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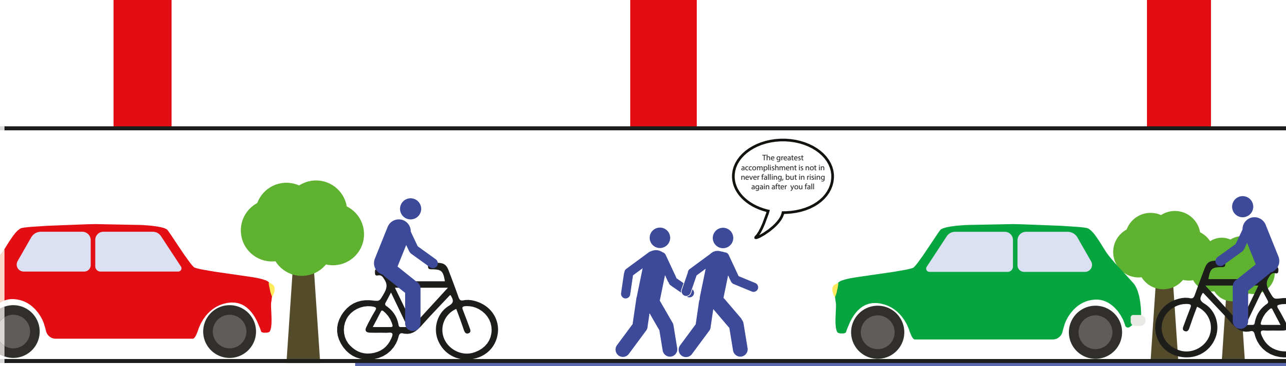
Title: A comprehensive approach to assess walking ability and fall risk using the Interactive Walkway
Issue Date: 2019-05-08



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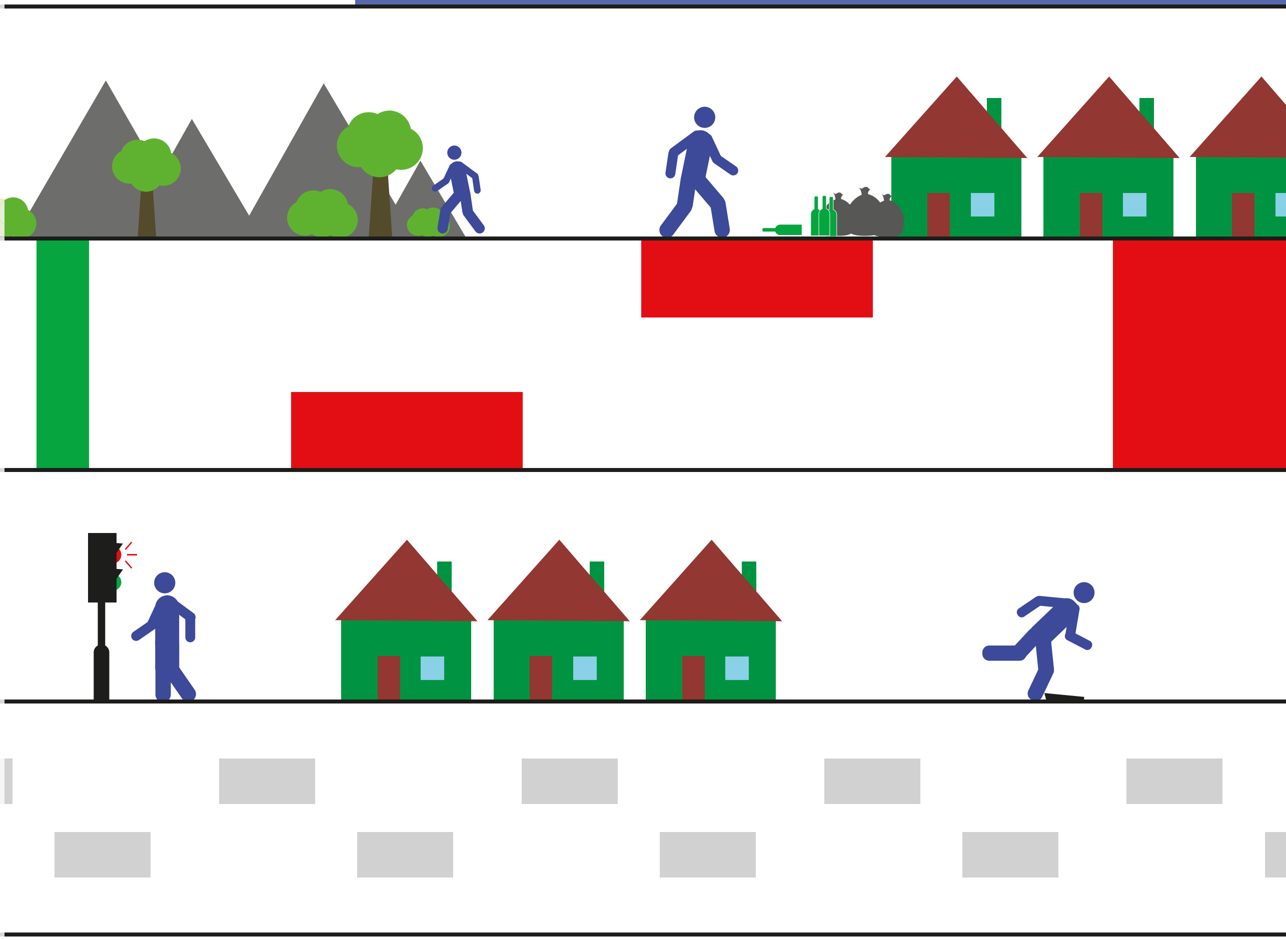

Daphne Geerse

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The research presented in this thesis was part of the research program Technology in Motion (TIM [628.004.001]), which was financed by the Netherlands Organisation for Scientific Research (NWO).

Financial support for this thesis has kindly been provided by the Parkinson Vereniging.

Cover design	Remco Wetzels
Lay-out	Daphne Geerse
Printed by	Ridderprint | www.ridderprint.nl
ISBN	978-94-6375-325-8

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Proefschrift

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
op gezag van Rector Magnificus prof. mr. C.J.J.M. Stolker,
volgens besluit van het College voor Promoties
te verdedigen op woensdag 8 mei 2019
klokke 13:45 uur

door

Daphne Jeane Geerse
geboren te Haarlem
in 1990

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Copromotoren

Dr. J. Marinus

Dr. M. Roerdink (Vrije Universiteit Amsterdam)

Promotiecommissie

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Chapter 1

General introduction

Gait and balance impairments in neurological disorders

Stroke and Parkinson's disease (PD) are two highly prevalent neurological disorders, with estimated prevalence rates in the Netherlands of 3,425 per 100,000 for stroke [1] and 1,350 per 100,000 for PD [2]. These neurological disorders can lead to a great variety of motor and non-motor symptoms [3-5]. Gait and balance impairments are among the most serious motor consequences of these disorders, because they negatively influence the ability to walk and loss of this ability has a significant impact on the quality of life of these patients [6-8]. In addition, fallers seem to experience greater impairments in walking ability compared to non-fallers [9-12]. A thorough insight into gait and balance impairments of patients is thus essential to provide the best treatment for regaining or maintaining their walking ability in order to reduce the risk of falling.

