Effects of lower limb orthotic devices in people with neurological disorders

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Lysanne de Jong

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Contents

Chapter 1

General introduction

One of the basic activities of daily living is walking, which enables us to get around in and outside the house[1]. Also when performing daily life activities, such as household activities, grocery shopping or leisure-time activities, we walk and move from one place to another. Being able to walk and perform these daily life activities is an important contributor to independent living[2], social participation[3], and quality of life[4].

Gait capacity

Independent and safe walking in daily life requires a good gait capacity. Human gait capacity can be described by a model containing three aspects: 1) stepping, 2) postural equilibrium (often referred to as 'dynamic balance') and 3) gait adaptability[5].

Stepping

Stepping is defined as the cyclical pattern of limb and trunk movements while moving forward. This cyclical stepping pattern can be divided into different phases based on the distance and/or time between gait events (i.e. spatiotemporal parameters) (Figure 1). The description of the gait pattern during the different phases of gait is most often based on the position and orientation of the body segments and joints (joint kinematics) and on the forces and energy involved (kinetics).

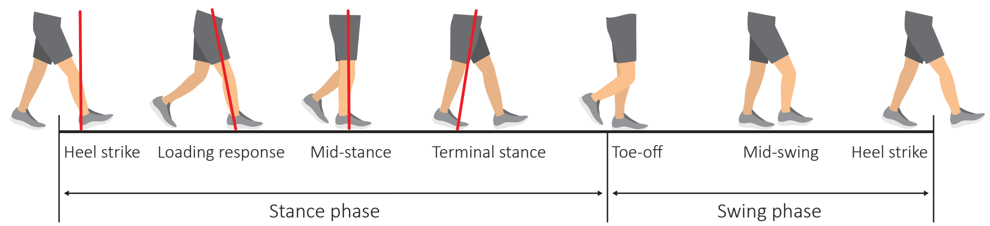

Figure 1. – The gait cycle, divided into the stance phase (i.e. heel strike to toe-off) and the swing phase (toe-off to heel strike). Different gait events can be determined during the gait cycle: heel strike, loading response, mid-stance, terminal stance, toe-off and mid-swing. The ground reaction force is indicated with the red line.

Dynamic balance

Dynamic balance is needed to keep the body stable and upright during walking. The concept of 'dynamic balance' is often based on the inverted pendulum model (see Box 1). In this model, stable and upright gait is maintained by controlling the extrapolated center of mass (XCoM) within the changing base of support (BoS), taking into account the inertial forces[6,7]. To achieve stable and upright gait, the foot or center of pressure (CoP) should be placed at a minimal distance in the medial-lateral direction from the XCoM. Based on the relation between the CoM-CoP kinematics, outcome measures like the ‘margin of stability’ and ‘foot placement strategy’ are used to describe dynamic balance control during walking (see for explanation Box 1).

Gait adaptability

Walking is a context dependent activity[8]. In daily life, we do not always walk in a controlled environment where every step can be identical, but we come across obstacles and unexpected changes. To step over an obstacle, precisely place the foot, or walk on uneven terrain we need to adapt our gait pattern[9]. The ability to adjust the basic stepping pattern and balance to these environmental changes is referred to as ‘gait adaptability’.

Box 1. Inverted pendulum model

A simple model to describe walking is the inverted pendulum model, where the inverted pendulum represents the stance leg and the point mass on top the center of mass (CoM)[10]. Walking is modelled as a falling movement of the inverted pendulum, representing the stance phase. The falling movement can be stopped by taking a step with the contra-lateral leg. Thus, the contralateral leg turns into the stance leg, repeating the movement of falling and taking a next step.

Stable and upright gait is achieved when the position of the CoM is controlled relative to the base of support (BoS) or center of pressure (CoP). Since walking is a dynamic activity, the concept of the extrapolated center of mass (XCoM) was proposed by Hof et al.[11], taking into account both the position and velocity of the CoM. In the anterior-posterior direction, the (X)CoM moves outside the BoS during single stance and is controlled again by taking a step, as described by the inverted pendulum model. In the medial-lateral direction, instability is created when the (X)CoM moves to the lateral border of the BoS. To control the position and velocity of the CoM, individuals apply control mechanisms like contraction of the hip and ankle muscle to influence body motion (hip and ankle strategy) or by adjusting the location or timing of foot placement (foot placement strategy).

Many outcome measures of dynamic balance are based on the CoM-CoP kinematics. The margin of stability (MoS) is a widely used measure to quantify dynamic balance and is defined as the distance between the edge of the BoS and the XCoM. Other measures of dynamic balance are based on the foot placement strategy, describing the relation between the CoM velocity and the foot placement (CoM-CoP distance at heel strike).

Individuals with neurological disorders

Neurological disorders like spinal cord injury (SCI), stroke and hereditary motor and sensory neuropathy (HMSN) are a major cause of disability worldwide[12]. Individuals with neurological disorders often experience sensory and motor deficits, like muscle weakness[13–16] and impaired muscle coordination[17], with an impact on their gait capacity. Indeed, with regard to stepping, an abnormal gait pattern with deviating kinematics and kinetics at the level of the hips, knees and ankles has been found in several neurological disorders[18–20]. Furthermore, people with neurological disorders tend to walk slower with shorter and wider steps[21]. Likewise, dynamic balance[22–25] and gait adaptability[26,27] are also often seriously affected in individuals with neurological disorders. Reduced gait capacity in these individuals contributes to impaired mobility, participation and quality of life.

In both central and peripheral neurological disorders, sensorimotor and morphological abnormalities at the level of the foot and ankle are often observed. Within the brain and spinal cord, the pyramidal tract is responsible for voluntary movements with the strongest projections onto the peripheral nerves innervating the distal muscles[28,29]. As a consequence, lesions of the pyramidal tract will result in disturbed motor control of the foot and ankle, most often showing characteristics of a ‘spastic paresis’. Peripheral nerves are responsible for the communication between the pyramidal nerves and the muscles. Damage to the peripheral nerves will lead to impaired motor control, which is characterized by signs of a ‘flaccid paresis’[30]. Peripheral polyneuropathies typically start with affecting the distal muscles, also resulting in problems at the level of the foot and ankle.

Hence, a common symptom in both central and peripheral neurological disorders is weakness of the distal muscles. For instance, weakness of the ankle dorsiflexors will result in foot drop, while reduced ankle (‘push-off’) power due to calf muscle weakness will lead to reduced propulsion of gait[19]. The inability to lift the feet during the swing phase and push off properly during the stance phase of gait will result in stumbling, tripping and poor balance, which increases the risk of falling. In addition, both central and peripheral disorders lead to prolonged muscular imbalance around the ankle joint and hindfoot, which predisposes to the development of a so-called ‘pes equinovarus’. Likewise, imbalance of the intrinsic and extrinsic foot muscles increases the likelihood of developing foot deformities such as ‘pes cavus’. The ankle-foot deformities typically start as dynamic (i.e. redressable) features, but tend to become structural (i.e. non-redressable) in time.

Together with sensory impairments, motor impairments and ankle-foot deformities may have a huge impact on the gait capacity of people with either central of peripheral neurological disorders. It is important to realize that impairments at the level of the foot and ankle may also have consequences at the level of the knee and hip joints. For instance, to compensate for foot drop or pes equinus, increased hip and knee flexion during the swing phase is often observed in people with peripheral disorders, whereas a ‘circumduction’ movement at the pelvis and hip is often observed in people with central (pyramidal) disorders[31]. In addition, in both types of neurological disorders knee hyperextension during the stance phase is common as a biomechanical consequence of limited ankle mobility at the ankle joint or as a compensation for proximal muscle weakness[32].

Rehabilitation

The main goal of rehabilitation is to optimize daily functioning and social participation. In people with neurological disorders, training of gait capacity is often an important component of rehabilitation to achieve this goal[33]. Such training may be aimed at improving muscle strength, but more frequently it is aimed at sensorimotor control and coordination to improve dynamic balance and gait adaptability, like sustaining perturbations and negotiating obstacles. With the enhancement of dynamic balance and gait adaptability skills, the gait pattern may improve as well, but many studies have shown that the basic spatiotemporal and kinematic characteristics of gait in people with neurological disorders are difficult to change. Hence, despite the effort of training, many individuals remain with an impaired gait pattern[34]. An intervention that is commonly prescribed to further improve the gait capacity in individuals with neurological disorders and that more directly impact joint kinematics, kinetics and stepping is the use of orthotic devices. Orthotic devices are externally worn medical devices that compensate for lost function and impede unwanted movements or counteract excessive muscle activity[35]. The two most important orthotic devices include ankle-foot-orthoses (AFOs) and orthopedic footwear. Both types of orthotic devices directly affect ankle-foot biomechanics and may indirectly even have an effect at the level of the hip and knee.

Ankle-Foot Orthosis

An AFO encompasses the foot, ankle and part of the lower limb, up to just below knee level. Different AFOs are available on the market, varying in design and material. AFOs can be prefabricated, also known as off-the-shelf AFOs[36], or custom-made, molded on the individual's foot and lower limb. In terms of design, AFOs can be hinged, allowing small ankle movements, or non-hinged, and they can have a ventral or dorsal shell. Commonly used materials for AFOs are carbon composites or thermoplastics like polypropylene. Which AFO is prescribed depends on the individual's underlying impairments and the specific gait deviations that need to be accommodated in order to improve gait, mobility, and daily functioning.

The efficacy of AFOs for improving gait capacity has been investigated in different neurological disorders. AFOs improved stepping (in terms of spatiotemporal parameters, kinematics and/or kinetics) in people with stroke[37], various neuromuscular diseases[38–40], and after spinal cord injury[41,42]. Individuals wearing an AFO generally walk faster, and with larger and narrower steps than without AFO. Furthermore, gait efficiency is often improved by decreasing the energy consumption during walking[43]. Only few studies investigated the effect of an AFO on dynamic balance and gait adaptability yielding various results. In terms of dynamic balance control, wearing an AFO improved postural responses to perturbations in individuals with walking disorders[44]. However, the impeding effect of an AFO on ankle motion induced a decreased gait stability in children with cerebral palsy[45]. In addition, gait adaptability in individuals with stroke wearing an AFO was found to be reduced compared to healthy controls[46].

To further improve the efficacy of AFOs for optimizing gait capacity, several influential factors have been investigated. One of the most important factors is AFO alignment, which corresponds to the orientation of the ground reaction force (GRF) in relation to the joint rotation centers. By making small adjustments to the heel height of the AFO-footwear combination or the angle between the ventral shell and footplate of the AFO, the orientation of the GRF can be manipulated until optimal AFO alignment is achieved[47]. This process is often referred to as 'AFO tuning'. The literature states that optimal alignment is reached when the GRF is as close as possible to the knee joint center[48]. An alternative parameter representing the orientation of the GRF in relation to the knee joint center is the shank-to-vertical angle (SVA) during midstance. The SVA is defined as the angle between the anterior surface of the shank and the absolute vertical in the global sagittal plane (Figure 2)[49]. It is assumed that a SVA in midstance between 7° and 15°, with an optimum of 10° to 12°, indicates optimal GRF orientation with respect to the knee[49]. In clinical practice, joint kinematics and kinetics, including the SVA, are usually assessed by performing a 2D- or 3D-gait analysis. A promising alternative for 2D- and 3D-gait analysis that can be used outside the lab are movement sensors (see Box 2). However, the process of AFO tuning in the clinic is currently not supported by the use of objective measurements. Hence, to improve the process of AFO prescription, the need for simple and quick measurement methods is urgent.

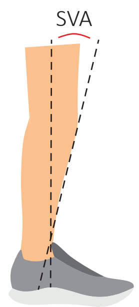

Figure 2. Shank-to-Vertical Angle (SVA)

Orthopedic footwear

Orthopedic footwear is commonly prescribed to individuals that merely have foot problems or to individuals who need an AFO but who cannot be fitted with an AFO due to foot deformities. Orthopedic footwear is custom-made and molded to the individual's foot shape. Its aim determines its characteristics, like shaft height. For example, low orthopedic footwear is prescribed to compensate for structural foot deformities in order to achieve plantigrade foot loading during standing and walking and/or to reduce pain due to excessive

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local foot pressure as a result of deformity. If additional compensation for leg muscle weakness is needed, high orthopedic footwear, sometimes with integrated orthotic support, can be prescribed, which often reaches to well above ankle level.

Although the clinical (experience-based) evidence for AFOs is abundant, the literature on the efficacy of orthopedic footwear in neurological disorders is still scarce. Only few studies investigated the effect of orthopedic footwear on gait capacity in people with stroke and HMSN[20,52,53]. These studies found that stepping, in terms of gait speed and spatiotemporal gait characteristics, was improved in individuals with stroke and HMSN wearing custom-made orthopedic footwear[20,53]. To our knowledge, no investigation of the effect of orthopedic footwear on dynamic balance or gait adaptability in neurological disorders has been published so far.

Box 2. Movement sensors

A movement sensor or inertial measurement unit (IMU) generally contains an accelerometer, gyroscope and magnetometer. An IMU measures acceleration, angular velocity, and the magnetic field vector in its own 3D local coordinate system[50] (Figure 3). By combining the raw data of these three measurement systems (sensor fusing), the sensor orientation in space can be assessed. By attaching multiple IMUs to different body segments, joint kinematics can be derived from the orientation of the IMUs relative to each other. Multiple studies have proven the validity and reliability of these IMUs in gait analysis[50,51]. Since IMUs are relatively cheap, easy to use and not restricted to a lab setting, their use has become a popular alternative for lab-based gait analysis.

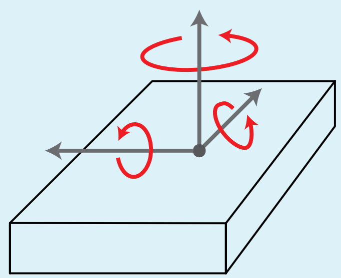

Figure 3. Inertial Measurement Unit (IMU)

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Aim and outline of this thesis

The general aim of this thesis is to study the effects of lower limb orthotic devices in people with neurological disorders. This thesis consists of two parts. **Part one** investigates the assessment of effects of orthotic devices on gait capacity, whereas **part two** evaluates the effects of orthopedic footwear on gait capacity.

In **part one, chapter 2a** starts with a study on the validity, inter-rater reliability and optimal shank location of a single IMU to measure the SVA in healthy controls. Subsequently, the validity of a single IMU at an optimal shank location was assessed in individuals with incomplete spinal cord injury wearing an AFO in **chapter 2b**. Furthermore, the responsiveness of the SVA to changing heel heights of the AFO-footwear combination was determined in this chapter. **Chapter 3** addresses the test-retest reliability of six dynamic balance measures during walking in healthy controls and in individuals with neurological disorders.

Part two focuses on the effect of orthopedic footwear on the three aspects of gait capacity (as described above) in individuals with HMSN. **Chapter 4** describes the effects of orthopedic footwear on postural stability during standing and on stepping and dynamic balance during walking. Participants performed a quiet standing task and a two-minute walk test both with orthopedic footwear and with minimally supportive flat footwear. In **chapter 5** the performance of these individuals on a precision stepping task is presented to assess the effects of orthopedic footwear on gait adaptability.

In **chapter 6**, a summary and general discussion of the work described in this thesis is given.

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Part I

Assessment of effects of orthotic devices on gait capacity

Chapter 2a

A single inertial measurement unit on the shank to assess the shank-to-vertical angle

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Abstract

The Shank-to-Vertical Angle (SVA) is a commonly used parameter to describe orthotic alignment. 3D gait analysis (3DGA) or 2D video analysis are usually used to assess the SVA, but are not always feasible in clinical practice. As an alternative, an Inertial Measurement Unit (IMU) attached and aligned to the shank might be used. This study aimed to investigate the validity, inter-rater reliability and optimal location of a single IMU on the shank to assess the SVA. Thirteen healthy participants (7m/6f, mean age: 45 ± 18 years) were recorded during quiet standing and barefoot walking using a 3D motion capture system and, simultaneously, with IMUs on the shank. The IMUs were anatomically placed and aligned at two different locations, i.e. anterior, in line with the tibial tuberosity and midline of the ankle (anterior IMU), and lateral, in line with the lateral epicondyle and lateral malleolus (lateral IMU). For each participant, the IMUs were placed by two different researchers. A paired t-test, Bland Altmann analysis (mean difference, repeatability coefficient) and intraclass correlation coefficient (ICC) between the 3DGA and both IMUs, and between raters, was performed. Although validity and reliability of the lateral IMU was low, good validity and inter-rater reliability was found for the anterior IMU (mean difference walking Rater1: -0.7 ± 2.1, p=0.27, ICC=0.83 and Rater2: -0.4 ± 1.9, p=0.46, ICC=0.86). Hence, a single IMU placed at the anterior side of the shank is a valid and reliable method to assess the SVA during standing and walking in healthy adults.

Introduction

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Ankle-Foot-Orthoses (AFOs), often in combination with orthopedic footwear (AFO-FC), are commonly prescribed to improve gait in patients with neurological disorders, such as spinal cord injury and stroke. The basic working mechanism of an AFO is to influence sagittal joint kinematics and kinetics by manipulating the ground reaction force (GRF) in relation to the joint rotation centers[1]. AFOs have shown to normalize joint kinematics and kinetics[2,3], improve spatiotemporal parameters[4,5] and, moreover, improve energy expenditure and gait capacity[2,6]. However, the AFO effectiveness depends mainly on the alignment of the AFO, which should be individually optimized[7].

To optimize AFO alignment, fine adjustments are made to the AFO-FC, which is often referred to as tuning[1]. These adjustments include adding heel wedges to incline the shank, and adjust footplate stiffness or footwear. In general, optimal AFO alignment is assumed when the GRF is as close as possible to the knee joint center during midstance, i.e. minimizing the knee flexion-extension moment[8]. A 3D gait analysis (3DGA) or 2D video analysis with force vector overlay can be used to assess the GRF in relation to the knee joint rotation center. However, these methods are restricted to a lab setting, expensive and time consuming (3DGA) and prone to errors (3DGA and 2D video) and therefore not always feasible in the outpatient clinic. As an alternative to the GRF in relation to the knee joint center, the Shank-to-Vertical Angle (SVA) at midstance is suggested as a parameter to evaluate AFO-FC tuning. The SVA, which is the angle between the anterior surface of the tibia and the vertical in the global sagittal plane[9], represents appropriate GRF alignment to the knee. Moreover, it has been shown responsive to increasing the AFO-FC's heel height while wearing rigid AFOs[1,7,8,10]. It is assumed that an SVA at midstance between 7° and 15°, with an optimum of 10° to 12° indicates optimal GRF alignment to the knee[9].

As an alternative to 2D and 3D gait analysis, Inertial Measurement Units (IMUs) have been shown to adequately measure joint kinematics during walking and can be used to assess shank movement[11–13]. Moreover, IMUs can be used at relative low costs and outside a lab setting. For adequate measurements, a sensor-to-segment alignment, commonly determined with calibration postures or calibration movements, is advised. Considering that this is time consuming and has also its limitations, this would make it less applicable in clinical practice. Sensor-to-segment alignment might however be achieved by placing the IMUs in a way that the IMU's local coordinate system corresponds to the anatomical coordinate system, therewith avoiding the need of calibration. Yet, it is unknown whether this approach is accurate for assessing shank kinematics.

This study investigated the use of a single IMU on the shank to assess the SVA, without using standard sensor-to-segment calibration. The following three aims were studied: 1) to examine the validity of a single IMU on the shank to assess the SVA, 2) to examine the inter-rater reliability of a single IMU on the shank to assess the SVA, and 3) to determine the optimal location of the IMU on the shank to achieve IMU-to-shank alignment. It was hypothesized that a single IMU on the shank is a valid and reliable method, with ICCs above 0.8 and error values (standard deviations) lower than 2°, to assess the SVA.

Methods

Participants

Thirteen healthy adults (7 male, mean (SD) age: 45 (18) years) participated. Exclusion criteria were balance or gait problems, and leg or foot deformities. All participants signed written informed consent before the start of the study. Measurement procedures were in accordance with the Declaration of Helsinki. The study was approved by the regional medical ethics committee of Arnhem-Nijmegen (2018-4647) and by the internal review board of the Sint Maartenskliniek.

Equipment

Data were collected at the gait laboratory of the Sint Maartenskliniek. This laboratory consists of a 10 camera motion capture system (Vicon, Oxford, USA) and a force plate (Kistler Instruments, Hampshire, UK) embedded in the middle of a ten meter walkway. The motion capture system recorded marker data with 100 Hz, while the sample frequency of the force plate was 2400 Hz. Two IMUs (APDM, Portland, USA) were placed on the shank, which sampled at a frequency of 128 Hz. A trigger was implemented to synchronize the three systems.

Measurement procedure

Prior to the measurements, anthropometric data were collected. Subsequently, participants were instrumented with 20 markers according to the Plug-in Gait model and three additional markers on the shank by one researcher (LJ) (Figure 1A). The IMUs were placed by two researchers at two locations on the shank: 1) anterior side in which the longitudinal axis of the IMU (Z_{ant}) was aligned with the line connecting tibial tuberosity and midline of the ankle (anterior IMU), and 2) lateral side in which the longitudinal axis of the IMU (Z_{lat}) was aligned with the line connecting lateral epicondyle and lateral malleolus (lateral IMU) (Figure 1A). The researchers placed the IMU by visual inspection in a way that the IMU was aligned with the shank in the frontal and transverse plane of the shank, which corresponds to the coordinate system of the lab (Figure 1B). For each participant either the right or left leg was assessed, which was randomized across all participants.

Participants performed a standing and walking task. During the standing task, participants were asked to stand still with slightly bended knees for 5 seconds. During the walking task, participants walked barefoot at a comfortable speed along the 10 meter walkway. When five correct trials were recorded (i.e. no irregular walking pattern observed, and a clean hit on the force plate of a single foot of the instrumented leg), the measurement was completed. To assess the inter-rater reliability of the IMU placement, the IMUs were independently placed by two raters. The first rater (LJ) placed the IMUs and participants performed the tasks. Subsequently, the IMUs were removed while the markers remained on the participant's body. Afterwards, a second researcher (WO) placed the IMUs on the shank and the tasks were performed again. The order of the two researchers placing the IMUs was randomized across participants.

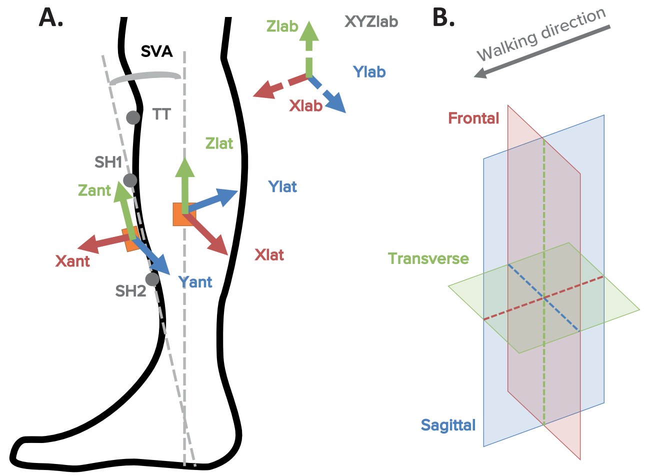

Figure 1. A. Schematic overview of the lower leg with additional markers (grey dots), IMUs (orange rectangles), and the corresponding coordinate systems: XYZant for the anterior IMU, XYZlat for the lateral IMU, and XYZlab for coordinate system of the lab to express the shank markers. SVA: Shank-to-Vertical Angle, TT: Tibia tuberosity, SH1: shank marker 1, SH2: shank marker 2. B. Schematic overview of the frontal (red), sagittal (blue) and transverse (green) plane and the corresponding axes Xlab (red), Ylab (blue) and Zlab (green) of the lab.

Data analysis

Marker data of the 3DGA was filtered with a zero lag, second order Butterworth filter with a cutoff frequency of 10 Hz and force plate data with a zero lag, second order Butterworth filter with a cutoff frequency of 7 Hz. Heel strikes and toe-offs were determined by the vertical component of the GRF. Heel strikes and toe offs were identified as the instant the vertical GRF respectively exceeded and dropped below the threshold of 25N. Midstance was defined as 50% between heel strike and toe off. The SVA measured with 3DGA (SVA_{3DGA}) was calculated as the angle in degrees between the anterior side of the shank, defined by the two markers at the anterior side of the shank (SH1 and SH2), and the vertical in the sagittal plane of the lab using the following equation:

$$SVA_{3DGA} = atan\left(\frac{posX_{SH1} - posX_{SH2}}{posZ_{SH1} - posZ_{SH2}}\right) * \frac{180}{\pi}$$

, in which $posX_{SH1}$ and $posX_{SH2}$ are the position of the shank markers on the X-axis and $posZ_{SH1}$ and $posZ_{SH2}$ the position of the shank markers on the Z-axis of the global coordinate system of the lab (Figure 1).

Acceleration, angular velocity and quaternion data of the IMU was used for data analysis of the IMU. Heel strike and toe off were determined based on the angular velocity[14]. In the angular velocity signal, heel strike and toe-off were represented by two sharp negative peaks, whereas a large positive peak represented mid swing. Firstly, the large positive peaks were detected. Heel strikes and toe-off were defined at the instants of the first and last negative peak after and before a large positive peak, respectively. These instants were used to determine midstance at 50% between heel strike and toe off. Quaternions were transformed into rotation matrices, which were used to compute the SVA in degrees measured with the IMUs. The rotation of Z_{ant} around Y_{ant} for the anterior IMU and of Z_{lat} around X_{lat} for the lateral IMU were used to calculate the SVA. The following equations were used:

$$SVA_{IMUant} = 90 - atan\left(\frac{R_{IMUant_{1,3}}}{R_{IMUant_{3,3}}}\right) * \frac{180}{\pi}$$

$$SVA_{IMUlat} = 90 - atan\left(\frac{R_{IMUlat\_1,3}}{R_{IMUlat\ 2,3}}\right) * \frac{180}{\pi}$$

, in which R_{IMUant} and R_{IMUlat} are the rotation matrices of the anterior and lateral IMU, respectively.

