, we subdivided the two perturbations types into "response non paretic leg" (NPL) and "response paretic leg" (PL). All perturbation types started 80 to 90 milliseconds after FC was detected. The maximum ML displacement was 0.045 meter and the maximum peak deceleration of the belt speed was $3.9 m/s^2$, see figure 5.2 for an illustration.

To summarize, we explored a total of six different gait perturbations. Four ML gait perturbations divided into contralateral and ipsilateral and response with either NPL or PL. The final two AP decelerating gait perturbations were divided into “response non paretic leg” (NPL) and “response paretic leg” (PL).

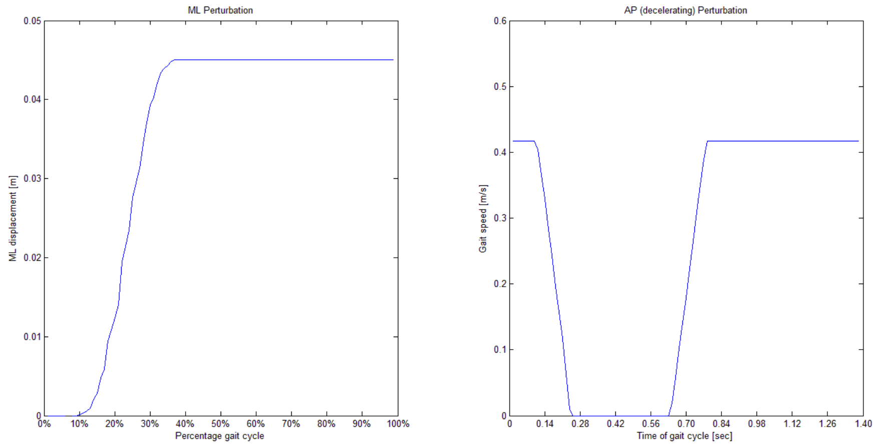

Figure 5.2: Left panel gait perturbation in medio-lateral direction relative to the gait cycle and anterior-posterior direction, right panel in absolute time.

Data analysis

Discrete gait events like FC were detected using a center of pressure method [127]. Based on these FC events and markers placed at the heel, lateral malleolus and toe on both feet, we calculated step time and the BoS gait characteristics: step length and step width. The whole body CoM was determined using a 14 body segment model [128]. Subsequently, dynamic stability expressed as the MoS in forward (FW) and ML direction was determined at FC [56]. A larger MoS indicates a increased dynamic stability.

For steady-state gait, the average of these parameters was calculated over 60 strides. The final two perturbations were free of handrail support and were used for further evaluation. Response characteristics were determined at FC of up to six steps after the perturbation. All analyses were performed using custom written Matlab programs (Matlab 2013B).

Fall status

Falls were detected using a 'fall calendar' and monthly phone calls during six months follow-up. A fall was defined as 'any unanticipated event that results in a participant coming to the ground, floor or lower level' [20]. Falls were excluded if the cause was clearly different from a loss of balance, such as when fainting or experiencing an epileptic seizure.

Statistics

Participants were assigned to the fallers group of stroke survivors if they had experienced at least one fall during follow-up and otherwise in the non fallers group of stroke survivors. Demographic and stroke specific characteristics were compared using an independent samples t-test or for not normally distributed variables a Mann Whitney U test. Dichotomous variables such as use of a walking aid and sex were examined using a chi square test.

Steady-state gait characteristics were compared between groups using an independent samples t test. Next, we examined the perturbed gait characteristics. We first assessed if and how many steps the characteristics after perturbation deviated from state steady gait. We used a dependent samples t test to compare each step after the perturbation, with steady-state gait. Results indicated that at least one out of five examined gait characteristics significantly deviated up to six steps after the perturbation (see appendix A). For further analysis, we therefore included 6 steps. We performed a mixed model ANOVA with steps as our within factor, and fall status as our between subjects factor. The dependent variable was the characteristic of interest. If a main effect of group or interaction effect with group was found, independent samples t tests per step were performed to determine in which step(s) groups differed from each other. Similar analysis were performed with preferred steady-state gait speed as covariate, to test for a possible confounding effect, results are shown in Appendix B. A p-value of <.05 was considered significant; all statistical analysis were performed in SPSS version 23.

Results

A total of 38 stroke survivors successfully completed the gait assessments. Fifteen (39%) stroke survivors reported at least one fall. Demographic and stroke specific characteristics did not differ between both groups of stroke survivors, except for the use of a walking aid which was more often used in the fallers group, see also table 5.1.

Steady-state gait

Gait characteristics of the groups were similar during steady-state gait at a fixed speed, except for step time of the paretic leg and step length of the non paretic leg, which were significantly lower in the F group, see appendix A.

Table 5.1: Demographic and stroke specific characteristics.

	NF-SS (23)	F-SS (15)	
	Mean (sd)	Mean (sd)	P-value
Age(y)	**55.0 ± 12.2**	**65.4 ± 6.7**	**.02**
Gender (female / male)	13 / 10	7 / 8	.74
Hemiparetic side (right / left)	16 / 7	10 / 5	1
Time since stroke (months)	73.8 ± 53	104 ± 89	.25
Number of strokes >1	3	0	.53
Weight (kg)	87 ± 19	83 ± 20.1	.67
Length (cm)	172 ± 10	171 ± 13	.73
BMI (kg/m^2)	29.5 ± 6.5	28.7 ± 6.1	.78
FAC score	**4.6 ±1.1**	**4.1 ± 0.9**	**.04**
Use of walking aid (no / yes)	**19 / 4**	**10 / 5**	**<.01**
Use of medicines (no / yes)	2 / 21	2 / 13	1
MMSE (max 30)	28.3 ± 2.1	27.6 ± 2.0	.41
Preferred gait speed (m/s)	**0.72 ± 0.3**	**0.5 ± 0.28**	**.02**

Mean ± standard deviation from demographic and stroke specific characteristics.P-values are based on independent sample t-test, Mann-Withney U test or chi-square tests. Significant differences are printed in bold.

Perturbations

Medio-lateral contralateral perturbations

Overall, contralateral gait perturbations when responding with the non paretic leg (figure 5.3 contralateral NPL) resulted in similar gait characteristics to steady-state gait in the first step, but step length was increased during the second and third step. In addition, step width increased from the second step onwards. MoS ML increased in the first step, (figure 5.4 contralateral NPL, for statistics see appendix A). No main effects of group or interaction effects with group were found for any of the five gait characteristics, for this perturbation type (table 5.2).

Contralateral gait perturbations when responding with the paretic leg (figure 5.3, contralateral PL) showed increased step times for the first step after perturbation, and increased step-widths from the second step onward. MoS values in the ML direction differed from the second step onwards except for the fifth step after gait was perturbed (figure 5.4 contralateral PL and appendix A). No main effects of group or significant interaction effects with group were found for any of the five gait characteristics, for this perturbation type, see table 5.2.

Medio-lateral ipsilateral perturbations

Both ipsilateral gait perturbations, (figure 5.3, ipsilateral) caused a similar change in BoS and step time characteristics for both legs. We found significantly reduced step times in comparison to steady-state step times. Step lengths were reduced for the first two steps and step width increased for all steps after the ipsilateral gait perturbations. When the NPL responded retributions resulted in an increased MoS in ML direction in the first, third and fifth step, moreover FW MoS was reduced in the second step compared to steady-state values (see figure 5.4 ipsilateral NPL and appendix A). When the PL responded ipsilateral perturbations resulted in a increased MoS in ML direction for the second, fourth and sixth step after gait was perturbed. Furthermore MoS in FW direction was reduced in the second and third step compared to steady-state values (see figure 5.4 ipsilateral PL and appendix A).

A main effect of group was found for step time when the NPL responded. Post hoc analyses revealed a significant by ($p<.01$) shorter step time in the F group in the first step after perturbation. In addition when the PL responded, main effects for group were found for step time and step length (see table 5.2). Post-hoc analyses revealed a shorter step time, thus quicker response for the F group during the first and second step after perturbation ($p=.03$ and $p=.01$). Moreover step length was reduced in the F group during the first step after perturbation ($p<.01$). Furthermore, significant interactions between group and step were found for step width and MoS in FW direction when the PL responded, table 5.2. Post-hoc analysis revealed no significant differences between groups in step width, but did reveal a significantly lower MoS in FW direction in the second step in the group of fallers compared to group of non fallers, indicating a reduced dynamic stability ($p<.001$).

Finally for all perturbation types and responding gait characteristics, results were the same when preferred steady-state gait speed was included as a covariate, see appendix B.

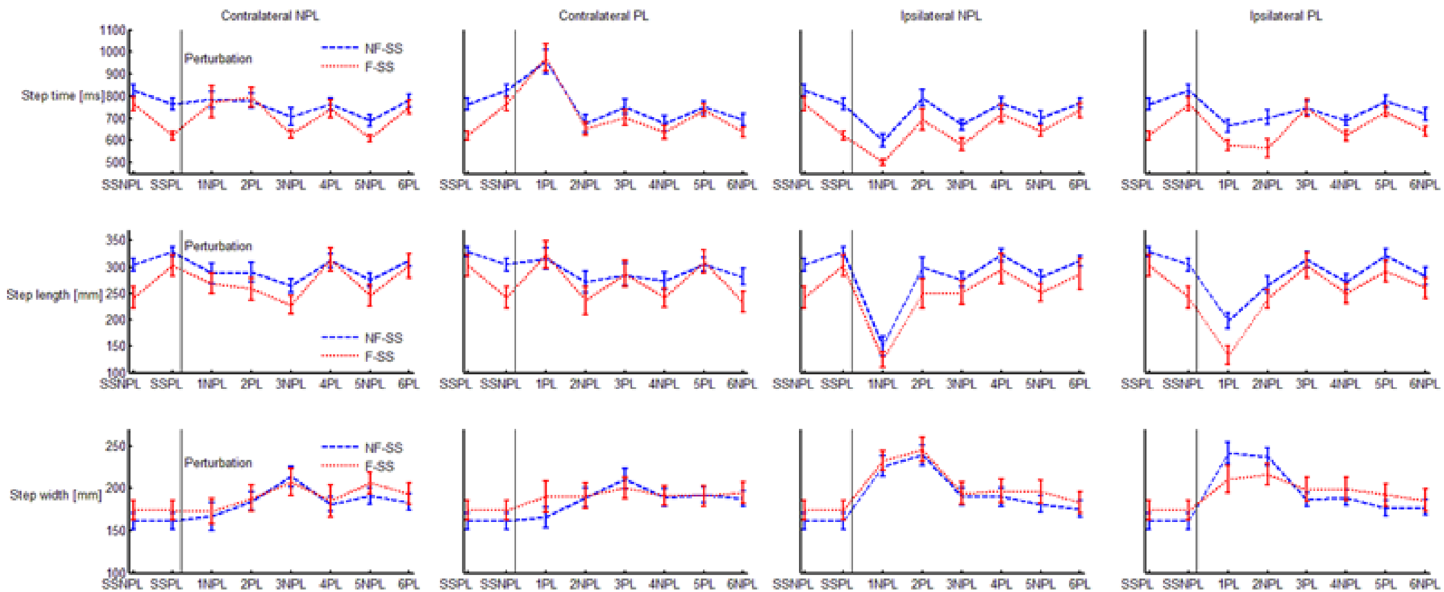

Figure 5.3 Step time and base of support (BoS) gait characteristics during steady state (SS) and after gait was medio-lateral perturbed for the paretic leg (PL) and non paretic leg (NPL).

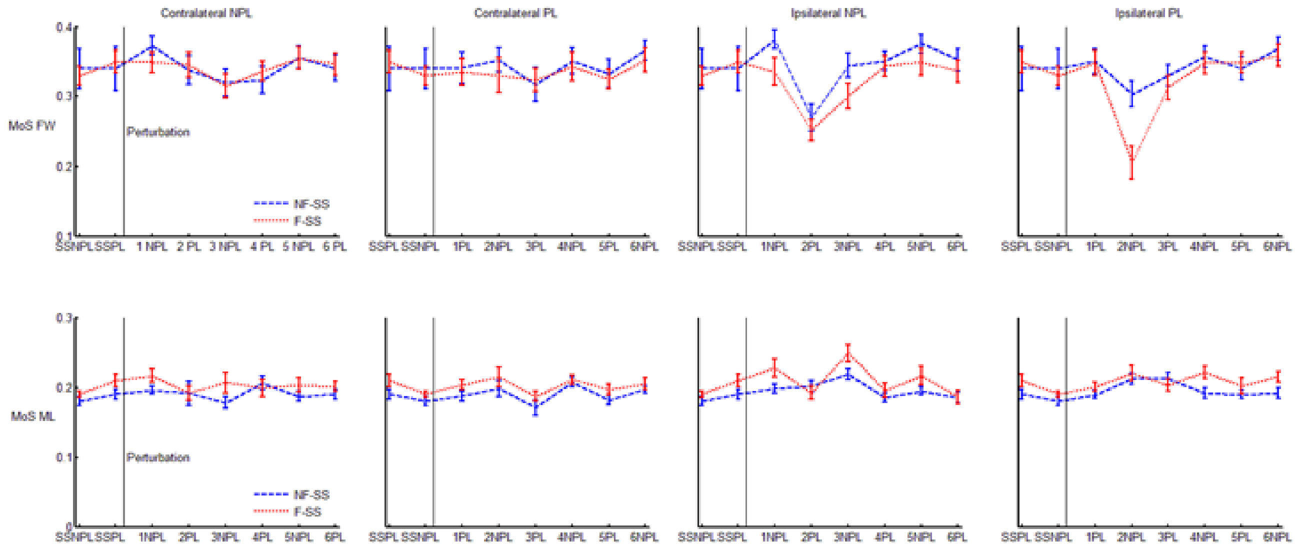

Figure 5.4. Margins of Stability (MoS) in the forward (FW) and medio-lateral (ML) direction during steady state (SS) and after gait was medio-lateral perturbed for the paretic leg (PL) and non paretic leg (NPL).

Table 5.2: Mixed model ANOVA for ML gait perturbations. With the gait characteristic as dependent variable. Number of steps as within factor and group as between effect. Significant group and interaction effects are printed in bold.