The archetypal gait impairment after stroke is hemiparetic gait, which is characterized by temporal and/or spatial asymmetry [13,14]. In addition, gait impairments in stroke patients often result in slower walking speeds, smaller step lengths, increased step times, reduced cadences and wider steps than healthy controls [15-17]. In PD patients, a different gait pattern is seen. Parkinsonian gait is characterized by a shuffling gait with a stooped posture and reduced arm swing [18]. Compared to healthy controls, slower walking speeds, smaller step lengths and increased cadences have been found [18]. Additionally, PD patients may also suffer from episodic gait impairments, such as freezing of gait (FOG) [6]. The gait impairments listed above can be evaluated objectively using 3D gait analyses. The results of these analyses provide a good understanding of the disease-specific gait impairments and severity of the motor symptoms.

In the clinic, extensive 3D gait analyses are often not performed, mainly due to the costs and time required to conduct the analysis. In contrast, subjectively-scored assessments examining disease-specific motor impairments are often administered. These include, for example, examinations of isolated limb movements with the Fugl-Meyer Assessment in stroke patients or the comprehensive Movement Disorder Society version of the Unified Parkinson's Disease Rating Scale in PD patients. Although these clinical tests provide useful information about the motor symptoms, they fail to reflect their influence on the walking ability of patients and are often time consuming. The most commonly used outcome measure of walking ability in the clinic is walking speed assessed over short distances, for example using the 10-meter walking test. It is a simple and cost effective outcome measure [19] and has been found to be associated with falls [20-25], hospitalization [23,24] and life expectancy [24,25] in older adults. Furthermore, generic gait and balance assessments examining functional mobility and balance outcomes, such as the Timed-Up-and-Go test and the Berg Balance Scale, are also frequently used clinical tests.

Although valuable, quantitative 3D gait analyses and clinical tests do not account for the full repertoire of walking skills needed for safe walking in order to prevent falls [26]. There is thus a need for a more comprehensive assessment of walking ability that incorporates factors directly associated with walking-related fall risk. A more task-specific assessment of walking ability could help identify people at risk of falling as well as help personalize treatments by targeting the identified risk factors.

The tripartite model of walking ability

Walking ability is defined as the ability to walk independently and safely from one place to the other [27]. In order to determine what should be in a comprehensive assessment of walking ability, we need to consider what walking ability entails. The tripartite model [26] is quite instrumental in that regard. This model comprises three overlapping components that are required for independent and safe walking (Figure 1.1). The person needs to be able to 1) generate effective stepping and 2) maintain balance while walking. These two components are often assessed with standard clinical tests, such as the 10-

meter walking test and the Berg Balance Scale. However, people should not only be able to walk safely in fairly simple and predictable environments, but should also be able to modify and adapt walking to both expected and unexpected changes in the environment in order to walk safely in everyday life [28], as reflected in the third component of the tripartite model: walking adaptability. The tripartite model was substantiated by the neural control frameworks put forward by Forssberg [29] and Grillner & Wallen [30], since differential neural control systems underlie walking adaptability and steady-state walking (for a review, see Balasubramanian et al. [26]). The three components of walking ability overlap (Figure 1.1) and the extent to which the various components are involved during walking depends upon the environmental and situational context, which is inherently variable and therefore imposes different demands on walking [27].

Walking adaptability is defined as the ability to modify walking to meet behavioral task goals and demands of the environment [26]. This component was previously described by Patla & Shumway-Cook [27], who proposed a theoretical framework where walking ability is not just the property of the individual to generate stepping and maintain balance, but reflects an interaction between the individual and the environment. Patla & Shumway-Cook [27] defined eight environmental domains that describe the complexity of the situation. Balasubramanian et al. [26], in turn, proposed nine domains, changing some domains of Patla & Shumway-Cook [27] and introducing domains as abilities of the individual to handle these situations. The domains consisted of obstacle negotiation (e.g., stepping over a doorstep), temporal constraints (e.g., walking faster to cross a street), cognitive dual-tasking (e.g., talking while walking), terrain demands (e.g., walking in a forest), ambient demands (e.g., walking in the dark), postural transitions (e.g., turning), motor dual-tasking (e.g., walking while holding a glass), physical load (e.g., walking with a heavy backpack) and maneuvering in traffic (e.g., walking around people in a busy shopping street). The demand on a particular domain and the number of domains involved may vary per environment, which clearly illustrates the challenge of assessing walking ability.

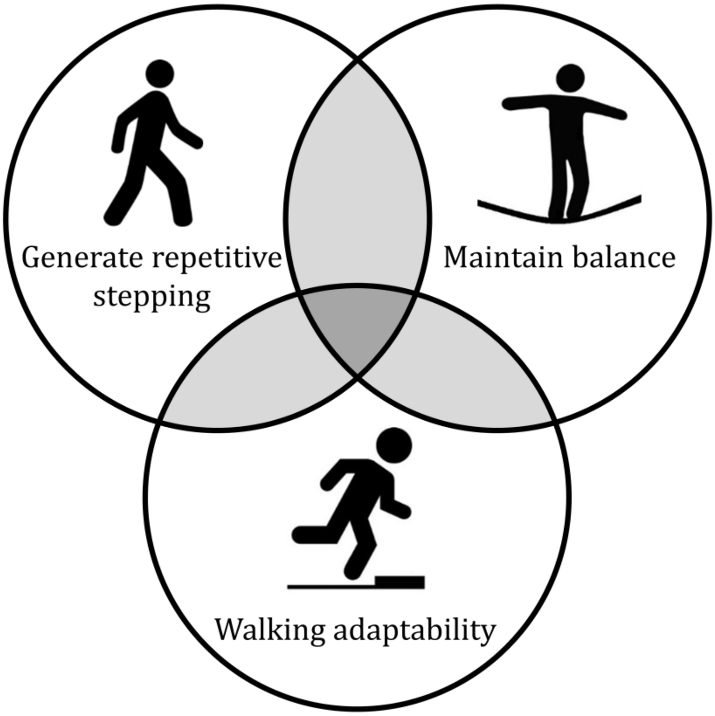

Figure 1.1 Tripartite model of walking ability.