A potential difference in SVA as measured by 3DGA or IMU, can be explained by the malalignment between the IMU axes and 3DGA axes and/or the difference in the timing of midstance. The angular difference between the IMU and 3DGA axes was calculated as the angle between Z_{ant} and the vector between the shank markers SH1 and SH2 in all three planes of the lab coordinate system (Figure 1). The timing difference in midstance was calculated as the difference in midstance in milliseconds between the 3DGA and IMUS.

All data processing and analyses were performed using MATLAB 2018b (The MathWorks Inc, Natick, MA, USA).

Statistical analysis

Validity and inter-rater reliability were estimated using paired t-test (α=0.05), Bland Altmann analysis (mean difference, repeatability coefficient) and intraclass correlation coefficient (ICC) between the SVA_{3DGA} and both SVA_{IMUant} and SVA_{IMUlat} for each rater, and between the raters, respectively. The IMU location with the smallest standard deviation (SD) of the mean difference between the SVA_{3DGA} and SVA_{IMU} was considered as the optimal IMU-to-shank alignment. A paired t-test between midstance estimated with 3DGA and the IMUs was performed to reveal differences in the timing of midstance.

Results

Validity

The mean SVA_{3DGA} for standing was 15.6° (±5.7°) and 13.7° (±4.7°) for rater 1 and 2, respectively. The SVA_{3DGA} was significantly different from the SVA_{IMUant} for rater 1 (17.6° ± 5.1°, p=0.003), and from the SVA_{IMUlat} for rater 1 (8.8° ± 4.7°, p<0.001) and rater 2 (9.3° ± 4.7°, p<0.001) (Table 1).

For walking, the mean SVA_{3DGA} was 13.7° (±2.7°) and 13.8° (±2.7°) for rater 1 and rater 2, respectively (Figure 2). The SVA_{IMUant} at midstance was not significantly different from SVA_{3DGA} for rater 1 (14.4° ± 2.9°, p=0.26) and rater 2 (14.1° ± 2.8°, p=0.52) (Table 1 and Figure 3). The SVA_{IMUlat} at midstance was significantly smaller compared to SVA_{3DGA} for rater 1 (6.3° ± 3.4°, p<0.001) and rater 2 (9.3° ± 3.0°, p<0.001) (Table 1 and Figure 3).

Table 1. Validity. Mean differences, repeatability coefficients, and Intraclass correlations coefficients (ICCs) of the SVA between the 3DGA and both IMUs for both raters for standing and walking.

		Anterior IMU		Lateral IMU	
		Rater1	*Rater2*	*Rater1*	*Rater2*
Standing	Mean difference (SD)	-2.0° (1.9°)*	-0.9° (1.9°)	6.8° (3.5°)*	4.4° (3.4°)*
	Repeatability coefficient	3.7°	3.8°	6.9°	6.7°
	ICC	0.94	0.94	0.59	0.69
Walking	Mean difference (SD)	-0.7° (2.1°)	-0.4° (1.9°)	7.4° (2.8°)*	4.5° (3.2°)*
	Repeatability coefficient	4.2°	3.7°	5.6°	6.2°
	ICC	0.83	0.87	0.25	0.27

SD: standard deviation.
* Significant differences between the 3D gait analysis and the IMU (p<0.01).

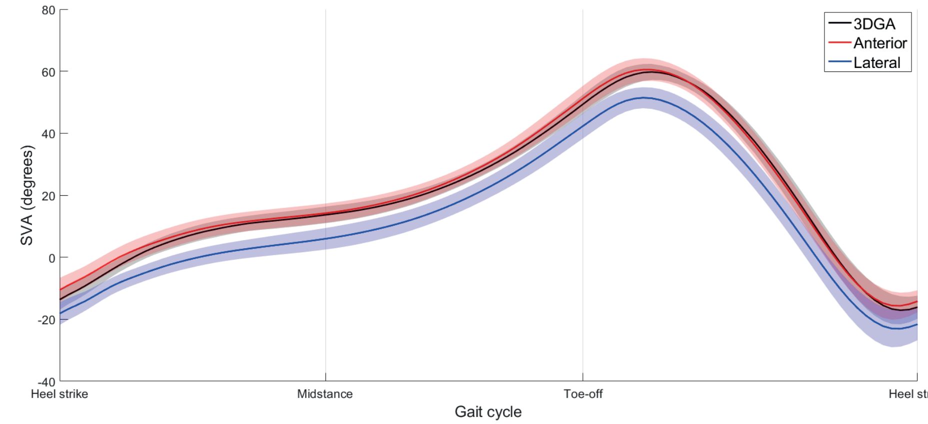

Figure 2. Mean and standard deviation (shaded areas) of the Shank-to-Vertical Angle (SVA) during the gait cycle for 3DGA, the anterior IMU and the lateral IMU of Rater 1.

Inter-rater reliability

No significant differences during standing between the raters were found for the SVA_{3DGA} (p=0.08) and SVA_{IMUlat} (p=0.70), whereas a significant difference was found for the SVA_{IMUant} (p=0.006). During walking, no significant differences at midstance between the raters were found for the SVA_{3DGA} (p=0.78) and the SVA_{IMUant} (p=0.67). A significant difference in SVA_{IMUlat} at midstance between raters was found (p=0.003) (Table 2).

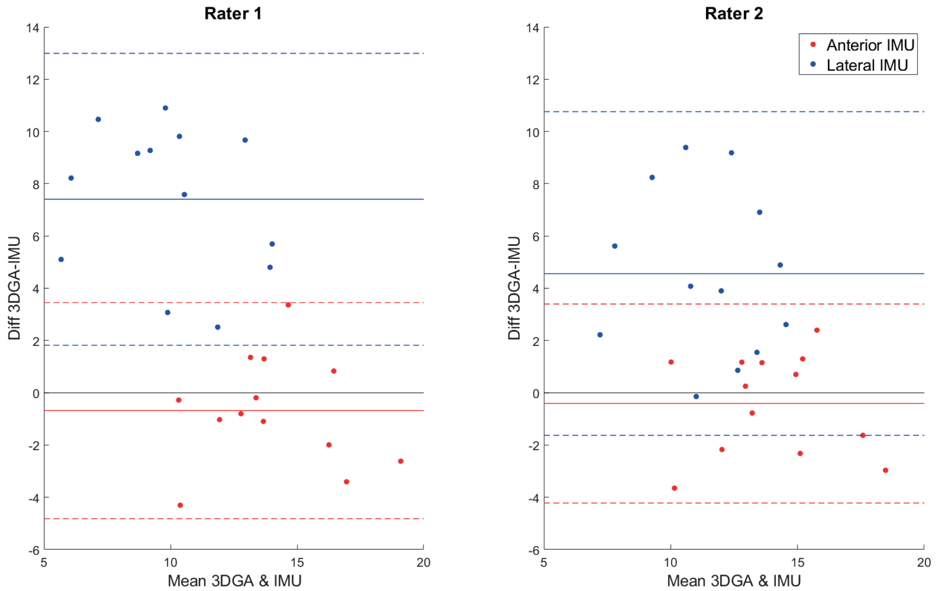

Figure 3. Bland Altman plots of the SVA at midstance for both raters, showing mean difference (solid lines) and limits of agreement (dashed lines) for both IMUs.

Table 2. Inter-rater reliability. Mean differences, repeatability coefficients, and Intraclass correlations coefficients (ICCs) of the SVA for 3D gait analysis (3DGA) and both IMU locations for standing and walking.

		3DGA	Anterior IMU	Lateral IMU
Standing	Mean difference (SD)	2.0° (3.8°)	3.1° (3.3°)*	-0.5° (4.4°)
	Repeatability coefficient	7.4°	6.5°	8.6°
	ICC	0.83	0.76	0.73
Walking	Mean difference (SD)	-0.07° (0.71°)	0.3° (2.4°)	-2.9° (2.8°)*
	Repeatability coefficient	1.4°	4.7°	5.7°
	ICC	0.98	0.79	0.62

SD: standard deviation.
* Significant difference between the 3D gait analysis and the IMU ($p<0.01$).

Differences between the 3DGA and IMU

The angular difference between the 3DGA and IMU at midstance is presented in Table 3. The timing of midstance differed significantly between 3DGA and the anterior IMU with a 6.0 (± 9.4, p=0.040) and 6.6 (±9.8, p=0.031) ms earlier midstance for the IMU for rater 1 and rater 2, respectively. For the lateral IMU, midstance was determined 9.0 (±9.6, p=0.006) and 14.3 (±12.7, p=0.002) ms earlier for rater 1 and rater 2, respectively.

Table 3. Angular difference between the 3DGA and both IMUs for both raters for walking.

	Anterior IMU		Lateral IMU	
Plane	***Rater1***	***Rater2***	***Rater1***	***Rater2***
Frontal	1.2° (±3.1°)	2.3 (±3.6°)	-0.3° (±3.1°)	2.4° (±3.0°)
Sagittal	0.5° (±2.1°)	0.1° (±1.8°)	2.6° (±2.7°)	2.3° (±3.0°)
Transverse	-7.2° (±13.0°)	-8.3° (±11.7°)	-8.5° (±14.9°)	-7.0° (±10.7°)

Values are reported as mean (SD)

Discussion

The present study investigated the validity, inter-rater reliability and optimal location for IMU-to-shank alignment to assess the SVA while standing and walking in healthy adults. The anterior IMU showed the best validity and reliability. The reported ICCs of above 0.80 for the anterior IMU indicated good validity, which were similar to the ICCs reported for 3DGA kinematics in the sagittal plane (ICC>0.80)[15]. Likewise, the SDs of the difference with the 3DGA of 2° for the anterior IMU correspond to the reported and acceptable SDs for 3DGA sagittal plane kinematics (SD < 4°)[15]. Furthermore, the inter-rater reliability of the anterior IMU to assess the SVA was good and comparable to 3DGA with ICCs above 0.75 and SDs below 4°[15]. Hence, validity and inter-rater reliability was similar to 3DGA indicating that the anterior IMU is an adequate method to assess the SVA.

Our main outcome was the difference in SVA between the 3DGA and IMU. Since the markers were not removed, the difference in SVA_{3DGA} between the raters was a measure of consistency of the standing and walking task by the participants. We observed a small difference of 2° during standing and almost identical SVA_{3DGA} during walking. This indicates that they stood slightly different during the standing task, but walked similar after the raters placed the IMU. Therefore, the difference in SVA_{IMU} between the raters was related to differences in placement. The difference between SVA_{3DGA} and SVA_{IMUant} could be mainly caused by accuracy of the sensor fusion algorithms to assess the orientation, malalignment by placement and/or differences in assessing the timing of midstance. The main disturbances in orientation assessment by the IMU, linear acceleration and magnetic field distortion, seem to minimally affect the IMU due to slowing of the shank during midstance (Figure 2) and sensor-to-segment alignment, respectively. Since the difference in midstance timing was only 6 ms, malalignment seems the main cause. Alignment was checked by calculating the angular difference between the longitudinal axis of the anterior IMU (Z_{ant}) and the vector between the shank markers. The mean angular difference of maximum 2.3° in the sagittal and frontal plane for the anterior IMU indicates adequate alignment with the shank. However, the large mean angular difference of around 8° and SD of around 12° in the transverse plane suggests difficulty to align the IMU in the transverse plane. Malalignment of the IMU could have introduced a shift of the IMU's reference frame, resulting in cross talk (i.e. not measuring the SVA in solely the sagittal plane). Moreover, it could introduce a more

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variable error between the methods and raters. This variable error, represented by the SD and repeatability coefficient, was clearly larger between 3DGA and the anterior IMU in comparison to the measurements with the 3DGA. To improve the accuracy of the IMU-to-shank alignment, the use of an alignment tool or addition of a calibration could be a solution to control the orientation of the IMU in the shank's anatomical coordinate system. The alignment tool will give a better indication of the orientation of the IMU relative to the shank, which could be used as a guidance to place the IMU. A simple calibration method of squats could be used to identify misalignment of the IMU.

In conclusion, a single IMU placed at the anterior side of the shank is a valid and reliable method to assess the SVA during standing and at midstance during walking in healthy adults. To be useful in clinical practice, the IMU needs to be valid, reliable and responsive to AFO tuning in patients walking with an AFO as well.

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Chapter 2b

Assessment of the shank-to-vertical angle while changing heel heights using a single inertial measurement unit in individuals with incomplete spinal cord injury wearing an ankle-foot-orthosis

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Abstract

Previous research showed that an Inertial Measurement Unit (IMU) on the anterior side of the shank can accurately measure the Shank-to-Vertical Angle (SVA), which is a clinically used parameter to guide tuning of ankle-foot orthoses (AFOs). However, in this context it is specifically important that differences in the SVA are detected during the tuning process, i.e. when adjusting heel height. This study investigated the validity of the SVA as measured by an IMU and its responsiveness to changes in AFO-footwear combination (AFO-FC) heel height in persons with incomplete Spinal Cord Injury (iSCI). Additionally, the effect of heel height on knee flexion-extension angle and internal moment was evaluated. Twelve persons with an iSCI walked with their own AFO-FC in three different conditions: 1) without a heel wedge (refHH), 2) with 5mm heel wedge (lowHH) and 3) with 10mm heel wedge (highHH). Walking was recorded by a single IMU on the anterior side of the shank and a 3D gait analysis (3DGA) simultaneously. To estimate validity, a paired t-test and intraclass correlation coefficient (ICC) between the SVA_{IMU} and SVA_{3DGA} were calculated for the refHH. A repeated measures ANOVA was performed to evaluate the differences between the heel heights. A good validity with a mean difference smaller than 1 and an ICC above 0.9 was found for the SVA during midstance phase and at midstance. Significant differences between the heel heights were found for changes in SVA_{IMU} (p=0.036) and knee moment (p=0.020) during the midstance phase and in SVA_{IMU} (p=0.042) and SVA_{3DGA} (p=0.006) at midstance. Post-hoc analysis revealed a significant difference between the ref and high heel height condition for the SVA_{IMU} (p=0.005) and knee moment (p=0.006) during the midstance phase and for the SVA_{IMU} (p=0.010) and SVA_{3DGA} (p=0.006) at the instant of midstance. The SVA measured with an IMU is valid and responsive to changing heel heights and equivalent to the gold standard 3DGA. The knee joint angle and knee joint moment showed concomitant changes compared to SVA as a result of changing heel height.

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Introduction

Persons with an incomplete spinal cord injury (iSCI) experience sensory and motor deficits, such as muscle weakness, spasticity and impaired muscle coordination[1,2]. These motor deficits often result in an abnormal walking pattern and an increased fall incidence[1–4]. Although many persons with iSCI regain some walking capacity within the first six months, they often do not fully recover to their normal walking pattern[5]. To further improve walking in persons with iSCI, an Ankle-Foot Orthosis (AFO) is often prescribed[6]. An AFO promotes normal joint kinematics and kinetics and improves spatiotemporal gait parameters and gait efficiency[7–10].

To optimize the effect of the AFO, the AFO footwear combination (AFO-FC) should be properly aligned[11]. Optimal alignment can be achieved by making fine adjustments to heel height, footplate stiffness and/or footwear, which is often referred to as tuning. The goal of AFO tuning is to align the ground reaction force (GRF) as close as possible to the knee joint center to minimize the knee flexion-extension moment[12]. In clinical practice, AFO tuning can be quantified by the Shank-to-Vertical Angle (SVA), which is the angle between the anterior surface of the tibia and the vertical in the global sagittal plane[13]. When the shank is tilted posteriorly, the SVA is considered reclined, and the SVA is considered inclined when the shank is tilted anteriorly. An inclined SVA at midstance between 7° and 15°, with an optimum of 10° to 12°, facilitates appropriate orientation of the GRF in relation to the joint rotation centers[13]. Literature has shown that increasing the heel height of rigid AFO-FCs affected the sagittal knee angle and knee joint moment, which were reflected by an increase in the SVA[14].

Recent research has shown that an inertial measurement unit (IMU) on the anterior side of the shank is a valid and reliable instrument to measure the SVA in healthy individuals[15,16]. An advantage of this approach is that you do not require an expensive gait lab and time-consuming 3D gait analysis, which is considered as the gold standard, to measure the GRF in relation to the knee joint center. Therefore, IMUs are promising as an easy and low-cost alternative to guide AFO tuning. However, assessment of the SVA using an IMU also needs to be valid in individuals with neurological disorders wearing an AFO. Moreover, for AFO tuning it is specifically important that differences in the SVA measured with an IMU are detected during the tuning process, i.e. when adjusting heel height.

This study investigated the use of a single IMU on the shank for assessing the SVA at midstance in iSCI patients while wearing an AFO. The two main aims of this study were: 1) to examine the validity of an IMU to assess the SVA, and 2) to examine the responsiveness of the SVA measured with an IMU while changing the AFO-FC's heel height. The SVA was measured by IMUs and 3D gait analysis (3DGA) as gold standard. As a secondary aim, the effect of heel height on the sagittal knee joint angle and knee joint moment were evaluated. It is hypothesized that an IMU is a valid method to assess the SVA in individuals with iSCI wearing an AFO and that the SVA measured with an IMU is responsive to changing heel heights and equivalent to 3DGA. The SVA measured with an IMU, as well as the SVA measured with 3DGA, knee joint angle and knee joint moment, are expected to increase during midstance with increasing heel height.

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Materials and methods

Participants

Persons with an iSCI who visited the Sint Maartenskliniek between June and December 2019 were screened for eligibility by a rehabilitation physician. Participants were included if they were 1) between 18-80 years old, 2) using an AFO with plantar flexion restriction, 3) using their AFO for a minimum of one month and 4) able to walk 10 meters without a walking aid with and without AFO.
All participants gave written informed consent in accordance with the Declaration of Helsinki. The study was approved by the internal review board of the Sint Maartenskliniek and the regional medical ethics committee of Arnhem-Nijmegen (2018-4647).
Participants characteristics, like the American Spinal Injury Association (ASIA) Impairment Scale[17], level of the lesion, time since injury and Medical Research Council (MRC) scale for muscle strength[18] were extracted from the medical record.

Equipment

The study was conducted on a 10 meter walkway in the gait laboratory of the Sint Maartenskliniek. This laboratory is equipped with a 10-camera motion capture system (Vicon, Oxford, USA) and a force plate (Kistler Instruments, Hampshire, UK). One IMU (APDM, Portland, USA) was placed on the shank. Data were recorded at 100 Hz for the motion capture system, 2400 Hz for the force plate and 128 Hz for the IMU. The three systems were synchronized with a trigger.

Measurement procedure

Reflective markers were placed on the participant according to the Plug-in Gait lower body model. Three additional markers were attached to the shank to assess the SVA (Figure 1A). The IMU was placed on the anterior side of the shank with the vertical axis of the IMU aligned with the line connecting tibial tuberosity and midline of the ankle[15]. The researcher visually inspected if the IMU was aligned with the shank in a way the that anterior-posterior axis (Ximu) pointed in the walking direction (Figure 1B). For each participant, the IMU was placed on the most affected leg with AFO. If the AFO consisted of an anterior shell, the IMU and the shank makers (SH1 and SH2) were placed on the AFO.
Participants performed a walking task with their own AFO-FC in three conditions, commonly used during the tuning process in clinical practice, in randomized order: 1) without a heel wedge (refHH), 2) with 5mm heel wedge (lowHH) (Figure 1C) and 3) with 10mm heel wedge (highHH) (Figure 1D). Participants were instructed to walk at a comfortable speed along the 10-meter walkway. The measurement was completed when five successful trials were recorded (i.e. no irregular walking pattern observed, and a clean hit on the force plate of a single foot of the affected leg).

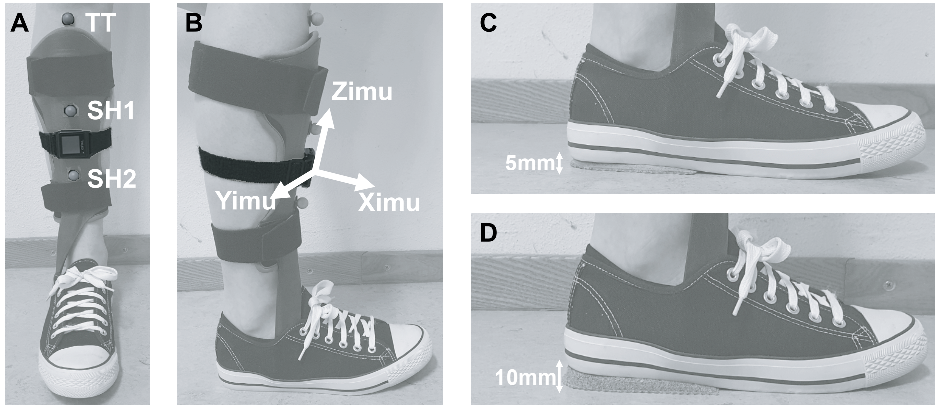

Figure 1. A. Frontal view of the lower leg with additional markers on tibia tuberosity (TT) and the shank (SH1 and SH2). B. Sagittal view of the lower leg with the corresponding coordinate system of the IMU (XYZimu). C. Sagittal view of 5mm heel wedge (lowHH). D. Sagittal view of 10mm heel wedge (highHH).

Data analysis

The SVA measured with the IMU (SVA_{IMU}) was calculated as described previously[15], using the quaternion data of the IMU. Quaternions were transformed into rotation matrices. The SVA_{IMU} was computed by the rotation of Z around Y, using the following equation:

$$SVA_{IMU} = 90 - \text{atan}\left(\frac{R_{IMU_{1,3}}}{R_{IMU_{3,3}}}\right) * \frac{180}{\pi}$$

in which R_{IMU} is the rotation matrix of the IMU.
The SVA measured with the 3DGA (SVA_{3DGA}) was calculated using the marker data. Marker data were filtered using the Woltring cross-validity quintic spline routine (MSE=20)[19]. The SVA_{3DGA} was defined as the angle between the two markers at the anterior side of the shank (SH1 and SH2), and the vertical in the sagittal plane, and calculated using the following equation:

$$SVA_{3DGA} = 90 - atan\left(\frac{posX_{SH1} - posX_{SH2}}{posZ_{SH1} - posZ_{SH2}}\right) * \frac{180}{\pi}$$

in which posX and posZ are the position of the shank markers on the anterior-posterior and vertical axis, respectively. Knee flexion-extension angles and internal moments were calculated using the Vicon Plug-In-Gait model and software.
Heel strike and toe-offs were calculated for the IMU using certain peaks in the angular velocity data during walking as has been previously described[15,20]. Position and acceleration of the foot markers were used to determine heel strikes and toe-offs for the 3DGA. Heel strike was defined as the mean of the instant that the vertical position of the heel marker

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was lowest and the heel marker maximally decelerated. Toe-off was defined as the mean of the instant that the vertical position of the toe marker increased and started to accelerate. The SVA_{IMU}, SVA_{3DGA}, knee angle and knee moment were calculated at the instant of midstance, which was defined as defined as 50% between heel strike and toe-off. Because instants only reflect one specific point in time, instants could be more prone to error since a timing difference of a few samples affects the outcome, whereas the average during a phase will be less susceptible to this timing difference. Hence, we also calculated the average SVA_{IMU}, SVA_{3DGA}, knee angle and knee moment during the midstance phase, defined as 10-30% of the gait cycle[21]. To examine possible effects later on in the stance phase, average knee moment during terminal stance, defined as 30-50% of the gait cycle[21], was also calculated.

A timing difference between the instant of midstance was determined to explain possible differences between SVA_{IMU} and SVA_{3DGA}. The difference in the instant of midstance in seconds between the IMU and 3DGA was calculated as the timing difference. Since kinematics and kinetics are influenced by walking speed, walking speed for all heel height conditions was assessed. Walking speed was calculated as stride length divided by stride time based on 3DGA.

All data processing and analyses were performed using MATLAB 2018b (The MathWorks Inc, Natick, MA, USA).

Statistical analysis

In total 9 outcome measures were calculated, of which were 4 at midstance, 4 as the average during midstance phase and 1 at terminal stance. The SVA_{IMU}, SVA_{3DGA}, knee angle and knee moment at midstance and during midstance phase, and knee moment during terminal stance were averaged over five successful trials per condition. Participant characteristics were analyzed using descriptive statistics and presented as means ± standard deviations (SD).

Validity was estimated using a paired t-test and intraclass correlation coefficient (ICC) between the SVA_{IMU} and SVA_{3DGA} for the refHH. To estimate repeatability, the standard deviation for each participant across trials was calculated and averaged over all participants for the SVA_{IMU} and SVA_{3DGA}.

For analyzing the responsiveness, a repeated measures ANOVA (α=0.05) was conducted to examine differences in the SVA_{IMU}, SVA_{3DGA}, knee angle and knee moment between the heel height conditions (refHH, lowHH and highHH). Post hoc testing with Bonferroni correction (α=0.05/3=0.0167) was performed to evaluate which conditions were significantly different from each other. Effect sizes (Cohen's *d)* were calculated by dividing the mean difference between conditions by the standard deviation of the mean difference between conditions[22].

Results

Participants

Twelve persons with an iSCI (ten males/two females) with an average age ± SD of 55 ± 14 years were included in this study. More detailed participant characteristics are provided in Table 1. Due to technical issues with the motion capture cameras after moving the lab (e.g. missing markers), joint kinematics and kinetics could not be calculated accurately for three participants, who were therefore excluded from the knee angle and knee moment analyses.

Table 1. Participant characteristics (n=12).

Characteristics	Mean ± SD
Age (years)	55.0 ± 14.1
Gender, male/female	10/2
Height (cm)	182.4 ± 8.7
Weight (kg)	90.0 ± 19.9
ASIA Impairment Scale, grade C/D	1/11
Level of the lesion, C1-8/T1-12/L1-5	4/4/4
Time since injury	161 ± 212
Affected leg, left/right	6/6
MRC plantar flexors, 0/1/2/3/4/5	3/1/2/4/1/1
MRC dorsal flexors, 0/1/2/3/4/5	1/2/0/5/3/1
AFO type, dynamic*/hinged**	11/1

* dynamic anterior shell carbon fiber AFO; ** spring-hinged AFO with anterior shell.