Contralateral perturbation First response Non Paretic Leg			
Gait characteristic	Effect	F	P-value
Step time	Steps	5.21	.01
	Group	0.35	.56
	Steps*Group	0.73	.45
Step length	Steps	2.33	.11
	Group	2.12	.15
	Steps*Group	0.17	.83
Step width	Steps	8.94	<.01
	Group	0.01	.96
	Steps*Group	0.25	.69
MoS FW	Steps	4.64	.02
	Group	0.21	.65
	Steps*Group	.792	.43
MoS ML	Steps	1.20	.29
	Group	1.45	.24
	Steps*Group	0.94	.36
Contralateral perturbation First response Paretic Leg			
Step time	Steps	30.6	<.01
	Group	0.15	.69
	Steps*Group	0.37	.63
Step length	Steps	4.89	.02
	Group	0.14	.70
	Steps*Group	.61	.51
Step width	Steps	3.95	.04
	Group	0.11	.73
	Steps*Group	1.48	.23
MoS FW	Steps	.59	.45
	Group	0.08	.77
	Steps*Group	.26	.62
MoS ML	Steps	6.45	<.01
	Group	1.61	.21
	Steps*Group	000	.99
Ipsilateral perturbation First response Non Paretic Leg			
Step time	Steps	24.3	<.01

	Group	**7.34**	**.01**
	Steps*Group	.022	.96
Step length	Steps	27.2	<.01
	Group	3.61	.07
	Steps*Group	.212	.76
Step width	Steps	25.3	<.01
	Group	0.11	.73
	Steps*Group	.03	.96
MoS FW	Steps	28.6	<.01
	Group	3.06	.09
	Steps*Group	0.87	.39
MoS ML	Steps	8.10	<.01
	Group	3.01	.09
	Steps*Group	3.0	.08
Ipsilateral perturbation First response Paretic Leg			
Step time	Steps	10.8	<.01
	Group	**4.35**	**.05**
	Steps*Group	2.84	.07
Step length	Steps	34.9	<.01
	Group	**4.35**	**.04**
	Steps*Group	1.35	.26
Step width	Steps	17.3	<.01
	Group	0.60	.44
	Steps*Group	**5.54**	**<.01**
MoS FW	Steps	19.3	<.01
	Group	3.01	.09
	Steps*Group	**5.98**	**<.01**
MoS ML	Steps	5.26	<.01
	Group	0.13	.71
	Steps*Group	1.41	.25

GG is Greenhouse Geiser correction. MoS is margin of stability. P-value for main effect of steps and interaction (Steps*Group) is Greenhouse-Geiser corrected.

Anterior-posterior decelerating gait perturbations

After gait was perturbed with a deceleration of the split belt, (figure 5.5) independent from which leg responded, the first step response was a shorter step (both in terms of time and length). Moreover step width was increased for all consecutive steps after the perturbation. MoS did not differ compared to steady-state values when the NPL responded. MoS in the ML direction increased for the first and second step if the PL responded and MoS in FW was reduced in the third step (figure 5.6 decelerating PL and appendix A). No main effect of group was found for neither responding leg. Two significant interaction effects between steps and group on step width were found for both perturbation types (see table 5.3). However post hoc analysis revealed no differences in step widths between groups.

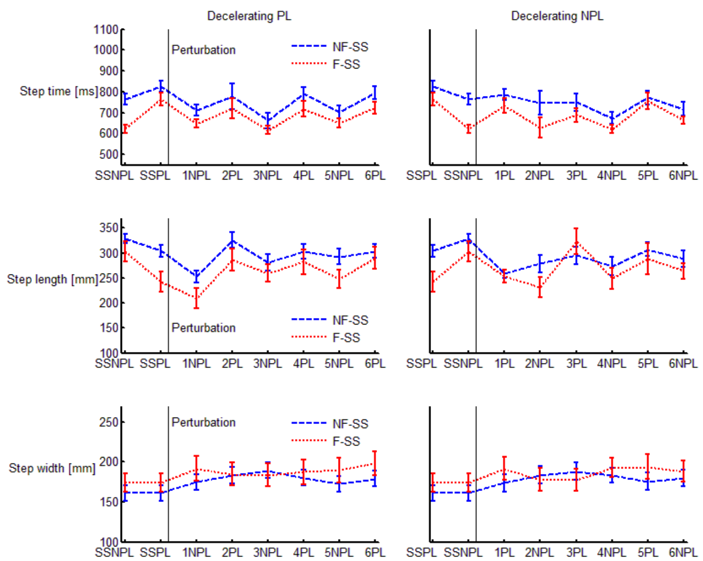

Figure5.5: Step time and base of support (BoS) gait characteristics during steady state (SS) and after gait was anterior-posterior perturbed for the paretic leg (PL) and non paretic leg (NPL).

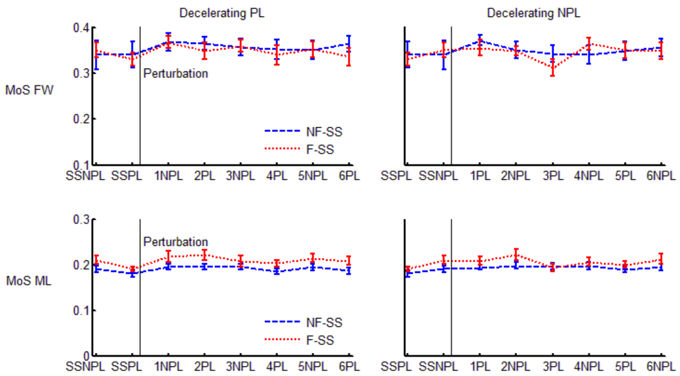

Figure 5.6: Margins of Stability (MoS) in the forward (FW) and medio-lateral (ML) direction during steady state (SS) and after gait was anterior-posterior perturbed for the paretic leg (PL) and non paretic leg (NPL).

Table5.3: Mixed model ANOVA for AP gait perturbations. With the gait characteristic as dependent variable. Number of steps as within factor and group as between effect. Significant group and interaction effects are printed in bold.

Decelerating FW perturbation First response Non Paretic Leg			
Gait characteristic	Effect	F	P-value
Step time	Steps	0.86	.40
	Group	0.77	.39
	Steps*Group	.026	.94
Step length	Steps	5.04	.02
	Group	.08	.79
	Steps*Group	1.91	.17
Step width	Steps	.383	.61
	Group	.001	.99
	Steps*Group	**3.88**	**.04**
MoS FW	Steps	4.81	.01
	Group	.406	.53
	Steps*Group	.704	.49
MoS ML	Steps	2.60	.10
	Group	1.02	.33
	Steps*Group	2.07	.15

Decelerating FW perturbation First response Paretic Leg			
Step time	Steps	6.18	.01
	Group	0.48	.49
	Steps*Group	.26	.69
Step length	Steps	8.53	<.01
	Group	2.01	.17
	Steps*Group	.08	.86
Step width	Steps	.55	.55
	Group	.06	.80
	Steps*Group	**6.15**	**<.01**
MoS FW	Steps	.75	.44
	Group	.02	.88
	Steps*Group	.48	.55
MoS ML	Steps	.47	.55
	Group	2.73	.11
	Steps*Group	.48	.54

GG is Greenhouse Geiser correction. MoS is margin of stability. P-value for main effect of steps and interaction (Steps*Group) is Greenhouse-Geiser corrected.

Discussion

Our aim was to explore whether differences exist in responses to external gait perturbations between a group of stroke survivors that experienced a fall in daily life, and a group that did not. The gait perturbations resulted in significant deviations in gait characteristics, which indicates that gait adjustments were made. We found that both groups of stroke survivors react largely similar to the gait perturbations. More specifically, the strategy of reacting with longer/shorter steps to certain gait perturbations was similar, as step times did not differ between groups. In addition, those responses were similar to what we expected for ML perturbations illustrated in figure 5.1. Furthermore, BoS characteristics showed similar decreasing trends over consecutive steps between groups. However, for ipsilateral ML perturbations the F group reacted quicker and with a reduced step length in the first step. Nevertheless, MoS values between groups were similar and MoS values did not deviate from steady-state MoS values (table 5.2 and figure 5.4 and 5.6). Therefore, it seems that both groups of stroke survivors were able to adequately respond to the gait perturbations. However, after gait was perturbed with an ipsilateral perturbation and the paretic leg (PL) responded fallers showed a significantly lower MoS in FW direction during the second step, suggesting lower stability. This is somewhat puzzling, because this perturbation disturbs gait in the ML direction. Possibly, widening the step while maintaining FW MoS when stepping with the paretic leg was challenging for this group.

To better understand this finding, we extended our analysis by studying the velocity of the center of mass in FW direction and the trunk angle for this particular gait perturbation in the FW direction. While the fallers group were able to increase their step width sufficiently and thereby restoring ML MoS, this came at the expense of a reduced step length, due to constant treadmill speed. This led to a more rearward position on the treadmill. To compensate for this change in position on the treadmill, fallers group attempt to regain speed by creating a larger forward momentum by a more forward shifted trunk during the second step, which then led to a smaller FW MoS. Although MoS in FW direction was decreased in the F group it may not be representative for everyday life situations where we would expect that one would try to slow down or even stop during the second step rather than trying to speed up. Thus, gait characteristic responses from the second step onward when the perturbations are applied on a treadmill with a constant belt speed may not be representative for real-life situations.

At present, only a few studies have applied larger external gait perturbations in stroke survivors [51, 53, 58]. While Krasovsky et al (2013) found a larger global response in terms of strategy and timing of gait rhythm after gait was perturbed in stroke survivors compared to healthy older adults [58], Kajrolkar et al (2014) concluded that stroke survivors have a preserved ability to adjust gait characteristics and maintain dynamic stability [51]. Our AP decelerating perturbations tended to cause a backward fall, however, contrary to the studies of Kajrolkar et al. (2014) and Kajrolkar and Bhatt (2016) our participants did not make a backward step, instead all participants were able to continue to move forward. It is interesting to see that apparently small differences in onset and magnitude of the perturbation can result in such different responses.

Our study is not comparable to any previous study executed in stroke survivors, since to the best of our knowledge this was the first study assessing differences in responses to larger external gait perturbations between fallers and non fallers in stroke. Our results indicate that perturbation responses are not useful as predictors of fall risk, which is different from perturbations during standing [39]. This suggests that priority should be given the study of steady-state gait characteristics in stroke survivors are more promising regarding predicting fall risk [39, 119]. Nevertheless, gait perturbations might be useful in fall prevention programs, as perturbation based gait training appears to be effective in fall prevention in older adults and in people with Parkinson’s disease [70].

There is a number of possibilities that might explain our limited findings. First, perturbations applied might lack ecological validity. Second, the perturbation magnitude may have been too small. MoS in the first step after gait perturbations were equal or even slightly increased in comparison to steady-state values, which may indicate that the perturbation magnitude was not challenging enough to differentiate between groups. Each perturbation type was repeated four (ML perturbations) and eight (decelerating perturbations) times, however due to handrail grasping we analyzed only the final two perturbations and thereby gathering the average response. From a different perspective, we may argue that perhaps only the response to the first gait perturbation is relevant for fall risk, as during a perturbation in daily life, people have only one chance to respond adequately and thereby prevent an actual fall incidence. Finally, it may be that small differences between groups are present, yet not found in this study due to the limited sample size.

Another methodological consideration is the gait speed during the perturbations. We used a fixed speed thereby making sure that the applied perturbations were similar across participants. Changing the treadmill speed to somebody's preferred speed means that the applied perturbation is executed over another percentage of the gait cycle as the duration of the gait cycle will change with speed while the duration of the ML displacement does not. Adjusting gait speeds would thus actually result in different gait perturbations, which makes it unfair to compare between participants. However, perturbing gait at preferred speed is more ecologically valid, since most perturbations experienced during gait in daily life will occur at preferred speed. Nevertheless, in this case it would remain unclear whether differences between groups would be due to how they respond or due the fact that perturbations were different. However, given the problems associated with designing “matched” perturbations at subjects preferred speeds, we choose to perturb subjects at a fixed speed. Finally our sample of stroke survivors may not be representative of the entire population based on the ratio male/female participants.

Conclusion

In conclusion, this study found limited differences in gait perturbation responses between stroke survivors that fell and that did not fall during follow-up. Although step length after an ipsilateral perturbation when the paretic leg responded was reduced in our group of fallers, this did not result in smaller MoS values than in non-fallers. Furthermore the FW MoS during the second step after a medio-lateral ipsilateral gait perturbation where the paretic leg responded differed between fallers and non-fallers, but this was most likely not directly caused by the perturbation itself but rather by the need to keep up with the belt speed. Our results do not support the use of gait characteristic responses to predict fall risk. However, our sample size was limited, and a larger cohort might reveal differences which were not found in the present study.

Appendix A. Between group comparison

Steady state gait characteristic	T value	P value
Step time non paretic leg	1.4	.16
Step time paretic leg	**3.8**	**<.01**
Step length non paretic leg	**2.5**	**.02**
Step length paretic leg	1.2	.25
Step width	-0.8	.43
MoS FW non paretic leg	0.3	.78
MoS FW paretic leg	-0.1	.91
MoS ML non paretic leg	-0.8	.42
MoS ML paretic leg	-1.7	.09
Variability of steady-state gait characteristics		
Step time non paretic leg	-1.8	.07
Step time paretic leg	**-2.5**	**.02**
Step length non paretic leg	-1	.31
Step length paretic leg	**-2.1**	**.04**
Step width	-1.7	.1
MoS FW non paretic leg	-1.9	.07
MoS FW paretic leg	**-2.1**	**.04**
MoS ML non paretic leg	**-3.2**	**<.01**
MoS ML paretic leg	**-2.4**	**.02**

Comparison of steady state gait characteristics and variability of steady-state gait characteristics between groups.

Appendix B. Mixed model ANCOVA for ML gait perturbations. Similar to table 5.2 in the manuscript the effect of ML gait perturbations on gait with the gait characteristic as dependent variable, number of steps as within factor and group as between effect. Furthermore, steady-state gait speed was insert as a covariate to adjust for differences in preferred steady-state gait speed. Significant group and interaction effects are printed in bold.