Comprehensive assessment of walking ability

When measuring walking ability in the clinic, there are several points to consider. First, we would like to address all components of the tripartite model to provide a completer picture of a person's walking ability than currently obtained with standard clinical tests. Although good clinical tests assessing stepping and balance already exist, there is currently no good assessment of walking adaptability [26]. Walking-related falls often occur due to trips, slips or misplaced steps [31-35], suggesting that people have problems adapting walking. Walking adaptability therefore seems to be related to fall risk and appears to be an important component of safe walking. Second, for an assessment to be useful in the clinic, there are certain practical requirements that need to be taken into account. Assessments should not take up too much time and should be cheap, easy to use and patient-friendly. Furthermore, while some clinical tests use subjectively scored assessments, objective examinations of motor function are preferred. Nevertheless, the most important point is that a comprehensive assessment provides valid and meaningful information about someone's walking ability. Such an assessment may help physicians and physiotherapists to characterize a person's walking ability, to select the best treatment for a specific person, and to monitor changes in walking ability over time or in response to the selected treatment.

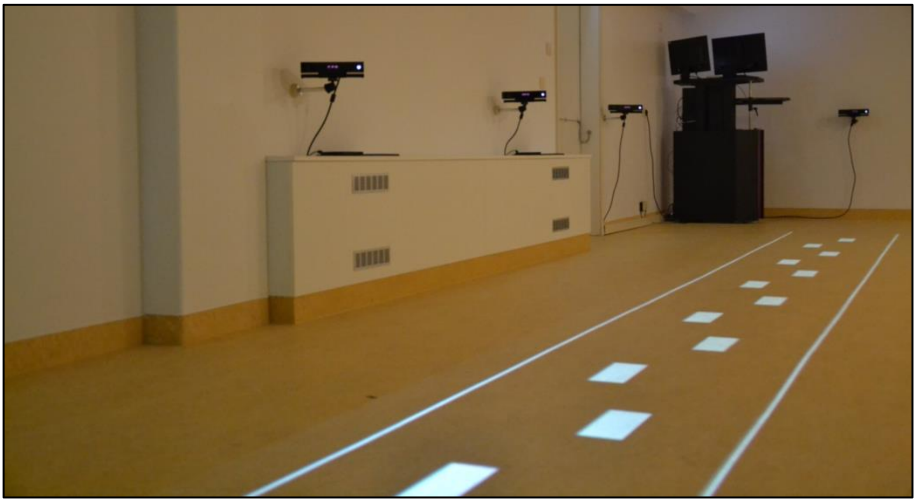

Figure 1.2 The Interactive Walkway with visual context projected onto the walkway.

The Interactive Walkway

The Interactive Walkway (IWW; Figure 1.2; [36]) is a system that may be used to address all components of walking ability and meets all practical requirements mentioned above. With the IWW, a quantitative gait assessment may be performed to gain more insight into gait impairments, which may provide information about the stepping and balance components of walking ability. The IWW is an 8- or 10-meter walkway instrumented with an integrated multi-Kinect v2 set-up for markerless registration of 3D full-body kinematics during walking. This multi-Kinect v2 set-up may be a good alternative for other 3D motion registration systems, since it is patient-friendly, cost-efficient and easy to use. Besides performing quantitative gait assessments, the IWW may also be used to assess walking adaptability. The IWW is equipped with a projector to augment the entire walkway with (gait-dependent) visual context, such as obstacles, sudden-stop-and-start cues and stepping targets. Using the real-time processed integrated Kinect data, obstacles can suddenly appear at the position one would step next, demanding a step adjustment under time pressure demands. The so-elicited gait-environment interactions potentially allow for assessing various walking-adaptability aspects and domains (e.g., the ability to avoid obstacles, suddenly stop or start, perform accurate goal-directed steps) in a safe manner. Taken together, the IWW has great potential to provide a comprehensive assessment of walking ability while fulfilling the practical assessment requirements of being efficient, unobtrusive, patient-friendly, low-cost and objective.

Aims and outline of this thesis

Although the IWW seems promising, it remains still unknown if 1) it can provide a valid assessment of walking ability and, if so, 2) what its clinical potential is for assessing walking ability and fall risk in stroke patients and PD patients. The aim of my thesis is to gain insight into these two aspects.

Part 1: Can the IWW be used for a valid comprehensive assessment of walking ability?

In the next three chapters, studies to validate the IWW are described. In **Chapter 2**, the validity of the IWW for quantitative gait assessments is evaluated in a group of 21 healthy subjects. The 10-meter walking test is conducted at comfortable and maximum walking speed, while 3D full-body kinematics is concurrently recorded with the multi-Kinect v2 set-up of the IWW and a gold-standard motion-registration system. In **Chapter 3** the between-systems agreement and sensitivity to task and subject variations for various walking-adaptability assessments on the IWW is addressed. Under varying task constraints, 21 healthy subjects perform obstacle-avoidance, sudden-stops-and-starts and goal-directed-stepping tasks. Outcome measures are concurrently determined with the IWW and a gold-standard motion-registration system. Based on the insights obtained in these two studies, we performed another validation study, described in **Chapter 4**, with the aim to systematically evaluate the effects of distance to the sensor, body side and step length on estimates of foot placement locations calculated with Kinect's ankle body points in a group of 12 healthy subjects. Estimates of foot placement locations are required to quantify spatial gait parameters and outcome measures of walking adaptability. The results of **Chapters 2 to 4** were used to improve the IWW set-up before it was used to examine the clinical potential of the IWW for assessing walking ability and fall risk in stroke patients and PD patients (**Chapters 5 to 7**).

Part 2: What is the clinical potential of the IWW for assessing walking ability and fall risk?

Stroke and PD are two neurological disorders that are highly prevalent and that have a severe impact on the walking ability of patients. In **Chapter 5**, the potential of the IWW as a new technology for assessing walking ability in stroke patients is evaluated. In total, 30 stroke patients and 30 age- and sex-matched healthy controls perform clinical tests as well as quantitative 3D gait assessments and various walking-adaptability tasks using the IWW. The known-groups validity of the assessments is examined as well as the added value of assessing walking adaptability over standard clinical tests. A similar study evaluating the expected added value of IWW assessments in 30 PD patients is described in **Chapter 6**. Again, the known-groups validity of all assessments is examined. Furthermore, the IWW outcome measures are related to commonly used clinical test scores to indicate their added value. Finally, the added value of IWW outcome measures over clinical tests scores for discriminating PD patients with and without FOG is examined.

The final objective of this thesis is to gain insight into the potential merit of the IWW for assessing fall risk in these patient groups. As indicated above, walking adaptability seems to be an important risk factor for falls, so including it in an assessment would potentially allow for a better identification of (future) fallers. The aim of **Chapter 7** is to evaluate the potential merit of the IWW to identify fallers and risk factors for future falls in a cohort with 30 stroke patient, 30 PD patients and 30 healthy controls. This study comprises subject characteristics, clinical gait and balance tests, a quantitative gait assessment and a walking-adaptability assessment. The results will provide insight into the (relative) importance of stepping, balance and walking adaptability for independent and safe walking. In **Chapter 8** a summary of the main conclusions, a general discussion of the results and suggestions for future research are outlined to further develop the IWW as a comprehensive assessment of walking ability to assess fall risk.