Validity

The mean SVA_{IMU} was 11.3° ± 4.3° during midstance phase and 13.4° ± 4.2° at midstance, whereas the mean SVA_{3DGA} was 10.6° ± 4.2° during midstance phase and 13.6° ± 4.6° at midstance (Table 2). The mean ± SD difference between the SVA_{IMU} and SVA_{3DGA} for refHH during midstance phase was -0.69° ± 2.2° (t(11)=-1.10 p=0.294) and 0.18° ± 2.6° (t(11)=0.247, p=0.809) at midstance. The ICCs were 0.93 and 0.91 for the midstance phase and the instant of midstance, respectively. The standard deviation across trails over the participants was 2.2° ± 1.2° for the SVA_{IMU} and 1.5° ± 1.6° for the SVA_{3DGA} during the midstance phase, and 2.1° ± 1.2° for the SVA_{IMU} and 0.95° ± 0.47° for the SVA_{3DGA} at midstance. The instant of midstance was 0.011 ± 0.014 (t(11)=2.71, p=0.020) seconds earlier for the IMU compared to 3DGA for the refHH.

Heel height conditions

Mean and standard deviations in SVA_{IMU}, SVA_{3DGA}, knee angle and knee moments for the heel height conditions are shown in Table 2. The mean SVA_{IMU}, SVA_{3DGA}, knee angle and knee moment during the gait cycle are shown in Figure 2. No statistical difference in walking speed was found between the heel height conditions. The repeated measures ANOVA revealed a significant main effect of heel height for the SVA_{IMU} ($F(11,2)=3.87$, $p=0.036$) and knee moment ($F(8,2)=5.03$, $p=0.020$) during the midstance phase (see Table 3 for differences between conditions). At midstance, SVA_{IMU} ($F(11,2)=3.68$, $p=0.042$) and SVA_{3DGA} ($F(11,2)=6.51$, $p=0.006$) were significantly different between the heel heights. Post-hoc testing showed a significant difference between the refHH and highHH for the SVA_{IMU} ($p=0.005$) and knee moment ($p=0.006$) during the midstance phase and for the SVA_{IMU} ($p=0.010$) and SVA_{3DGA} ($p=0.006$) at the instant of midstance. No significant differences for the other comparisons (refHH-lowHH and lowHH-highHH) were found. No main effect of heel height was found for SVA_{3DGA}, knee angle during the midstance phase, for the knee angle and knee moment at the instant of midstance and knee moment during terminal stance.

Table 2. Mean ±SD values of the SVA_{IMU} (n=12), SVA_{3DGA} (n=12), knee flexion angle (n=9) and internal knee flexion moment (n=9) during midstance phase and at midstance, and internal knee flexion moment (n=9) during terminal stance for the different heel height conditions.

Conditions	RefHH	LowHH	HighHH	F	p
Midstance phase					
SVA_{IMU} (°)	11.3 ± 4.3	12.4 ± 4.8	13.2 ± 4.3	3.87[a]	0.036
SVA_{3DGA} (°)	10.6 ± 4.2	10.9 ± 4.3	11.2 ± 4.2	2.51[a]	0.104
Knee angle (°)	20.2 ± 4.3	21.5 ± 3.8	21.6 ± 3.1	3.56[b]	0.053
Knee moment (Nm/kg)	0.28 ± 0.12	0.31 ± 0.12	0.33 ± 0.12	5.03[b]	0.020
Instant of midstance					
SVA_{IMU} (°)	13.4 ± 4.2	14.6 ± 4.5	15.3 ± 3.5	3.68[a]	0.042
SVA_{3DGA} (°)	13.6 ± 4.6	14.5 ± 4.3	14.8 ± 4.3	6.51[a]	0.006
Knee angle (°)	11.4 ± 6.3	12.7 ± 5.3	12.8 ± 5.2	3.03[b]	0.077
Knee moment (Nm/kg)	0.07 ± 0.16	0.11 ± 0.13	0.12 ± 0.14	3.27[b]	0.065
Terminal stance phase					
Knee moment (Nm/kg)	0.07 ± 0.16	0.10 ± 0.16	0.11 ± 0.15	2.24[b]	0.139
Gait characteristics					
Walking speed (m/s)	0.85 ± 0.18	0.84 ± 0.17	0.83 ± 0.17	1.66[a]	0.214

[a] degrees of freedom: 11,2; [b] degrees of freedom: 8,2.

Table 3. Mean ± SD differences and effect sizes (ES) between the heel height condition of SVA_{IMU}, SVA_{3DGA}, knee angle and knee moment during midstance phase and at midstance, and knee moment during terminal stance.

Conditions	Ref - Low		Low - High		Ref - High	
	Mean ± SD	ES	Mean ± SD	ES	Mean ± SD	ES
Midstance phase						
SVA_{imu} (°)	1.1 ± 2.6	0.40	0.80 ± 2.4	0.33	1.9 ± 1.8*	1.03
SVA_{3DGA} (°)	0.32 ± 1.1	0.28	0.27 ± 0.6	0.44	0.59 ± 0.9	0.65
Knee angle (°)	1.3 ± 1.8	0.69	0.16 ± 1.6	0.10	1.4 ± 1.9	0.76
Knee moment (Nm/kg)	0.04 ±0.07	0.54	0.02 ± 0.05	0.39	0.05 ± 0.04*	1.43
Instant of midstance						
SVA_{imu} (°)	1.2 ± 2.7	0.44	0.6 ± 2.3	0.28	1.8 ± 2.0*	0.89
SVA_{3DGA} (°)	0.9 ± 1.4	0.69	0.3 ± 1.0	0.26	1.2 ± 1.2*	0.98
Knee angle (°)	1.3 ± 1.9	0.70	0.04 ± 1.5	0.03	1.4 ± 2.3	0.61
Knee moment (Nm/kg)	0.04 ±0.08	0.50	0.01 ± 0.04	0.23	0.05 ± 0.06	0.84
Terminal stance phase						
Knee moment (Nm/kg)	0.03 ± 0.07	0.13	0.01 ± 0.04	0.08	0.04 ± 0.05	0.17

* Significant differences between the conditions ($p < 0.0167$).

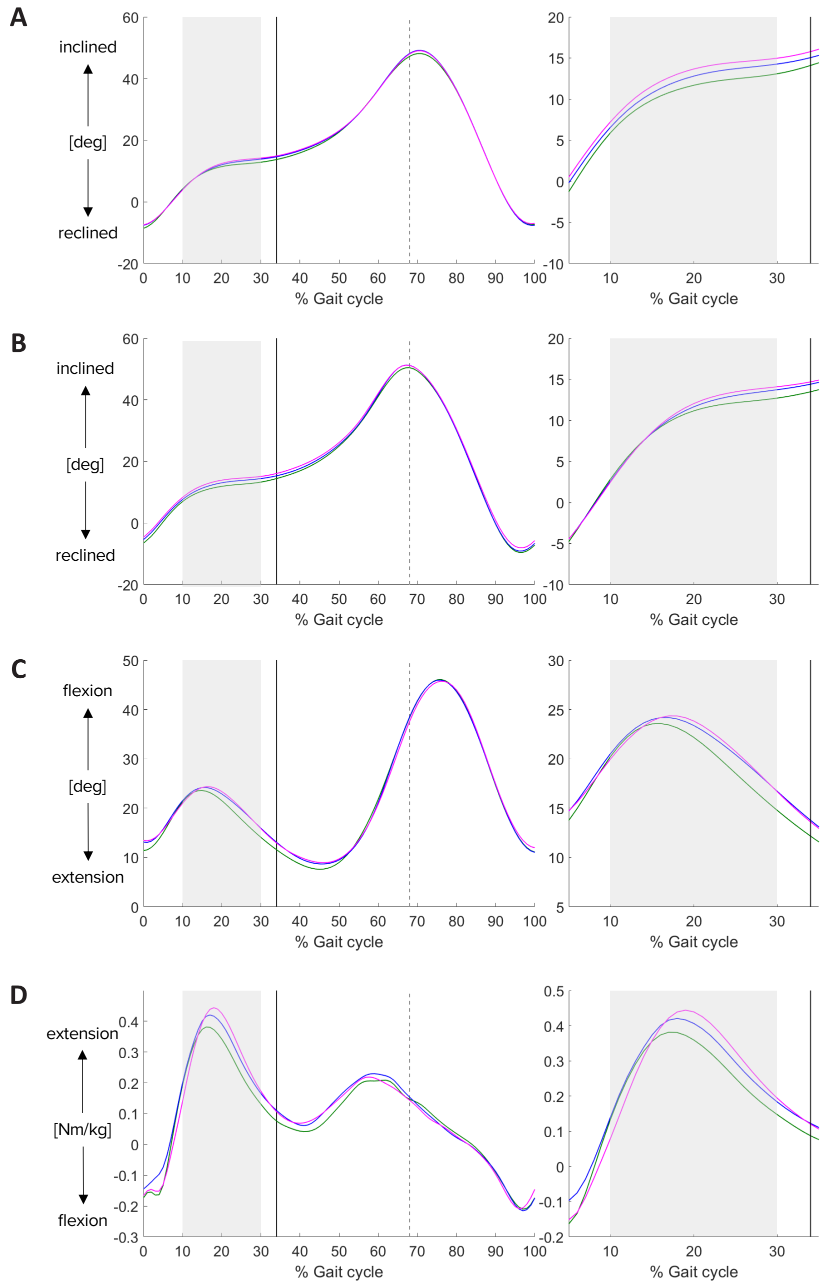

Figure 2. Mean SVA$_{IMU}$ [deg] (A), SVA$_{3DGA}$ [deg] (B), knee flexion-extension angle [deg] (C) and internal knee flexion-extension moment [Nm/kg] (D) during the gait cycle for refHH (green), lowHH (blue) and highHH (pink). The shaded area indicates the midstance phase (10-30%), the black line indicates the instant of midstance (34%) and the dashed line indicates toe off (68%).

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Discussion

This study investigated the use of a single IMU to assess the SVA while changing heel heights in persons with iSCI. The validity was good with small mean differences and high ICCs above 0.9. The SVA increased as a result of increasing heel heights, which was assessed by the IMU and 3DGA. Additionally, we found that an increase in heel height resulted in concomitant changes in knee joint moment at midstance. Knee joint angle did not reach statistical significance as a result of increasing heel height.

The small difference and standard deviation together with the high ICCs in SVA between IMU and 3DGA supports the validity of assessing the SVA with an IMU as has shown before[15,16]. Likewise, the standard deviation of 2° across trials corresponded to the intra-session standard deviation of the SVA measured with a smartphone[16]. The timing difference in midstance of 0.01 second between IMU and 3DGA was comparable to the timing difference in healthy controls, indicating the IMU is able to determine midstance accurately[15].

The significant main effect of heel height for the SVA indicated responsiveness of the SVA to changes in AFO-FC heel height. In contrast to previous study with high heel height differences above 10 mm[14], a strength of our study is that we tested the participants with heel height conditions of 5 and 10mm in accordance to clinical practice. The SVA measured by the IMU and 3DGA was only significantly different between the reference and high heel height condition in the post-hoc analysis. Since no differences of the low heel height with the reference and high heel height condition were found in the SVA, our results indicate that subtle changes in heel height are not reflected by the SVA in this study population. We found a larger mean and standard deviation for the differences in SVA between the heel heights measured with the IMU compared to 3DGA. The effect sizes, ranging from 0.26 to 1.03 (Table 3), were nearly similar indicating that the responsiveness of the SVA measured by an IMU is equivalent to the gold standard 3DGA.

In the current study, we also assessed the kinetics and kinematics of the lower limb to evaluate the alignment of an AFO. The knee joint moment at midstance was significantly different between conditions whereas the knee joint angle was nearly significant, indicating both parameters were influenced by AFO-FC heel height. This is in line with previous literature which found an increase in knee flexion angle and internal knee extensor moment as a result of an increased heel height[12,14,23,24]. Remarkably, the SVA had the same effect size as the knee joint moment between the heel height conditions (see Table 3), indicating that the responsiveness of the SVA corresponds to the responsiveness of the knee joint moment.

We evaluated the outcome measures SVA, knee angle and knee moment during midstance phase and at midstance. Because comparable results were found for all outcome measures, we prefer to use the outcome measures at midstance since the instant midstance can be easily detected when using IMUs and/or video. Furthermore, the instant of midstance corresponds to the clinically used definition of midstance, i.e. the instant when the swing leg passes the stance leg in the walking direction.

The inability to measure subtle changes, especially between the low and high heel height condition, could be explained by the great variability in response on increasing heel heights. Moreover, the AFOs were already tuned in clinical practice. As a result, participants may have counteracted the increase to prevent larger knee angles and moments in order to retain stability during stance and an efficient walking pattern. The ability to counteract the changing heel heights could be due to the familiarity of the participants to walk with their AFOs and/or their walking ability. Another explanation of the small differences could be the use of small heel height differences. Previous literature on AFO tuning using heel height adjustments used higher heel heights to increase the SVA[14]. Accordingly, this study found larger differences in SVA between conditions. However, these large heel heights do not reflect clinical practice. The great variability in the SVA measured by the IMU can be due to the movement of the IMU during and between trials. The IMU was attached to the shank using an elastic band around the calf muscle. Since most participants walked with an anterior supported AFO, there could be some movement between the shank and carbon fiber shell of the AFO, pulling on the elastic band, causing the IMU to slide down or sideways. We recommend attaching the IMU with double side tape to prevent movement of the IMU. The use of an anterior supported AFO resulted also in the attachment of the shank markers on the AFO in stead of on the skin. It could be possible that the shank itself was not in contact with the anterior shell, resulting in a different orientation of the shank and AFO. However, due to the working mechanism of these AFOs and the inclusion of subjects with individually fitted AFOs, we believe that the shank is pushed against the anterior shell during midstance. Hence, the orientation of the shank will be similar to the orientation of the anterior shell, resulting in a correct measurement of the SVA with the shank markers on the AFO. Another explanation that needs to be addressed is the small sample size. Only 12 persons with iSCI participated in this study, and only 9 were included in the analyses for the knee angle and knee moment. This sample size was too low to find a main effect for knee angle and differences between the reference and low heel height. For clinical applications, however, the effect size should be large enough to reveal significant differences in such a small sample size.

Although the SVA is an important measure in clinical practice, and differences between heel height conditions can be measured[12,14,23,24], evidence for the relationship between the SVA and optimal AFO alignment is still scarce. The mean SVA of 11 degrees during midstance phase with the reference heel height (see Table 2) does support the idea that there is an optimum in SVA between 10 and 12 degrees[13]. However, the standard deviation of 4 degrees indicates that individuals deviate from this optimum. Therefore, adding an extra outcome parameter to the SVA could give more information on the optimal alignment of the AFO. The effect size between the reference and low heel height was highest for the knee angle. The knee angle can be easily measured by attaching an IMU to the thigh in addition to the shank for the SVA. Measuring SVA and knee angle during AFO tuning in a large population is needed to increase the understanding of optimal alignment of an AFO.

2

Conclusions

The SVA measured with an IMU is valid and responsive to changing AFO-FC heel height and is equivalent to the gold standard 3DGA. The knee joint angle and knee joint moment showed corresponding changes indicating that the SVA reflects changes in AFO alignment.

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2

Chapter 3

Test-retest reliability of stability outcome measures during treadmill walking in patients with balance problems and healthy controls

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Abstract

Background: Improvement of balance control is an important rehabilitation goal for patients with motor and sensory impairments. To quantify balance control during walking, various stability outcome measures have described differences between healthy controls and patient groups with balance problems. To be useful for the evaluation of interventions or monitoring of individual patients, stability outcome measures need to be reliable.

Research question: What is the test-retest reliability of six stability outcome measures during gait?

Methods: Patients with balance problems (n=45) and healthy controls (n=20) performed two times a two-minute walk test (2MWT). The intraclass correlation coefficient (ICC) and Bland-Altman analysis (coefficient of repeatability; CR) were used to evaluate the test-retest reliability of six stability outcome measures: dynamic stability margin (DSM), margin of stability (MoS), distance between the extrapolated centre of mass (XCoM) and centre of pressure (CoP) in anterior-posterior (XCoM-CoP_{AP}) and medial-lateral (XCoM-CoP_{ML}) direction, and inclination angle between centre of mass (CoM) and CoP in anterior-posterior (CoM-$CoP_{AP\text{-}angle}$) and medial-lateral (CoM-$CoP_{ML\text{-}angle}$) direction. A two way mixed ANOVA was performed to reveal measurement- and group-effects.

Results: The ICCs of all stability outcome measures ranged between 0.51 and 0.97. Significant differences between the measurements were found for the DSM (p=0.017), XCoM-CoP_{AP} (p=0.008) and CoM-$CoP_{AP\text{-}angle}$ (p=0.001). Significant differences between controls and patients were found for all stability outcome measures (p<0.01) except for the MoS (p=0.32). For the XCoM-CoP distances and CoM-CoP angles, the CRs were smaller than the difference between patients and controls.

Significance: Based on the ICCs, the reliability of all stability outcome measures was moderate to excellent. Since the XCoM-CoP_{ML} and CoM-$CoP_{ML\text{-}angle}$ showed no differences between the measurements and smaller CRs than the differences between patients and controls, the XCoM-CoP_{ML} and CoM-$CoP_{ML\text{-}angle}$ seem the most promising stability outcome measures to evaluate interventions and monitor individual patients.

3

Introduction

Many patients with neurological and/or musculoskeletal disorders have difficulty maintaining their balance during standing and walking[1,2]. As a consequence, patients have a higher risk of falling, which can result in physical injuries, decreased social participation and reduced quality of life[3,4]. Because balance control plays an important role in performing daily activities[5], improving balance control is an important rehabilitation goal.

In clinical practice, balance control has commonly been assessed and evaluated by clinical assessment tools like the Berg Balance Scale, Timed Up and Go and Activities-Specific Balance Confidence Scale[6,7]. These tools are easy to use, quick to perform and inexpensive[7,8]. However, most outcome measures of these clinical assessment tools are subjective, show ceiling effects and/or are not responsive to small changes[7,9]. Furthermore, these outcome measures do not reflect the underlying mechanisms of balance control[7].

The biomechanically underlying mechanism of static balance control is the ability to stabilize the centre of mass (CoM) above the base of support (BoS)[10,11]. However, in dynamic situations the CoM can be outside the BoS without losing balance. Therefore, the concept of the extrapolated centre of mass (XCoM) has been proposed for dynamic situations[12]. The XCoM is a state of the CoM taking into account both the instantaneous position and velocity of the CoM. Dynamic balance control is the ability to control the position of the XCoM with respect to the BoS. During walking the XCoM is not always within the BoS which is natural and necessary for forward progression[12,13]. To maintain balance during walking, the foot needs to be correctly placed to control the (X)CoM relative to the BoS[5,14]. Based on the control mechanism between the (X)CoM and foot placement (BoS and CoP), various stability outcome measure, like the dynamic stability margin (DSM)[15], margin of stability (MoS)[12], XCoM-CoP distance[13] and CoM-CoP inclination angles[16], have been proposed in the literature. The DSM is based on the distance interaction between the XCoM and the front line of the BoS[15], while the MoS[12] and XCoM-CoP distance[13] use the XCoM-CoP interaction to assess balance control. In addition, CoM-CoP inclination angles, defined as the angle between the line connecting the CoM and CoP and the vertical line passing through the CoP, are also used as an outcome measure for balance control during walking[16]. The above-mentioned stability outcome measures have been used to describe differences in balance control during walking between healthy controls and (patient) groups with balance problems. For example, the MoS of above-knee amputees was larger compared to healthy controls[17]. In elderly fallers the XCoM-CoP distance in the anterior-posterior distance (XCoM-CoP_{AP}) and the anterior-posterior CoM-CoP inclination angle (CoM-$CoP_{AP\text{-}angle}$) were reduced[13,16], whereas the medial-lateral CoM-CoP inclination angle (CoM-$CoP_{ML\text{-}angle}$) was larger compared to healthy elderly[16]. Furthermore, stroke patients with better balance control, represented by a higher Berg Balance Scale score (>45), reported larger DSM values than stroke patients with a lower Berg Balance Scale score (≤45)[15]. These results illustrated that the above-mentioned stability outcome measures were able to distinguish between patients and controls, indicating construct validity.

In addition to validity, these stability outcome measurements should be reliable to be useful for the evaluation of interventions and monitoring of individual patients. However, the reliability of these stability outcome measures has not been evaluated yet. Therefore, the purpose of this study was to evaluate the test-retest reliability of six different stability outcome measures (DSM, MoS, XCoM-CoP_{AP}, XCoM-CoP_{ML}, CoM-$CoP_{AP\text{-}angle}$ and CoM-$CoP_{ML\text{-}angle}$) during gait in patients with balance problems and healthy controls.

Methods

Participants

Between May 2016 and November 2017, 56 patients and 22 healthy controls were recruited in the Sint Maartenskliniek Nijmegen. Patients were included if: 1) referred to GRAIL (Gait Real-time Analysis Interactive Lab) training for balance and gait training by a rehabilitation physician, 2) 18 years or older, and 3) could walk independently for two minutes without assistance at the beginning of their training period (Functional Ambulation Categories (FAC) ≥ 3). Patients were divided into three categories based on their diagnosis: spinal cord injury (SCI), stroke, and the diverse group with diagnoses including amputation, total knee prosthesis or other neurological disorders than SCI or stroke. The healthy controls were also 18 years or older and did not have any balance or gait problems and neurological or lower limb impairments.

All participants gave written informed consent in accordance with the Declaration of Helsinki. The study was approved by the regional medical ethics committee of Slotervaart Hospital and Reade (P1613/P1614) and by the internal review board of the Sint Maartenskliniek.

Experimental protocol

All participants performed twice a 2-minute walk test (2MWT) on an instrumented split-belt treadmill in the self-paced mode (GRAIL, Motek Medical BV, the Netherlands). The patients performed the 2MWT on two separate days within one week at the beginning of their training sessions. The healthy controls performed both 2MWTs on the same day with a minimum of four hours in between the measurements.

Twelve reflective markers were placed on the following anatomical landmarks of the lower leg: anterior superior iliac spine (ASIS) and posterior superior iliac spine (PSIS), femoral lateral epicondyle, lateral malleolus, metatarsal II and the calcaneus. Marker position was captured by an eight-camera motion capture system (VICON, Oxford, UK) with a sample frequency of 100 Hz. Force data were collected with two embedded force plates underneath each treadmill belt and sampled with 1000 Hz.

The speed of the treadmill was automatically controlled in the self-paced mode using the position of the pelvis[18] . The position of the pelvis was continuously compared to the zero line, located at the middle of the treadmill. Walking forward or backward relative to the zero line resulted in an acceleration or deceleration, respectively. The sensitivity of the self-paced mode (how fast the treadmill reacts at changes in position of the pelvis) was set at 1.0 or 1.5

(setting ranged between 1 and 5), while the maximum acceleration or deceleration was set at 0.25 m/s^2.

Prior to the measurements, participants performed multiple practice trials to familiarize themselves with walking on the GRAIL in the self-paced mode. During these trials, the participants practiced starting and stopping the treadmill, and controlling the speed of the treadmill to reach their steady state walking speed. On the first measurement day, participants received at least three practice trials. During the first practice trial, starting and stopping the treadmill, and controlling the speed were practiced for 60 seconds. The other practice trials were focused on controlling the treadmill during the start-up phase to reach their steady state walking speed and lasted approximately 30 seconds. If participants were not able to control the speed of the treadmill after three trials, additional practice trials were performed until the participants were able to reach a comfortable walking speed within 20 seconds. On the second measurement day, one practice trial was performed for approximately 30-45 seconds. During the 2MWT measurements, participants were instructed to walk as far as possible at a comfortable walking speed in two minutes[19]. To assure safety, all participants wore a safety harness without providing any weight support.

Data analysis

Force plate data were filtered with a zero lag, second order low pass Butterworth filter with a cut-off frequency of 7 Hz. The position of the CoP was calculated using force plate data[20]. To obtain a continuous CoP signal, the CoP trajectory of each foot was weighted by the relative magnitude of the vertical component of the ground reaction force of the corresponding foot[21].

The position data of the markers were low pass filtered with a zero lag, second order Butterworth filter with a 10 Hz cut-off frequency. The position of the CoM was estimated by the average of the four pelvis markers[22]. The XCoM was calculated according to Hof et al.: $XCoM = p_{CoM} + \frac{v_{CoM}}{\omega_0}$ [12]. With p_{CoM} representing the instantaneous position of the CoM, v_{CoM} the instantaneous velocity of the CoM and $\omega_0 = \sqrt{g/l_0}$, in which g is the acceleration of gravity and l_0 the maximum height of the CoM.

Using the position data of the foot markers, heel strikes and toe offs were identified. Heel strikes were defined as the instant at which the velocity of the calcaneus marker started moving backwards, while toe offs were defined as the instant at which the velocity of the metatarsal II marker started moving forward. Steps were defined as the period from heel strike to contralateral heel strike, and strides were defined as the period from heel strike to ipsilateral heel strike. To remove the start-up phase, the first 20 seconds of the data were excluded for analysis. For each participant a constant number of 50 steps was used for analysis.