Contralateral perturbation First response Non Paretic Leg			
Gait characteristic	Effect	F	P-value
Step time	Steps	5.46	<.01
	Group	0.25	.62
	Steps*Group	0.96	.44
Step length	Steps	1.22	.27
	Group	0.56	.45
	Steps*Group	0.10	.99
Step width	Steps	0.34	.88
	Group	1.27	.26
	Steps*Group	0.60	.70
MoS FW	Steps	0.70	.62
	Group	0.01	.99
	Steps*Group	0.32	.89
MoS ML	Steps	3.85	<.01
	Group	0.16	.70
	Steps*Group	0.40	.85
Contralateral perturbation First response Paretic Leg			
Step time	Steps	5.55	<.01
	Group	0.01	.91
	Steps*Group	0.73	.59
Step length	Steps	3.24	<.01
	Group	0.03	.88
	Steps*Group	0.17	.97
Step width	Steps	0.83	.53
	Group	0.81	.37
	Steps*Group	0.76	.58
MoS FW	Steps	1.19	.32
	Group	0.01	.99
	Steps*Group	0.32	.89
MoS ML	Steps	5.91	<.01
	Group	1.12	.29
	Steps*Group	1.31	.26

Ipsilateral perturbation First response Non Paretic Leg			
Step time	Steps	8.28	<.01
	Group	1.96	.17
	Steps*Group	0.51	.76
Step length	Steps	2.43	.04
	Group	0.93	.34
	Steps*Group	0.09	.99
Step width	Steps	2.71	.02
	Group	0.03	.85
	Steps*Group	0.17	.97
MoS FW	Steps	1.56	.17
	Group	0.79	.38
	Steps*Group	0.67	.64
MoS ML	Steps	9.60	<.01
	Group	1.32	.26
	Steps*Group	0.26	.93
Ipsilateral perturbation First response Paretic Leg			
Step time	Steps	15.0	<.01
	Group	2.1	.16
	Steps*Group	0.62	.68
Step length	Steps	7.04	<.01
	Group	0.96	.33
	Steps*Group	0.73	.61
Step width	Steps	1.11	.36
	Group	0.06	.79
	Steps*Group	**3.64**	**<.01**
MoS FW	Steps	11.4	<.01
	Group	0.19	.67
	Steps*Group	1.62	<.20
MoS ML	Steps	3.20	<.01
	Group	1.20	.28
	Steps*Group	1.10	.36

GG is Greenhouse Geiser correction. MoS is margin of stability. P-value for main effect of steps and interaction (Steps*Group) is Greenhouse-Geiser corrected.

CHAPTER 6

EXPECTED GAIT PERTURBATIONS

Virtual obstacle crossing in chronic stroke survivors: reliability and association with fall risk. Michiel Punt, Sjoerd M. Bruijn, Harriet Wittink, Ingrid G. van de Port, Gijs Wubbels, Jaap H. van Dieën, Gait & Posture (under review)

Abstract

Background. Stroke survivors often fall during walking. To reduce fall risk, gait testing and training with avoidance of virtual obstacles is gaining popularity. However, it is unknown whether and how virtual obstacle crossing is associated with fall risk.

Objective. The present study assessed whether obstacle crossing characteristics are reliable and associated with fall risk in community dwelling chronic stroke survivors.

Method. We recruited twenty-nine community dwelling chronic stroke survivors. Participants crossed five virtual obstacles with increasing lengths. After a break, the test was repeated to assess test-retest reliability. For each obstacle length and trial, we determined; success rate, leading limb preference, pre and post obstacle distance, margins of stability, toe clearance, and crossing step length and speed. Subsequently, fall incidence was monitored using a fall calendar and monthly phone calls over a six-month period.

Results. Test-retest reliability was poor, but improved with increasing obstacle-width. Twelve participants reported at least one fall. No association of fall incidence with any of the obstacle crossing characteristics was found.

Conclusion. Given the absence of height of the virtual obstacles, obstacle avoidance may have been relatively easy, allowing participants to cross obstacles in multiple ways, increasing variability of crossing characteristics and reducing the association with fall risk. These finding cast some doubt on current protocols for testing and training of obstacle avoidance in stroke rehabilitation.

Introduction

About 30 to 50% percent of all chronic stroke survivors report at least one fall each year [7] and these falls often result in injuries and medical costs[103]. One of the causes of a fall may be unsuccessful negotiation of an obstacle, resulting in a trip. Indeed, it has been found that obstacle crossing is challenging for elderly and for stroke survivors, as it often results in tripping [23, 133].

Crossing obstacles demands adequate gait adjustments. Several gait adjustments during obstacle crossing in a over ground setting were found to be different in stroke survivors compared to age matched controls [59, 63, 65]. For instance, stroke survivors showed a reduced toe clearance of the affected limb while crossing the obstacle and they also placed their foot at a less favorable position behind the obstacle[59]. Moreover, during over ground obstacle crossing, the peak velocity of the center of mass (CoM) in the medio-lateral (ML) direction was higher in stroke survivors as compared to controls[63, 65]. These gait changes may reduce safety, and it has been shown that the ability to negotiate obstacles successfully is reduced in stroke survivors compared to age matched control groups [60, 62, 65, 134]. Although these differences in over ground obstacle crossing may to some extent explain the higher fall rates in stroke survivors compared to the general older population [62, 63, 65, 66], at present it remains largely unknown whether measures derived from over ground obstacle crossing are associated with falls in stroke survivors. Only one study did find that fall prone stroke survivors were indeed less successful in obstacle crossing as compared to non-fallers [64].

In recent years, obstacle crossing using a virtual environment has gained popularity for testing and training during rehabilitation after a stroke [135, 136]. Training generally aims to enhance the ability to perform stepping adjustments and thereby the ability to walk safely through more complex environments and as such perhaps prevent falls. However, little is known about the reliability and validity of virtual obstacle crossing as a diagnostic tool for fall risk, or as a model for daily life gait. Finally, results found in over ground obstacle crossing may be not transferable to virtual obstacle crossing due to the differences in the experimental set up. For instance, virtual obstacles are two dimensional, and there is no penalty when hitting the obstacle whereas hitting a real obstacle will result in a trip. Therefore, the main aims of the present experiment were to assess test-retest reliability of characteristics of virtual obstacle crossing and their association with fall risk. We note here that the data reported were obtained from participants of a previous study that found that steady-state gait characteristics were associated with fall risk [137].

Methods

Participants were community dwelling persons after stroke in the chronic phase, recruited via flyers in hospitals, physical therapy practices, general practitioners and national peer group meetings. Prior to the study, all participants gave written informed consent and the medical ethical committee 'Noord Brabant', The Netherlands approved the research protocol (NL49126.028.14).

Participants were excluded if their Functional Ambulation Category (FAC) was lower than three [84], Mini Mental State Examination (MMSE) was lower than 24 [85] and if they had severe cardiovascular, respiratory, musculoskeletal or other neurological disorders that could affect gait performance. Furthermore, stroke survivors who were institutionalized in for instance a nursing home were excluded as well. The measurements were performed during a single visit at the rehabilitation center Revant, Breda, The Netherlands.

Experimental set up

Data collection was performed using the Gait Real-time Analysis Interactive Lab (GRAIL, Motekforce Link b.v., The Netherlands). The GRAIL is equipped with ten infrared cameras (Bonita B10, Vicon Motion Systems, Oxford, UK), a dual belt treadmill with two embedded force platforms (Motekforce Link b.v., The Netherlands) and a synchronized virtual environment. A custom-developed application to control the GRAIL was written in DFlow software (Motekforce Link b.v., The Netherlands). Light planes projected on the treadmill, created with the DFlow software, functioned as obstacles to be crossed. Full-body kinematics were collected by tracking forty-seven markers on anatomical landmarks [126].

Obstacle crossing protocol

For safety reasons, participants wore a fall harness that did not restrict motion, nor provided body weight support. All participants first familiarized themselves with treadmill walking, and were instructed to walk without support of the treadmill sidebars and a walking aid. The obstacle crossing task was executed at a gait speed of 0.41m/s (1.5km/h) to make sure that the perturbation size was the same among all participants, moreover, 0.41m/s was feasible for all participants.

The obstacle crossing task contained five virtual obstacles. The virtual obstacles were two-dimensional, and had no height. The width of the obstacle was equal to the width of the treadmill, the length of the first out of five obstacles was 7cm, each of the subsequent obstacles increased in steps of 7 cm towards 35 cm. The appearance of the obstacle (in both time and position) was determined by the mid-swing phase position of the right limb, plus three times the stride time and stride length based on three previously performed strides, see figure 6.1A. Given the provided time and space between obstacle appearance and actual obstacle crossing, participants were free to decide whether to cross the obstacle with their paretic or non-paretic limb. To improve the ecological validity of our experiment, the only instruction given was to cross the obstacle, no instruction was given on how to cross the obstacle. Finally, after a break of ten minutes the experiment was repeated to assess test-retest reliability. To assess associations with fall risk, we used data from the first set of 5 obstacles.

Data analysis

Gait events (foot contacts (FC), foot off) were detected based on the trajectory of the center of pressure [127]. The whole body CoM was determined using a 14 body segment model [128]. Subsequently dynamic stability expressed as the Margin of Stability (MoS) in forward (FW) and mediolateral (ML) directions, was determined at FC [56]. All crossing attempts were included for all analysis regardless of whether the attempt was successful or not.

We calculated several measures that reflect how, and how well, participants performed the obstacle crossing tasks, further referred to as crossing characteristics. First, we determined two dichotomous variables; 1) lead limb, i.e. the limb which first crossed the obstacle (paretic or non-paretic limb) further referred to as ‘Leading Limb Preference’(LLP) and 2) success rate. Since some participants placed their foot in the middle of the obstacle, it was not always clear whether an unsuccessful foot placement was intended as a crossing step, or a last step before crossing. We defined a crossing step, as a step wherein the anterior-posterior (AP) position of the toe marker was beyond the mid-line of the obstacle. A crossing step was defined unsuccessful if the position of the virtual obstacle in the progression direction overlapped with the position of the foot during the stance phase. Both dichotomous variables were determined for each obstacle length. Second, we determined seven continuous crossing characteristics, (Figure 6.1B): (1) toe clearance (i.e. vertical distance between lead limb toe and the ground halfway crossing the obstacle), (2) pre-obstacle-distance (i.e. the distance between the toe marker of the final foot placement prior to obstacle crossing and the beginning of the obstacle), (3) post-obstacle-distance (i.e. the distance between the end of the obstacle and the heel marker of the leading limb). (4) crossing length (i.e. the step length of the lead limb, when crossing the obstacle) (5) crossing speed (i.e. the crossing step length divided by the step time of the leading limb), (6 and 7) MoS in ML and FW direction at FC directly after obstacle crossing.

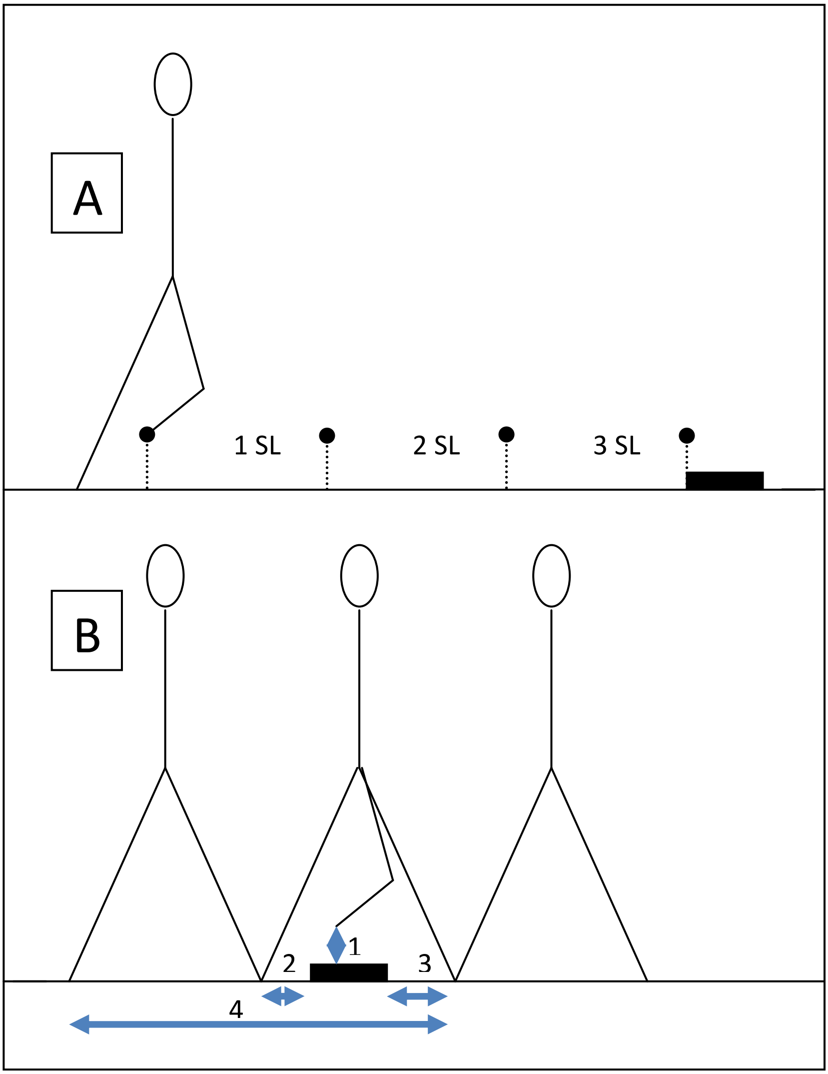

Figure 6.1A: Time and place of the appearance of the obstacle. SL is stride length. Figure6. 1B: spatial crossing characteristics.

Fall status

For six months after the lab visit, fall status was determined by monthly phone calls, and a fall diary was used to report when, and how the fall occurred. We defined a fall as 'any unanticipated event that results in a participant coming to the ground, floor or lower level' [20]. We excluded falls that had a clearly different cause than a loss of balance, such as fainting or an epileptic seizure. Participants that experienced at least one fall were classified as fall prone stroke survivors.