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Chapter 2

Kinematic validation of a multi-Kinect v2 instrumented 10-meter walkway for quantitative gait assessments

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Published in PLoS One 2015;10(10):e0139913

Walking ability is frequently assessed with the 10-meter walking test (10MWT), which may be instrumented with multiple Kinect v2 sensors to complement the typical stopwatch-based time to walk 10 meters with quantitative gait information derived from Kinect's 3D body point's time series. The current study aimed to evaluate a multi-Kinect v2 set-up for quantitative gait assessments during the 10MWT against a gold-standard motion-registration system by determining between-systems agreement for body point's time series, spatiotemporal gait parameters and the time to walk 10 meters. To this end, the 10MWT was conducted at comfortable and maximum walking speed, while 3D full-body kinematics was concurrently recorded with the multi-Kinect v2 set-up and the Optotrak motion-registration system (i.e., the gold standard). Between-systems agreement for body point's time series was assessed with the intraclass correlation coefficient (ICC). Between-systems agreement was similarly determined for the gait parameters walking speed, cadence, step length, stride length, step width, step time, stride time (all obtained for the intermediate 6 meters) and the time to walk 10 meters, complemented by Bland-Altman's bias and limits of agreement. Body point's time series agreed well between the motion-registration systems, particularly so for body points in motion. For both comfortable and maximum walking speeds, the between-systems agreement for the time to walk 10 meters and all gait parameters except step width was high (ICC ≥ 0.888), with negligible biases and narrow limits of agreement. Hence, body point's time series and gait parameters obtained with a multi-Kinect v2 set-up match well with those derived with a gold standard in 3D measurement accuracy. Future studies are recommended to test the clinical utility of the multi-Kinect v2 set-up to automate 10MWT assessments, thereby complementing the time to walk 10 meters with reliable spatiotemporal gait parameters obtained objectively in a quick, unobtrusive and patient-friendly manner.

Introduction

Walking speed is associated with falls [1-3], adverse events [4,5] and life expectancy [6] in older adults. A standardized clinical test often used to assess walking speed is the 10-meter walking test (10MWT). However, the 10MWT only provides a single performance measure (i.e., walking speed derived from the time to walk 10 meters), reflecting just one aspect of walking ability. To yield a more comprehensive evaluation of walking ability, quantitative gait assessments (e.g., step length, cadence and step width) may be conducted using high-end motion-registration systems. Yet, even the best motion-registration systems yield limitations when conducting quantitative gait assessments in clinical settings (e.g., costs, patient-preparation time, calibration procedures, marker occlusion, and delays in availability of results; [7]).

A promising motion-registration system to instrument the 10MWT is the Microsoft Kinect sensor, a RGB-D camera that was launched in 2011 in combination with a Software Development Kit for 3D human-pose estimation, originating from the gaming industry [8]. The development of 3D human-pose estimation software, using a large and highly varied training dataset of paired depth images and ground truth body parts to train very deep decision forests for efficient and accurate body part recognition [8], was a major undertaking by Microsoft. It successfully eliminated the need for markers and calibration procedures, thereby enabling fast and patient-friendly 3D full-body motion registration (Figure 2.1). This motion-registration system has gained enormous interest from developers and scientists in the context of assessment and rehabilitation of balance, posture and gait (e.g., [9-18]), since it allows for motion registration in a quick and affordable manner. Recently, the second generation of the Kinect sensor has been introduced. Key differences with the previous Kinect v1 sensor are that the Kinect v2 sensor is a time-of-flight camera with an increased resolution of the depth image, a wider field of view and improved body point tracking [19], possibly leading to improved results.

Several studies have demonstrated that spatiotemporal gait parameters can be validly obtained using a single Kinect v1 sensor [9,11,13,14,17], and recently also for a single Kinect v2 sensor [15]. However, these studies only analyzed a few steps since accurate body point tracking with the Kinect sensor is only possible between 0.8 and 4.0 meters from the Kinect v1 sensor and between 0.5 and 4.5 meters from the Kinect v2 sensor due to the limited field of view and poorer depth-image quality at greater distances. One way to cover a larger volume, such as the walkway of the 10MWT, is to use multiple spatially and temporally integrated Kinect sensors. Hereby measurement volume may be increased, while preserving good quality depth images for accurate body point tracking. This supposedly allows for the parametrization of a large number of steps during walking from high quality 3D body point's time series. In view of Kinect's v2 higher resolution depth images, improved body point tracking and enlarged area for accurate body point tracking, the current study will explore the potential of a multi-Kinect v2 set-up for instrumenting the 10MWT.

The objective of this study is to determine the usability of a multi-Kinect v2 set-up to quantitatively assess gait during the 10MWT. Because the multi-Kinect v2 set-up has not yet been validated for 3D full-body motion registration, its performance will be compared to a gold standard in 3D measurement accuracy (i.e., the Optotrak active-marker 3D optical tracking system, Northern Digital Inc., Waterloo, Canada). The between-systems agreement will be examined for raw data (i.e., body point's time series) and spatiotemporal gait parameters (e.g., step length, cadence and step width). In addition, the between-systems agreement for the performance measure of the 10MWT (i.e., time to walk 10 meters) will be assessed between the multi-Kinect v2 set-up, the Optotrak motion-registration system (i.e., the gold-standard reference) and the stopwatch (i.e., the clinical standard).

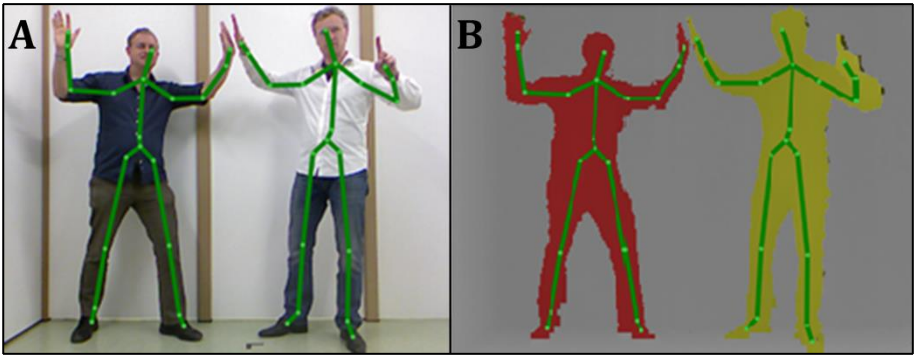

Figure 2.1 RGB image (A) and depth image (B) with the corresponding body points derived with the human-pose estimation software of Kinect v1.