Stability outcome measures

Six stability outcome measures based on the position of the (X)CoM relative to the foot placement (BoS and CoP) were determined. The DSM was calculated as the shortest distance from the XCoM to the front line of the BoS during double support[15]. Since the exact edge of the front line of the BoS was not available, the front line of the BoS was defined by a line through the metatarsal II markers of the left and right foot (Figure 1A). The MoS was defined as the shortest distance in the medial-lateral direction between the XCoM and CoP at the initial start of the single support phase of each step (Figure 1B)[12]. The XCoM-CoP distance was defined as the shortest distance between the XCoM and CoP calculated at the instant of heel strike in the anterior-posterior direction (XCoM-CoP_{AP}) and in the medial-lateral direction (XCoM-CoP_{ML}) (Figure 1C-D)[13]. The CoM-CoP inclination angle in the anterior-posterior (CoM-$CoP_{AP\text{-}angle}$) and medial-lateral direction (CoM-$CoP_{ML\text{-}angle}$), is defined as the angle between the line connecting the CoM and CoP and the vertical line passing through the CoP[16]. The peak inclination angle was defined as the difference between the minimal and maximal angle within one stride (Figure 1E-F). The stability outcome measures were calculated for each leg separately. If no difference between the legs were found, the results for the affected leg of the patients and left leg of the controls were reported. All data processing and analyses were performed using MATLAB R2009b (The MathWorks Inc, Natick, MA, USA).

Statistical analysis

Subject demographics between groups were compared with an ANOVA (α=0.05). Test-retest reliability for each stability outcome measure was estimated using the intraclass correlation coefficient (ICC (3,1)). ICCs were calculated for each patient group separately (SCI, stroke and diverse), all patients together, and the controls. In addition, Bland-Altman analyses were performed: limits of agreement were calculated to determine the coefficient of repeatability (CR)[23]. Differences in the six stability outcome measures and walking speed between the two measurement and the patient groups were assessed with a two way mixed model ANOVA (α=0.05), with measurement (1 and 2) as within factor and the groups (SCI, stroke, diverse and controls) as between factor. To indicate whether the stability outcome measures could be useful for monitoring individual patients, CRs were compared to the differences between patients and controls. The differences between the patient groups and the control group were determined and tested with post-hoc independent t-tests with Bonferroni correction (α=0.017). To establish an ICC of at least 0.6 with statistical significance (α=0.05 and β=0.80), we aimed to include at least 15 participants per subgroup[24].

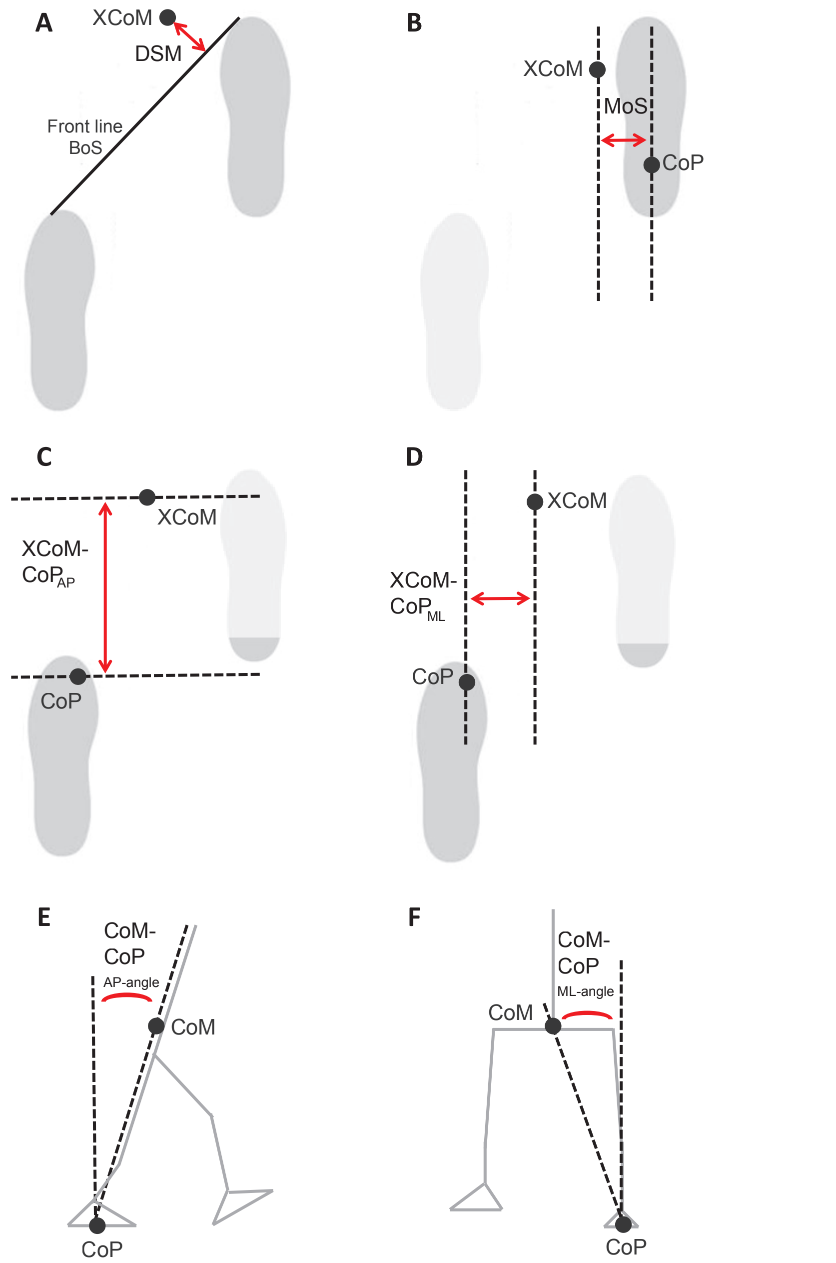

Figure 1. Stability outcome measures based on the position of the centre of mass (CoM), extrapolated centre of mass (XCoM), centre of pressure (CoP) and/or base of support (BoS). A. Dynamic stability margin (DSM); B. Margin of stability (MoS); C. Distance XCoM-CoP_{AP}; D. Distance XCoM-CoP_{ML}; E. CoM-$CoP_{AP\text{-}angle}$ and F. CoM-$CoP_{ML\text{-}angle}$. Darkened segments of the footprints represent foot contact.

Results

Participants

In total, 78 participants were included in this study. Data of ten patients and two healthy controls were incomplete due to technical reasons (e.g. no recording or incomplete marker data). One patient was excluded because he was not able to control self-paced walking. For data analysis, data of the remaining 45 patients and 20 healthy controls were used. One patient did not reach 50 steps during both measurements. For the analysis of this patient, we included 41 and 49 steps instead of 50 for measurement 1 and 2, respectively. Subject demographics are reported in Table 1. No significant differences in subject demographics, except for time post-injury, between the groups were found.

Table 1. Subject demographics.

	Patients			Controls	*p*
	SCI	Stroke	Diverse*		
N	15	15	15	20	
Gender (M/F)	11 / 4	7 / 8	9 / 6	8 / 12	0.195
Age (year)	57.7 ± 11.5	54.9 ± 15.6	58.8 ± 14.6	48.6 ± 17.7	0.232
Weight (kg)	84.1 ± 6.7	75.3 ± 19.6	82.8 ± 14.3	80.4 ± 15.3	0.379
Height (cm)	178.5 ± 7.3	171.1 ± 10.3	174.5 ± 10.3	177.2 ± 6.8	0.102
Post-injury (months)**	27.3 ± 26.9	10.7 ± 14.5	54.9 ± 72.1	-	0.034
Walking speed (m/s)**	0.93 ± 0.33	0.73 ± 0.29	0.91 ± 0.29	1.53 ± 0.28	<0.001

Values are displayed as mean ± SD.
* The group diverse included the following diagnoses: brain tumour, contusion, amputation (n=2), total knee prosthesis (n=3), acquired brain injury, autosomal dominant cerebellar ataxia, neuropathic pain, Guillain-Barré syndrome, encephalomyelitis, brain trauma, hereditary spastic paraplegia, vestibular disorder and pain complaints of ankle and foot.
** Significant difference between the groups ($p<0.05$).

For walking speed a significant main effect for groups ($p<0.001$) and measurements ($\Delta=0.06$, $p<0.001$) was found. Post-hoc testing revealed significant differences between the controls and all patient groups (SCI: $\Delta=0.60$, $p<0.001$; stroke: $\Delta=0.80$, $p<0.001$; diverse: $\Delta=0.62$, $p<0.001$).

Test-retest reliability

The ICCs of all stability outcome measures for all groups are shown in Table 2 and ranged between 0.51 (MoS in the controls) and 0.97 (CoM-CoP$_{ML\text{-}angle}$ in the diverse patient group).

Table 2. Intraclass Correlations Coefficients (ICC) for all stability outcome measures and all groups.

	Patients				Controls
	All	SCI	Stroke	Diverse	
DSM	0.77	0.79	0.83	0.70	0.60
MoS	0.92	0.89	0.81	0.95	0.51
XCoM-CoP$_{AP}$	0.88	0.94	0.83	0.83	0.93
XCoM-CoP$_{ML}$	0.84	0.86	0.84	0.84	0.80
CoM-CoP$_{AP\text{-}angle}$	0.88	0.95	0.82	0.83	0.87
CoM-CoP$_{ML\text{-}angle}$	0.94	0.92	0.89	0.97	0.88

SCI: spinal cord injury; DSM: dynamic stability margin; MoS: margin of stability; XCoM: extrapolated centre of mass; CoP: centre of pressure; CoM: centre of mass; AP: anterior-posterior; ML: medial-lateral

Outcomes of measurement 1 and 2, mean differences and CR are presented in Table 3. The two way mixed ANONA revealed a significant main effect for groups for the DSM ($p<0.001$), XCoM-CoP$_{AP}$ ($p<0.001$), XCoM-CoP$_{ML}$ ($p=0.003$), CoM-CoP$_{AP\text{-}angle}$ ($p<0.001$) and CoM-CoP$_{ML\text{-}angle}$ ($p<0.001$). In addition, a significant main effect for measurements was found for the DSM ($p=0.017<0.001$), XCoM-CoP$_{AP}$ ($p=0.008$) and the CoM-CoP$_{AP\text{-}angle}$ ($p=0.001$). Interaction effects between groups and measurements were not found for any of the stability outcome measures ($p>0.05$). Post-hoc tests revealed significant difference between the controls and all patients groups for the DSM, XCoM-CoP$_{AP}$, XCoM-CoP$_{ML}$, CoM-CoP$_{AP\text{-}angle}$ and the CoM-CoP$_{ML\text{-}angle}$ (all $p<0.001$).

Table 3. Measurement scores, mean differences and coefficient of repeatability (CR) of the (most) affected leg for patients and left leg for healthy controls.

			Measurement scores		Mean difference	CR
			Measurement 1 (mean ± SD)	Measurement 2 (mean ± SD)	Test 2 – Test 1 (mean ± SD)	
DSM (mm)*	Patients	All	20.9 ± 28.8	27.0 ± 28.8	6.1 ± 18.8	36.8
		SCI	22.8 ± 22.8	28.1 ± 20.4	5.3 ± 13.6	26.7
		Stroke	14.0 ± 32.3	18.5 ± 34.3	4.5 ± 19.6	38.4
		Diverse	26.0 ± 31.0	34.5 ± 29.5	8.5 ± 23.0	45.0
	Controls**		49.8 ± 20.6	54.1 ± 17.5	4.4 ± 17.0	33.2
MoS (mm)	Patients	All	28.7 ± 25.5	28.0 ± 21.6	-0.6 ± 9.7	19.1
		SCI	26.1 ± 22.8	27.4 ± 19.3	1.4 ± 10.2	19.9
		Stroke	35.3 ± 16.3	32.2 ± 13.8	-2.9 ± 9.2	17.9
		Diverse	24.7 ± 34.5	24.3 ± 29.5	-0.4 ± 10.0	19.7
	Controls		17.9 ± 13.1	21.4 ± 15.3	3.4 ± 14.1	27.6
XCoM-CoP$_{AP}$ (mm)*	Patients	All	377.3 ± 154.9	398.5 ± 143.6	21.2 ± 71.2	139.5
		SCI	394.5 ± 158.5	413.7 ± 153.2	19.3 ± 50.2	98.4
		Stroke	317.9 ± 144.3	345.7 ± 125.1	27.8 ± 75.5	148.0
		Diverse	419.7 ± 153.2	436.2 ± 144.8	22.9 ± 65.0	172.1
	Controls**		684.9 ± 137.0	711.6 ± 158.0	26.7 ± 49.7	97.5
XCoM-CoP$_{ML}$ (mm)	Patients	All	125.0 ± 26.6	124.6 ± 29.1	-0.3 ± 16.2	31.7
		SCI	125.8 ± 21.1	121.4 ± 25.9	-4.4 ± 12.4	24.3
		Stroke	128.7 ± 30.7	127.4 ± 31.8	-1.3 ± 18.3	35.9
		Diverse	120.5 ± 28.2	125.1 ± 31.1	4.6 ± 16.9	33.2
	Controls**		100.2 ± 19.3	94.2 ± 22.3	-6.0 ± 12.2	24.0
CoM-CoP$_{AP\text{-}angle}$ (°)*	Patients	All	13.9 ± 4.9	14.6 ± 4.5	0.7 ± 2.3	4.4
		SCI	14.0 ± 4.7	14.6 ± 4.9	0.5 ± 1.5	3.0
		Stroke	11.9 ± 4.1	12.9 ± 3.7	1.1 ± 2.3	4.4
		Diverse	15.9 ± 5.2	16.4 ± 4.4	0.5 ± 2.9	5.7
	Controls**		22.7 ± 4.2	24.2 ± 4.7	1.6 ± 1.8	3.6
CoM-CoP$_{ML\text{-}angle}$ (°)	Patients	All	11.5 ± 2.4	11.5 ± 2.5	0.00 ± 0.83	1.6
		SCI	11.3 ± 1.7	11.3 ± 1.7	0.02 ± 0.70	1.4
		Stroke	11.9 ± 1.9	11.8 ± 2.1	-0.06 ± 0.95	1.9
		Diverse	11.2 ± 3.4	11.2 ± 3.5	0.03 ± 0.87	1.7
	Controls**		8.4 ± 1.6	8.3 ± 1.5	-0.11 ± 0.77	1.5

SCI: spinal cord injury; DSM: dynamic stability margin; MoS: margin of stability; XCoM: extrapolate centre of mass; CoP: centre of pressure; CoM: centre of mass; AP: anterior-posterior; ML: medial-lateral; SD: standard deviation.
* Significant difference between test 1 and test 2 ($p<0.05$).
** Significant difference between patient groups and controls ($p<0.001$).

Discussion

This is the first study evaluating the test-retest reliability of the stability outcome measures, DSM, MoS, XCoM-CoP$_{AP}$, XCoM-CoP$_{ML}$, CoM-CoP$_{AP\text{-}angle}$ and CoM-CoP$_{ML\text{-}angle}$, during treadmill walking in patients with balance problems and healthy controls. ICCs ranged between 0.51 and 0.97. Significant differences between measurements were found for the DSM, XCoM-CoP$_{AP}$ and CoM-CoP$_{AP\text{-}angle}$. All stability outcome measures, except the MoS, showed significant differences between controls and patient groups, supporting the literature and indicating construct validity of these stability outcome measures[13,15–17].

Based on the ICCs, a moderate to excellent test-retest reliability was found for all stability outcome measures in patients and controls on group level. The ICCs of the XCoM-CoP$_{AP}$, XCoM-CoP$_{ML}$, CoM-CoP$_{AP\text{-}angle}$ and CoM-CoP$_{ML\text{-}angle}$ were good (ICC>0.80[25]) for all groups. These ICCs were comparable to the ICCs reported for spatiotemporal and kinematic parameters like step length, step width and knee flexion/extension (ICC>0.85) in healthy controls, stroke and SCI patients[26–28]. The ICCs of the DSM and MoS, ranging between 0.51 and 0.95, corresponded to the ICCs found for the kinematic and kinetic parameters ankle dorsi-plantar flexion and peak knee extension moment (0.65-0.79)[26]. The ICCs of the healthy controls were in general lower than the ICCs of the patients which may be explained by the smaller between-subject variability in healthy controls (more homogenous group). Since the ICC is a relative measure depending on both the between-subject variability and test-retest variability, similar test-retest variability in combination with smaller between-subject variability resulted in lower ICC values.

Between the measurements, no significant differences were found for the MoS, XCoM-CoP$_{ML}$ and CoM-CoP$_{ML\text{-}angle}$ whereas DSM, XCoM-CoP$_{AP}$, CoM-CoP$_{AP\text{-}angle}$, and walking speed were significantly different. The increased walking speed suggests a learning effect, which has been found previously for walking tests like the six minute walk test[29]. When the walking speed increases, the XCoM will be situated more forward in the AP-direction. As a consequence, the distance between the XCoM and the BoS or CoP will increase, which results in larger values of the AP-direction based stability outcome measures (the DSM, XCoM-CoP$_{AP}$, CoM-CoP$_{AP\text{-}angle}$). Therefore, the increase in AP-direction based stability outcome measures in the second measurement seems to be related to the increase in walking speed. The systematic increase in walking speed, indicating a learning effect for the AP-direction based stability outcome measures, was probably caused by unfamiliarity with the treadmill and testing procedures on the first measurement day[30]. To reduce the learning effect, additional trials for practicing walking in the self-paced mode may be necessary.

To evaluate the reliability on an individual level, CRs of the stability outcome measures were used. The CR represents the difference between two repeated measures for 95% of pairs of measurements and sets the boundary of the minimal change that can be detected[23]. A weighted comparison between the six stability outcome measures is difficult since the CR is an absolute index in the same unit as the stability outcome measure. To be useful for monitoring of individual patients, the CR should be at least smaller than the differences between patients and controls. Therefore, we compared the CRs to the difference between the patients and controls. All stability outcome measures, except for the MoS, indicated significant lower balance control in patients compared to controls. The CRs of the XCoM-CoP distance and CoM-CoP angle in both AP- and ML-direction were smaller than the differences between patients and controls and may therefore useful for monitoring individual patients. The XCoM-CoP$_{ML}$ and CoM-CoP$_{ML\text{-}angle}$ seem the most promising stability outcome measures for evaluation of interventions and monitoring of individual patients since these two stability outcome measures show high ICCs, no learning effects, independency of walking speed and smaller CRs compared to the differences between patients and controls. Further research should determine whether the stability outcome measures could be useful in clinical practice. The stability outcome measures should be able to distinguish between patients with different levels of balance control (i.e. fallers and non-fallers) and to detect improvements during and after interventions for improving balance control.

A limitation of this study is that test and retest for patients took place on separate days within one week. Disadvantage of this procedure is that subject conditions could differ between the days. However, performing two measurements on one day was not feasible in clinical practice since patients experience fatigue after exercise. Another limitation is the limited number of observations, especially in the subgroups, which affects the precision of the estimation of the CRs and confidence intervals. We recommend to confirm the CRs in a larger and independent sample.

Conclusion

The test-retest reliability of the DSM, MoS, XCoM-CoP$_{AP}$, XCoM-CoP$_{ML}$, CoM-CoP$_{AP\text{-}angle}$ and CoM-CoP$_{ML\text{-}angle}$ for both patients and controls was moderate to excellent. No significant differences between measurements were found for the MoS, XCoM-CoP$_{ML}$ and CoM-CoP$_{ML\text{-}angle}$, whereas a learning effect was found for the DSM, XCoM-CoP$_{AP}$, and CoM-CoP$_{AP\text{-}angle}$. All stability outcome measures, except for the MoS, showed significant differences between the controls and all patient groups. For the XCoM-CoP distance and CoM-CoP angle in both AP- and ML-direction, the CRs were smaller than the difference between patients and controls. Hence, the XCoM-CoP$_{ML}$ and CoM-CoP$_{ML\text{-}angle}$ seem the most promising stability outcome measures to evaluate interventions and monitor individual patients.

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Part II

Effects of orthopedic footwear

Chapter 4

Effects of orthopedic footwear on postural stability and walking in individuals with Hereditary Motor Sensory Neuropathy

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Abstract

Background: Orthopedic footwear is often prescribed to improve postural stability during standing and walking in individuals with Hereditary Motor Sensory Neuropathy. However, supporting evidence in literature is scarce. The aim of this study was to investigate the effect of orthopedic footwear on quiet standing balance, gait speed, spatiotemporal parameters, kinematics, kinetics and dynamic balance in individuals with Hereditary Motor Sensory Neuropathy.

Methods: Fifteen individuals with Hereditary Motor Sensory Neuropathy performed a quiet standing task and 2-minute walk test on customized orthopedic footwear and standardized footwear. Primary outcome measures were the mean velocity of the center of pressure during quiet standing and gait speed during walking. Secondary outcome measures included center of pressure amplitude and frequency during quiet standing, and spatiotemporal parameters, kinematics, kinetics, and dynamic balance during walking. Two-way repeated measures ANOVAs and paired t-tests were performed to identify differences between footwear conditions.

Findings: Neither quiet standing balance nor dynamic balance differed between orthopedic and standardized footwear, but orthopedic footwear improved spatiotemporal parameters (higher gait speed, longer step length, shorter step time and smaller step width) during walking. Moreover, less sagittal shank-footwear range of motion, more frontal shank-footwear range of motion, more dorsiflexion of the footwear-to-horizontal angle at initial contact and more hip adduction during the stance phase were found.

Interpretation: Orthopedic footwear improved walking in individuals with Hereditary Motor Sensory Neuropathy, whereas it did not affect postural stability during quiet standing or dynamic balance. Especially gait speed and spatiotemporal parameters improved. An improved heel landing at initial contact for all footwear and reduced foot drop during swing for mid and high orthopedic footwear contributed to the gait improvements wearing orthopedic footwear.

Introduction

Hereditary Motor Sensory Neuropathy (HMSN) is the most common inherited neuromuscular disorder (prevalence 1:2500 people)[1]. HMSN is characterized by bilateral distal muscle weakness and sensory impairments, starting in the feet and lower legs[2]. Due to weakness of the foot muscles, foot deformities develop such as pes cavus and claw toes[3]. These foot deformities cause secondary abnormalities at the level of the hindfeet (varus), knees (hyperextension), and hips/pelvis (anterior tilt). The walking pattern associated with HMSN is characterized by foot drop, impaired push-off, and overloading of the lateral foot edge during roll-off[4]. In addition, compensatory kinematic adjustments at the knee and hip joints are observed[2,5–8]. Overall, people with HMSN show a relatively low gait speed[5], shortened step length[9] and enlarged step width[7,9] compared to persons without impairments. In addition, postural instability during standing[10–12] and walking[2,5,9,11], and increased risk of falling[13,14] have been reported.

To improve postural stability during standing and walking, orthopedic footwear is commonly prescribed to people with HMSN[15,16]. Low orthopedic footwear aims to enable plantigrade foot loading during standing and walking by compensating for structural foot deformities, while high orthopedic footwear (with integrated orthotic support) may additionally compensate for weakness of the lower leg muscles during walking. However, formal evidence for the efficacy of orthopedic footwear in people with HMSN is hardly available. Only two studies investigated the effect of orthopedic footwear on standing and walking in individuals with HMSN[8,17]. One study (n=10) investigated orthopedic footwear during quiet standing. With orthopedic footwear, people with HMSN showed a tendency towards lower center of pressure (CoP) velocities characterized by a marked reduction of sway amplitude in the frontal plane, which coincided with a higher sway frequency in this plane[17]. The second study, a case study, found that orthopedic footwear enhanced gait speed, cadence and step length[8]. Furthermore, they reported better postural stability and no falls when the subject wore orthopedic footwear.

Generally, gait capacity can be categorized in three components to understand functional walking: (1) stepping, (2) postural stability, and (3) gait adaptability[18]. Stepping is defined as moving forward with a cyclical pattern of limb and trunk movements, usually quantified by spatiotemporal parameters and by joint kinematics and kinetics. While moving forward, the body must maintain postural stability to keep the center of mass (CoM) within the changing base of support, taking into account inertial forces, usually quantified by dynamic balance measures describing the CoM relative to the base of support or CoP. In daily life, the stepping pattern and basic postural stability during walking must also be adjustable to changing environmental demands, which is commonly referred to as gait adaptability.

This present study is focused on the effects of orthopedic footwear on postural stability during quiet standing (static balance) as well as on stepping and postural stability during walking (dynamic balance) in individuals with HMSN. To this end, we compared measures of quiet standing balance as well as spatiotemporal parameters, kinematics, kinetics, and dynamic balance during walking when subjects wore their own customized orthopedic

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footwear with wearing minimal supportive, flexible footwear. We hypothesized a lower CoP velocity during quiet standing and higher gait speed during walking with the orthopedic footwear compared to minimal supportive, flexible footwear.

Method

Participants

Individuals with HMSN who visited the Sint Maartenskliniek between January 2017 and March 2018 were screened for eligibility by a rehabilitation physician. Inclusion criteria were: 1) diagnosed with HMSN, 2) between 18-70 years old, and 3) provided with customized orthopedic footwear for a minimum of two months to improve postural stability and/or to prevent falling. Exclusion criteria were: 1) inability to walk independently for 2 minutes without assistance, 2) pain and/or pressure sores related to the orthopedic footwear, 3) surgery of the lower extremities less than one year ago, and 4) other disorders influencing the gait pattern. The following demographic characteristics were registered upon inclusion: age, sex, height, and weight. In addition, clinical characteristics, like HMSN disease type and Medical Research Council (MRC) Scale scores[19] for muscle strength of the ankle dorsal- and plantar flexors were extracted from the medical records.
All participants gave written informed consent in accordance with the Declaration of Helsinki. The study was approved by the internal review board of the Sint Maartenskliniek and the regional medical ethics committee of Arnhem-Nijmegen (2018-4306).