Statistics

For all crossing characteristics, we determined the test-retest reliability. For both dichotomous crossing characteristics, Kappa statistics were used. Reliability of continuous crossing characteristics was determined through intra-class correlation (ICC), absolute agreement [102], single measures. Reliability of dichotomous crossing characteristics was defined as moderate for kappa between 0.41 – 0.6, substantial for kappa between 0.61 – 0.8, or almost perfect for kappa between 0.81 - 1 [138] and reliability for continuous crossing characteristics was considered adequate if ICC was ≥ 0.75 [139].

Demographic and stroke specific characteristics between fallers and non-fallers were compared using a Mann Whitney U test. Between group differences for the dichotomous variables LLP and success rate were examined using a Chi square test. Normality of the continuous variables was examined using a Kolmogorov-Smirnov test. We used a mixed model ANOVA with group as between and obstacle length as within factors. If an interaction with group was found, independent samples t tests were used to determine which condition(s) differed between groups.

Results

A group of twenty-nine stroke survivors derived from a larger cohort [137] participated in the obstacle crossing task. After a six-month follow up, twelve stroke survivors (41%) reported at least one fall, and were classified as fall prone stroke survivors (F). The remaining seventeen stroke survivors (59%) were classified as non-fall prone stroke survivors (NF). None of the reported falls were excluded due to the fall exclusion criteria. The participants in the fall prone group were significantly older and used a walking aid more often, see table 6.1 for statistics. Due to missing marker data, we were not able to estimate center of mass position for all participants, therefore results regarding the MoS are based on twenty-four participants, including nine participants with prospective falls.

Table 6.1: Mean and SD and between group differences in demographic and stroke specific characteristics. Significant between group differences are printed in bold.

Demographic characteristics	NF-SS (17)	F-SS (12)	p-value
Age (years)	55.5 (12.3)	64.6 (8.2)	**.03**
Length (cm)	171.8 (10)	169.9 (11)	.64
Weight (kg)	90.2 (20)	76.9 (16)	.07
Male (%)	50%	66%	.39
Use walking aid (%)	25%	66%	**.03**
Use of medication (%)	87%	83%	.75

Reliability of crossing characteristics

Dichotomous crossing characteristics LLP and success rate were not reliable (Table 6.2). Test-retest reliability of pre- and post-obstacle distance was inadequate for the smaller obstacles but was adequate (0.65- 0.78) for obstacles with a length of 21cm or higher. Reliability of crossing step length, and crossing speed was inadequate with ICC values around 0.4. Test-retest reliability of toe clearance was around 0.7 across the obstacle lengths. Reliability of MoS in the ML direction ranged between 0.6 and 0.8, while reliability for MoS in FW direction was inadequate.

Association with falls

Dichotomous crossing characteristics LLP and success rate were not different between groups (see table 6.3 for percentages and table 6.4 for p-values per obstacle length). No interaction effect with group or main effect of group was found for any of the crossing characteristics. Pre-obstacle-distance decreased and step length and FW MoS increased when obstacle length increased (main effect of obstacle length, Table 6.4).

Table 6.2: Test-retest reliability for dichotomous and continuous obstacle crossing characteristics for all five obstacle lengths. MoS is margins of stability, FW is forward, ML is medio-lateral.

Obstacle	7cm obstacle	14cm obstacle	21cm obstacle	28cm obstacle	35cm obstacle
Crossing characteristics	Kappa	Kappa	Kappa	Kappa	Kappa
Success rate	.32	.51	.81	.51	.31
Leading limb	.40	.17	.26	.51	.24
Crossing characteristics	ICC (CI)	ICC (CI)	ICC (CI)	ICC (CI)	ICC (CI)
Pre obstacle distance	.41 (0 -.71)	.57 (.24 - .79)	.70 (.41 - .86)	.65 (.33 - .84)	.72 (.42 - 87)
Post obstacle distance	.39 (0 - .69)	.48 (.12 - .74)	.67 (.36 - 85)	.79 (.57 - .91)	.78 (.57 - 90)
Step length	.39 (-.01-.69)	.16 (-.26 - .5)	.28 (-.15-.62)	.16 (-.24 -.52)	.36 (0 - .66)
Crossing speed	.46 (.06 - .73)	.21 (-.2 - .55)	.26 (-.1 - .6)	.21 (.01 - .54)	.63 (.3 - .82)
Toe clearance	.74 (.45 - .88)	.71 (.43 - .86)	.74 (.49 - .88)	.62 (.30 - .82)	.76 (.52- .89)
MoS ML	.59 (.21 - .81)	.80 (.56 - .91)	.63 (.24 - .84)	.62 (.25 - .83)	.66 (.29 -.85)
MoS FW	.45 (.05 - .73)	.14 (-.25-.52)	.22 (-.19-.58)	.26 (-.22-.62)	.40 (-.05-.72)

Table 6.3. Mean and standard deviation (SD) from continuous crossing characteristics for both groups. Success rate as percentage of successful crossings attempts per group for each LPO size. In addition Leading limb preference (LLP) as percentage of crossing attempts leading with the paretic leg per group for each LPO size. Significant differences for dichotomous crossing characteristics based on Chi Square statistics are printed in bold. NF is the none fall prone group. F is the fall prone group. cm is millimeter. Dis is distance.

Obstacle	7cm obstacle		14cm obstacle		21cm obstacle		28cm obstacle		35cm obstacle	
Group	NF	F	NF	F	NF	F	NF	F	NF	F
Success rate (%)	50	50	62	41	68	50	68	41	68	41
LLP (%)	50	33	44	50	44	33	25	41	31	41
Crossing characteristic										
Pre-obstacle	33 ±14	29.1 ±13.7	23.3 ±14.2	21.2 ±9.1	17.7 ±6.7	21.1 ±14.2	14.5 ±7.7	11.8 ±10.6	12.7 ±6.3	10.7 ±9.1
Post-obstacle	-4 ±7.2	-2 ±8.9	4.5 ±7.6	3 ±9	5.1 ±6.2	-1 ±12.9	2.7 ±6	-3.0 ±12.9	1.4 ±7.0	-1.9 ±11.5
Step length	59.3 ±10	46.8 ±15.2	60.3 ±7.7	51.2 ±14.3	65.2 ±12	53.1 ±17.1	67.7 ±8.2	57.8 ±15	70.7 ±9.6	60.5 ±13.4
Crossing speed	63.4 ±18.9	63.7 ±33.8	72.7 ±22.8	59.5 ±22.3	76 ±13.8	60.7 ±24.5	70.2 ±14.5	69.1 ±25.8	71.7 ±16	66.6 ±24.1
Toe-clearance	11.9 ±4.1	12.3 ±4.3	11.3 ±4.3	11.3 ±2.9	11.5 ±3.9	12.1 ±3.9	11 ±3.5	10.7 ±2.4	12 ±3.7	11.1 ±3.1
MoS ML	0.19 ±0.05	0.20 ±0.04	0.19 ±0.04	0.22 ±0.05	0.18 ±0.04	0.21 ±0.05	0.19 ±0.03	0.20 ±0.05	0.19 ±0.03	0.20 ±0.05
MoS FW	0.53 ±0.07	0.44 ±0.09	0.51 ±0.04	0.51 ±0.11	0.54 ±0.05	0.57 ±0.11	0.53 ±0.04	0.48 ±0.10	0.56 ±0.05	0.50 ±0.07

Table 6.4. Chi square p-values per obstacle length for success rate and leading limb preference. Main and interaction effects for continuous crossing characteristics. Significant Values are printed in bold.

Obstacle length	7 cm	14 cm	21 cm	28 cm	35 cm	
Success rate (P-value)	.87	.22	.26	.12	.12	
LLP (P-value)	.46	.64	.18	.30	.49	
Main effects	Obstacle length		group		Interaction	
Crossing characteristic	F-value	P-value	F-value	P-value	F-value	P-value
Pre-obstacle-distance	**29.2**	**<.001**	0.19	.66	0.97	.41
Post-obstacle-distance	**2.80**	**.04**	1.79	.19	2.47	.07
Step length	**16.3**	**<.001**	0.15	.69	0.35	.79
Crossing speed	.95	.42	0.99	.33	1.87	.14
Toe clearance	1.59	.20	0.0	.99	0.65	.58
MoS ML	0.54	.65	1.51	.23	1.08	.36
MoS FW	**3.47**	**.03**	1.48	.23	2.84	.07

Discussion

As virtual obstacle crossing has gained popularity in stroke rehabilitation for training and testing, and since falls occur during obstacle negotiation in daily life[23, 133], we explored whether a virtual obstacle crossing task can function as a diagnostic tool for fall risk. Specifically, the main purpose of the present experiment was to determine test-retest reliability of obstacle crossing characteristics and their association with fall risk in community dwelling chronic stroke survivors. Contrary to our expectations, the results indicated no differences between groups, neither for the dichotomous, nor for the more reliable continuous crossing characteristics. This is in contrast with results from an previous study which found that fall prone stroke survivors were more likely to fail an over ground obstacle crossing task [64]. Additionally, previous studies found a greater ML velocity of the CoM during over ground obstacle crossing in fallers than in non-fallers [63, 65]. This greater velocity requires a greater deceleration after obstacle crossing, which may hamper safety. However, we found that despite this greater velocity, fall prone stroke survivors were equally able to regulate their MoS in ML direction compared to non-fallers. While stroke survivors generally compensate their increased ML trunk displacement by an increased step width compared to a general older population[15, 131], these differences were not found between fallers and non fallers, neither during steady-state gait [Punt 2017B], nor during obstacle crossing tasks as step-width after obstacle was similar between both groups (17.4cm versus 17.5cm for non-fallers versus fallers).

Interestingly, test-retest reliability for pre and post obstacle distance improved when obstacle length increased from 21cm onwards, and these ICC values are similar to earlier findings [61]. Furthermore, poor reliability of leading limb preference and success rate has also been reported previously [60]. Reliability of toe clearance was lower in our study as compared to a previous report [61], where ICCs were around 0.8. Previous studies assessed real obstacle crossing in over ground walking, we assessed crossing of virtual obstacles on a treadmill. There are several differences between virtual and actual obstacle crossing which have to be taken into account when interpreting the results. While over ground obstacle crossing of a real obstacle can actually result in a trip, which may result in some degree of fear, this is not the case when using a virtual obstacle. Another important limitation of a virtual obstacle is the absence of height of the obstacles. This latter difference may explain the limited test-retest reliability of toe clearance in our study. It may also be that obstacle crossing was relatively easy due to the absence of obstacle height. Such a relatively easy task may not perturb gait enough, so that participants maintain their regular gait pattern. To successfully overcome more challenging obstacles, participants are forced to optimize pre-obstacle-distance, which will limit the possibility of varying crossing characteristics. This may lead to smaller variation within participants, and thus more reliable crossing characteristics. Note that in our experiment, the obstacles with greater length resulted in more reliable crossing characteristics. Obviously, more reliable crossing characteristics can be more sensitive to differentiate between fallers and non-fallers, because true differences do not get buried in noise. Moreover, our results support this suggestion as we did find a nearly significant interaction between group and obstacle length on post-obstacle-distance (see table 4, p=.07). We highly recommend future studies to carefully read these recommendations and follow along as we still think that this paradigm can reveal relevant information for evaluation and diagnostic purposes during rehabilitation, especially because we are not the first to report large variance in obstacle crossing behavior[140].

In contrast to previous studies, we did not separately analyze obstacle crossing with the affected and unaffected limb as leading limb. During a pilot experiment, we discovered that not all stroke survivors were able to follow instructions on which limb should be leading during obstacle crossing. This may be related to constraints imposed by the treadmill, as this requires the participant to maintain gait speed in contrast to over ground walking. Although this may appear to be a disadvantage, it may more realistically reflect daily-life situations, where time to adapt may be limited and may not allow crossing an obstacle with the preferred limb. Furthermore, a previous study indicated that obstacle crossing characteristics between affected and unaffected limb appear to be small, and thus there may be no or very limited information to be obtained with respect to fall risk [61]. Yet, at present it remains unknown if a separation of paretic and non paretic limb on obstacle crossing characteristics revealed other insights in regard to evaluation and diagnostic assessments in stroke survivors.

Despite the fact that training with virtual obstacles holds promise as a few pilot studies did find improvements in the ability to adjust step placements [135, 136], our findings suggest that caution may be needed regarding implementation of these interventions. More successful virtual obstacle avoidance or improved avoidance characteristics on the treadmill may not reflect reduced fall risk in daily life.

A limitation in our study design was that we explored test-retest reliability of crossing characteristics during a single visit rather than two separate visits. On average, participants improved their success rate by 20% during the second trial. Although this improvement was not significant, a learning effect may have affected our reliability results. Another limitation is that our study did not explore variability of pre-obstacle distance over multiple trials, a variable that was recently reported to discriminate older from younger adults [141]. Finally, our limited sample size might have not revealed small between group differences. However, for the purpose of fall prediction at an individual level, such small group differences are not meaningful.

Conclusion

In conclusion, obstacle crossing characteristics in chronic stroke survivors, as determined in our protocol, are neither suitable for evaluation of the ability to make step adjustments nor for the prediction of fall risk among stroke survivors, because test-retest reliability was poor and no differences in obstacle crossing characteristics were found between fallers and non-fallers. However, it is worth to explore reliability of crossing characteristics and their association with fall risk for a set of more challenging obstacles, as more challenging obstacles may improve reliability and sensitivity of the crossing characteristics.

CHAPTER 7

IMPROVING GAIT STABILITY?

Does a perturbation based gait intervention enhance gait stability in fall prone stroke survivors? A pilot study. Michiel Punt, Sjoerd M. Bruijn, Ingrid G. van de Port, Ilona J.M. de Rooij, Harriet Wittink , Jaap H. van Dieën, Clinical Biomechanics (under review)

Abstract

Background. Falls are a common problem among stroke survivors. Fall prevention training programs that have been shown to be effective for healthy older adults are not effective and consequences of falls are more severe in stroke survivors. A recent review indicated that perturbation based training (PBT) interventions are effective in reducing falls in older adults and people with Parkinson's disease. At present, it is unknown whether this type of intervention is effective in stroke survivors.

Objective. We determined whether PBT can enhance gait stability in stroke survivors.