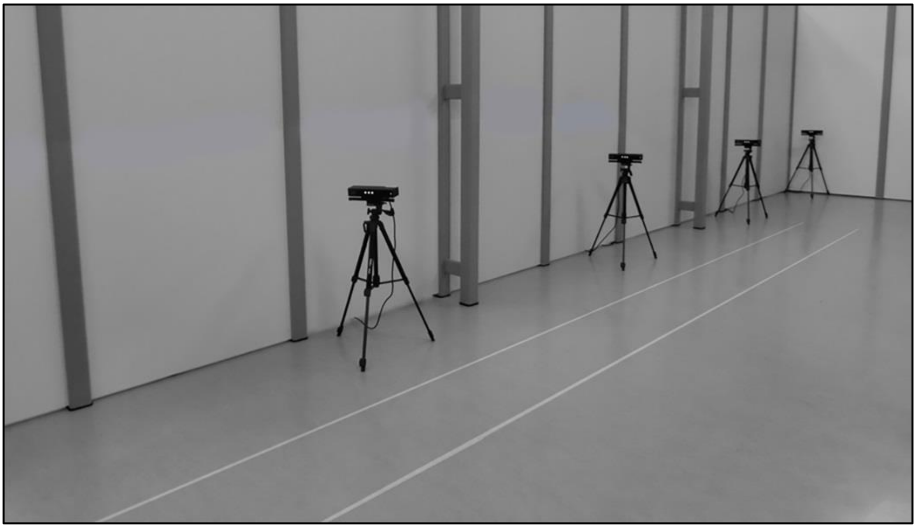

Figure 2.2 Overview of the multi-Kinect v2 set-up.

Methods

Subjects

A heterogeneous group of 21 healthy subjects in terms of gender (11 males, 10 females), age (mean [range]: 30.2 [19-63] years), height (176.1 [158-190] cm) and weight (70.5 [53-83] kg) took part in this experiment. Subjects did not have any medical condition that would influence walking.

Ethics statement

The current study was approved by the ethics committee of the Department of Human Movement Sciences (VU University Amsterdam, Amsterdam). All subjects provided written informed consent prior to participation. The subjects in Figure 2.1 have given written informed consent, as outlined in the PLOS consent form, to publish this photograph.

Experimental set-up and procedure

Full-body kinematics was recorded with four spatially and temporally integrated Microsoft Kinect v2 sensors and the Optotrak system (Northern Digital Inc., Waterloo, Canada). The multi-Kinect v2 set-up is displayed in Figure 2.2. The four Kinect v2 sensors were positioned on tripods alongside a walkway of 10 by 0.5 meters at a height of 0.75 meters. The sensors were placed 0.5 meters from the left border of the walkway with an angle of 70 degrees relative to the walkway direction. The first sensor was positioned at 4 meters from the start of the walkway. The other three sensors were placed at inter-sensor distances of 2.5 meters. In addition, five Optotrak cameras (i.e., a combination of two Optotrak 3020 and three Optotrak Certus cameras, which are all compatible with each other) were positioned around the walkway to cover the same area as the multi-Kinect v2 set-up. The so-obtained Optotrak set-up ensured sub-millimeter accuracy throughout the 10-meter walkway. The coordinate systems of the multi-Kinect v2 set-up and the Optotrak system were aligned using a spatial calibration grid.

The Kinect for Windows Software Development Kit (SDK 2.0, www.microsoft.com) provides, with a sampling rate of 30 Hz, the 3D positions of 25 body points (Figure 2.3B). These body points are: head, neck, spine shoulder, spine mid, spine base and left and right shoulder, elbow, wrist, hand, thumb, hand tip, hip, knee, ankle and foot. For motion registration with the Optotrak system (Northern Digital Inc., Waterloo, Canada, using First Principles data acquisition software with a sampling rate of 60 Hz), subjects were asked to wear tight-fitting shorts and a t-shirt to limit clothing-related marker occlusion. Smart Marker Rigid Bodies (Northern Digital Inc., Waterloo, Canada) were attached to the head, upper arms, forearms, lower abdomen, upper legs, lower legs and feet (Figure 2.3A), allowing for 6 degrees of freedom tracking of body segments. In addition, 30 anatomical landmarks were digitized using a 3-marker digitizing probe to define various body point positions (so-called virtual markers) on abovementioned body segments. Smart markers were also placed on the sternum, hands and feet. The body points represented by Optotrak's virtual markers and/or smart markers were selected to closely match Kinect's body points (see Supplement 2.1), although sometimes arbitrary positional differences between the body point's time series of the two motion-registration systems could not be prevented because 1) the exact definitions of the body points given by the human-pose estimation algorithms of Kinect v2 are not known and 2) virtual markers and smart markers are by definition positioned at the contours of the body while Kinect v2 body points are typically estimated within the body. For example, the smart marker representing Kinect's spine shoulder was placed on the sternum (see Supplement 2.1), which deviates in AP direction from the within-body spine shoulder given by the human-pose estimation algorithm of Kinect v2, thus resulting in a between-systems positional mismatch. Positions of the neck, spine mid, thumbs and hand tips body points were not tracked with the Optotrak system due to the limited number of available smart markers, rendering a total of 19 out of aforementioned 25 body points eligible for a between-systems agreement analysis (as specified in Supplement 2.1).

Before conducting the experiment, the quality of the depth image of the subject was checked since some textiles are known to corrupt the infrared radiation emitted by the previous Kinect v1 sensor, making human-pose estimation less accurate [17]. No problems were encountered with clothing of the subjects, possibly owing to the improved properties of the Kinect v2 sensor. Subsequently, subjects performed the 10MWT at two different walking speeds, namely comfortable walking speed (CWS) and maximum walking speed (MWS). Both conditions were performed three times in a fixed order (i.e., three times CWS followed by three times MWS). Subjects were instructed to start walking at the fourth, high-pitched beep of a standardized auditory start command (i.e., three low-pitched beeps followed by one high-pitched beep) and to continue walking until they had fully crossed the finish line. The standardized auditory start command was synchronized with the multi-Kinect v2 set-up. Synchronization between the two motion-registration systems was achieved by a synchronization movement (i.e., ab- and adduction of both arms) that participants performed prior the auditory start command of each trial. Motion registration started before the synchronization movement and ended well after the subject had passed the 10-meter line. Time to walk 10 meters (i.e., from final beep onset until the moment that the most forward ankle passed the 10-meter line, according to the recommendations of Graham et al. [20]) was determined using a stopwatch. A video showing body point's time series simultaneously for both measurement systems during the 10MWT is available in the supplementary material (see Supplement 2.2). This video also includes the synchronization movement and the standardized auditory start command.

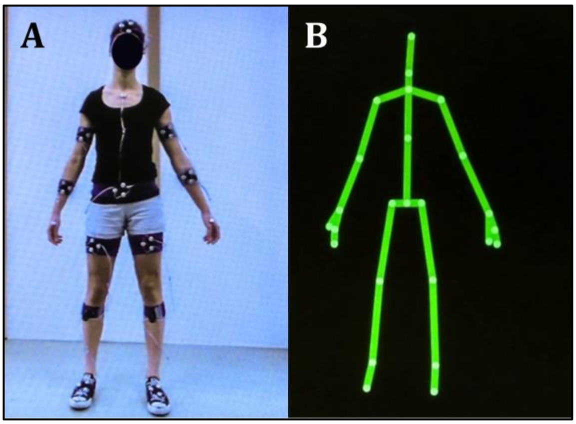

Figure 2.3 Body point determination with the Optotrak and Kinect v2 systems. (A) Subject with all markers of the Optotrak system; (B) Same subject with body points derived with the human-pose estimation algorithm of Kinect v2.