Footwear

Orthopedic footwear (Figure 1A) was custom made for each individual and molded to the individual's foot shape. The insole, an internal footwear feature, especially accommodates the foot deformity to relieve pain and pressure and to assist a neutral position of the hind foot. The aim is to accept plantar flexion of the first metatarsal (deepening of MT1)[20] by lowering the insole under MT1, without changing the position of the ankle joint (no increase in ankle plantar flexion). External footwear features like shaft height, heel adjustment en forefoot apex position, are based on the individual's characteristics, e.g. muscle strength and walking pattern, and treatment purpose. Common footwear features include shaft height, heel adjustment and forefoot apex position. Shaft height was defined as the height of the supplement in the shaft in relation to the ankle joint. Low orthopedic footwear consists of a shaft height below the level of the ankle, whereas the shaft height of mid and high orthopedic footwear is above the level of the ankle in order to control the movement of the ankle joint in the frontal plane. Adjustments to the heel can be made by rounding off the posterior edge (beveled heel) to decrease ankle dorsiflexion work in loading response or by adding a lateral flare to the heel (flared heel) to increase stability in the frontal plane[21]. The forefoot rocker can be influenced by the position of the apex (forefoot apex position)[22], which is the position where the outsole begins to curve upwards under the forefoot. A neutral apex position is at the MTP joints, whereas the apex position could also be placed

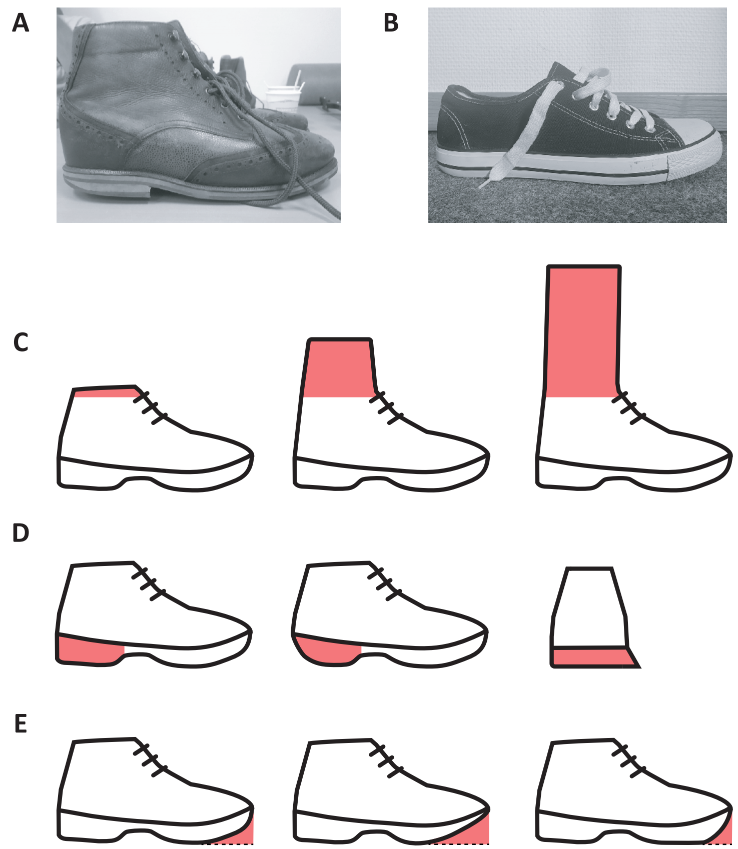

Figure 1. Overview of the footwear. A. Example of orthopedic footwear. B. Standardized footwear. C. Shaft height: low height, mid height and high height. D. Heel adjustments: no adjustment, beveled heel and flared heel (posterior view) E. Forefoot apex position: neutral, proximal, distal.

more proximal or distal to achieve an early or delayed forefoot rocker, respectively. Standardized footwear consisted of a minimal supportive sneaker with a flexible shaft made of canvas and a flat rubber sole without heel-to-toe drop (Figure 1B).

Assessments

Participants visited the research department of the Sint Maartenskliniek once. Prior to the balance and gait measurements, the American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Scale[23] score and the classification of foot deformity proposed by Louwerens[20] were determined by the primary researcher (LdJ). This researcher also assessed footwear features of the customized orthopedic footwear and its intensity of use. The three footwear features included shaft height, heel adjustment and forefoot apex positioned, and were categorized in three levels. Shaft height was scored as follows: 'low height' below the ankle joint, 'mid height' max 10 cm above the ankle joint, and 'high height' >10 cm above ankle joint (Figure 1C). Heel adjustments were categorized in: 'no adjustment', in which the posterior edge was perpendicular to the ground, 'beveled heel', in which the posterior edge of the heel was rounded off or 'flared heel', in which the heel was extended with a lateral flare (Figure 1D). Forefoot apex position was classified as: 'neutral' in which is the apex position coincides with the MTP joints, 'proximal', in which the apex position is closer to the heel or 'distal', in which the apex position is closer to the toes (Figure 1E).

Subsequently, participants were instrumented with 20 markers according to the Plug-in Gait lower body model (Plug-in-Gait, Vicon Motion Systems Ltd., Oxford, UK). The foot markers were placed on the footwear. Balance measurements were performed on a platform with integrated force plate (AMTI , Watertown, MA, USA) collecting force data at a sampling rate of 500 Hz. Gait measurements were performed on an instrumented treadmill, the Gait Real-time Analysis Interactive Lab (GRAIL, Motek Medical BV, the Netherlands). Marker position was captured by a ten-camera motion capture system (Vicon, Oxford, UK) at a sample frequency of 100 Hz. Force data were collected with two force plates embedded underneath the treadmill belt and sampled at 1000 Hz.

Participants first performed three practice trials to familiarize themselves with walking on the GRAIL. Thereafter, participants completed two tasks in the following, fixed order: 1) quiet standing task and 2) 2-minute walk test (2MWT). These two tasks were performed with customized orthopedic footwear that participants brought to the assessment, and with minimal supportive, flexible, flat sneakers, referred to as standardized footwear, that was provided on site. Participants were fitted into the standardized footwear without any additional modifications. After completion of both tasks with one type of footwear, participants changed to the other type of footwear. The order of measurements was randomized across participants.

Quiet standing

During the quiet standing task, participants stood upright on the force platform with their feet against a foot frame (medial sides of the heels 8.4 cm apart; each foot out-toeing at a 9° angle from the sagittal midline)[24]. Participants were instructed to stand as still as possible for 30 seconds either with open or closed eyes. Both conditions were performed twice, starting with eyes open followed by eyes closed.

2-Minute Walk Test

The 2MWT was performed once per footwear condition on the GRAIL in a self-paced mode, i.e. the treadmill speed was automatically controlled by continuously comparing the position of the pelvis to the midline of the treadmill[25]. Walking forward or backward relative to the midline resulted in treadmill acceleration or deceleration, respectively. Participants were instructed to walk as far as possible in two minutes[26].

Data analysis and outcome measures

For quiet standing, signals were processed using a custom-made program after a 16-bit AD-conversion[27,28]. CoP during standing (CoP_{st}) was calculated as the point of application of the resultant of the ground reaction forces in the anterior-posterior (AP) and medial-lateral (ML) directions, separately. The CoP data was low-passed filtered (cut-off frequency 6Hz). Firstly, the root mean square (RMS) amplitude of the CoP displacement ($aCoP_{st}$) [mm] in both AP and ML directions was calculated. Then, after a first-order differentiation, the RMS velocity of the CoP ($vCoP_{st}$) [mm/s] in either direction was calculated as the primary outcome measure. The mean CoP frequency ($fCoP_{st}$) in each direction was determined as the ratio between $aCoP_{st}$ and $vCoP_{st}$, using the following equation: $fCoP_{st} = vCoP_{st} / (aCoP_{st} \times \sqrt{2} \times 4)$[17].

Marker data of the 2MWT were filtered using the Woltring cross-validity quintic spline routine (MSE=20) before running the Vicon Plug-In-Gait model and software[29]. Thereafter, marker and model data was filtered using a zero lag, fourth-order low-pass Butterworth filter (cut-off frequency 20 Hz). Instants of heel strike and toe-off were identified using the markers on both feet as described by Zeni et al.[30]. Midstance was defined at 50% between heel strike and toe off.

The primary outcome measure for walking was gait speed. Secondary outcome measures included spatiotemporal parameters, joint kinematics and kinetics, and dynamic balance measures. The first 20 seconds of the 2MWT were excluded from all analyses to remove the starting phase of walking. All outcome measures were averaged over steps between the 20th and 120th second of the 2WMT and calculated for each leg separately. The most affected leg, based on MRC of the dorsal- and plantar flexors, was used for analysis. If no differences were present, the leg was randomly selected.

Gait speed was defined as the mean treadmill speed [m/s]. Step length [cm] and step width [cm] were determined for each step and defined as the AP and ML distance between the heel markers at heel strike, respectively. Step time [s] was defined as the mean time between a heel strike on one side to the subsequent heel strike of the contralateral foot. The standard deviation over all steps was used to calculate the variability of the step length, step time and step width.

Due to placement of the markers on the footwear, not the ankle angle inside the footwear but the angle of the shank relative to the footwear was measured. Kinematics (angles) and kinetics (internal moment and power) between the shank and footwear, and of the knee and hip joints in the sagittal and frontal planes were calculated per gait cycle using the Vicon Plug-In-Gait model and software. Furthermore, the shank-to-vertical angle and the footwear-to-horizontal angle were calculated per gait cycle. The shank-to-vertical angle was defined as the angle between the knee and shank-footwear joint center, and the vertical in the sagittal plane[31], whereas the footwear-to-horizontal was defined as the angle between the toe and heel marker, and the horizontal in the sagittal plane[32]. The shank-to-vertical angle at midstance and the footwear-to-horizontal at heel strike were determined for each gait cycle. Kinetic data were excluded from analysis when the foot had hit both force plates during the stance phase. Range of motion (RoM) [deg] was calculated as the maximal minus the minimum joint angle during one gait cycle. Peak moment [Nm/kg] and peak power [W/

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kg] were defined as the maximum joint moment and power during the stance phase, respectively. Propulsive force was estimated by the propulsive impulse [N/s/kg], which was calculated as the time integral of the positive anterior ground reaction force during the stance phase[33].

Dynamic balance assessment was based on the relation between the CoM or extrapolated center of mass (XCoM) and base of support or the CoP during walking (CoP_w). The CoM was estimated using the average of the four pelvis markers[34]. The XCoM was calculated using the equation proposed by Hof[35]. The CoP_w was calculated using force plate data that was filtered using a zero lag, fourth-order low-pass Butterworth filter (cut-off frequency 20 Hz). A continuous CoP_w signal was obtained by the weighted average of the CoP_w values derived from both force plates[36].

As a measure of dynamic balance, we calculated the XCoM-CoP_{ML} [cm], which is the shortest distance between the XCoM and CoP at the instant of heel strike in the ML direction[37]. Lower values indicate better postural stability during walking. The XCoM-CoP_{ML} was reported to be reliable in previous studies[38].

Statistical analysis

The COP outcomes of the two quiet standing task performances in the same condition (footwear, vision) were averaged into a mean value per condition per subject. Then, a two-way repeated-measures ANOVA (α=0.05) was performed to determine the effects of footwear (orthopedic vs. standardized) and vision (eyes open vs. eyes closed) on the CoP measures. To evaluate walking, paired t-tests (α=0.05) were used to determine the effects of footwear on the group means for gait speed, spatiotemporal parameters, joint kinematics and kinetics, and dynamic balance. Statistical Parametric Mapping (SPM) was performed to assess where in the gait cycle differences between footwear were present for the joint kinematics and kinetics[39].

Results

Participants

Demographics, clinical characteristics, MRC scores and orthopedic footwear features of the 15 participants enrolled in this study are displayed in Table 1. For one patient, no MRC scores were available. Due to missing markers during the 2MWT, kinematic and kinetic parameters could not be calculated for three other participants, whom were therefore excluded from the kinematic and kinetic analyses.

Quiet standing

No main or interaction effect of footwear was found for any outcome measure during quiet standing (Table 2). Higher $vCoP_{st}$, $aCoP_{st}$, and $fCoP_{st}$ values in both the AP and ML directions were found during eyes closed compared to eyes open, irrespective of footwear.

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Table 1. Participants' demographic and clinical characteristics (n=15).

Characteristics	Mean ± SD	Frequency
Age [years]	49.6 ± 14.8	
Sex, male/female		10/5
Height [cm]	179.4 ± 9.8	
Weight [kg]	82.0 ± 17.9	
HMSN disease type, 1/2/4		9/5/1
AOFAS Ankle-Hindfoot Scale score	78 ± 14	
MRC score ankle plantar flexors, 0/1/2/3/4/5*		1/2/7/0/3/1
MRC score ankle dorsal flexors, 0/1/2/3/4/5*		3/1/4/4/1/2
Orthopedic footwear features		
Shaft height, low/mid/high		4/9/2
Heel adjustment, no/beveled/flared		2/11/2
Forefoot apex position, normal/proximal/distal		6/9/0
Use of orthopedic footwear		
Days per week, 0/1/2-3/4-5/6-7		0/0/0/1/14
Hours per day, <1/1-4/4-8/8-12/>12		0/0/0/8/7

HMSN: Hereditary Motor Sensory Neuropathy, AOFAS: American Orthopedic Foot and Ankle Society, MRC: Medical Research Council
* n=14

2-Minute Walk Test

Orthopedic footwear significantly improved gait speed (t(14)=4.1, *P*=.001), step length (t(14)=4.0, *P*=.001), step time (t(14)=-2.9, *P*=.01) and step width (t(14)=-4.2, *P*=.001) compared to standardized footwear (Table 3).

Figure 2 shows the kinematics and kinetics of the shank-footwear, knee and hip joints in the sagittal (Figure 2A) and frontal (Figure 2B) planes during the gait cycle. SPM revealed that the hip showed lower extension moments during loading response (6-7%) and terminal stance (44%) with orthopedic compared to standardized footwear (P=0.002 and P=0.01, respectively). The shank-to-vertical angle was more reclined during terminal swing (91-93%) with orthopedic footwear (P=0.04). During initial contact (1-4%) and terminal swing (93-100%), the footwear-to-horizontal was more in dorsiflexion with orthopedic footwear (P=0.02 and P=0.02, respectively). In the frontal plane, the hip angle showed more adduction during midstance (18-29%) with orthopedic footwear (P=0.01). The shank-footwear showed higher varus moments during loading response (6%, P=0.02) with orthopedic footwear.

Across the gait cycle, orthopedic footwear showed a decrease in shank-footwear RoM in the sagittal plane (t(11)=-2.8, *P*=.02) and an increase in shank-footwear RoM in the frontal plane (t(11)=3.4, *P*=.006).Lower shank-footwear peak power was found for walking with orthopedic footwear (t(11)=-2.8, *P*=0.02). The footwear-to-horizontal angle at heel strike was more in dorsiflexion with orthopedic footwear compared to standardized footwear (t(11)=-4.5, *P*=0.001). No significant differences between footwear conditions were found for any other kinematic or kinetic outcome measure (Table 4).

Table 2. Outcomes of the quiet standing task

	Eyes open			Eyes closed			Shoes		Task		Shoes × Task	
	Orthopedic footwear	Standardized footwear	Mean difference	Orthopedic footwear	Standardized footwear	Mean difference	F	*P*	F	*P*	F	*P*
$aCoP_{st}$ AP [mm]	4.8 ± 1.7	5.4 ± 2.6	-0.5 ± 2.0	9.3 ± 4.6	9.5 ± 3.8	-0.3 ± 3.3	.57	.46	41	<0.001	0.09	.16
$aCoP_{st}$ ML [mm]	3.1 ± 1.7	4.1 ± 2.3	-1.0 ± 1.6	5.2 ± 4.0	6.9 ± 3.8	-1.7 ± 4.0	4.3	0.06	27	<0.001	.7	.42
$vCoP_{st}$ AP [mm/s]	14.7 ± 4.5	17.1 ± 8.5	-2.4 ± 9.0	36.5 ± 19.2	36.9 ± 18.3	-0.4 ± 20.9	.01	.92	33	<0.001	2.3	.16
$vCoP_{st}$ ML [mm/s]	8.1 ± 4.5	10.8 ± 6.8	-2.6 ± 7.2	16.3 ± 13.9	24.6 ± 18.7	-8.3 ± 19.3	2.8	.12	16	0.001	2.2	.15
$fCoP_{st}$ AP [Hz]	0.56 ± 0.12	0.58 ± 0.16	0.58 ± 0.16	0.72 ± 0.21	0.69 ± 0.19	0.02 ± 0.19	.00	.99	15	0.002	1.1	.32
$fCoP_{st}$ ML [Hz]	0.49 ± 0.15	0.48 ± 0.14	0.48 ± 0.14	0.58 ± 0.17	0.57 ± 0.17	0.02 ± 0.24	.04	.85	11	0.005	.00	.97

CoP: center of pressure, aCoP: RMS CoP amplitude, vCoP: RMS CoP velocity, fCoP: mean CoP frequency, AP: anterior-posterior, ML: medial-latera
Bold: significant difference between footwear conditions (*P*<.05)

The XCoM-CoP_{ML} showed no significant difference between orthopedic footwear (11.6 ± 2.3) and standardized footwear (12.2 ± 2.1; t(14)=-1.7, *P*=0.11).

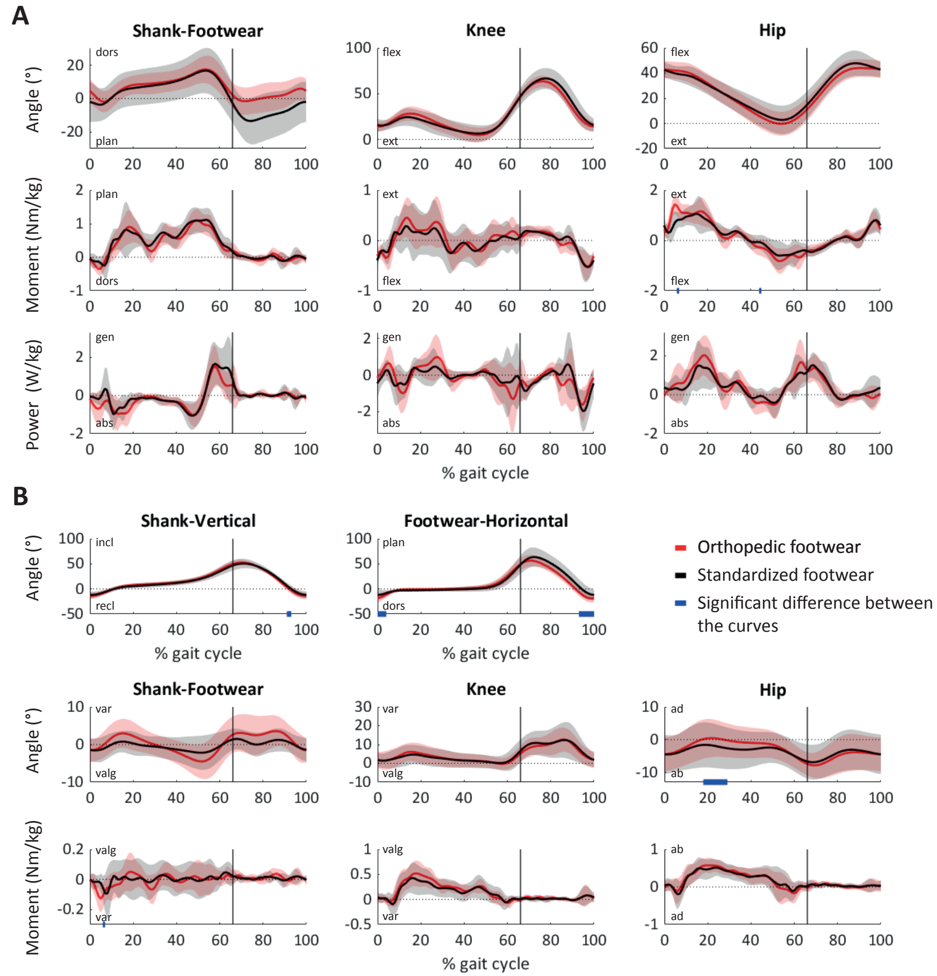

Figure 2. Kinematics (angles) and kinetics (internal joint moment and power) of the 2MWT in the sagittal (A) and frontal (B) planes for orthopedic footwear (red line) and standardized footwear (black line). Lines represent the mean values and shaded areas the standard deviations. Blue horizontal bars on the X-axis indicate differences between the curves.
dors: dorsiflexion, plan: plantar flexion, flex: flexion, ext: extension, gen: generation, abs: absorption, incl: inclination, recl: reclination, var: varus, valg: valgus, ad: adduction, ab: abduction.

Table 3. Spatiotemporal outcomes of the 2MWT

Outcome	Orthopedic footwear	Standardized footwear	Mean difference	*P*
Gait speed [m/s]	1.33 ± 0.28	1.10 ± 0.35	0.23 ± 0.22	**.001**
Step length [cm]	66 ± 13	58 ± 17	8.5 ± 8.2	**.001**
Step time [s]	0.49 ± 0.04	0.52 ± 0.05	-0.03 ± 0.04	**.01**
Step width [cm]	12 ± 3.9	15 ± 4.4	-2.8 ± 2.6	**0.001**
Step-length variability [cm]	31 ± 9.4	38 ± 16	-7 ± 14	0.08
Step-time variability [s]	0.01 ± 0.01	0.03 ± 0.02	-0.01 ± 0.02	0.10
Step-width variability [cm]	33 ± 7.7	36 ± 11	-2.4 ± 7.4	0.23

Bold: significant difference between footwear conditions (*P*<.05)

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Table 4. Kinematic and kinetic outcomes of the 2MWT

Outcome		Orthopedic footwear	Standardized footwear	Mean difference	*P*
Sagittal plane					
Propulsive impulse [N/s/kg]		0.25 ± 0.06	0.22 ± 0.1	0.03 ± 0.07	.16
Ankle	RoM [deg]	24 ± 8.2	33 ± 13	-9.3 ± 11.6	**.02**
	Peak moment [Nm/kg]	1.6 ± 0.5	1.7 ± 0.8	-0.09 ± 0.5	.58
	Peak power [W/kg]	2.6 ± 1.2	3.8 ± 2.0	-1.2 ± 1.5	**.02**
Knee	RoM [deg]	62 ± 6.6	64 ± 7.3	-1.7 ± 5.9	.34
	Peak moment [Nm/kg]	0.9 ± 0.4	0.8 ± 0.4	0.07 ± 0.2	.34
	Peak power [W/kg]	2.6 ± 1.0	2.6 ± 1.5	0.04 ± 1.3	.92
Hip	RoM [deg]	48 ± 4.7	48 ± 8.7	0.16 ± 6.9	.94
	Peak moment [Nm/kg]	1.8 ± 0.4	1.7 ± 0.6	0.19 ± 0.6	.29
	Peak power [W/kg]	3.2 ± 1.1	2.8 ± 1.2	0.39 ± 1.0	.20
Shank-to-vertical angle [deg]		10 ± 3.5	9.4 ± 4.0	0.92 ± 2.4	.21
Foot-to-horizontal angle [deg]		-18 ± 7.1	-13 ± 9.1	-5.4 ± 4.2	**.001**
Frontal plane					
Ankle	RoM [deg]	11 ± 3.5	7.4 ± 3.3	2.8 ± 2.4	**.006**
	Peak moment [Nm/kg]	0.21 ± 0.1	0.22 ± 0.1	0.02 ± 0.1	.74
Knee	RoM [deg]	18 ± 3.6	19 ± 4.6	-1.2 ± 2.3	.37
	Peak moment [Nm/kg]	0.66 ± 0.2	0.63 ± 0.3	0.08 ± 0.1	.55
Hip	RoM [deg]	12 ± 3.7	11 ± 2.8	0.72 ± 2.5	.37
	Peak moment [Nm/kg)]	0.79 ± 0.1	0.76 ± 0.2	0.04 ± 0.1	.50

RoM: range of motion
Bold: significant difference between footwear (*P*<.05)

Discussion

Orthopedic footwear improved stepping, whereas it did not affect postural stability during quiet standing (static balance) or walking (dynamic balance) in individuals with HMSN. More specifically, with orthopedic footwear, walking improved in terms of gait speed and spatiotemporal parameters (increased step length and decreased step time and step width). Interestingly, reduced step width may still indicate some improvement in frontal plane postural stability. Generally, there was a limited impact on gait kinematics or kinetics, but we observed a decrease in sagittal and an increase in frontal shank-footwear RoM, a decreased sagittal shank-footwear peak power, more dorsiflexion of the footwear-to-horizontal angle at initial contact and more hip adduction during the stance phase. Improved heel landing at initial contact for all orthopedic footwear and reduced foot drop during swing for mid and high orthopedic footwear seemed to be the main contributors to gait improvement when wearing orthopedic footwear.

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Compared to healthy controls, individuals with HMSN showed larger values of RMS CoP amplitude and velocity[27]. In line with a previous study, no significant effect of footwear on CoP velocity during quiet standing was found[17], neither with eyes open nor with eyes closed. In contrast with this previous study, we did not find a trade-off between CoP amplitude and frequency in the ML direction, which is probably attributable to the fact that the control condition in the previous study was barefoot instead of using standardized footwear. If a positive effect of footwear was present, it could have been eliminated by the proximal forefoot apex position of most orthopedic footwear, which decreased the base of support and might negatively affect postural stability. As CoP velocity is closely related to the velocity and acceleration of the body's CoM during quiet standing, it seems safe to conclude that orthopedic footwear in people with HMSN has no beneficial effect on static balance compared to standardized footwear.

Individuals with HMSN walked slower on both footwear conditions compared to healthy controls with the same age[38]. Congruent with our hypothesis and in line with the case study by Guzian et al.[8], gait speed and spatiotemporal parameters improved when our subjects with HMSN were walking with orthopedic footwear compared to standardized footwear. Moreover, thirteen out of the fifteen participants showed an increase in gait speed exceeding the minimal clinically important difference (MCID) of 0.10 m/s[40]. The increase in gait speed was due to 10% increase in step length and 6% increase in cadence. Remarkably, the increase in step length was not reflected by an increase in propulsive force nor in sagittal shank-footwear power. Moreover, the sagittal shank-footwear peak power was reduced in orthopedic footwear. Instead, orthopedic footwear decreased the sagittal shank-footwear RoM during the gait cycle compared to standardized footwear, which was caused by reduced plantar flexion during the end of the swing phase and at initial contact (Figure 1). This reduced plantar flexion was also represented by an increased dorsiflexion of the footwear-to-horizontal angle during terminal swing and at initial contact. No clear differences were found in knee or hip kinematics or kinetics in the sagittal plane, nor in the shank-to-vertical angle. Hence, the main effect of orthopedic footwear may be that it enables individuals

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to load the foot properly[41] due to decreased foot drop during initial contact for all orthopedic footwear and during swing for mid and high orthopedic footwear. As a consequence, subjects were able to walk with a heel strike instead of a mid- or forefoot landing, which may have resulted in a more efficient first rocker. This heel contact and improved efficiency of the first rocker has most likely contributed to an increase in both step length and cadence, leading to a higher walking speed.