Methods. Ten chronic stroke survivors who experienced falls in the past six months participated in the PBT. Participants performed 10 training sessions over a six-week period. The gait training protocol was progressive and each training contained, unexpected gait perturbations and expected gait perturbations. Evaluation of gait stability was performed by determining steady-state gait characteristics and daily-life gait characteristics. We previously developed fall prediction models for both gait assessment methods. Here, we evaluated whether predicted fall risk was reduced after PBT according to both models.

Results. Several steady-state gait characteristics significantly improved and consequently predicted fall risk was reduced after the PBT. Daily-life gait characteristics, however, did not change and thus predicted fall risk based on daily-life gait remained unchanged after the PBT.

Conclusion. A six week PBT resulted in more stable gait on a treadmill and thus lower predicted fall risk. However, the more stable gait on the treadmill did not transfer to a more stable gait in daily life.

Introduction

Falls are common in community dwelling stroke survivors [22] and patients after stroke are more often frequent fallers than older adults [7]. In addition, hip fractures resulting from a fall more often lead to immobility in stroke survivors [8]. Other consequences of falls are loss of independence and social isolation [8]. These consequences underline the importance of developing effective fall prevention programs for stroke survivors.

While a recently updated review indicated that effective fall prevention programs exist for older adults [142], a review on fall prevention in stroke survivors found no effective programs [69]. Fall prevention programs generally aim to improve physical activity and thereby physical functioning. By participating in fall prevention programs, fall prone stroke survivors may be able to improve their physical activity level to some extent. However, this improvement in physical activity might lead to more falls, due to an increase in exposure. This may explain the ineffectiveness of fall prevention programs for stroke survivors. Training may need to improve gait stability in fall prone stroke survivors before exposure is increased by stimulating daily walking activities.

In comparison to conventional treadmill training of gait stability, perturbation based training (PBT) may offer a more ecologically valid training approach. PBT has shown promise in reducing the numbers of falls in older adults and people with Parkinson’s disease [70]. At present, it is unknown whether this type of intervention is effective for decreasing falls in stroke survivors.

Most falls occur during walking[22, 29] and we recently found that gait characteristics either derived from daily life gait or from a laboratory gait assessment are the predictors of fall risk in stroke survivors[137] . Therefore, as a first step in the development of an effective fall prevention program, we studied whether PBT enhances gait stability in ambulatory chronic stroke survivors who are prone to falls.

We assessed the effect of a perturbation based gait training on three outcomes. We assessed whether steady-state and daily-life gait characteristics improved, whether predicted fall risk decreased and whether participants were able to progressively increase training workload.

methods

participants

Participants were recruited from the rehabilitation centre Revant, Breda, The Netherlands, through day care centers and by contacting participants that already participated in our previous studies [143]. Stroke survivors were included if they were at least 12 months post stroke, had a Functional Ambulation Category score of 3 or higher [84], reported at least one fall in the six months prior to inclusion in the study, were free of other disorders which could have affected gait such as Parkinson's disease and were able to walk on the treadmill without handrail support.

Intervention

The intervention was executed on the Gait Real-time Analysis Interactive Lab (GRAIL, Motekforce Link bv, Amsterdam, The Netherlands). For technical details about the GRAIL and perturbation characteristics see our previous studies [143]. The participants received ten perturbation based gait training sessions in a six-week period. Prior to each training session, four reflective markers were placed on the pelvis, and one marker one each lateral malleolus. The markers were use to collect gait kinematics. In addition, participants wore a safety harness that prevented falls but did not restrict motion, nor provided body weight support. Each training session lasted at least 30 minutes and could last up to 1 hour, depending on the physical condition of the participant. A custom-designed virtual reality application allowed us to adjust each training session to the abilities of the participant. Each training session started with a warming up trial without gait perturbations, followed by multiple trials with unexpected gait perturbations and multiple trials with expected gait perturbations. The length of each trial and the number of trials performed during a single training session depended on the physical condition of the participant.

Unexpected gait perturbations

Unexpected, gait perturbations included simulated trips and slips (induced by belt deceleration or acceleration) as well as medio-lateral (ML) belt translations. The intensity of the perturbations was set at one of five different levels [143]. The interval between perturbations ranged from 4 to 2 strides. The perturbation was triggered at one of three moments in the gait cycle: foot contact, mid stance or toe off. The perturbations were applied to both the paretic and non-paretic limb.

Expected gait perturbations

Expected gait perturbations were created by virtual obstacles, which were projected on the treadmill. The width of the obstacles ranged from 7 cm up to 49 cm in steps of 7 cm. The interval between presentation of obstacles ranged from 4 to 2 strides. The obstacles could be targeted to one of the limbs by projecting the virtual obstacle on only one side of the treadmill. In some cases the virtual targeted both limbs, by projecting it on both sides of the treadmill, forcing both limbs to cross the obstacle.

Progression of training load

The settings within each training session for both unexpected and expected gait perturbations, were varied as much as possible such that participants were exposed to a variety of different gait perturbations. Furthermore, the default gait speed during the training sessions was comfortable gait speed. From this comfortable gait speed, gait speed was frequently increased and decreased by the researcher, in order to practice gait and gait perturbations at all kind of gait speeds.

The settings were adjusted between training sessions, such that training load was progressively increased. After each training session the patient's rate of perceived exertion[144] was determined and based on the judgment of the researcher and the performance of the participant in previous training sessions, gait speed, walking time, frequency and intensity of the perturbations were in- or decreased for the upcoming training session. Finally, after several training sessions, participants received an additional task, a visual Stroop task together with the gait perturbations. This Stroop task functioned as a cognitive dual task, which made the training session more challenging and was aimed at establishing a more automated response after gait was perturbed. For a visual demonstration of the intervention see the electronic supplement.

Primary outcomes gait stability

Before and after the training period, gait stability was assessed by determining steady-state gait characteristics and daily life gait characteristics.

Steady-state gait characteristics

We assessed steady-state gait characteristics in a standardized laboratory setting. The assessment of steady-state gait characteristics was performed twice. First gait characteristics were determined at preferred gait speed. Second steady-state gait characteristics were determined at the same gait speed between pre- and post-assessments regardless of any changes in preferred gait speed within the participant between assessments, to eliminate effects of gait speed on gait variability[145] which together with gait speed is one of the most important predictors for fall risk [111].

Data analysis for determining steady-state gait characteristics was consistent with our previous study [137]. Briefly, participants walked on the GRAIL treadmill. Data were collected for 60 consecutive strides using Vicon Nexus and transferred to Matlab 2013B (The MathWorks Inc., Natick, MA). The gait events foot contact (FC) and foot off (FO) were determined using the Center of Pressure (CoP) [127]. Spatial, temporal, variability and local dynamic stability gait characteristics were determined over the 60 consecutive strides [137].

Daily life gait characteristics

Daily-life gait characteristics were assessed using accelerometry. For daily-life gait stability assessment, we applied the same data collection and analysis method as in our previous experiment [119, 137]. Briefly, participants wore a tri-axial accelerometer (McRoberts, The Hague, The Netherlands) at the lower back during seven consecutive days. Gait episodes were detected by a previously validated algorithm [108]. Quantity and frequency of gait activity were expressed as number of walking minutes per day and number of walking bouts per day. Next, qualitative gait characteristics that have been shown to predict fall risk in older adults [47] and stroke survivors [119] were estimated. For a detailed explanation on how daily life characteristics were estimated see Rispens et al [46].

Predicting fall risk

Fall risk was predicted based on steady-state gait characteristics and based on daily-life gait characteristics using our previous established fall prediction models [137]. For steady-state gait characteristics only the trial at preferred gait speed was evaluated by the steady-state fall risk prediction model, because the model requires gait speed as input. Moreover, prior to entering the data into the prediction model, we adjusted the steady-state fall risk prediction model to a new model without Margin of Stability (MoS) measures because in our present study we were not able to determine MoS due to the limited marker set up. We re-evaluated the performance of this model, which appeared to be exactly the same as in our previous study [137]. For our daily-life fall prediction model, no modifications were made.

Secondary outcomes training workload

Training load per session was assessed by (1) determining the number of walking minutes per training session over the three walking conditions (steady-state, unexpected and expected). (2) The number of minutes walked combined with a visual Stroop task. (3) The average gait speed per training session, (4) the intensity of unexpected, expected gait perturbations and the (5) frequency of gait perturbations.

Statistics

Non-parametric Wilcoxon signed rank tests were used to assess differences between steady-state and daily-life gait characteristics before and after the PBT. In addition, if significant differences were found, we calculated the effect size per gait characteristic, by dividing the Z value derived from the Wilcoxon signed rank test divided by the square root of N. Wherein N is the summed number of participants in the pre- and post-assessments. Effect sizes of 0.1 correspond with a small effect, 0.3 with a medium effect and 0.5 with a large effect[146].

Changes in input parameters of the fall risk prediction models, which were principal component scores [137] as well as in the predicted fall risk, the output of the model, were examined using Wilcoxon signed rank tests. The evaluation was performed for both the steady-state fall prediction model and the daily-life fall prediction model.

Finally, non-parametric Friedman tests were used to determine differences in the secondary outcome measures, training workload among the training sessions.

Results

All included participants were at least 12 months post stroke, and reported at least one fall in the previous six months. Seven out of ten participants completed all training sessions. See table 7.1 for demographic detail. Two participants missed one training session due to the flu, and one participant missed a training session due to an urgent private meeting. All ten participants performed the steady-state gait assessments before and after the intervention. Due to a technical failure of the accelerometer, one participant (number 8) was not included in the results of daily-life gait characteristics.

Primary outcomes

Steady-state gait characteristics

Gait speed and step length for both the paretic and non-paretic limb increased significantly with respectively large to medium effect sizes after the PBT. Stride time variability, step time variability for both limbs and swing time variability for the paretic limb significantly decreased after PBT, with large to medium effect sizes (table 7.2). No significant effects of PBT were found for local dynamic stability. Results for the steady-state gait characteristics measured at the same preferred gait speed between both assessments are reported in table 7.3. No significant differences were found.

Table 7.1: Demographics.

#	gender	Age	Length	mass	BMI	Paretic side	TSS	FAC	Co-morbidities
1	Male	65	190	90	23.6	Left	4	3	
2	Female	49	182	83	25.1	Right	3	4	
3	Female	64	170	113	39.1	Left	10	3	
4	Male	63	172	78	26.4	Right	2	3	
5	Female	58	163	65	24.4	Right	2	5	
6	Male	70	172	76	25.6	Right	4	3	scoliosis
7	Male	50	190	89	24.6	Left	20	5	Broken hip due to fall
8	Male	61	171	85	29.1	Right	4	4	
9	Male	67	168	85	29.5	Left	1.2	5	
10	Male	68	185	105	30.8	left	1.5	3	epileptic

TSS is time since stroke.

Daily-life gait characteristics

The quantity of walking, expressed as number of walking minutes per day, showed an increasing trend after PBT, but this did not reach statistical significance. The number of walking bouts did increase significantly (table 7.4). Of the gait quality characteristics, stride time increased and the smoothness of walking (index of harmonicity in the VT direction) decreased after PBT (table 7.4).

Table 7.2: Laboratory based steady-state qualitative gait characteristics. Prior (T0) and after (T1) the perturbation based gait intervention. Gait speed was preferred gait speed.

	T0	T1				
Gait characteristics	Mean ± SD	Mean ± SD	dif	Z-score	P-value	ES
Spatio temporal gait characteristics						
Gait speed	**0.46 ± 0.2**	**0.62 ± 0.2**	0.16	**-2.81**	**<.01**	**0.63**
Step length PL	**318 ± 73**	**388 ± 101**	70	**-2.19**	**.03**	**0.49**
Step length NPL	**210 ± 109**	**270 ± 122**	60	**-2.70**	**<.01**	**0.60**
Step time PL	0.75 ± 172	0.71 ± 152	-48	-1.78	.07	
Step time NPL	0.59 ± 120	0.56 ± 101	-34	-1.78	.07	
Swing time PL	0.51 ± 149	0.47 ± 125	-34	-1.27	.20	
Swing time NPL	0.32 ± 83	0.30 ± 64	-12	-1.37	.17	
Stride time	1.35 ± 0.21	1.27 ± 0.15	-0.08	-1.88	.06	
Step width	343 ± 30	343 ± 54	0	-0.35	.72	
Symmetry gait characteristics						
Step length SI	0.25 ± 0.23	0.22 ± 0.24	-0.03	-0.06	.95	
Step time SI	0.11 ± 0.14	0.11 ± 0.15	0	-0.41	.67	
Swing time SI	0.21 ± 0.22	0.20 ± 0.21	-0.01	-1.12	.26	
Variability gait characteristics						
Stride time	**0.10 ± 0.06**	**0.07 ± 0.05**	-0.03	**-2.59**	**<.01**	**0.58**
Step length PL	53 ± 23	51 ± 24	-2	-0.15	.87	
Step length NPL	48 ± 17	52 ± 30	4	-0.56	.57	
Step time PL	**80 ± 49**	**56 ± 39**	-24	**-2.59**	**<.01**	**0.58**
Step time NPL	**67 ± 37**	**54 ± 29**	-13	**-1.88**	**.05**	**0.42**
Swing time PL	**83 ± 44**	**63 ± 39**	-20	**-1.98**	**.04**	**0.44**
Swing time NPL	65 ± 44	50 ± 24	-15	-1.37	.16	
Step-width	22 ± 5.7	22 ± 4.8	0	-0.76	.44	
Smoothness gait characteristics						
IH VT	0.44 ± 0.21	0.46 ± 0.22	0.02	-1.17	.24	
IH ML	0.96 ± 0.02	0.95 ± 0.04	-0.01	-0.15	.87	
IH AP	0.59 ± 0.22	0.62 ± 0.23	0.03	-0.15	.87	
Stability gait characteristics						
LDE VT	1.47 ± 0.13	1.52 ± 0.20	0.05	-1.07	.29	
LDE ML	1.82 ± 0.37	1.79 ± 0.43	-0.03	-1.07	.29	
LDE AP	1.83 ± 0.32	1.82 ± 0.47	-0.01	-0.15	.87	

PL is the paretic limb, NPL the non paretic limb. SI is symmetry index.
LDE is the local divergence exponent.

Table7.3: Laboratory based steady-state qualitative gait characteristics. Prior (T0) and after (T1) the perturbation based gait intervention. Gait speed was preferred gait speed at pre assessment.