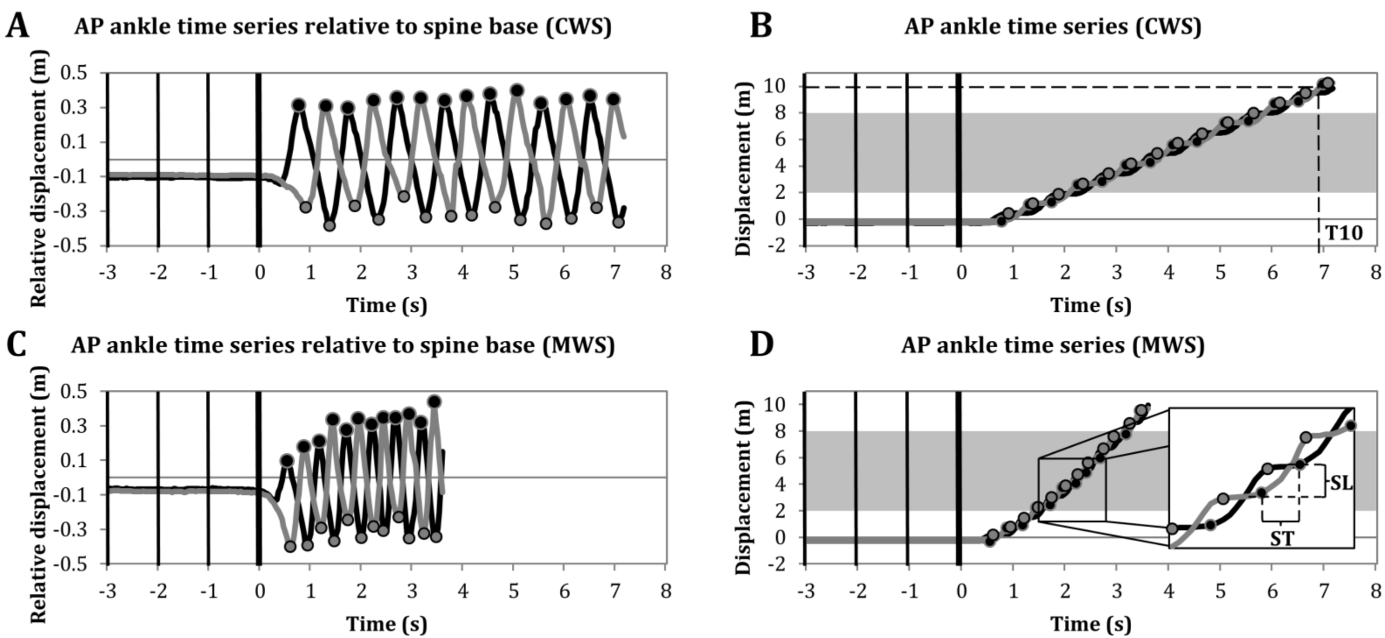

Figure 2.4 Overview of the analysis of spatiotemporal gait parameters. Analyses for comfortable walking speed (CWS; panels A and B) and maximum walking speed (MWS; panels C and D) conditions are based on anterior-posterior (AP) displacement data of the left (black lines) and right (gray lines) ankles as a function of time for the multi-Kinect v2 set-up. AP ankle time series relative to the spine base (panels A and C) were used to estimate instants of foot contact (black dots) and foot off (gray dots) for each step. Step location was defined as the median value of the AP ankle time series during the single-support stance phase (i.e., the horizontal plateaus delimited by foot off and foot contact events of the contralateral foot in panels B and D). Vertical bars represent the four beep onsets of the auditory start command. The shaded area in panels B and D represent the 6-meter window from which spatiotemporal gait parameters were derived. Dashed lines in panels B and D schematically define the time to walk 10 meters (T10), step time (ST) and step length (SL).

Data pre-processing

The 3D positional data of body points were first pre-processed per Kinect sensor separately. Inferred body points (i.e., when a body point was not visible due to for example occlusion, Kinect's human-pose estimation software inferred its position) were considered as missing values. Moreover, since the sampling frequency of the Kinect system is not constant (i.e., apart from 20 outliers in inter-sample intervals for multiple subjects but confined to one Kinect sensor, the remaining inter-sample intervals ranged from 32 to 34 ms), the body point's time series were linearly interpolated using Kinect's timestamps to ensure a constant sampling frequency of 30 Hz, without filling in the parts with missing values. Data points not adhering to the requirements for valid human-pose estimation (e.g., minimum of 15 tracked body points out of the 25 body points, tracked data points for the head and at least one foot and no outliers in segment lengths) were removed from the time series. Subsequently, data of the four Kinect sensors were combined by taking for each sample the 3D positions of the body points of a validly estimated human pose. If, for a given sample, more than one sensor contained valid human-pose data, the associated body point's 3D positions were averaged for that specific sample. Optotrak data were down-sampled to 30 Hz. Subsequently, the cross-covariance and time lag were determined for paired time series in the mediolateral (ML) and vertical (V) direction of the elbows, wrists and hands during the synchronization movement. These time series were first interpolated with a spline algorithm in case of missing data. The median of the time lags was used to temporally align the time series of the two motion-registration systems. Time-synchronized 3D body point's time series of both systems are presented as supplementary material, starting from final beep onset until the moment that for both systems the most forward ankle passed the 10-meter line (see Supplement 2.3). Body point's time series with more than 50 percent of missing values were excluded from further analyses. No time series were excluded for the multi-Kinect v2 set-up, whereas 17 out of 2,394 time series were excluded for Optotrak, including two time series of the ankles from which gait parameters were derived. The missing values of the remaining data were interpolated with a spline algorithm. The so-obtained time series were used for assessing the between-systems agreement in body point's time series (see *Data analysis*) and for the quantification of several gait parameters, as specified in the next paragraph.