In addition to improvements in the sagittal plane, orthopedic footwear also caused changes in the frontal plane. Participants wearing orthopedic footwear walked with a 20% (3cm) smaller step width compared to standardized footwear, suggesting improved postural stability in the frontal plane. Yet, the smaller step width did not induce a significant decrease in the distance between the XCoM and CoP at heel strike. Movement of the shank-footwear and hip in the frontal plane was increased when wearing orthopedic footwear, which is probably an epiphenomenon of the smaller step width and the longer step length. When the swing leg is placed closer to the line of progression, the hip is more adducted during midstance. The increased shank-footwear RoM in the frontal plane should be interpreted with caution due to the limitations of the used marker model. The marker model treats the foot as a rigid model, only registering movement of the foot relative to the shank, which includes varus/valgus and foot deformities in the same curve.

A few limitations of this study need to be addressed. Since the markers were placed on the footwear, we did not measure the ankle angle inside the footwear. However, the heel-to-toe drop at the lateral side of the footwear was near zero in both footwear types. This was supported by an almost similar shank-to-vertical angle during the whole gait cycle in both footwear. Therefore, we expect that the ankle kinematics and kinetics will be almost similar to the shank-footwear kinematics and kinetics. Furthermore, the offset ankle angle inside the footwear (i.e. maximum 0.5 cm heel-to-toe-drop results in maximum 2 degrees) is within the measurement error of sagittal joint angles[42]. Another limitation is that participants were not used to walk on the standardized footwear. However, practice trials were performed to familiarize themselves with walking with standardized footwear. The standardized footwear were flat flexible sneakers without any support function minimizing the influence on the walking pattern.

Although orthopedic footwear is commonly prescribed to individuals with balance and gait problems due to HMSN, this is the first study to support its beneficial effects on the gait pattern in a larger group of affected individuals. Unfortunately, our sample size does not allow relating the effects of individual orthopedic footwear features to specific kinematic and kinetic gait characteristics. Therefore, for future research, it is important to relate individual footwear features to specific gait characteristics in people with HMSN using larger sample sizes. Furthermore, other balance and stability measures, like foot placement strategy[43] or reactive balance control[44], could be investigated to assess other dimensions of the gait capacity.

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Chapter 5

Orthopedic footwear has a positive influence on gait adaptability in individuals with Hereditary Motor and Sensory Neuropathy

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Submitted

Abstract

Background: Individuals with Hereditary Motor and Sensory Neuropathy (HMSN) are commonly provided with orthopedic footwear to improve gait. Although orthopedic footwear has shown to improve walking speed and spatiotemporal parameters, its effect on gait adaptability has not been established.
Research question: What is the effect of orthopedic footwear on gait adaptability in individuals with HMSN?
Methods: Fifteen individuals with HMSN performed a precision stepping task on an instrumented treadmill projecting visual targets, while wearing either custom-made orthopedic or standardized footwear (i.e. minimally supportive, flexible sneakers). Primary measure of gait adaptability was the absolute Euclidean distance [mm] between the target center and the middle of the foot (absolute error). Secondary outcomes included the relative and variable error [mm] in both anterior-posterior (AP) and medial-lateral (ML) directions. Dynamic balance was assessed by the prediction of ML foot placement based on the ML center of mass position and velocity, using linear regression. Dynamic balance was primarily determined by foot placement deviation in terms of root mean square error. Another aspect of dynamic balance was foot placement adherence in terms of the coefficient of determination (R^2). Differences between the footwear conditions were analyzed with paired t-tests (α=0.05).
Results: The absolute error, relative error (AP) and variable error (AP and ML) decreased with orthopedic footwear, whereas the relative error in ML-direction slightly increased. As for dynamic balance, no effect on foot placement deviation or adherence was found.
Significance: Gait adaptability improved with orthopedic compared to standardized footwear in people with HMSN, as indicated by improved precision stepping. Dynamic balance, as a possible underlying mechanism, was not affected by orthopedic footwear.

Introduction

Hereditary Motor and Sensory Neuropathy (HMSN) disease is an inherited progressive polyneuropathy that affects the sensory and motor nerves of the peripheral nervous system. HMSN is the most common hereditary neuromuscular disorder and can occur in the myelin structure (type 1) or the axons (type 2) of the peripheral nerves[1]. As a result, there is reduced motor control and sensory loss in the feet and legs[2]. Over time, the weak neural signals to the muscles will cause muscle atrophy and muscle weakness[2], which can result in foot deformities like pes cavus and claw toes[3]. Sensorimotor disturbances and foot deformities together result in low gait speed[4] and increased risk of falling[5], indicating a decreased gait capacity.
Human gait capacity can be described by a tripartite model of 1) stepping, 2) dynamic balance, and 3) gait adaptability[6]. The first aspect (stepping) refers to the cyclical pattern of limb movements during gait. This gait pattern is specified by spatiotemporal parameters and joint kinematics and kinetics. The second aspect (dynamic balance) is defined as the ability to keep the Center-of-Mass (CoM) within the base of support during gait. The third aspect (gait adaptability) refers to the ability to adjust the gait pattern and dynamic balance to changing environmental demands.
Orthopedic footwear is often provided to individuals with HMSN who experience gait impairments[7]. In general, orthopedic footwear aims to accommodate foot deformity and enable plantigrade foot loading. Additional orthotic support may be integrated in the orthopedic footwear to compensate for muscle weakness to further enhance stability in the stance phase and foot clearance in the swing phase. Our research group recently investigated the effects of orthopedic footwear on two aspects of gait capacity: stepping (i.e. spatiotemporal parameters and joint kinematics and kinetics) and dynamic balance (i.e. CoM – Center-of-Pressure (CoP) kinematics)[8]. We found that orthopedic footwear enhanced walking speed and step length, and decreased step width, whereas no effects on dynamic balance could be established compared to standardized footwear. The effect of orthopedic footwear on gait adaptability in people with HMSN has never been investigated.
Hence, in this follow-up study, the aim was to investigate the effects of orthopedic footwear on gait adaptability in individuals with HMSN by assessing the performance on a precision stepping task while walking with either orthopedic or standardized footwear. Dynamic balance control during the precision stepping task was assessed to obtain insight in possible underlying mechanisms of improvement.

Methods

Participants

In total, 15 individuals with HMSN participated in this study. Participants were included if they were 1) between 18 and 80 years old, and 2) used customized orthopedic footwear for a minimum of two months to improve postural stability and/or to prevent falling. Participants were excluded if they were 1) unable to walk independently for 2 minutes, 2) experienced

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pain and/or pressure sores related to the orthopedic footwear, 3) had surgery of the lower extremities less than one year ago, or 4) were diagnosed with other neurological or musculoskeletal disorders influencing the walking pattern.

Demographic information like age, sex, height and weight were registered at inclusion. From the medical records, clinical information (HMSN disease type and Medical Research Council (MRC) Scale scores[9] of the ankle dorsi- and plantarflexors) were extracted.

All participants gave written informed consent in accordance with the Declaration of Helsinki. The study was approved by the internal review board of the Sint Maartenskliniek and the regional medical ethics committee of Arnhem-Nijmegen (2018-4306).

Intervention

All participants brought their custom-made orthopedic footwear to the assessments. This footwear had previously been provided through the outpatient clinic of the Sint Maartenskliniek in close collaboration between the treating physician (orthopedic surgeon or physiatrist) and the orthopedic shoe technician. The orthopedic footwear was molded to the individual foot shape, the insole accommodating the foot deformity while assisting in achieving or maintaining a position of the hindfoot as neutral as possible. Other individual footwear features were prescribed based on clinical characteristics (muscle strength, walking pattern and treatment goal). Common footwear features concerned shaft height, heel adjustment/height and forefoot apex position. Eleven participants wore orthopedic footwear with a shaft height above the ankle joint. Eleven participants had a beveled heel (i.e. posterior edge rounded off), two participants a flared heel (i.e. extended with a lateral flare), while two participants had no heel adjustments. The forefoot apex position was proximal to the metatarsal joints in nine participants and was aligned with the metatarsal joints in six participants.

Assessment

All participants visited the GRAIL (Gait Real-time Analysis Interactive Lab, Motek Medical BV, the Netherlands) of the Sint Maartenskliniek once. The GRAIL is an instrumented dual belt treadmill, equipped with a 10-camera motion capture system (VICON, Oxford, United Kingdom) and two embedded force plates underneath each treadmill belt. Marker position data was collected at a sample frequency of 100 Hz, whereas force plate data was sampled at 1000 Hz.

Before the start of the measurement, functional outcome and pain of the ankle and hindfoot were assessed using the American Orthopedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Scale score[10]. The classification of foot deformity proposed by Louwerens[11] was used to describe the position and flexibility of the first metatarsal and hindfoot.

Afterwards, reflective markers were placed on anatomical landmarks of the participants according to the Plug-In-Gait lower body model, while all foot markers were placed on the footwear. To indicate the anterior border of the footwear, an additional marker was placed at the tip of the footwear anterior to the metatarsal II marker and in line with the metatarsal II and heel marker on the sagittal axis.

Participants first performed a baseline measurement to familiarize themselves with walking on the GRAIL, and to assess spatiotemporal gait parameters during regular walking with orthopedic footwear. After the baseline measurement, participants completed a precision stepping task of two minutes with either orthopedic or standardized footwear (each participant completed both conditions). The order of the footwear was randomized across all participants.

Baseline measurement

During the baseline measurement, participants walked two minutes in a self-paced mode and two minutes at a preferred fixed speed. In the self-pace mode, the speed of the treadmill was automatically controlled by continuously comparing the position of the pelvis to the midline of the treadmill. Walking forward or backward relative to the midline resulted in acceleration or deceleration, respectively. Participants were instructed to walk at a comfortable walking speed for 2 minutes. The mean walking speed over the last 1 minute and 45 seconds was considered as the preferred walking speed. Subsequently, participants walked 2 minutes at this preferred fixed speed to assess step length and step width during regular walking.

Precision stepping task

The precision stepping task lasted two minutes and was performed at the preferred walking speed, determined during the baseline measurement. Rectangular stepping targets (length and width identical to the participant's footwear) were projected on the treadmill. During the task, the stepping targets followed an irregular stepping pattern based on variations in step length and step width as determined during the baseline measurement. The step length varied across -20%, -10%, 0%, +10%, and +20% of the baseline step length, whereas step width varied across -10 cm, 0 cm, and +10cm of two times the baseline step width (Figure 1). Participants were instructed to step as accurately as possible within the borders of the stepping targets. Correct foot placement was defined as the middle of the foot within 5 cm of the target center.

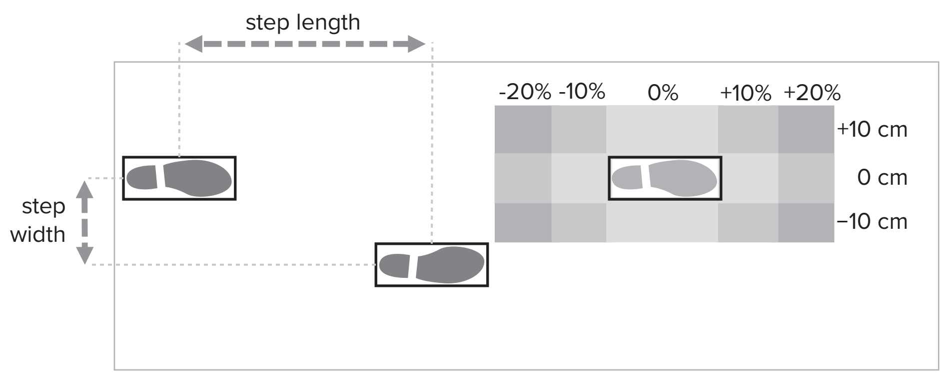

Figure 1. Precision stepping task, with black rectangles following the regular stepping pattern and with shaded rectangles as variation options in anterior-posterior and medial-lateral direction.

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All participants practiced stepping on the stepping targets once for approximately two minutes while they followed their own stepping pattern using the baseline step length and doubled baseline step width. During practicing, participants received real-time feedback regarding the foot placement in relation to the target. When the foot was placed correctly (<5 cm), the target lightened up green and a sound was played. In the case of incorrect foot placement, no sound or light was presented. No feedback was given during the actual precision stepping task.

Data analysis

Marker data were filtered using the Woltring cross-validity quintic spline routine (MSE=20). Subsequently, force plate and filtered marker data were filtered using a zero lag, fourth-order low-pass Butterworth filter with a cut-off frequency of 20 Hz.

Identification of heel strikes and toe-offs was based on the velocity of the foot markers[12]. The instant at which the velocity of the calcaneus marker started moving backwards was defined as a heel strike. Toe off was defined as the instant at which the velocity of the metatarsal II marker started moving forward[12]. Midstance was defined as 50% between heel strike and toe off.

To assess precision stepping performance, the distance between the target center and the middle of the foot at midstance was calculated. The middle of the foot was determined as the mean position of the tip of the footwear and the heel marker. The primary measure of gait adaptability was the absolute error [mm] defined as the absolute Euclidean distance between the target and foot (Figure 2A). Secondary outcomes included the relative error and the variable error. The relative error [mm] was the distance between the target and foot in both anterior-posterior (AP) and medial-lateral (ML) directions (Figure 2B and 2C, respectively). Positive values indicated an overshoot (anterior or lateral to the target), whereas negative values indicated an undershoot (posterior or medial to the target). The variable error [mm] was defined as the within-subject standard deviation of the distance between the target and the foot across steps in both AP and ML directions (Figure 2D and 2E, respectively).

Dynamic balance was assessed by analyzing the relation between the CoM kinematics and the foot placement (FP) in ML-direction (i.e. the foot placement strategy) using linear regression. The ML foot placement was predicted based on the ML CoM position and velocity at heel strike[13,14], using the following formula:

$$FP = \beta_{pos} \cdot COM + \beta_{vel} \cdot \dot{COM} + \varepsilon$$

in which β_{pos} and β_{vel} are the regression coefficients of the CoM position and velocity, respectively, and ε the model error. CoM was estimated using the average of the four pelvis markers[15]. The CoM position was defined with respect to the calcaneus marker of the stance leg at midstance. The CoM position and velocity were demeaned. Foot placement was defined as the demeaned ML distance between the left and right calcaneus markers at midstance.

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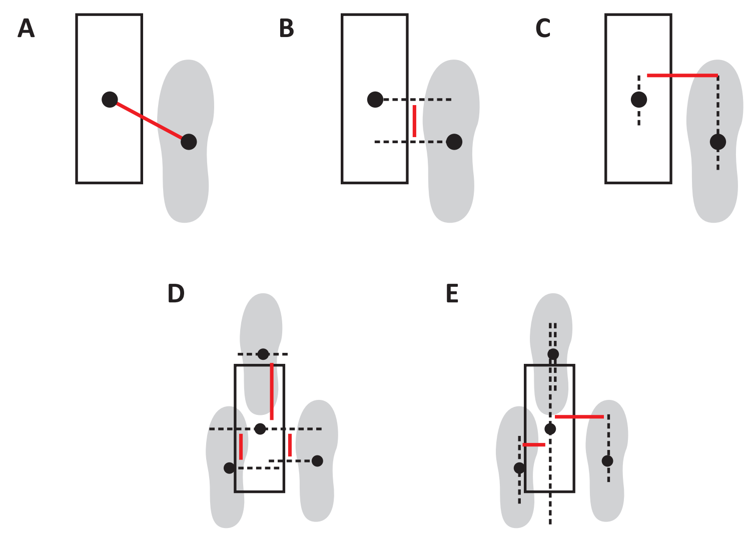

Figure 2. Outcome measures for the precision stepping task. Black rectangles indicate the stepping targets and grey feet, the placement of the foot. The target center and middle of the foot are indicated with black dots. The red lines represent the absolute error (A), relative error in AP-direction (B) and ML-direction (C), and variable error in AP-direction (D) en ML-direction (E).

We primarily determined the root mean square error (RMSE) of the linear regression to assess the accuracy of the foot placement strategy and referred to this measure as foot placement deviation [mm]. To verify adherence to the foot placement strategy, the coefficient of determination (R^2) of the linear regression was calculated and referred to as foot placement adherence. All data processing and analyses were performed using MATLAB 2018b (The MathWorks Inc, Natick, MA, USA).

Statistical analysis

Means and standard deviations of the absolute, relative and variable errors were individually calculated for the left and right leg together. Individual foot placement deviation and adherence were first determined for each leg separately, and then averaged for the left and right leg. To analyze the group differences between both footwear conditions a paired t-test (α=0.05) was performed using MATLAB 2018b (The MathWorks Inc, Natick, MA, USA).

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Results

Participants

Fifteen individuals with HMSN (10 males/5 females) and with an average age of 50 ± 15 years old participated[8]. Their mean height was 179 ± 10 cm and mean weight was 82 ± 18 kg. Nine participants were diagnosed with HMSN disease type 1, five with HMSN disease type 2, and one with HMSN disease type 4h. The mean AOFAS Ankle-Hindfoot scale of all participants was 78 ± 14 points. The MRC-scale scores of the ankle plantar flexors were below 3 for ten participants, 4 for three participants, and 5 for one participants. The MRC-scale scores of the ankle dorsiflexors were below 3 for eight participants, 3 for four participants, 4 for one participant and 5 for two participants.

Gait adaptability

The mean preferred walking speed during the precision stepping task was 0.83 ± 0.22 m/s. A significant difference between footwear conditions was found for the primary outcome measure: absolute error (t(14)=-2.9, *P*=0.01) (Table 1). Furthermore, all secondary outcome measures showed significant differences between footwear conditions: relative error in both AP-direction (t(14)=2.4, *P*=0.03) and ML-direction (t(14)=-2.3, *P*=0.03), and the variable error in both AP-direction (t(14)=-3.2, *P*=0.01) and ML-direction (t(14)=-2.3, *P*=0.04) (Table 1). Remarkably, while the absolute error, relative error (AP) and variable error (AP and ML) decreased with orthopedic footwear, the relative error in the ML-direction slightly increased.

Table 1. Precision stepping task outcomes

Outcome	Orthopedic footwear	Standardized footwear	Mean difference	*p*
Absolute error [mm]	54 ± 22	66 ± 25	-12 ± 16	**0.01**
Relative error AP [mm]	-33 ± 27	-45 ± 25	12 ± 20	**0.03**
Relative error ML [mm]	-18 ± 7.3	-13 ± 8.9	-4.2 ± 7.0	**0.03**
Variable error AP [mm]	35 ± 7.9	43 ± 14	-7.9 ± 9.5	**0.01**
Variable error ML [mm]	26 ± 7.9	33 ± 15	-6.9 ± 12	**0.04**

Bold: significant difference between footwear conditions (p<0.05).

Dynamic balance

The foot placement deviation and adherence did not show significant differences between footwear conditions (Table 2).

Table 2. Dynamic balance outcomes

Outcome	Orthopedic footwear	Standardized footwear	Mean difference	*p*
Foot placement deviation [mm]	29 ± 3.7	31 ± 6.3	-1.4 ± 7.9	0.50
Foot placement adherence	0.71 ± 0.07	0.68 ± 0.10	0.03 ± 0.09	0.23

Bold: significant difference between footwear conditions (p<0.05).

Discussion

Orthopedic footwear improved gait adaptability in individuals with HMSN. The absolute error of foot placement decreased, as well as the relative error in AP-direction and the variable errors in AP- and ML-direction. Only the relative error in ML-direction showed a slight increase. At the same time, no effects on dynamic balance in terms of foot placement deviation or adherence were found with orthopedic footwear.

The mean absolute error of 66 mm with standardized (conventional) footwear as observed in the current study is in line with the stepping error found in individuals with diabetic peripheral neuropathy[16] or with Parkinson's disease[17]. With orthopedic footwear, the mean absolute error improved to 54 mm, which was still higher compared to healthy controls of comparable age (38 mm)[16]. In the literature, the difference in absolute stepping error between individuals with balance problems and healthy controls ranges from 17 to 22 mm[16–19]. Against this background, the improvement of about 12 mm in absolute stepping error with orthopedic compared to standardized footwear as observed in the current study can be considered clinically relevant.

Improvement in absolute error was mainly due to a decrease in relative error in the AP-direction. With orthopedic footwear individuals placed their foot on average 12 mm closer to the target in the AP-direction, while in the ML-direction the foot was placed on average 4 mm more medially to the target. The latter observation may be related to the fact that orthopedic footwear is generally wider than standardized footwear. Consequently, the markers placed at metatarsal II and the anterior border of the orthopedic footwear are placed more medially compared to standardized footwear, resulting in a more medial determination of the position of the middle of the foot compared to standardized footwear. Nevertheless, the variable error in both the AP- and ML-direction was smaller with orthopedic footwear, indicating that foot placement relative to the target was more consistent than with standardized footwear. Together, the smaller relative error in AP-direction and the more consistent foot placement in both AP- en ML-direction demonstrate that individuals with HMSN were able to place their foot more precisely while wearing orthopedic footwear compared to standardized footwear.

In line with our previous study, orthopedic footwear did not affect dynamic balance. The higher foot placement deviation of 30 mm and lower foot placement adherence of around 0.7 compared to healthy controls[13,14,20,21], suggests an impaired foot placement strategy.

The impaired foot placement strategy can most likely be attributed to the sensory impairments of HMSN individuals that are specifically present in the ankles and feet. Accordingly, the sensory information to estimate the state of the CoM and placement of the feet in space during walking is reduced or delayed. Since the interaction between the CoM and CoP was comparable between footwear conditions, orthopedic footwear did not seem to influence the sensory input from the feet.

Some limitations of this study need to be addressed. During the precision stepping task, foot placement was imposed, but earlier research showed that restricted foot placement did not influence foot placement adherence[20]. Furthermore, during precision stepping, multiple stepping targets were visible on the treadmill, giving individuals the opportunity to proactively plan their next steps, which implies that our precision stepping task is not able to assess reactive gait adaptations. Because reactive gait adaptations are also an important aspect of gait adaptability, the effect of orthopedic footwear on reactive gait adaptability should further be investigated.

In conclusion, gait adaptability in people with HMSN improved with orthopedic compared to standardized footwear, as indicated by better precision stepping. This improvement in anticipatory gait adaptability could not be explained by a congruent change of dynamic balance. Therefore, future research should focus on elucidating the underlying mechanisms of improved gait adaptability with orthopedic footwear in HMSN, with the aim to further optimize footwear features and to investigate whether targeted balance and gait training with orthopedic footwear might have additional clinical value.

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Chapter 6

Summary and general discussion

The general aim of this thesis was to investigate the effects of lower limb orthotic devices in individuals with neurological disorders. The first part focused on the assessment of the effects of orthotic devices on gait capacity in general. In the second part, the effects of orthopedic footwear on gait capacity in individuals with Hereditary Motor and Sensory Neuropathy (HMSN) were assessed. This chapter starts with a summary of the main findings, followed by a discussion of theoretical considerations and clinical implications. Directions for future research will close the chapter.

Summary

In the first part of this thesis, measures to assess the effects of orthotic devices on different aspects of gait capacity were evaluated. Adequate orthotic alignment is essential for its efficacy, which is often evaluated by the shank-to-vertical angle (SVA). With the use of an inertial measurement unit (IMU), shank movement can be measured quickly and easily outside a lab setting. Therefore, we investigated the use of an IMU on the shank to determine the SVA in **chapter 2**. In **chapter 2a**, we assessed the validity, inter-rater reliability, and optimal location of a single IMU on the shank to determine the SVA in healthy subjects. Participants were simultaneously recorded with 3D gait analysis and IMUs on two locations on the shank during quiet standing and barefoot walking. The anterior IMU, when anatomically placed in line with the tibial tuberosity and midline of the ankle, showed the best validity and inter-rater reliability for measuring the SVA.

In **chapter 2b**, the anterior IMU was investigated in individuals with incomplete spinal cord injury (iSCI) wearing an AFO to assess its validity and responsiveness to changes in heel height of the AFO-footwear combination (AFO-FC). Additionally, the effects of heel height on knee flexion-extension angle and internal knee moment were evaluated. People with iSCI walked with their own AFO-FC without a heighted heel as well as with a 5 mm and 10 mm heel wedge. Walking was recorded using 3D gait analysis while wearing the anterior IMU on the shank. The SVA measured with the anterior IMU was valid and responsive to changing heel height, and was equivalent to the gold standard 3D gait analysis. The knee flexion-extension angle and internal knee moment showed changes congruent with changing heel height.

Another important aspect of gait capacity in relation to the efficacy of orthotic interventions is dynamic balance. For dynamic balance, multiple outcome measures have been described in the literature, but it remains unclear which outcome measure(s) are most applicable to assess gait capacity in clinical practice. Therefore, in **chapter 3**, the test-retest reliability of six dynamic balance measures was assessed. Individuals with balance problems and healthy subjects performed a two-minute walk test on an instrumented treadmill twice. All dynamic balance measures showed moderate to excellent reliability. However, based on the absence of learning effects and a coefficient of repeatability smaller than the group difference between individuals with balance problems and healthy individuals, two outcome measures seemed most promising: the distance between the extrapolated center of mass (XCoM) and the center of pressure (CoP) at heel strike, and the peak angle of the line connecting the center of mass (CoM) and the CoP with the vertical line passing through the CoP during a gait cycle, both in the medial-lateral direction.