	T0	T1				
Gait characteristics	Mean± SD	Mean± SD	dif	Z-score	P-value	ES
Spatio temporal gait characteristics						
Gait speed	0.46 ± 0.2	0.46 ± 0.2	-	-	-	
Step length PL	300 ± 70	334 ± 85	34	-1.27	.20	
Step length NPL	200 ± 94	198 ± 86	-2	-0.35	.72	
Step time PL	0.77 ±163	0.78 ±161	0.01	-1.07	.28	
Step time NPL	0.62 ±114	0.62 ±123	0	-0.25	.79	
Swing time PL	0.51 ±138	0.51 ±144	0	-0.35	.72	
Swing time NPL	0.33 ± 86	0.30 ± 65	-0.03	-1.48	.13	
Stride time	1.39 ±180	1.40 ±186	0.01	-0.25	.79	
Step width	342 ± 28	350 ± 46	8	-1.17	.24	
Symmetry gait characteristics						
Step length SI	0.23 ± 0.2	0.28 ± 0.2	0.05	-1.1	.28	
Step time SI	0.11 ± 0.1	0.11 ± 0.1	0	-0.76	.44	
Swing time SI	0.20 ± 0.2	0.24 ± 0.2	0.04	-1.27	.20	
Variability gait characteristics						
Stride time	102 ± 62	91 ± 49	-11	-0.86	.38	
Step length PL	54 ± 23	51 ± 17	-3	-0.05	.96	
Step length NPL	49 ± 17	52 ± 18	3	-0.45	.64	
Step time PL	82 ± 46	74 ± 41	-8	-1.1	.28	
Step time NPL	68 ± 34	64 ± 34	-4	-0.66	.51	
Swing time PL	85 ± 40	76 ± 35	-9	-0.86	.38	
Swing time NPL	68 ± 42	62 ± 36	-6	-1.1	.28	
Step-width	21 ± 5	21 ± 5	0	-0.15	.87	
Stability gait characteristics						
LDE VT	1.45 ± 0.1	1.52 ± 0.2	0.07	-1.27	.20	
LDE ML	1.81 ± 0.3	1.95 ± 0.4	0.14	-1.58	.11	
LDE AP	1.85 ± 0.3	1.88 ± 0.4	0.03	-0.25	.79	

PL is the paretic leg, NPL the non paretic leg. SI is symmetry index. LDE is the local divergence exponent.

Table 7.4: Accelerometer derived quantitative gait characteristics.
Prior (T0) and after (T1) the perturbation based gait intervention.

Gait characteristics	T0	T1				
Quantitative measures	Mean ± SD	Mean ± SD	dif	Z-score	P-value	ES
Gait activity	17 ± 11	21.9 ± 9.7	4.9	-1.36	.17	
Walking bouts / day	**76.5±38**	**99.6±37.2**	**23**	**-2.19**	**.02**	**0.51**
Monitoring time	5.9 ± 1	5.5 ± 1.6	-.4	-0.77	.44	
Qualitative measures						
Gait speed (m/s)	0.59±0.14	0.54± 0.11	-.05	-0.77	.44	
Stride time (s)	**1.29±0.45**	**1.47±0.19**	**.18**	**-2.38**	**.02**	**0.56**
SD VT	1.35±0.51	1.31±0.36	-.04	-0.06	.95	
SD ML	1.49±0.58	1.49±0.39	0	-0.18	.85	
SD AP	1.23±0.55	1.28±0.40	.05	-0.89	.37	
HR VT	0.99±0.08	0.99±0.04	0	-0.18	.85	
HR ML	1.25±0.19	1.27±0.17	.02	-0.06	.95	
HR AP	0.98±0.11	0.91±0.07	-.07	-1.59	.11	
IH VT	**0.29±0.11**	**0.18±0.09**	**-.11**	**-2.07**	**.04**	**0.49**
IH ML	0.51±0.21	0.59±0.20	.08	-1.12	.26	
IH AP	0.34±0.17	0.35±0.15	.01	-0.88	.37	
Amplitude (psd) VT	0.2 ±0.06	0.27±0.05	-.02	-0.53	.59	
Amplitude (psd) ML	0.49±0.26	0.51±0.21	.02	-0.41	.67	
Amplitude (psd) AP	0.36±0.11	0.39±0.16	.03	-0.53	.59	
Width (psd) VT	1.16±0.20	1.29±0.23	.13	-1.24	.21	
Width (psd) ML	1.09±0.48	0.94±0.22	-.15	-0.05	.95	
Width (psd) AP	1.15±0.39	0.98±0.39	-.17	-0.89	.37	
LDE/stride VT	1.05±0.55	1.18±0.21	.13	-1.36	.17	
LDE/stride ML	1.18±0.75	1.06±0.19	.12	-0.77	.44	
LDE/stride AP	1.14 ±0.72	1.06 ±0.24	0.08	-0.77	.44	

psd is power spectral density, LDE is local divergence exponent.

Predicted fall risk

Nine out of ten participants significantly improved their steady-state gait after the PBT as reflected in the input principal component score of the fall prediction model (p=.005) and in the predicted probability of falling (p=.027) (figure7.1 upper panel). For daily-life gait, no changes after the PBT were observed in model input scores (p=.30) nor in predicted probability of falling (p=.35)(figure 7.1 lower panel).

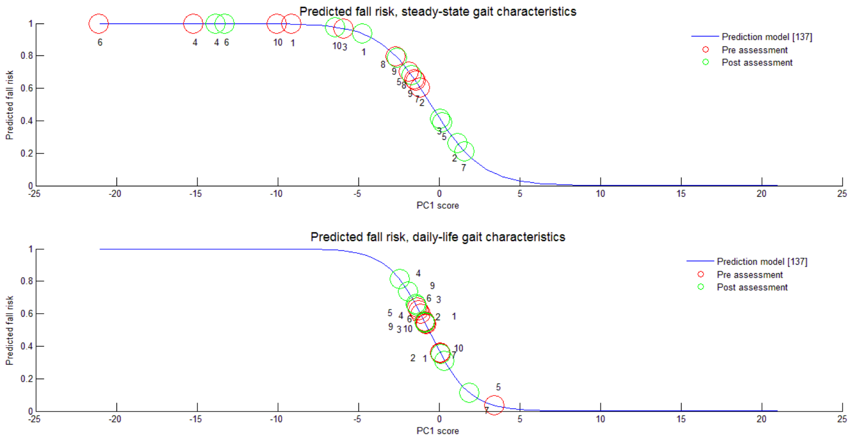

Figure 7.1: Fall predictions based on steady-state gait characteristics (upper graph) and fall predictions based on daily life gait characteristics (lower graph). Participants scores compared to before (red circles) and after the intervention (green circles). Numbering indicate individual score values for each participant. For daily life prediction model, numbering on the right side of the prediction model correspond to the scores after the intervention(green circles). Participants had a reduced fall risk according to the steady-state gait characteristics based fall prediction model, but not according to daily life gait characteristics based fall prediction model.

Training load

Figure 7.2 illustrates the progressively increasing training load of the PBT. As some participants missed a training session and a Friedman test excludes these participants from the analysis, we removed the three incomplete training sessions from our statistical analysis. For the remaining seven training sessions, all participants were able to increase (1) training time (p<.01), (2) combining gait perturbations with a Stroop task (p<.01), (3) increase gait speed(p<.01), (4) perturbation intensity(p<.01) and (5) perturbation frequency(p<.01) over the course of the PBT sessions.

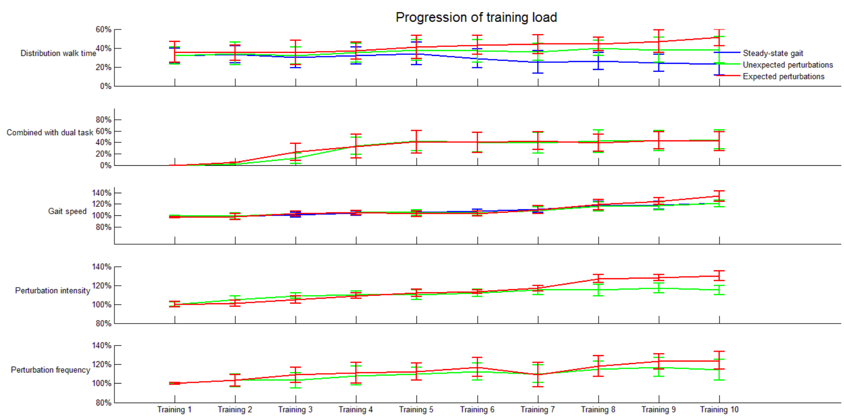

Figure 7.2: training load was progressively increased over training sessions. (1) Relative to the first training session, training time spend in steady-state gait is reduced, while time spend in unexpected gait and expected gait training is increased. (2)Moreover, time spend in unexpected and expected gait while simultaneously performing a dual task was increased. In addition, gait speed (3) (relative to baseline) increased, (4) perturbation intensity relative to the first training session was increased. (5) Fifth graph, perturbation frequency relative to the first training session, 100% corresponds with 4 strides between each perturbation, a increase in percentage is a reduction in strides between perturbations.

Discussion

The main purpose of the present investigation was to explore whether a perturbation based intervention can enhance gait stability in fall prone ambulatory chronic stroke survivors. We found that several steady-state gait characteristics associated with fall risk in stroke survivors [137] were significantly improved after PBT. Additionally, our prediction model based on steady-state gait indicated a lower predicted fall risk. This is in line with a recent fall intervention study in Parkinson's disease, which showed improved spatio-temporal gait parameters after a single perturbation training compared to a control group with regular gait training [147]. However, daily-life gait characteristics indicated no improvement of gait quality after the PBT. Consequently, the daily-life fall risk prediction model indicated a similar fall risk after the PBT as before the intervention. Thus it seems that PBT enhances gait stability in a standardized laboratory setting, yet this does not translate to a daily-life setting.

There are several issues that need to be addressed to place the present results into perspective. We did not apply a statistical correction for multiple comparisons, because this was a pilot study examining whether gait stability improves after PBT. Thus our results require further validation in a larger pre-registered trial. We determined gait characteristics at preferred gait speed. During the post-intervention assessment, preferred gait speed was higher, which may be related to the increase in gait speed during training over the intervention period (figure 7.2). The improvements in gait quality could (in part) be caused by the increased gait speed. For example, it is known that gait variability, which is an important variable in our fall prediction model [137], decreases with increasing gait speed [145]. The fact that gait characteristics did not change when participants were tested at a fixed speed, while gait characteristics did change when tested at preferred speed, which was higher during the post assessment, raises the question to what extent changes in gait characteristics were fully caused by differences in gait speed. To gain a better understanding we determined the correlation coefficients between change in speed and changes in gait characteristics between pre and post assessment, for all significantly changed gait characteristics. Correlations ranged from -0.15 towards 0.15, except for step length of the non paretic limb which was correlated 0.67. Moreover, previous literature has shown that local divergence exponents (LDE) in ML direction increase with gait speed over a specific range (0.4 to 0.6 m/s) of speeds [148]. Interestingly, our participants gained gait speed over this range on average, while their LDE ML values decreased although not significantly so. All in all, this suggests that improvements in gait quality were not mediated by changes in speed alone.

In this study, we aimed to expose participants to many repetitions of as many different kinds of perturbations as possible, thereby improving the ecological validity of the training, because in daily life one may be exposed to a wide range of perturbation types. Pai & Bhatt (2007) indicated that, at least in older adults, feed forward control improves when experiencing gait perturbations in training sessions, thereby creating more adequate responses [149]. This finding is supported by our study, as we found that participants were able to handle more, and larger perturbations during their training sessions and even were able to combine these with a visual Stroop task. Actual improvement of gait was shown in the steady-state gait characteristics. These characteristics quantify how people walk in steady-state conditions without external perturbations. We did not evaluate whether the quality of the perturbation responses was improved, because in contrast to steady-state gait characteristics [137], measures derived from gait perturbations were found not to be associated with fall risk in stroke survivors [143] & [Punt et al 2017C under review in G&P]. However, the lack of transfer of the improved steady-state gait characteristics to daily-life conditions does not necessarily imply that PBT is not useful in fall prone stroke survivors. It may be that this type of intervention improves participants' ability to deal with perturbations such as the ones that the PBT focused on and as such have a positive impact on fall incidence. Especially because previously several studies already found promising results that stroke survivors are able to improve their ability t handle expected perturbations [135, 136].

When interpreting the daily-life gait characteristics results, it should be kept in mind that despite their value in assessing fall risk [46, 47, 119], daily-life assessments are prone to many confounding effects. After the PBT intervention, participants walked more often (significantly more bouts), and walked more minutes per day (although not significantly so). It may be that such behavioral changes coincide with more frequent walking in complex environments and conditions that would lead to less smooth, more variable and less stable walking and hence negatively affect gait characteristics. This might explain the lack of improvement of daily-life gait characteristics.

Conclusion

In conclusion, a perturbation based gait intervention improved steady-state gait characteristics at preferred gait speed and reduced the predicted fall risk in fall prone chronic stroke survivors. These improvements did not transfer to gait in daily life and thus neither reduced fall risk predictions from daily-life gait data. The progression that could be realized during the training indicates that participants improved their ability to deal with expected and unexpected gait perturbations. The positive effects in steady-state gait and potential effects on perturbations responses warrant further study to determine the effect of a perturbation based gait training on fall incidence in stroke survivors.

CHAPTER 8

EPILOGUE

Summary

To ultimately reduce fall incidence in stroke survivors, we first need to know who is at increased risk for falls. Therefore, the first aim of this thesis was to study the ability of a variety of gait assessments to predict fall risk in ambulatory chronic stroke survivors. The second aim was to explore whether we can improve gait stability in fall-prone stroke survivors.

Assessing gait in daily life provides insight in the amount, frequency and quality of gait in stroke survivors. Quantification of gait activity in daily life by accelerometry may be more challenging in stroke survivors as compared to healthy older adults, due to the reduced gait speed and consequent smaller amplitudes of the acceleration time series during gait. In **chapter 2,** we investigated criterion validity and test-retest reliability of several basic quantitative gait characteristics like number of steps and walking distance. Thirty-three chronic stroke survivors participated during the first test for criterion validity, twenty-seven participants performed a second test to obtain test-retest reliability. The gait assessment was performed on a treadmill to determine the number of steps and distance at comfortable walking speed and at 15% below and above comfortable walking speed. Furthermore, over ground gait was detected by performing a six-minute walk test on a twenty meter pathway. The results indicated that the amount of gait can be quantified validly and reliably by using accelerometers located at the lower back.