Several gait parameters were calculated from the body point's time series, separately for both measurement systems. The following spatiotemporal gait parameters were all determined for the intermediate 6 meters (i.e., from the 2-meter to the 8-meter line), reducing the effect of gait acceleration and deceleration on the gait parameters [21]. Walking speed (in cm/s) was defined as the distance travelled between the 2-meter and 8-meter line on the walkway divided by the time, using the data of the spine shoulder. For the other gait parameters, estimates of foot contact and foot off were required, stemming from respectively the maxima and minima of the anterior-posterior (AP) time series of the ankles relative to that of the spine base [22] (Figures 2.4A and 2.4C). For spatial gait parameters, first left and right step locations were determined, defined as the median value of the left and right ankle position in the AP and ML direction during the respective single-support stance phases (i.e., between foot off and foot contact of the contralateral foot). Based on these AP and ML step locations, various spatial gait parameters were determined. Step length (in cm) was calculated as the AP difference of consecutive step locations (Figure 2.4D). Stride length (in cm) was calculated as the AP difference of consecutive ipsilateral step locations. Moreover, step width (in cm) was estimated by taking the absolute ML difference of consecutive step locations. Cadence (in steps/min) was calculated from the number of steps in the time interval between the first and last estimate of foot contact. Step time (in s) was calculated as the time interval between two consecutive instants of foot contact (Figure 2.4D). Consequently, stride time (in s) was calculated as the time interval between two consecutive ipsilateral instants of foot contact. For step length, stride length, step width, step time and stride time, median values within the 6-meter window were used as outcome measures per trial since Baldewijns et al. [9] demonstrated superior agreement between registration systems on a per walk basis.

The performance measure of the 10MWT, that is the time to walk 10 meters (in s), was defined as the time from final beep onset until the moment that the most forward ankle passed the 10-meter line (Figure 2.4B). For comparison with the stopwatch score, serving as the clinical reference, the time to walk 10 meters was also determined from data of the multi-Kinect v2 set-up and the Optotrak system, the latter serving as the gold-standard reference.

Data analysis

First, the between-systems agreement was calculated for the body point's time series from final beep onset until the moment that the most forward ankle passed the 10-meter line. For the AP direction, the trend was removed using a bidirectional, second-order Butterworth high-pass filter (cutoff frequency of 0.5 Hz) to reduce the effect of a large within-subject variation (increasing from 0 to 10 meter) on the agreement statistic, which would become arbitrarily high [23]. The agreement between the time series of the two motion-registration systems was calculated for each body point in the AP, ML and V direction by means of the intraclass correlation coefficient for consistency ($ICC_{(C,1)}$; [24]). We selected $ICC_{(C,1)}$ in view of abovementioned somewhat arbitrary between-systems mismatches in body point's time series (see Supplement 2.1). The average $ICC_{(C,1)}$ was constructed over all trials per system, body point and direction for each subject. From these values, the average $ICC_{(C,1)}$ over subjects was calculated for each system, body point and direction, including confidence intervals.

Second, the between-systems agreement for spatiotemporal gait parameters was calculated. Spatiotemporal gait parameters were based on specific within-system time series' features (e.g., minima or maxima, consecutive step locations) and hence less susceptible to arbitrary systematic between-systems positional differences in body point's time series. Therefore, the ICC for absolute agreement ($ICC_{(A,1)}$; [24]) was selected. The agreement in the time to walk 10 meters obtained with the multi-Kinect v2 set-up, the Optotrak system (gold standard) and a stopwatch (clinical standard) was also assessed using $ICC_{(A,1)}$.

In line with Cicchetti [25], we regard ICC values above 0.60 as good and ICC values above 0.75 as excellent. $ICC_{(A,1)}$ values were complemented by mean differences and precision values obtained with a Bland-Altman analysis (i.e., the bias and the limits of agreement, respectively; [26]). Since large differences were expected between CWS and MWS conditions for all gait parameters, leading to large within-subject variation that would arbitrarily inflate the between-systems agreement [23], the agreement for gait parameters and time to walk 10 meters was analyzed separately for both conditions. In line with Flansbjer et al. [27], the average time to walk 10 meters was constructed over the three trials per condition per subject. For the spatiotemporal gait parameters the average was hence also constructed over the three trials per condition per subject. For each condition, at least two trials had to be valid (i.e., less than 50 percent of missing values and, for the time to walk 10 meters, data around the 10-meter line and no error in pressing the stopwatch) in order to compute the average over the trials. This resulted in the exclusion of one subject for further analysis of the between-systems agreement for the time to walk 10 meters for the MWS condition.

Results

Agreement between body point's time series

The agreement ($ICC_{(C,1)}$) between the body point's time series of the multi-Kinect v2 set-up and the gold-standard Optotrak motion-registration system for all 19 matched body points in AP (detrended), ML and V directions are listed in Table 2.1. Apart from the hips, there was a good to excellent agreement in body point's time series between the two motion-registration systems in the

AP direction. Furthermore, all gait parameters were derived from time series with high (i.e., ML time series of the right ankle) or excellent levels of agreement (all other time series), as highlighted in Table 2.1 (bold values). Figure 2.5 shows an example of a part of the AP (detrended) and ML time series of the left and right ankle for the multi-Kinect v2 set-up and the Optotrak system during a CWS trial with corresponding $ICC_{(C,1)}$ values (as well as $ICC_{(A,1)}$ values to illustrate the effect of a systematic between-systems mismatch in body point's time series on ICC values).

Table 2.1 Between-systems agreement ($ICC_{(C,1)}$ with 95% CI) for body point's time series in anterior-posterior (AP; detrended), mediolateral (ML) and vertical (V) directions. Bold values represent agreement for time series from which spatiotemporal gait parameters were derived.

	AP	ML	V
Head	0.736 (0.709-0.762)	0.753 (0.714-0.792)	0.832 (0.801-0.863)
Spine shoulder	**0.777 (0.747-0.808)**	0.744 (0.709-0.780)	0.870 (0.850-0.890)
Spine base	**0.864 (0.852-0.877)**	0.824 (0.797-0.850)	0.790 (0.752-0.828)
Left shoulder	0.746 (0.671-0.821)	0.734 (0.658-0.810)	0.824 (0.740-0.908)
Left elbow	0.917 (0.847-0.987)	0.764 (0.685-0.842)	0.567 (0.488-0.646)
Left wrist	0.970 (0.961-0.980)	0.903 (0.884-0.922)	0.879 (0.853-0.906)
Left hand	0.973 (0.966-0.980)	0.903 (0.882-0.923)	0.900 (0.880-0.921)
Right shoulder	0.787 (0.761-0.813)	0.751 (0.712-0.790)	0.849 (0.813-0.885)
Right elbow	0.936 (0.919-0.953)	0.794 (0.760-0.828)	0.628 (0.569-0.688)
Right wrist	0.939 (0.908-0.971)	0.850 (0.787-0.914)	0.773 (0.711-0.834)
Right hand	0.911 (0.868-0.953)	0.828 (0.763-0.893)	0.693 (0.622-0.763)
Left hip	0.479 (0.418-0.540)	0.736 (0.693-0.779)	0.572 (0.506-0.637)
Left knee	0.942 (0.922-0.963)	0.786 (0.739-0.833)	0.221 (0.152-0.289)
Left ankle	**0.970 (0.955-0.984)**	**0.871 (0.844-0.898)**	0.392 (0.342-0.442)
Left foot	0.923 (0.866-0.980)	0.842 (0.781-0.904)	0.443 (0.396-0.491)
Right hip	0.386 (0.308-0.465)	0.749 (0.709-0.789)	0.616 (0.571-0.661)
Right knee	0.847 (0.804-0.890)	0.587 (0.525-0.650)	0.163 (0.128-0.198)
Right ankle	**0.911 (0.891-0.932)**	**0.744 (0.708-0.781)**	0.198 (0.133-0.262)
Right foot	0.819 (0.786-0.852)	0.685 (0.641-0.729)	0.279 (0.234-0.325)

Abbreviations: $ICC_{(C,1)}$ = intraclass correlation coefficient for consistency; CI = confidence interval.