In the second part of this thesis, the effects of orthopedic footwear on the three aspects of gait capacity (stepping, dynamic balance and gait adaptability) were investigated in individuals with HMSN. In **chapter 4**, The effects of orthopedic footwear on postural stability during standing, stepping and regular walking were investigated. Fifteen individuals with HMSN performed a quiet standing task and a two-minute walk test with customized orthopedic footwear and with minimally supportive, flexible and flat footwear (regular footwear). Compared to regular footwear, orthopedic footwear improved stepping in terms of gait speed and spatiotemporal parameters, whereas it did not affect postural stability during quiet standing or regular walking.

In **chapter 5**, the effects of orthopedic footwear on gait adaptability were investigated. The same individuals as in chapter 4 performed a precision stepping tasks with both orthopedic and regular footwear. The participants stepped more precisely and consistently on the targets while wearing orthopedic footwear, which indicated improved proactive gait adaptability. Yet, dynamic balance, as a potential underlying mechanism, was not significantly different between orthopedic footwear and regular footwear.

Discussion

In chapter 2, we assessed the validity, inter-rater reliability and responsiveness to change of an IMU that estimated the SVA. Although, this showed to be a valid and reliable measurement method, the validity and reliability of the SVA itself were not addressed. In chapter 2b, a standard deviation across trials of around 2° was found for the SVA, indicating good test-retest reliability. Nevertheless, the construct validity of the SVA remains ambiguous. Although the SVA is described and used in clinical studies to tune AFOs, it remains unclear to what extent the SVA reflects the construct 'AFO alignment'. Using the outcomes of an IMU in clinical practice can only be sensible if we understand which SVA results in optimal AFO alignment and how this is related to optimal AFO efficacy, i.e. improvement of the gait capacity.

Similarly, the measures described in chapter 3 have been used in healthy subjects and individuals with balance and gait problems to assess the construct 'dynamic balance'. They showed moderate to good test-retest reliability, but how they relate to underlying mechanisms of dynamic balance is unknown. Whether these measures truly reflect dynamic balance and gait capacity in general has never been established. Furthermore, these measures are difficult to interpret, especially when compared to clinical outcome measures. In order to validate and interpret new measures of dynamic balance, they need to be compared to clinical aspects of dynamic balance.

The studies described in chapters 4 and 5 indicated that orthopedic footwear improved both stepping and gait adaptability in people with HMSN. Yet, static and dynamic balance was not influenced by orthopedic footwear. How can this discrepancy be understood? Orthotic devices directly target gait biomechanics, which are important determinants of stepping and gait adaptability. Stepping and (proactive) gait adaptability were assessed at the level of specific task performance. Apparently, orthopedic footwear provides better conditions for effective task performance without affecting the interaction between the CoM and CoP. Further research needs to be conducted to understand this apparent discrepancy.

Ankle-foot impairments in neurological disorders

Individuals with neurological disorders commonly experience gait impairments in daily life[1–4]. They can show a wide range of gait abnormalities (e.g. toe clawing, pes cavus, pes equinovarus, foot drop, knee hyperextension), of which most are not associated with merely one disorder. Different disorders can lead to similar gait impairments (e.g. foot drop in stroke or HMSN), while people with the same disorder can experience different gait impairments. Moreover, not all gait abnormalities are so-called primary deficits that are directly caused by the neurological dysfunction (such as foot drop)[5]. Several abnormalities can be considered secondary (e.g. knee hyperextension coinciding with pes equinus in people with stroke) or compensatory (e.g. increased hip flexion or pelvic tilt for foot drop in people with HMSN or stroke, respectively)[6–9]. Although it is not always easy to disentangle movement abnormalities in individual cases, from a clinical perspective it is essential to discriminate between primary, secondary and compensatory phenomena as precisely as possible to identify the best target(s) for treatment[5]. The most common primary deficits of the lower limb in people with neurological disorders are loss of motor control and muscle imbalance around the ankle and foot, often leading to the clinical picture of pes equinovarus[10–12]. In addition, people with central neurological disorders frequently show signs of concomitant spasticity or dystonia of lower leg muscles that aggravate the muscular imbalance around the ankle and foot. Over time, the risk of muscle or joint contractures in people with neurological disorders is substantial, which may lead to structural equinovarus deformity of the ankle and hindfoot. Together with forefoot deformities (e.g. pes cavus, pes adductus, claw toes) and sensory impairments, which are usually most prominent distally, the ankle-foot complex is an area of great clinical concern in many people with neurological gait impairments.

Treatment options for ankle-foot impairments in neurological disorders

Multiple options are available to treat ankle-foot impairments due to neurological disorders. Orthotic devices can be used to compensate for muscle weakness and counteract excessive muscle activity (e.g. a dynamic AFO) or to redress or accommodate ankle-foot deformities (e.g. a static AFO or orthopedic footwear). As an alternative, foot drop in people with central neurological disorders can be compensated by functional neuromuscular stimulation if there are no contractures or troublesome spasticity leading to ankle-foot deformity[13].

Spasticity or dystonia leading to ankle-foot deformity or impaired voluntary muscle control can be primarily treated with pharmacological interventions like neuromuscular blockade (e.g. intramuscular botulinum toxin injections)[14]. Muscle contractures are primarily treated with intensive stretching exercises or serial casting, but such conservative treatment options are usually more effective in children than in adults[15]. In adults, surgical treatment options (e.g. tendon lengthening, tendon transfer, tenotomy, hindfoot correction and arthrodesis) are often necessary to avoid a life-long dependency on (massive) orthopedic footwear. After adequate treatment of contractures and/or spasticity, remaining muscle weakness and imbalance around the ankle and hindfoot can often be treated with lightweight orthotic devices that can be worn in regular footwear or no orthotic device at all.
The treatment option that is primarily used for each specific type and severity of ankle-foot impairment can be different between clinical sites and is largely determined by daily practice and clinical experience of the treatment team. Our group has recently published two treatment algorithms to support such clinical decision making: one for upper motor neuron syndromes and one for HMSN[11,12]. In the treatment algorithm for upper motor neuron syndrome, a three-step hierarchical approach is proposed to target contractures first, followed by spasticity, and then muscle weakness, entering the next level if treatment is not indicated or successfully addressed at the previous level[11]. In the treatment algorithm for HMSN, a similar hierarchical approach is proposed starting with the treatment of ankle-foot deformities, followed by muscle weakness and sensory impairments[12]. In both treatment algorithms, a three-step strategy is used to select an appropriate intervention. In the case of failure of the other treatments included in the first steps, orthotic devices are considered to accommodate residual ankle-foot deformities or support weakened muscles. Therefore, an orthotic device is an important intervention in all steps of the treatment algorithm.

Optimal orthotic management in neurological disorders

Various types of orthotic devices can be prescribed to individuals with neurological disorders. Each AFO has specific biomechanical characteristics that are typically defined by its design (e.g. hinged or non-hinged, ventral or dorsal shell,) and materials used (e.g. carbon, polypropylene). In turn, the biomechanical principles an AFO is based on can be expressed in terms of mechanical properties (Table 1), such as alignment and stiffness.
The concept of individually optimized ankle stiffness has already been investigated. The effect of AFO stiffness on gait was first described in simulations[17] and in healthy people[18], and later also in individuals with non-spastic calf muscle weakness[19–21]. Based on the walking energy cost, gait speed, and gait kinematics and kinetics, optimal AFO stiffness was determined[20,22]. These studies showed that - on an individual level - optimized AFO stiffness decreased the walking energy cost compared to non-optimized AFOs, as often provided in usual care. However, stiffness-optimized AFOs did not affect gait biomechanics.
Next to stiffness, AFO alignment is an important determinant of AFO efficacy. Multiple studies have shown that so-called ‘tuned AFOs’ result in a more normal gait pattern compared to ‘non-tuned AFOs’[23–28]. AFO tuning focuses on modifying the AFO’s properties to manipulate the vector of the ground reaction force (GRF) in relation to the joint centers,

Table 1. Mechanical properties of an Ankle-Foot Orthosis (AFO)

Determinant	Description
AFO design	Type of AFO, e.g. hinged or non-hinged, ventral or dorsal shell
Ankle stiffness	The moment around the ankle exerted by the AFO per degree of ankle rotation[16]
Footplate stiffness	Stiffness of the AFO around the metatarsal-phalangeal (MTP) joint region
Neutral angle	The configuration (angle between the shell and footplate) of the AFO when no external moment is applied
AFO alignment	Alignment of the ground-reaction force vector in relation to the joint rotation centers

especially the knee joint rotation center[24]. Furthermore, the SVA has been proposed as a parameter of AFO alignment[26]. Both the GRF in relation to the joint centers and the SVA have been specifically addressed during midstance. Generally, the GRF vector should be as close as possible to the knee joint rotation center in both the sagittal and frontal plane, reducing the external joint moments to minimize the need for corrective internal joint moments[24]. For the SVA, an optimum between 10 and 12 degrees has been suggested[26], but clinical studies[29] (including Chapter 2b) have not yet provided conclusive evidence that this SVA range results in an optimal gait pattern. Furthermore, it is unknown if optimal AFO alignment reduces the energy costs of walking.
Optimization of AFO stiffness and alignment seems to be key to effective orthotic management, leading to an optimized gait pattern. From a biomechanical perspective, ‘normalization’ of joint kinematics and kinetics is regarded as an optimal gait pattern, implying that the gait pattern should show joint kinematics and ranging within the normal values obtained from healthy control subjects. However, the relation between such normalized joint kinematics and kinetics and optimization criteria such as walking energy costs and SVA remains unclear[30–32]. Although the Dutch guideline “Beenorthesen bij neuromusculaire aandoeningen”[33] and the above-mentioned algorithms from our research group[11,12] give some directions for optimization of orthotic devices in relation to specific gait impairments, no detailed guidelines for matching mechanical properties with specific patient characteristics are generally accepted.
In comparison to AFOs, even less is known about the optimization of mechanical properties of orthopedic footwear. The effects of different footwear features, such as heel height, shaft height and rocker profile on the postural stability and gait biomechanics have been investigated in healthy people. For instance, elevated heel height seems to decrease postural stability[34], gait speed[35] and stride length[36] and alter knee and ankle kinematics[37,38], whereas a high shoe collar seems to increase stability during standing and walking[39,40]. A more proximal or distal apex position and beveled heel change the application point of the GRF, resulting in altered gait kinematics and kinetics[41,42]. However, a guideline on how to relate gait impairments in people with neurological disorders to specific footwear features is lacking. In Chapter 4, we provided insight in the effects of orthopedic footwear on gait kinematics and kinetics and included a description of the footwear features. Since all

participants walked on both orthopedic and standardized footwear, the altered gait kinematics and kinetics could fairly be attributed to the individual's footwear features. However, more subjects need to be included to reliably assess this relationship.

For all orthotic devices, the optimization criteria that have been proposed are rather technical and often relate to merely one aspect of gait. Especially biomechanical efficacy and minimal energy cost of walking is strived for, whereas clinical efficacy (i.e. daily functioning and patient satisfaction) is just as important. Yet, hardly any studies have addressed the effects of orthotic devices on daily functioning and user satisfaction, even though these aspects are often most relevant to users. In other words, user perspective and preference have not yet been considered as optimization criteria. It is sometimes argued that individual preference may not be in accordance with an 'optimal gait pattern', but ignoring user perspective and preference may increase the risk of non-use of an otherwise 'optimal orthotic device'. Several studies have reported 6-80% non-use of orthotic devices[43–45]. Lack of improvement of gait capacity is certainly not the only factor determining low patient compliance. Lack of comfort, ease of use and cosmetic appearance are probably just as important[46]. By taking into account the user's view on all these factors during the prescription process, the user will feel more in charge of his/her own rehabilitation. Furthermore, the risk of non-use could be determined earlier on in the prescription process. Only when potential users are positive about an orthotic device, further optimization of the design, stiffness and alignment will be cost-effective. With the general emergence of shared decision-making in healthcare, the role of the user in orthotic management needs to be better defined. Regrettably, how user perspective and preference can be integrated in the prescription process of orthotic devices has not yet been investigated.

The optimization of an orthotic device to individual characteristics is only one aspect of the human-device interaction. Human motor control is as important as the technical aspects of the orthotic device. The orthotic device should therefore not only be optimized to an individual's characteristics, but the individual should also be optimally trained to control the device. Indeed, even when the mechanical characteristics of an orthotic device are optimal, its effectiveness will be reduced when the user is not able to control the device properly. Individuals wearing an AFO or orthopedic shoe for the first time usually show no immediate improvement of their gait capacity[47]. Such improvement is generally visible only after a few days or weeks of using the device due to habituation and motor learning. Feedback and training on how to use an orthotic device is therefore crucial to achieve optimal effectiveness. A short bout of gait training directly after delivery of an orthotic device could be a sensible first step in this direction.

One step further is the human-in-the-loop optimization, in which the orthotic device and the individual are optimized in a cyclical process based on their respective performance. In this process, the mechanical properties and alignment of the orthotic device are continuously adjusted to the performance of the user, while the user receives feedback on his/her performance. Especially in the field of exoskeletons[48,49] and lower limb prosthetics[50,51], human-in-the-loop optimization has shown promising results to optimize gait performance. It needs to be investigated whether similar results can be obtained with, for instance, AFOs, and whether such intensive optimization procedures are cost-effective.

Assessment of orthotic efficacy and gait in neurological disorders

Both the orthotic efficacy and the gait capacity / performance should be measured objectively to assess the effectiveness of orthotic devices in people with neurological disorders. A 3D gait analysis at the start of a rehabilitation process is commonly used to assess the individual gait deviations in order to decide which treatment options are indicated. At the end of the rehabilitation process, 3D gait analysis is often repeated to determine the effects of treatment. However, from the perspective of orthotic prescription, more regular assessments should take place during the rehabilitation process to ensure a fruitful interaction between the orthotic device and the human systems. Whether - at every point in time - an extensive assessment like 3D gait analysis is necessary, can be argued, particularly because 3D gait analysis is expensive, time-consuming and restricted to a lab-setting. If just a few parameters are important for the next step in the prescription process, assessment of a small set of gait parameters will be sufficient. Moreover, repeated assessment of a small set of gait parameters will be easier to implement in clinical practice. A good example is the SVA, possibly in combination with the knee angle or GRF in relation to the knee joint rotation center, as a determinant of AFO alignment. The SVA can be assessed with a simple measurement method such as an IMU on the shank, as we have shown in chapter 2. By adding an IMU on the thigh, the knee angle can be measured as well. Furthermore, we can think of a combination of pressure systems and IMUs to estimate the GRF in relation to the knee joint rotation center. Repeated assessment of simple parameters can also be applied as feedback to the users, provided that relevant parameters are monitored in real-time. For instance, feedback of a simple parameter or video can help to show why AFO changes may be necessary in the case of discrepancy between the biomechanical analysis and the user perspective.

An alternative for 3D gait analysis, often used in clinical practice and favored in studies on orthotic alignment, is 2D gait analysis using analogue video cameras. With the addition of a force plate to the 2D video analysis, the GRF vector can be projected onto the video, the so-called force-vector overlay. With dedicated software, the GRF vector can be estimated in relation to the joint centers by playing the video in slow motion. Nevertheless, 2D gait analysis including a force plate still requires a lab setting, which hampers implementation in smaller clinical practices.

2D video analysis without a force plate will be more affordable and realistic for all clinical settings. Although, it cannot provide a force-vector overlay. Furthermore, videos do not necessarily need to be taken with analogue cameras, but can also be captured by a mobile phone or iPad. There are apps specifically developed to add a stick figure or calculate joint kinematics on mobile devices. The accuracy of the so obtained joint kinematics depends on the localization of the joint centers, which is more reliable when joint markers are used. But markerless motion tracking with software like DeepLabCut and OpenPose is upcoming during the last few years. Although markerless motion capture systems yielded similar spatiotemporal parameters compared to 3D gait analysis, the estimation of joint centers and joint angles is not yet sufficiently accurate with 2D analysis[52,53]. Multi-camera motion capture minimizes the projection error present using a single camera, resulting in more

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comparable results to 3D marker-based systems. However, systematic differences in the estimation of joint centers are still present[54]. Moreover, it requires more space and is more expensive, thus less applicable in clinical practice.

A promising method that is applicable outside a lab setting is the use of IMUs (movement sensors). These IMUs have already been implemented in clinical settings to measure spatiotemporal gait parameters and joint kinematics. Even measures of dynamic balance (e.g. margin of stability) can be reliably assessed with IMUs[55]. As we have shown in Chapter 2, IMUs are also able to assess important determinants of orthotic alignment, such as the SVA. However, the SVA alone is not suitable to achieve optimal orthotic alignment, which requires information about the GRF vector in relation to the joint rotation centers as well. IMUs have shown to be able to measure the vertical GRF using biomechanical models or machine learning techniques[56]. Moreover, the first results of tracking the 3D GRF are promising[57,58], but further validation in individuals with gait impairments is needed. By estimating the GRF in relation to the joint rotation centers, three IMUs on the foot, shank and thigh are needed, which will probably increase time with the additional attachment of IMUs and a calibration trial.

Another portable technique that can be used to measure the GRF, are pressure systems like a pressure plate or pressure insoles. A pressure system measures the pressure distribution at the plantar surface of the foot. From this data, also the CoP trajectory and vertical GRF can be estimated. Moreover, using machine learning techniques, the fore-aft component of the GRF can be mapped[59,60].

Overall, analysis of orthotic efficacy and gait performance needs to be quick and easy to be widely implemented in daily clinical practice. Ideally, results are immediately available to be analyzed and interpreted in terms of orthotic alignment, stiffness, and human-device interaction. During AFO tuning, adjustments to the AFO alignment (e.g. by adding a heel wedge) should be immediately assessable to reach an optimum within an acceptable time slot. In addition, certified prosthetists and orthotists (CPOs) need to be able to perform and interpret these assessments. To this aim, additional training of CPOs during or after their regular education is required. Hence, implementation of point-of-care gait analysis during AFO tuning will only be successful if CPOs are properly trained and the assessments can be done within an acceptable spatial and temporal window.

Future perspectives on orthotic devices in neurological disorders

In general, orthotic devices have shown to improve gait capacity in individuals with neurological disorders[61,62]. Even though other treatment options such as serial casting, surgical or pharmacological interventions may be more suitable for some, orthotic devices will remain a widely applied intervention for individuals with residual muscle weakness and/or foot deformities.

Many different types of orthotic devices are available in clinical practice, supporting individuals with neurological disorders in daily life. However, some orthotic devices, especially solid AFOs and high orthopedic footwear, can hamper activities of daily living that require ankle range of motion, like walking the stairs or slopes, squatting, or ground play[62].

Furthermore, restricted ankle range of motion may impede the third rocker and therewith further reducing ankle push-off power, which is usually already reduced in individuals with neurological disorders[63].

A type of AFO that improves ankle push off power is the energy storing AFO (e.g. spring-like AFOs). An energy storing AFO stores energy during the stance phase when the ankle moves towards dorsiflexion while during push off, when the ankle moves towards plantarflexion, the energy is released[64,65]. The release of energy during push off supports ankle push off by increasing ankle moment and ankle power[66]. Although spring-like AFOs allow some ankle movement depending on the bending stiffness, ankle range of motion is still hampered. An AFO overcoming the problem of restricted ankle range of motion is a hinged AFO that allows ankle movement during the stance phase, which results in a more natural tibia progression and knee angle[31,67]. A hinged AFO with spring-like properties may combine the positive effects of increased push off and a natural gait pattern. However, a disadvantage of hinged AFOs is their size, which is why they usually do not fit in regular footwear, which may require the additional use of low orthopedic footwear. Technical developments decreasing the size of hinged AFOs are necessary to prevent the necessity of using additional orthopedic footwear and to improve cosmetic appearance, which will probably increase user compliance. Although spring-like (hinged) AFOs may increase ankle push off power, push off power is not totally restored. To support ankle push off power even more, powered AFOs have been developed providing assistive ankle torque, for instance using external power and electronics. In the last decades, several powered AFO have been developed and tested in a scientific setting, showing an increase in range of motion and power during push off[68,69]. However, powered AFOs are heavy, bulky, and expensive, which prevents clinical implementation. A next step would be to develop a comprehensive, powered AFO with a built-in energy source that can support natural walking for a substantial amount of time.

Another research field that has been growing in the last few years is the field of soft exoskeletons. Soft exoskeletons aim to provide a lightweight and comfortable solution to restore natural movement, with the advantage that they are relatively cheap, easy to use, and fit in regular footwear. A few soft AFO exoskeletons have been described in literature, showing promising results in healthy subjects and one stroke patient[70,71]. However, to assess the real potential of soft AFO exoskeletons, longitudinal studies including larger samples and individuals with neurological gait impairments should be performed.

To further optimize the effectiveness of orthotic devices, they should be more based on the individual user characteristics, like muscle strength, ankle range of motion, and type of gait deviation. A first step is to investigate how individual characteristics can better be matched to mechanical properties like AFO stiffness and alignment. In the future, an extensive measurement procedure aiming to individually adjust AFO stiffness and alignment, followed by determining its effect on individual gait capacity, is not desirable. Ideally, optimal individual AFO stiffness and alignment should be predicted by an algorithm taking the user's impairments and gait deviations as input parameters. To detect gait deviations, it needs to be determined which measurement tools are most suitable in clinical practice. Currently, we are comparing four measurement methods (i.e. 3D gait analysis, 2D video analysis with

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force vector overlay, markerless motion tracking, and IMUs) for determining AFO alignment, while applying different wedge heights under the forefoot and heel. The ultimate goal is to develop a combined scoring system indicating optimal alignment based on the gait biomechanics.

As described above, the role of the user in the prescription process needs to be better defined as well. Recently, we started a study investigating individual preference as a guidance in the decision-making process for off-the-shelf AFO prescription. In this study we try to assess if individuals are able to choose the AFO that is most suitable for them, immediately at delivery and after a 4-week trial period. Furthermore, we try to gain better insight in the AFO's underlying working mechanisms, i.e. the relation between AFO efficacy and gait biomechanics.

Future research should focus on the development of quick and easy assessments to better evaluate individual characteristics and gait deviations. Furthermore, user preferences should be integrated in these assessments. The ultimate goal is to develop a combined scoring system indicating an optimal orthotic device based on individual gait biomechanics and user preferences.

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Chapter 7

Nederlandse samenvatting

Mensen met neurologische aandoeningen ervaren vaak problemen met lopen. Om deze loopproblemen te verbeteren, worden orthopedische hulpmiddelen zoals enkel-voet orthesen (EVOs) of orthopedisch schoeisel voorgeschreven. Het algemene doel van dit proefschrift was om het effect van orthopedische hulpmiddelen te onderzoeken bij personen met neurologische aandoeningen. Het eerste deel richtte zich op de beoordeling van de effecten van orthopedische hulpmiddelen op de loopvaardigheid in het algemeen. In het tweede deel werden de effecten van orthopedisch schoeisel op de loopvaardigheid bij personen met Hereditaire Motorische en Sensorische Neuropathie (HMSN) onderzocht.

In het eerste deel van dit proefschrift werden diverse maten onderzocht om de effecten van orthopedische hulpmiddelen op het looppatroon te beoordelen. Voor de uitlijning van EVOs is de shank-to-vertical angle (SVA), ook bekend als de tibia-inclinatie hoek, een belangrijke determinant. Met behulp van een bewegingssensor kan de beweging van het onderbeen snel en gemakkelijk - ook buiten een laboratorium – worden gemeten. Daarom onderzochten we in **hoofdstuk 2** het gebruik van een bewegingssensor op het onderbeen om de SVA te bepalen. In **hoofdstuk 2a** hebben we de validiteit, interbeoordelaarbetrouwbaarheid, en optimale locatie van één enkele bewegingssensor op het onderbeen onderzocht voor het bepalen van de SVA bij gezonde proefpersonen. Deelnemers werden gelijktijdig gemeten met 3D gangbeeldanalyse en met twee bewegingssensoren op het de voorzijde (anterieure sensor) en laterale zijde van het onderbeen tijdens stil staan en blootsvoets lopen. De anterieure bewegingssensor, anatomisch geplaatst in lijn met de tuberositas tibiae en het midden van de enkel, toonde de beste validiteit en interbeoordelaarbetrouwbaarheid.
In **hoofdstuk 2b** werd de anterieure bewegingssensor onderzocht bij personen met een incomplete dwarslaesie die een EVO gebruikten. De validiteit en de responsiviteit op verandering in hielhoogte van de EVO-schoen combinatie werden beoordeeld. Bovendien werden de effecten van hielhoogte op de flexie-extensiehoek van de knie en het interne kniemoment geëvalueerd. Mensen met incomplete dwarslaesie liepen zowel met hun eigen EVO-schoen combinatie zonder hielhoogte als met een hielverhoging van 5 en 10 mm. Het lopen werd gelijktijdig geregistreerd met de anterieure bewegingssensor op het onderbeen en met 3D gangbeeldanalyse. De SVA gemeten met de anterieure bewegingssensor was valide, reageerde op veranderende hielhoogte, en bleek gelijkwaardig aan de SVA bepaald middels de gouden standaard (3D gangbeeldanalyse). De flexie-extensie hoek van de knie en het interne kniemoment toonden veranderingen overeenkomend met de veranderende hielhoogte.
Een ander belangrijk aspect van de loopvaardigheid in relatie tot de effectiviteit van orthopedische interventies is dynamische balans. Voor dynamische balans zijn meerdere uitkomstmaten beschreven in de literatuur, maar het blijft nog onduidelijk welke uitkomstmaten het meeste inzicht geven. Daarom werd in **hoofdstuk 3** de test-hertest betrouwbaarheid van zes dynamische balansmaten beoordeeld. Personen met evenwichtsproblemen en gezonde proefpersonen voerden tweemaal een twee-minuten wandeltest uit op een geïnstrumenteerde loopband. Alle dynamische balansmaten vertoonden een

matige tot uitstekende betrouwbaarheid. Echter, gebaseerd op de afwezigheid van leereffecten en een herhaalbaarheidscoëfficiënt kleiner dan het groepsverschil tussen individuen met evenwichtsproblemen en gezonde individuen, leken twee uitkomstmaten het meest veelbelovend: de afstand tussen het geëxtrapoleerde massamiddelpunt (XCoM) en het aangrijpingspunt van de grondreactiekracht (center of pressure, CoP) bij hielcontact, en de piekhoek tussen de lijn die het massamiddelpunt (CoM) verbindt met de CoP en de verticale lijn die door het CoP gaat tijdens de gehele gangcyclus, beide in de medio-laterale richting.