Over the past few years, fall risk assessment based on gait characteristics has mainly focused on healthy older adults. To determine whether fall prediction

models developed for older adults can also be applied to stroke survivors, **chapter 3** explored whether the same gait characteristics are associated with fall risk in stroke survivors as in older adults, or whether modifications are needed in either the cut-off value and/or regression coefficients of fall risk prediction models. A total of 106 participants were recruited, including 31 non-fall-prone stroke survivors, 25 fall-prone stroke survivors, 25 fall-prone older adults and 25 non-fall-prone older adults. All participants wore the accelerometer at the lower back during seven consecutive days. From the acceleration time series, quantitative and qualitative gait characteristics were determined. We created a binary logistic regression model to assess the ability to predict falls for each gait characteristic. We included health status and the interaction between health status (stroke survivors versus older adults) and gait characteristics in the model. Four interactions of gait characteristics with health status were found, suggesting that gait characteristics are differently associated with falls in stroke survivors as compared to healthy older adults. Given the interactions found, we concluded that specific fall prediction models are needed to predict fall risk in community dwelling chronic stroke survivors based on daily-life gait characteristics.

In **chapter 4,** we determined to what extent clinical physical therapy assessments, daily-life gait characteristics, steady-state gait characteristics and a combination of both types of gait characteristics are able to predict fall risk in chronic stroke survivors. In a group of forty stroke survivors, six physical and psychological assessments were administered. Subsequently, gait data were collected in daily life and in a laboratory setting. From this data, the most promising gait characteristics were determined. A fall calendar and monthly phone calls registered fall events over a six-months period. A total of 15 participants reported at least one fall. Univariate logistic regressions indicated that only one out of six clinical assessments was significantly associated with falls. Furthermore, several gait characteristics derived from both steady-state and daily-life gait revealed a significant association with falls. After data reduction through principal component analysis, the predictive ability of each method was determined by logistic regression. Results indicated that both gait assessment methods were able to predict fall risk, while clinical assessments showed a limited ability to predict fall risk. A combination of both gait assessment methods revealed no improvement in predicting fall risk. Clinicians might enhance currently used fall risk assessments in ambulatory chronic stroke survivors by applying one of either tested gait assessments.

Larger perturbations in gait arise from external sources like unexpected hard wind, slippery roads or for instance from other people walking in the same area. Whether people will actually fall due to such perturbations ultimately comes down to how adequate their response to the perturbation is. It may be that fall prone stroke survivors respond less adequately to unexpected gait perturbations, which could result in a increased risk of falls. In **chapter 5,** we addressed this hypothesis by assessing how stroke survivors respond to six types of gait perturbations. Thirty-eight chronic stroke survivors participated; fifteen experienced at least one fall during a six month follow up period. All participants performed multiple walking trials while medio-lateral belt translations and trips were applied at a fixed moment in the gait cycle. Base of support (BoS) gait characteristics, step time and margins of stability (MoS) were calculated during the first six steps after the gait perturbation. Results revealed that all types of gait perturbations resulted in significantly deviating BoS gait characteristics compared to steady-state gait characteristics. The deviating BoS gait characteristics resulted in similar MoS values compared to steady-state values. Gait characteristics did not differ between fall-prone and non-fall-prone stroke survivors. Thus, as MoS values did not differ and gait characteristics after perturbing gait were similar in the fall-prone and non-fall-prone groups, it seems that at least for the applied gait perturbations, fall-prone stroke survivors have a preserved ability to respond to external gait perturbations.

Falls may also be caused by unsuccessful negotiation of expected gait perturbations like obstacles. To walk safely in more complex environments like walking inside a home, adequate obstacle crossing is needed. In **chapter 6**, we explored whether obstacle crossing characteristics can be used as a diagnostic and evaluation tool for gait training, by determining associations of obstacle crossing characteristics with falls and by determining test-retest reliability. Twenty-nine stroke survivors participated in the experiment; twelve stroke survivors experienced at least one fall during the six-months follow up period. Five virtual, two dimensional, obstacles of increasing width needed to be crossed. After a break, the test was repeated to obtain test-retest reliability. The test-retest reliability was poor for most of the obstacle crossing characteristics, but reliability increased with increased obstacle width. No differences in crossing characteristics between fall-prone and non-fall-prone stroke survivors were found, indicating no diagnostic value for obstacle crossing characteristics. It is worth to further explore the reliability of crossing characteristics and their association to fall risk in a set up with more challenging obstacles than used in our experiment, as more challenging obstacles perturb gait more, and subsequently may improve reliability.

Fall prevention programs generally aim to improve physical activity and thereby physical functioning. Although fall-prone stroke survivors are perhaps able to improve physical function to some extent, this might be outweighed by the increased exposure to fall hazards and this could explain the ineffectiveness of current fall prevention programs. Therefore, in **chapter 7** we addressed the question, whether we can improve gait stability in fall-prone stroke survivors. We developed a perturbation based gait training intervention (PBT) using the GRAIL system. Ten fall-prone stroke survivors were recruited and followed a five-weeks training protocol with two training sessions each week. The PBT contained three parts: steady-state gait training, gait training with a great variety of unexpected gait perturbations and gait training with several expected gait perturbations like obstacle crossing tasks. Finally, the perturbations were combined with a visual Stroop task in order to make the training more challenging. Prior to, and after the PBT, gait stability was assessed using the fall prediction models developed in chapter 4. Steady-state gait characteristics were improved in nine out of ten participants and consequently predicted fall risk reduced. However, daily-life gait characteristics showed no clear improvements, and thus predicted fall risk remained similar after the PBT. Gait quantity, expressed as the number of walking bouts was increased after PBT. In conclusion, it seems that a PBT intervention improves gait stability in steady-state gait, yet it does not transfer to daily-life gait. These latter results, however, could be affected by confounding effects like changes in gait behavior, like for instance performing more small walking bouts inside home which may have lower gait quality.

General discussion.

Daily-life gait characteristics

A classification problem

A major topic throughout this thesis is the assessment of gait of stroke survivors in daily life. In chapter 2, we validated a gait detection algorithm and applied this algorithm to determine quantity of gait and to select the episodes of the acceleration signals classified as gait for determining quality of daily-life gait in chapters 3, 4 and 7. Although the algorithm was validated, it is unknown to what extent the algorithm classifies other cyclic activities like biking, stair negotiation, wheelchair riding and so on as gait. Multiple studies [150, 151], similar to our study, assessed validity in terms of correct quantification of gait. But very few have actually determined if and to what extent other activities are classified as gait. Importantly, those that did so, in either a mock up situation [152] and or in a real-world situation [153], indeed indicate that other activities can be misclassified as gait. Despite of these misclassifications of gait activity, which may result in random errors in estimating gait quality, we and previous authors were able to find valuable information with regard to the prediction of fall risk based on daily-life gait characteristics [44, 47, 107, 119]. Nevertheless, future studies may greatly benefit from more accurate gait detection algorithms. One obvious solution may be changing the sensor location on the body towards one where different activities will result in more distinguishable acceleration time series, like for example the upper leg. However, it seems that accelerations are most relevant with regard to fall risk when they are measured close to the center of mass [154]. It is therefore worth investigating more advanced algorithms using multiple sensors to obtain gravitational orientation, angular velocity and air pressure and thereby improve accuracy of activity classification [155].

Differences in gait behavior

Another potential confounder in the assessment of quality of daily-life gait, is the difference in gait behavior among participants. While for some stroke survivors qualitative gait characteristics are mainly derived from short-lasting walking bouts, others perform longer-lasting walking bouts as well. These differences of bout length will to a certain extent coincide with differences in the environment. Longer lasting bouts are likely performed outside, while shorter walking bouts are performed indoors, which often is a more complex environment, likely to affect those qualitative gait characteristics. To address this issue, we examined the relative contribution of short and long walking bouts to the estimation of gait characteristics in chapter 3. Interestingly, we found a clear difference between fallers and non-fallers and between stroke survivors and older adults, thus indicating that indeed gait behavior is a factor that needs to be taken into account. A simple solution may be comparing walking bouts of similar length. A recent study explored this option and used only walking bouts of at least 60 seconds, to minimize the risk of misclassification of activities, and to avoid potential confounding effects of gait behavior [156]. Although the results are promising, the drawback is that probably not all fall-prone stroke survivors perform such longer walking bouts on a regular basis, which makes practical application questionable.

Applying larger external perturbations

Giving the challenges of walking in the community, like avoiding obstacles or negotiating a slippery road, it seems insufficient to only assess steady-state walking, especially considering the fact that stroke survivors more often fall on the paretic side [21], indicating that perhaps adequate responses to perturbations are diminished in fall-prone stroke survivors. Moreover, as motor control deficits after a stroke can be quite different among stroke survivors, it would be naive to expect to find one single assessment that adequately assesses all these deficits at once, and consequently provides strong associations with fall incidence. Although some stroke survivors may perform well in steady-state gait, they may find avoiding obstacles challenging due to the nature of their impairments. We have tested this line of reasoning by determining the diagnostic value of responses to gait perturbation with respect to fall risk. Unfortunately, results from chapters 5 and 6 indicate no diagnostic value, neither of unexpected gait perturbations, nor of expected gait perturbations.

Unexpected gait perturbations

With regard to unexpected gait perturbations, an important aspect is the quantification of 'how' adequate the response is. The number of measures proposed to this end appears to grow continuously [18]. The measures applied in chapter 5, namely the margins of stability (MoS) and base of support (BoS) reflect to what extent stability is restored after a perturbation. Deriving information about fall risk from perturbation responses is challenging for several reasons. First, even at a fixed speed, participants' gait characteristics at baseline (steady-state) already differ between fall-prone and non-fall-prone groups. Thus, potential differences observed after the perturbation may be explained by the differences found in steady-state gait. Differences may also be masked by differences in the baseline; fallers may exhibit a more variable gait pattern during steady-state gait, which could obscure the perturbation responses. Second, perturbations were executed at a fixed gait speed, to make sure that the magnitude of the perturbation was equal for all participants. Yet, perhaps, handling the perturbation was 'easier' for participants whose preferred gait speed was close to the chosen fixed gait speed. Note that preferred gait speed differs between fallers and non-fallers (see table 5.1). To summarize, for unexpected gait perturbations, even if differences between fall-prone and non-fall-prone stroke survivors are present, it will be very challenging to identify these.

A different, largely unexplored, approach may to some extent be useful in assessing whether fall-prone stroke survivors have a diminished ability to respond to external unexpected perturbations. Assessing the maximum manageable perturbation size avoids the issues raised in this section and provides an objective measure of someone's ability to respond to perturbations. Research using this straightforward approach is limited. Several studies did perform these kinds of analyses and results are promising as they differentiate between younger and older adults [157] and indicate that the paretic leg of stroke survivors responds less adequate to perturbations [53]. Future studies may explore this option in greater detail, although this option may not be feasible for more fragile stroke survivors.

Expected gait perturbations

For a large part, the concerns raised for unexpected gait perturbations do not hold for the measures that were applied to assess expected gait perturbations in chapter 6. Nevertheless, the measures that quantify ability to cross an obstacle are prone to different issues. The most important challenge is the minimization of possibilities of negotiating an obstacle. Allowing to cross an obstacle in multiple ways may increase the variability of these measures, thereby reducing test-retest reliability. More challenging obstacles perturb gait more, and subsequently may improve reliability, making these measures more sensitive to differences between fallers and non-fallers.

Is stimulating gait activity dangerous?

A final discussion point regarding this thesis is the paradoxical effect that stimulating gait may have in stroke survivors. Increasing physical activity is beneficial for health related outcomes like blood pressure, premature death and reduces risk of adverse health outcomes, such as diabetes and obesity [158]. Moreover, specifically for stroke survivors, physical activity is likely to reduce the odds of experiencing a second stroke [159] and physical activity increases physical functioning [159] which may enhance participation in daily life. However, the downside of stimulating physical activity is that it can indirectly increase the risk of falls.

Van Schooten et al (2015) already reported that for people with low gait quality, the number of strides is a risk factor for falls [47]. Moreover, as mentioned, most falls occur during gait, and it has been reported that most falls occur in the morning [21, 22, 160]. In a post-hoc analysis based on acceleration data from chapters 3 and 4, we determined how stroke survivors distribute their gait activity over the day. The results revealed that 50% of all gait activity was performed during the first few hours of the day (figure 8.1). To some extent falls rates appear to correspond with the amount of gait activity in the same timeframe. Thus, it may be beneficial to improve gait stability prior to actually stimulating stroke survivors to walk more in daily life.

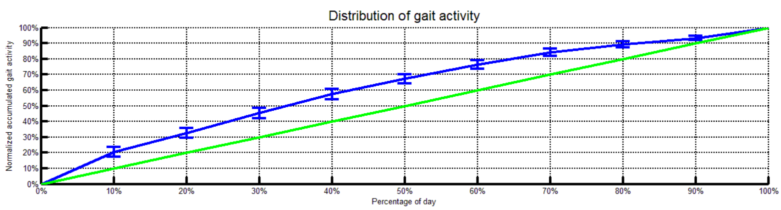

Figure 8.1: The accumulated gait activity of a group of stroke survivors over the day (blue line). Stroke survivors appear to be more active during the morning as their distribution line deviates from the green, uniform distribution. Error bars are confidence intervals.

In chapter 7, we studied whether a perturbation based gait training can improve gait stability in fall-prone stroke survivors by using the GRAIL (Motek Forcelink b.v.). The results found are somewhat puzzling and require further investigation. First, we evaluated gait stability by examining how our fall-prone stroke survivors performed in steady-state and in daily-life gait, while the intervention targeted the resistance against larger external perturbations. However, according to chapter 4, steady-state gait characteristics were associated with falls while chapters 5 and 6 indicated that larger external perturbations are not. This may raise the question why we performed such an intervention, and not just performed regular gait training. However, it has been established that regular gait training is ineffective in reducing falls among stroke survivors [69], while recent studies indicate that perturbation based training yields promising results [70, 149]. Moreover, Pai & Bhatt (2007) indicated that applying a perturbation paradigm enhances adaptive skills to adequately respond to perturbations [149]. Finally, a perturbation based gait intervention may have a leverage effect in terms of reducing fear of falling, better concentration while walking and being able to handle a greater variety of environmental challenges.

Interestingly, we found that after perturbation based gait training, fall-prone stroke survivors appeared to be somewhat safer walkers again (figure 7.1) i.e., their predicted fall risk decreased. However, at present, it is unknown whether this improvement will actually result in a reduced fall rate in daily life. Additionally, it should be kept in mind that based on daily-life gait characteristics, predicted fall risk did not differ between pre and post assessment.

Clinical implications

The results of chapter 4 indicate that steady-state and daily-life gait characteristics provide more accurate information regarding fall risk than currently used clinical fall risk assessments. Clinicians could start embedding a prediction model using gait characteristics into their clinical reasoning, to base their decisions on more accurate information. In order to assign all fallers to a fall prevention program, the cut-off values can be optimized to increase sensitivity at the cost of specificity and thereby detecting almost all fallers. Doing so would of course come at the cost of an increased number of non-fallers assigned to the fall prevention program as well.

A potential intervention could be the PBT described in chapter 7. As the intervention enables stroke survivors to train all challenging aspects of gait in daily life, it appears to be an ecologically valid training method. Initial results were encouraging albeit inconsistent between steady-state and daily-life gait. No evidence exists that a perturbation based intervention actually will results into a reduction of fall rates in stroke survivors [70]. Hence, further study is needed to test whether PBT can indeed be recommended for this population.

Future studies

In general, this thesis has presented fall risk predictions that are promising and better than existing fall risk predictions. Moreover, the intervention study indicates that at least stability of steady-state walking can be improved in chronic stroke survivors after normal rehabilitation and perturbation based training is therefore worth further investigation.

More specifically, we here provide evidence that quantity of gait activity as measured using an accelerometer is valid, but studies testing whether gait recognition algorithms classify other activities as gait are clearly lacking. Improvements in the classification of gait activity will reduce random error and potential bias in gait characteristics caused by misclassification by currently used classification algorithms. Consequently, gait characteristic estimates will improve, which may improve fall risk prediction. Second, larger studies should confirm the associations presented in this thesis and test these prediction models with an external validation procedure [48]. Third, as technology finds its way into clinical practice, new opportunities arise. Nowadays most rehabilitation centers in the Netherlands are capable of performing a gait assessment using a motion capture system similar to the set-up used in this thesis. Structuring this new information across these centers and combining it with long-term surveillance, obtaining information like fall incidence, will enable us to make more accurate predictions, which then help in better, 'data driven' decisions to prevent falls in the future. The intervention study in chapter 7 should be repeated on a larger scale to better understand the mechanism(s) of improvements in steady-state gait. Additionally, a control group and the measurement of fall incidence should be included to study effectiveness in the reduction of fall risk. Finally, the intervention could be applied earlier in the rehabilitation process, which might enhance its effectiveness.

Conclusion

This thesis aimed to determine to what extent gait characteristics are associated with falls. In addition, this thesis explored the potential of a perturbation based gait intervention to improve gait stability with the ultimate goal to reduce fall risk in chronic fall-prone stroke survivors.

The results indicate that assessing quantity and quality of gait is feasible and that these factors yield more information about fall risk than currently used fall risk assessments. Moreover, fall risk predictions based on daily-life gait characteristics should be stroke specific in order to improve accuracy. Assessing expected gait and unexpected gait stability revealed no information with regard to fall risk. However, other, perhaps more challenging gait perturbations may put things into a different perspective, as more challenging obstacles may improve reliability of crossing characteristics and thereby increase sensitivity to fall risk. Finally, a perturbation based gait intervention was able to significantly improve stability of steady-state gait, but this finding did not transfer to more stable gait in daily life.

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SAMENVATTING

Ongeveer 45% van alle mensen na een beroerte valt tenminste één keer per jaar. Een val kan leiden tot tijdelijk letsel zoals een gebroken heup. Ook leidt vallen bij mensen met een beroerte regelmatig tot chronische invaliditeit. Het voorkomen van vallen is daarom erg belangrijk en daarmee het uiteindelijke doel van dit onderzoek.

Een eerste stap naar het voorkomen van vallen is het identificeren van mensen met een verhoogd valrisico. Valrisico wordt bepaald door het afnemen van een balans test zoals een 'Berg balance scale' of een 'Time up and go test'. Hoewel deze testen enige voorspellende waarde hebben, zijn uitkomsten van verschillende studies vaak inconsistent en daarmee zeer beperkt bruikbaar in de praktijk.

De meeste vallen gebeuren tijdens het lopen. Mogelijk zijn er verschillen in de kwaliteit van lopen tussen mensen die wel en niet vallen. Het bestuderen van 'hoe' iemand loopt ofwel de kwaliteit van lopen, zou dus informatie kunnen opleveren over het valrisico. Deze hypothese is reeds onderzocht bij ouderen zonder beroerte. Het blijkt dat bij ouderen de kwaliteit van lopen voorspellend is voor het valrisico. Daarom heb ik in dit proefschrift het lopen bij mensen met een beroerte bestudeerd en onderzocht of de manier van lopen gerelateerd is aan valrisico.

Tot slot heb ik onderzocht of we het lopen van mensen met beroerte en een daarmee gepaard gaand verhoogd valrisico hebben kunnen verbeteren door middel van looptrainingen. Een belangrijk onderdeel hierbij was het creëren van een verstoring tijdens het lopen. Hiermee heb ik gepoogd zo goed mogelijk het dagelijks leven te simuleren.

Het meten van loopkarakteristieken

In dit proefschrift heb ik het lopen bij mensen met een beroerte op drie verschillende manieren gemeten. De kwaliteit van lopen wordt in deze dissertatie uitgedrukt in loopkarakteristieken. Bij elke methode heb ik bestudeerd in welke mate loopkarakteristieken voorspellend zijn voor het valrisico bij mensen met een beroerte.

Allereerst heb ik het lopen in een gestandaardiseerde, laboratoriumomgeving gemeten. Het voordeel van deze methode is dat alle factoren die het lopen kunnen beïnvloeden, zijn beperkt tot een minimum. Ten tweede heb ik het lopen van de deelnemers met behulp van een beweegmonitor bestudeerd in het dagelijks leven. Een sterk argument om deze methode te gebruiken is dat ik het lopen kan bestuderen op dezelfde locatie als waar de daadwerkelijke valincidenten plaatsvinden. Ten derde heb ik in dit proefschrift het lopen gemeten terwijl het lopen werd verstoord. Aangezien veel mensen met beroerte aangeven te zijn gevallen doordat ze struikelden of weggleden, lijkt het bestuderen van de reacties op een loopverstoring mogelijk informatie te kunnen opleveren over het valrisico. Immers, de adequaatheid van de reactie op een loopverstoring zal bepalend zijn of iemand daadwerkelijk valt of niet.

Loopkarakteristieken in het laboratorium.

Een belangrijke vraag is of loopkarakteristieken bij mensen met een beroerte beter het valrisico voorspellen dan de huidige conventionele testen. In hoofdstuk 4 hebben we onder andere loopkarakteristieken bepaald in een gestandaardiseerde laboratoriumomgeving. Ook hebben we een zestal veelgebruikte klinische testen bij dezelfde groep mensen afgenomen. Het onderzoek laat zien dat bepaalde loopkarakteristieken zoals loopsnelheid, variabiliteit van lopen, loopsymmetrie en de divergentie van het lopen voorspellend zijn voor vallen. Daarnaast blijkt uit hoofdstuk 4 dat deze loopkarakteristieken betere voorspellers zijn in vergelijking met de klinische testen. Loopkarakteristieken lijken dus een meerwaarde te hebben ten op zichtte van de huidige standaard testen.

Loopkarakteristieken in het dagelijks leven.

Het meten van loopkarakteristieken in het dagelijks leven heeft enkele methodologische uitdagingen. Een van deze uitdagingen is dat voorafgaand aan het bepalen van hoe iemand loopt in het dagelijks leven, het noodzakelijk is te bepalen wanneer iemand loopt. Vervolgens kunnen de als lopen geïdentificeerde stukken worden geanalyseerd om de loopkarakteristieken in het dagelijks leven te bepalen. In Hoofdstuk 2 heb ik daarom bepaald of we het lopen op een valide manier kunnen kwantificeren ten op zichtte van een gouden standaard, namelijk video-observatie. Ook heb ik bekeken of de bevindingen reproduceerbaar zijn door de test twee weken later te herhalen. De resultaten zijn valide en reproduceerbaar en daarmee bruikbaar voor het identificeren van loopactiviteit in het dagelijks leven. In hoofdstuk 3 en 4 zijn loopkarakteristieken in het dagelijks leven bepaald. In hoofdstuk 3 heb ik bepaald of de associatie tussen loopkarakteristieken en vallen anders is bij mensen met een beroerte dan bij mensen zonder beroerte. Uit de resultaten blijkt dat loopkarakteristieken gemeten in het dagelijks leven anders zijn geassocieerd met vallen dan bij mensen zonder een beroerte. Vervolgens heb ik in hoofdstuk 4 bepaald hoe accuraat loopkarakteristieken in het dagelijks leven valrisico voorspellen bij mensen met een beroerte. Uit de resultaten blijkt dat loopkarakteristieken in het dagelijks leven valrisico kunnen voorspellen en dat deze voorspellingen beter zijn dan de huidige klinische testen. Verder blijkt uit hoofdstuk 4 dat de voorspelling van valrisico op basis van loopkarakteristieken in het dagelijks leven even accuraat is als die op basis van de loopkarakteristieken gemeten in een laboratorium.

Het verstoren van lopen.

Een regelmatig gerapporteerde oorzaak van vallen is struikelen en uitglijden. Het bestuderen van de adequaatheid van reactie op een loopverstoring zou daarom kunnen bijdragen aan het identificeren van mensen met een verhoogd valrisico. Immers, mensen die adequater reageren op een loopverstoring zullen na een verstoring minder vaak vallen. Daarom heb ik in hoofdstuk 5 en 6 bestudeerd of de loopaanpassingen door een verstoring afwijken bij mensen met een beroerte en verhoogd valrisico, ten opzichte van mensen met beroerte en een laag valrisico. In hoofdstuk 5 heb ik zes verschillende, onverwachte loopverstoringen bestudeerd. Alle zes de verstoringen leidden tot een verandering van het looppatroon ten opzichte van onverstoord lopen. Echter, er werden geen verschillen gevonden in de loopaanpassingen nadat het lopen was verstoord tussen de twee groepen. In hoofdstuk 6 heb ik bestudeerd hoe dezelfde deelnemers als die uit hoofdstuk 5 het lopen aanpassen wanneer zij een verwachte verstoring tijdens het lopen ondergaan. Voorbeelden van verwachte loopverstoringen in het dagelijks leven zijn: het opstappen van een stoeprand en het overstappen van een drempel. Uit de resultaten blijkt dat er geen verschillen zijn in loopaanpassingen bij mensen met een beroerte tussen hoog en laag valrisico. Ook is in hoofdstuk 6 bestudeerd of de loopaanpassingen reproduceerbaar zijn voor evaluatieve doeleinden tijdens training. Uit de resultaten blijkt dat de loopaanpassingen meer reproduceerbaar worden naarmate de verwachte verstoringen moeilijker worden, door het vergroten van de obstakels.

Verbeteren van loopkarakteristieken

Nu we beter kunnen identificeren wie een verhoogd valrisico heeft, is de volgende vraag of we het valrisico in deze groep kunnen verlagen? Daarom heb ik in hoofdstuk 7 bestudeerd of een specifieke looptraining het valrisico kan verlagen bij mensen met een beroerte. Tien mensen met een beroerte hebben deelgenomen. De deelnemers waren in de 6 maanden voorafgaand aan de start van de interventie tenminste één keer gevallen.

De looptraining bestond uit een tiental trainingssessies en werd uitgevoerd in een periode van vijf weken. Naast de reguliere looptraining werd het lopen ook verstoord door middel van verwachte en onverwachte verstoringen. De intensiteit en frequentie van deze verstoringen werden in de loop van de trainingsperiode verhoogd. Tevens werd de training uitdagender doordat de deelnemers eveneens een visuele taak kregen in combinatie met de verstoringen. Voorafgaand en na afloop van de trainingssessies werd het lopen geëvalueerd aan de hand van de met vallen geassocieerde loopkarakteristieken. De resultaten laten zien dat de loopkarakteristieken gemeten in de laboratoriumomgeving aanzienlijk verbeterden en dat het voorspelde valrisico verminderde. Het lopen werd ook geëvalueerd met de loopkarakteristieken uit het dagelijks leven. Hieruit bleek dat de loopkarakteristieken in het dagelijks leven niet verbeterden en het voorspelde valrisico dus ook niet. Wel gingen de deelnemers meer lopen.

Conclusie

De resultaten van dit onderzoek geven aan dat het meten van loopkarakteristieken zowel in een laboratoriumomgeving als in het dagelijks leven meer accuraat is in het voorspellen van valrisico dan conventionele klinische testen. Het voorspellen van valrisico aan de hand van loopkarakteristieken tijdens loopverstoringen heeft niet geleid tot het voorspellen van vallen. Mogelijk kunnen andere type verstoringen en of andere verstoringsmaten wel leiden tot accurate voorspellingen van valrisico. Wel blijkt uit dit onderzoek dat looptraining gecombineerd met verstoringen tijdens het lopen kan leiden tot een verlaging van het voorspelde valrisico, hoewel het valrisico niet veranderde op basis van loopkarakteristieken uit het dagelijks leven.

Dit onderzoek kan het startpunt zijn voor het beter inschatten van valrisico bij mensen met een beroerte. Op basis van deze voorspelling kunnen maatregelen getroffen worden om een daadwerkelijke val te voorkomen. Een mogelijke maatregel zou de looptraining zoals omschreven in hoofdstuk 7 kunnen zijn, hoewel niet bekend is of dit daadwerkelijk leidt tot minder vallen.

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