In het tweede deel van dit proefschrift werden de effecten van orthopedisch schoeisel op de drie aspecten van de loopvaardigheid (stappen, dynamische balans en loopaanpassingsvermogen) onderzocht bij personen met HMSN. De effecten van orthopedisch schoeisel op de stabiliteit tijdens staan en lopen werden onderzocht in **hoofdstuk 4**. Vijftien personen met HMSN voerden een sta-taak en een twee-minuten wandeltest uit met op maat gemaakt orthopedisch schoeisel en met minimaal ondersteunend, flexibel en plat schoeisel (regulier schoeisel). Vergeleken met regulier schoeisel verbeterde orthopedisch schoeisel het lopen in termen van loopsnelheid en spatiotemporele parameters, terwijl het geen invloed had op de stabiliteit tijdens staan of lopen (dynamische balans).
In **hoofdstuk 5** werden de effecten van orthopedisch schoeisel op het loopaanpassingsvermogen onderzocht. Dezelfde personen als in hoofdstuk 4 voerden een precisiestaptaak uit met zowel orthopedisch als regulier schoeisel. Met orthopedisch schoeisel stapten de deelnemers preciezer en consistenter op de doelen, wat wees op een verbeterd loopaanpassingsvermogen. Er was geen verandering in dynamische balans.

Dankwoord

Dankwoord

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Sander, je liet ons vrij om het project zelf vorm te geven, maar op de achtergrond was je altijd op de hoogte. Door jouw klinische blik en manier van schrijven zijn alle artikelen en dit boekje naar een hoger niveau getild. Dank hiervoor!

Beste leden van de manuscriptcommissie, prof. Tanck, prof. Harlaar en prof. Houdijk, dank voor het lezen en beoordelen van dit proefschrift. Prof. Swinnen, prof. Bus en dr. den Boer, dank voor jullie deelname aan de oppositie. Jasper, ik denk met veel plezier terug aan het ISPO World congres in Japan!

Ten alle tijden kon ik terugvallen op het GaReC projectteam. Cock, ik heb je leren kennen als een gedreven man met veel aandacht voor de persoon. Met zowel een kritische blik als veel enthousiasme voor het vakgebied wist je altijd de juiste vragen te stellen. Dank voor het vertrouwen om mij aan te nemen bij OIM en de fijne samenwerking die volgde. Garik, of kan ik beter naamgever van het project zeggen?, dank voor al je enthousiasme en interesse in dit onderzoek. We gaan snel weer een biertje drinken! Viola, met jouw scherpe blik en kennis over gangbeeld en hulpmiddelen, konden we voor de inhoud altijd op je terugvallen. Fijn dat je na jouw overstap naar Klimmendaal nog zo betrokken bent gebleven! Peter en Johan, zonder jullie inhoudelijke kennis en ervaring in de paskamer had het onderzoek nooit zo dicht bij de praktijk kunnen staan. Dank voor al jullie input!

Een speciaal bedankje aan alle medeauteurs! Brenda, tijdens mijn stage heb ik veel geleerd over onderzoek doen en de begeleiding van stages. Dank dat ik het artikel over de stabiliteitsmaten mocht publiceren en al je hulp daarbij. Wieneke, wat fijn dat jij de tweede plakker was. Dank voor je hulp en gezelligheid tijdens de metingen en daarbuiten. Bart, heel veel dank voor het ontwikkelen van de staptaak op de GRAIL en al je technische hulp. Viola, Ilse en Marije, dank voor het meedenken en includeren van de deelnemers. Verder hebben de afgelopen jaren meerdere stagiaires mij geholpen bij het uitvoeren van de metingen. Jeske, Evi, Tom, Janneke, Femke, Celine, Esmee, Maaike en Milan, dank voor jullie hulp en gezelligheid!

Alle research collega's in het W-gebouw, bedankt voor de gezellige momenten bij het koffiezetapparaat, de cake van de week, jaarlijkse bingoavond, afdelingsuitjes, kerstdiners en alle andere borrels. Team Reva (Motorisch Functioneren) dank voor de fijne sfeer binnen het team en natuurlijk de gezelligheid tijdens alle congressen en (thema)borrels. Rosanne, ik ben blij dat we nog lang na mijn stage hebben mogen samenwerken en heel wat lol hebben beleefd op de borrels en congressen! Mitchel, wat fijn dat jij de extra onderzoeker (of toch mijn slaaf?) werd op het GaReC-project. Dank voor de goede samenwerking en gezelligheid tijdens al de metingen in het lab. Ik hoop dat je het project weer een stap verder kunt brengen! Eline, je bent de perfecte opvolger voor de organisatie van ReCoMe en de borrels. Gelukkig hebben we nog wat (halloween)borrels en congressen kunnen inhalen samen. Laten we het delen van een kamer, inclusief chips en bier in bed, erin houden!
Beste roomies van W0.03, Tim en Maartje, ik kon me geen betere kamergenootjes wensen! Het was altijd een gezellige boel met jullie! Ik kon altijd bij jullie terecht en we hebben genoeg champagne gepopt om onze behaalde doelen te vieren. Gelukkig is in tijden van corona de videokoffie geïntroduceerd en staat die nog wekelijks in de agenda om bij te kletsen.

OIM collega's, dank voor jullie ondersteuning tijdens dit project. In het speciaal OIM Nijmegen, Theo, Femke, Hans en Maarten, dank dat ik jullie mocht lastigvallen met al mijn vragen, het meedenken over de opzet en meehelpen met de inclusie. Afdeling Zorg, Cock, Peter, Johan, Jeroen, Tom, Irma, Marieke en Lotte, dank voor het warme bad waar ik in belandde bij OIM! Ik kijk uit naar onze verdere samenwerking binnen het team, met natuurlijk vis op dinsdag!

Gelukkig was er buiten promoveren om genoeg tijd voor ontspanning! Lieve vrienden en familie, dank voor alle mooie en gezellige momenten die ik met jullie heb mogen beleven!

Wat begon als groepje meisjes in de brugklas is uitgegroeid tot de Rangers, een hechte vriendinnengroep die ik na meer dan 15 jaar niet meer kan missen. Melanie, Iris, Carlijne, Liza, Susan, Elske en Anne, wat ben ik blij om jullie al zo lang om me heen te hebben! Dank voor alle etentjes, borrels, stapavonden, vakanties, dagjes en weekendjes weg. Melanie en Iris, hoe fijn dat ik met jullie, en Thomas natuurlijk, in de Rangercave heb mogen wonen. Dank dat jullie altijd een luisterend oor waren, dat het eten klaar stond, of we samen op de bank konden ploffen met een slechte serie. Inmiddels zijn deze activiteiten na het verhuizen vervangen door wijnproeverijen en mountainbike-middagen. Iris, ik ben blij dat we nog steeds zo dicht bij elkaar wonen, samen sporten, en altijd op de hoogte zijn wat er speelt. Dank dat ik altijd bij je terecht kan! Melanie, al bijna 30 jaar vriendinnen, en ook al woon je in Utrecht, ik heb het gevoel dat je altijd dichtbij bent. Ik ben blij dat je naast me staat als paranimf!

Dat een eerste werkgroep tijdens de opleiding BMW de fijne alumni-vriendengroep zou opleveren, had ik niet durven dromen. Mirre, Paulien, Evi, Majke, Renske, Sjoerd, Bas en Jochem, ik hoop dat we nog vaak een alumni-activiteit, -borrel, -etentje of weekend hebben! Dank voor de fijne sfeer en gezelligheid die altijd aanwezig is als we bij elkaar zijn. Mirre, wat hebben we veel gedeeld in de laatste jaren: samen Nijmegen ontdekken tijdens de introductie, tegelijkertijd promoveren (zelfs inleveren en verdedigen), thuiswerken tijdens corona, zeuren over jongens en daten, biertjes drinken, dansen in de kroeg en lekker op vakantie. Wat fijn dat je mijn paranimf bent!

Hoooooooiiii meiden! Marsha en Michelle, dank voor alle avonden dat ik met de Eetclub weer eens bij jullie mocht aanschuiven. Natuurlijk ook voor alle gezelligheid tijdens onze nachtjes weg en het hoogtepunt: ons tripje naar New York. Heerlijk eten, lekker drinken en veel lachen zijn altijd aanwezig met jullie. Jordy, we waren al vrienden toen jij aan mijn wieg stond en gelukkig is dat nog steeds zo. Dank dat de deur altijd openstaat voor een kop koffie, borrel of hapje eten.

Rosalie en Anouk, wat een leuke vriendschap wel niet kan ontstaan na een weekje Sziget! Op naar nog vele mooie borrelavonden, feestjes, 11/11 en weekendjes. Maarten's vreetzakken, dank voor de gezelligheid op de woensdagavond, in het speciaal tijdens de PR-taarten en Zevenheuvelenetentjes. Jolanda, onze snelle tijd op de zevenheuvelennacht verbeter ik nooit meer! Lieke, van sneeuwbalfeestjes naar huisgenoot, dankjewel voor alle gezellige avonden, vaak met slechte serie, en weekenden in huis. Ik denk met veel plezier terug aan alle corona-zaterdagavonden met baksels, afhaal/bezorg-maaltijden, wijn en bier, spelletjes en pubquizen!

Familie de Jong, jullie hebben ook echt fysiek bijgedragen aan dit boekje. Dankjewel dat jullie proefpersoon wilden zijn. Lieve Wendy, Daan en Rens, wat is het fijn dat jullie zo dichtbij wonen. Ik kijk altijd uit naar onze gezellige uitjes en etentjes! Oma, dankjewel voor alles!

Ik heb lang gedacht dat deze alinea niet nodig zou zijn, maar ben blij dat ik hem voor jou mag schrijven. De laatste loodjes wegen het zwaarst zeggen ze, maar door jouw knuffels en lieve woorden voelden ze een stuk minder zwaar. Lieve Paul, ik weet zeker dat er nog veel mooie dingen gaan gebeuren en kan niet wachten om dit samen met jou te beleven.

Lieve pap en mam, ik kan in woorden niet beschrijven hoe dankbaar ik jullie ben voor alles. Jullie hebben mij altijd gesteund en de ruimte gegeven om te doen wat ik wil. Ook al is dit soms onbekend terrein, jullie waren altijd geïnteresseerd en trots als er een artikel was gepubliceerd of ik een presentatie mocht geven. Ik kan me geen betere ouders wensen!

Curriculum vitae

Curriculum vitae

Lysanne de Jong was born on April 6th 1993 in Oss. After graduating from secondary school in 2011 at the Mondriaan College in Oss, she started the bachelor Biomedical Sciences at the Radboud University in Nijmegen. In 2014, she obtained her bachelor degree and started the master Biomedical Sciences at the Radboud University in the same year. During her masters, with a major in Clinical Human Movement Sciences, she became interested in the field of rehabilitation. Lysanne performed an internship at the University of Sydney, where she investigated the effect of locomotor training on general mobility and quality of life in people with spinal cord injury. During her final internship at the Sint Maartenskliniek, she studied the reliability and responsiveness of stability outcome measures. After her graduation in 2017, Lysanne started as a junior researcher on the Gait Rehabilitation Clinical decision tool (GaReC) project at the Sint Maartenskliniek in close collaboration with OIM Orthopedie. Currently, Lysanne is working as manager Research & Development at OIM Orthopedie.

List of publications

List of publications

This thesis

L.A.F. de Jong, Y.L. Kerkum, V.C. Altmann, A.C.H. Geurts, N.L.W. Keijsers. Effects of orthopedic footwear on postural stability and walking in individuals with Hereditary Motor Sensory Neuropathy. Clin Biomech (Bristol, Avon). 2022 Apr;94:105638. doi: 10.1016/j.clinbiomech.2022.105638.

L.A.F. de Jong, Y.L. Kerkum, T. de Groot, M. Vos-van der Hulst, I.J.W. van Nes, N.L.W. Keijsers. Assessment of the shank-to-vertical angle while changing heel heights using a single inertial measurement unit in individuals with incomplete spinal cord injury wearing an ankle-foot-orthosis. Sensors (Basel). 2021 Feb 2;21(3):985. doi: 10.3390/s21030985.

L.A.F. de Jong, Y.L. Kerkum, W. van Oorschot, N.L.W. Keijsers. A single inertial measurement unit on the shank to assess the shank-to-vertical angle. J Biomech. 2020 Jul 17;108:109895. doi: 10.1016/j.jbiomech.2020.109895.

L.A.F. de Jong, R.B. Van Dijsseldonk, N.L.W. Keijsers, B.E. Groen. Test-retest reliability of stability outcome measures during treadmill walking in patients with balance problems and healthy controls. Gait Posture. 2020 Feb;76:92-97. doi: 10.1016/j.gaitpost.2019.10.033.

Other publications

R.B. Van Dijsseldonk, **L.A.F. De Jong**, B.E. Groen, M. Vos-Van Der Hulst, A.C.H. Geurts, N.L.W. Keijsers. Gait stability training in a virtual environment improves gait and dynamic balance capacity in incomplete spinal cord injury patients. Front Neurol. 2018 Nov 20;9:963. doi: 10.3389/fneur.2018.00963.

J.P. Molenaar, N.C. Voermans, **L.A.F. de Jong**, D.F. Stegeman, J. Doorduin, B.G. van Engelen. Repeatability and reliability of muscle relaxation properties induced by motor cortical stimulation. J Appl Physiol (1985). 2018 Jun 1;124(6):1597-1604. doi: 10.1152/japplphysiol.00455.2017.

C. Quel de Oliveira, K. Refshauge, J. Middleton, **L.A.F. de Jong**, G.M. Davis. Effects of activity-based therapy interventions on mobility, independence, and quality of life for people with spinal cord injuries: a systematic review and meta-analysis. J Neurotrauma. 2017 May 1;34(9):1726-1743. doi: 10.1089/neu.2016.4558.

Conference abstracts (presenter)

L.A.F. de Jong, Y.L. Kerkum, N.L.W. Keijsers. The effect of orthopedic shoes on the gait adaptability in HMSN patients. ISPO World congress, Kobe, 2019 (oral presentation)

L.A.F. de Jong, Y.L. Kerkum, W. van Oorschot, N.L.W. Keijsers. Validity and inter-rater reliability of an inertial measurement unit to assess the shank-to-vertical angle. ISPO World congress, Kobe, 2019 (oral presentation)

L.A.F. de Jong, Y.L. Kerkum, W. van Oorschot, N.L.W. Keijsers. Is an inertial measurement unit valid and reliable for the assessment of the shank-to-vertical angle. ESMAC congress, Amsterdam, 2019 (oral presentation)

L.A.F. de Jong, Y.L. Kerkum, W. van Oorschot, N.L.W. Keijsers. Can an inertial measurement unit assess the shank-to-vertical angle in healthy individuals? ISPGR congress, Edinburgh, 2019 (poster presentation)

L.A.F. de Jong, Y.L. Kerkum. J. Jansens, N.L.W. Keijsers. The use of an inertial measurement unit to assess the shank-to-vertical angle in healthy individuals. RehabMove congress, Groningen, 2018 (poster presentation)

Conference abstracts (other)

L.A.F. de Jong, Y.L. Kerkum, V.C. Altmann, A.C.H. Geurts, N.L.W. Keijsers. Orthopedic footwear improves spatiotemporal gait characteristics and gait adaptability in individuals with Hereditary Motor and Sensory Neuropathy. ISPGR world congress, Montreal, 2022 (poster presentation)

M. Vos-van der Hulst, **L.A.F. de Jong**, T. de Groot, N.L.W. Keijsers. Inertial measurement units to asses shank-to-vertical angle in patients with incomplete spinal cord injury. ISCoS, Virtual, 2020 (poster presentation)

L.A.F. de Jong, R.B. van Dijsseldonk, B.E. Groen, N.L.W. Keijsers. Test-retest reliability of stability outcome measures during walking. Congress on NeuroRehabilitation and Neural Repair (NNR), Maastricht, 2019 (poster presentation).

L.A.F. de Jong, R.B. van Dijsseldonk, B.E. Groen, N.L.W. Keijsers. Test-retest reliability of stability outcome measures during treadmill walking. Congress of International Society of Biomechanics (ISB) and annual meeting of the American Society of Biomechanics (ASB), Calgary, 2019 (poster presentation).

L.A.F. de Jong, N.L.W. Keijsers, R.B. van Dijsseldonk, V.C. Altmann, B.E. Groen. The repeatability of stability outcome measures during treadmill walking in healthy controls and spinal cord injury patients. ESMAC congress, Trondheim, 2017 (oral presentation, nominated for best paper award)

Portfolio

Portfolio

Name PhD student: Lysanne A.F. de Jong
Department: Research (Sint Maartenskliniek)
Graduate School: Donders Graduate School

TRAINING ACTIVITIES	Year(s)	ECTS
Courses and Workshops		
BROK	2018	1.5
GRAIL operator level 1	2018	1
eCiep course	2018	0.66
Project management for PhD candidates	2019	2
(K)EVO Blok II: Orthesiologie bij neuromusculaire aandoeningen	2019	0.66
Donders Graduate School Day	2019, 2020	0.66
Effective Writing Strategies	2019	3
Scientific Integrity course	2019	0.33
The Art of Presenting Science	2019	1.5
Analytic Storytelling	2019	1
Design and Illustration	2020	1
MED-BMS61: Statistical modeling in observational research	2020	3
Loopbaanmanagement voor promovendi	2021	1
The art of finishing up	2021	1
Seminars & Lecturers		
(Inter)national Symposia and Congresses		
Verder in Beweging congres, Sint Maartenskliniek	2017, 2018, 2019, 2021	1
Society for Movement Analysis Laboratories in the Low Lands (SMALLL) congress	2017, 2018, 2019	1.25
International Society for Prosthetics and Orthotics (ISPO) NL congress *	2018, 2020, 2021	1.25
RehabMove congress #	2018	1.25
GRAIL symposium	2019	0.1
International Society of Posture and Gait Research (ISPGR) World congress #	2019	1.5
European Society for Movement Analysis in Adults and Children (ESMAC) congress *	2019	1.25
International Society for Prosthetics and Orthotics (ISPO) World congress*	2019	3

Other		
Refereeravond Revalidatiegeneeskunde Nijmegen-Arnhem-Den Bosch*	2019	0.25
Research lunch Sint Maartenskliniek	2017-2022	2
Journal club Sint Maartenskliniek & Radboudumc	2017-2018	2
Research Content Meeting (ReCoMe) Sint Maartenskliniek	2019-2022	2
Guest speaker webinar	2021	0.25
TEACHING ACTIVITIES		
Supervision of internships		
Supervision of Master student Biomedical Sciences (RU)	2018, 2019, 2021	5
Supervision of Bachelor student Biomedical Sciences (RU)	2019, 2020	3.33
Supervision of student Bewegingstechnologie (Haagse Hogeschool)	2020	2
Supervision of Master student Biomedical engineering (TU Delft)	2021	1.33
Supervision of Master student Human Movement Sciences (VU)	2022	2
Other		
GRAIL demo	2019	0.1
Meet the PhD	2021	0.1
Total		**49,3**

Oral and poster presentations are indicated with a * and # after the name of the activity, respectively

Research data management

Research data management

General information about the data collection

This research followed the applicable laws and ethical guidelines. Research Data Management was conducted according to the FAIR principles. The paragraphs below specify in detail how this was achieved.

Ethics

This thesis is based on the results of human studies, which were conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was given by all participants. All studies met the requirements for exemption from the medical ethics committee review determined by the medical ethics committee on Research Involving Human Subjects region Arnhem-Nijmegen (chapter 2 - dossier number 2018–4647, and chapter 4 & 5 - dossier number 2018-4306), and the medical ethics committee of Slotervaart-Reade (chapter 3 - dossier number P1613/P1614).

The studies described in chapters 2, 4 and 5 of this thesis are part of the GaReC project, which is co-funded by OIM Orthopedie and the PPP Allowance made available by Health ~ Holland, Top Sector Life Sciences & Health, to stimulate public-private partnerships. The study described in chapter 3 did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

FAIR principles

Findable

Data were stored on the server of the research department at the Sint Maartenskliniek: V:\research_reva_studies\797_OIM_onderzoek_algemeen, V:\research_reva_studies\ 721_GRAIL_2MWT, V:\research_reva_studies\827_sensor_drukplaat_GBA, and Y:\research_archief. The paper CRF files were stored at the research department (room W0.28) and will be transferred to the department's archive after publication of the study.

Accessible

All data will be available on reasonable request by contacting the staff
secretary of the research department at the Sint Maartenskliniek (secretariaat.research@maartenskliniek.nl) or the corresponding author.

Interoperable

Documentation was added to the data sets to make the data interpretable. The documentation contains links to publications, references to the location of the data sets and description of the data sets. The data were stored in the following file formats: .mat (MATLAB, Mathworks, USA) and .xlsx (Microsoft Office Excel). No existing data standards were used such as vocabularies, ontologies or thesauri.

Reusable

The data will be saved for at least 15 years after termination of the study concerned. Using these patient data in future research is only possible after a renewed permission by the patients as recorded in their informed consents.

Privacy

The privacy of the participants in this thesis has been warranted using encrypted and unique individual subject codes. The encryption key was stored separately from the research data and was only accessible to members of the project who needed access to it because of their role within the project.

**Donders Graduate School
for Cognitive Neuroscience**

Donders Graduate School for Cognitive Neuroscience

For a successful research Institute, it is vital to train the next generation of young scientists. To achieve this goal, the Donders Institute for Brain, Cognition and Behaviour established the Donders Graduate School for Cognitive Neuroscience (DGCN), which was officially recognised as a national graduate school in 2009. The Graduate School covers training at both Master's and PhD level and provides an excellent educational context fully aligned with the research programme of the Donders Institute.

The school successfully attracts highly talented national and international students in biology, physics, psycholinguistics, psychology, behavioral science, medicine and related disciplines. Selective admission and assessment centers guarantee the enrolment of the best and most motivated students.

The DGCN tracks the career of PhD graduates carefully. More than 50% of PhD alumni show a continuation in academia with postdoc positions at top institutes worldwide, e.g. Stanford University, University of Oxford, University of Cambridge, UCL London, MPI Leipzig, Hanyang University in South Korea, NTNU Norway, University of Illinois, North Western University, Northeastern University in Boston, ETH Zürich, University of Vienna etc.. Positions outside academia spread among the following sectors: specialists in a medical environment, mainly in genetics, geriatrics, psychiatry and neurology. Specialists in a psychological environment, e.g. as specialist in neuropsychology, psychological diagnostics or therapy. Positions in higher education as coordinators or lecturers. A smaller percentage enters business as research consultants, analysts or head of research and development. Fewer graduates stay in a research environment as lab coordinators, technical support or policy advisors. Upcoming possibilities are positions in the IT sector and management position in pharmaceutical industry. In general, the PhDs graduates almost invariably continue with high-quality positions that play an important role in our knowledge economy.

For more information on the DGCN as well as past and upcoming defenses please visit:
http://www.ru.nl/donders/graduate-school/phd/

Theses Sint Maartenskliniek

Theses Sint Maartenskliniek

Mulder, M. (2022). Going off-road. Exploring and mapping psoriatic arthritis. Radboud University Nijmegen, Nijmegen. The Netherlands.
Huiskes, V. (2022). The synergistic role of patients and healthcare providers in reducing drug-related problems. Radboud University Nijmegen, Nijmegen. The Netherlands.
Marsman, D. (2022). Polymyalgia rheumatica. Clinical characteristics and new treatment opportunities. Radboud University Nijmegen, Nijmegen. The Netherlands.
Alingh, J. (2021). Effect of robotic gait training on the post-stroke gait pattern. Evaluation of LOPES II. Radboud University Nijmegen, Nijmegen. The Netherlands.
Van Dijsseldonk, R. (2021). Step into the future: mobility after spinal cord injury.
Radboud University Nijmegen, Nijmegen. The Netherlands.
Pelle, T. (2021). Beating osteoarthritis by e-self management in knee or hip osteoarthritis. Radboud University Nijmegen, Nijmegen. The Netherlands.
Van Heuckelum, M (2020). Novel approaches to improve medication adherence in rheumatoid arthritis. Radboud University Nijmegen, Nijmegen. The Netherlands.
Mathijssen, E. (2020). The voice of patients with rheumatoid arthritis. Radboud University Nijmegen, Nijmegen. The Netherlands.
Bakker, S. (2019). Regional anesthesia and total knee arthroplasty. Anesthetic and pharmacological considerations. Radboud University Nijmegen, Nijmegen. The Netherlands.
Claassen, A. (2019). Strategies for patient education in rheumatic diseases. Radboud University Nijmegen, Nijmegen. The Netherlands.
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Minten, M. (2019). On the role of inflammation and the value of low dose radiation therapy in osteoarthritis. Radboud University Nijmegen, Nijmegen. The Netherlands.
Verhoef, L. (2019). Effective and efficient use of bDMARDs in rheumatoid arthritis. Radboud University Nijmegen, Nijmegen. The Netherlands.
Bekker, C. (2018). Sustainable use of medication. Medication waste and feasibility of redispensing, Utrecht University, Utrecht. The Netherlands.
Bikker, I.(2018). Organizing timely treatment in multi-disciplinary care. University of Twente, The Netherlands.
Bouman, C. (2018). Dose optimisation of biologic DMARDs in rheumatoid arthritis: long-term effects and possible predictors. Radboud University Nijmegen, The Netherlands.
Mahler, E. (2018). Contributors to the management of osteoarthritis. Utrecht University, The Netherlands.
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