Agreement of spatiotemporal gait parameters

The agreement statistics of the spatiotemporal gait parameters are presented in Table 2.2. Apart from step width, the between-systems agreement for spatiotemporal gait parameters was excellent for CWS ($ICC_{(A,1)} \geq 0.888$) and MWS ($ICC_{(A,1)} \geq 0.951$) conditions. This was supported by relatively small biases and narrow limits of agreement (Table 2.2). Step width showed a good between-systems agreement (CWS: 0.646, MWS: 0.705) with proportionally higher biases and wider limits of agreement (Table 2.2). Bland-Altman plots for spatiotemporal gait parameters are available in the supplementary material (see Supplement 2.4).

Table 2.2 Mean values, between-subjects standard deviations (SD) and agreement statistics (bias, limits of agreement [95% LoA] and intraclass correlation coefficient for absolute agreement [$ICC_{(A,1)}$]) for spatiotemporal gait parameters of comfortable walking speed (CWS) and maximum walking speed (MWS) conditions.

		Multi-Kinect v2 set-up mean ± SD	**Optotrak system mean ± SD**	**Bias (95% LoA)**	**$ICC_{(A,1)}$**
Walking speed (cm/s)	**CWS**	142.8 ± 11.7	143.9 ± 11.8	1.1 (0.1 2.1)	0.995
	MWS	220.2 ± 32.2	220.8 ± 31.7	0.6 (-1.4 2.6)	0.999
Cadence (steps/min)	**CWS**	115.9 ± 6.2	115.0 ± 5.9	-0.9 (-3.0 1.2)	0.974
	MWS	147.8 ± 21.9	145.7 ± 21.7	-2.1 (-7.4 3.3)	0.988
Step length (cm)	**CWS**	75.5 ± 5.7	75.4 ± 5.7	-0.1 (-1.4 1.2)	0.994
	MWS	92.5 ± 8.0	92.5 ± 7.8	-0.1 (-2.1 2.0)	0.992
Stride length (cm)	**CWS**	151.0 ± 11.3	151.1 ± 11.2	0.1 (-0.7 0.9)	0.999
	MWS	185.6 ± 15.7	185.4 ± 15.6	-0.1 (-1.6 1.4)	0.999
Step width (cm)	**CWS**	11.3 ± 2.1	10.0 ± 3.1	-1.3 (-5.2 2.6)	0.646
	MWS	12.1 ± 2.4	10.6 ± 3.4	-1.5 (-5.2 2.2)	0.705
Step time (s)	**CWS**	0.52 ± 0.03	0.52 ± 0.03	0.01 (-0.02 0.03)	0.888
	MWS	0.42 ± 0.05	0.42 ± 0.05	0.00 (-0.03 0.03)	0.951
Stride time (s)	**CWS**	1.04 ± 0.06	1.05 ± 0.06	0.01 (-0.02 0.04)	0.962
	MWS	0.82 ± 0.09	0.84 ± 0.10	0.01 (-0.02 0.04)	0.979

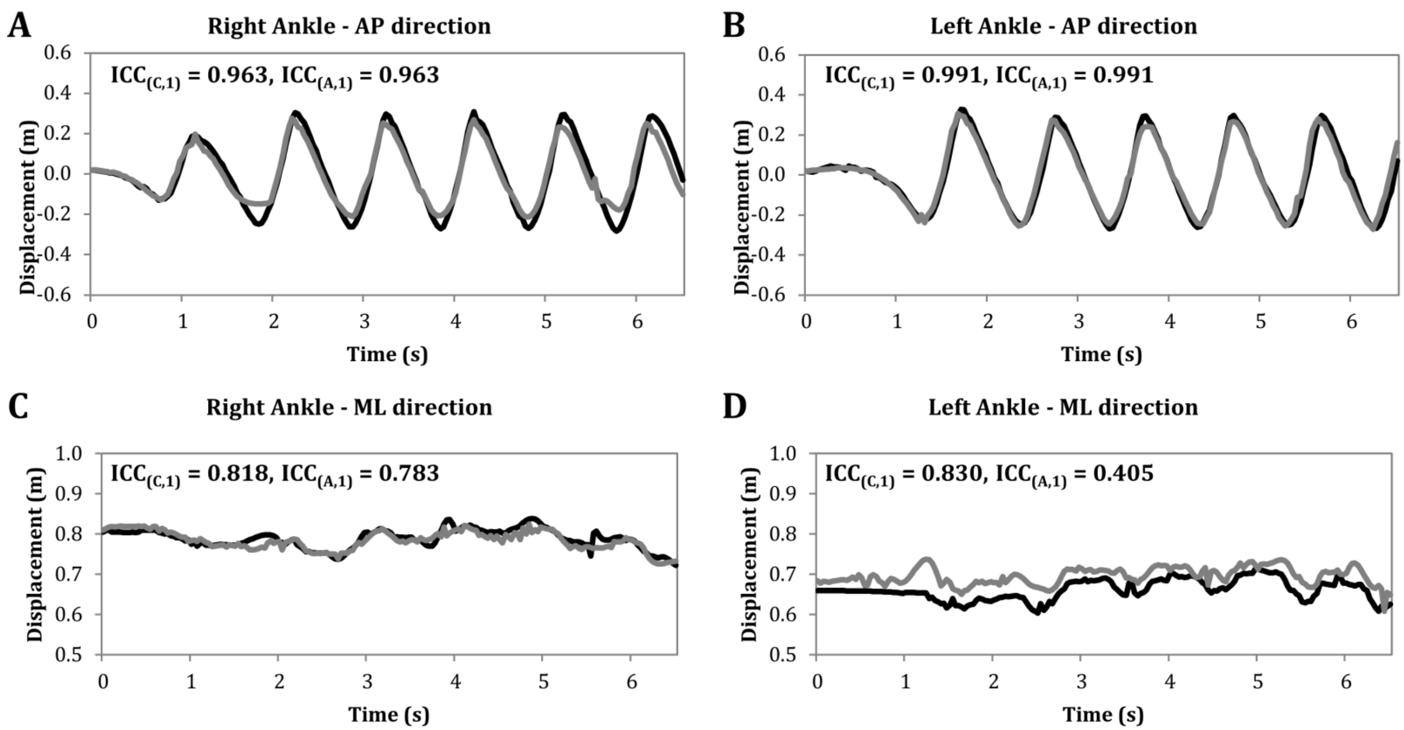

Figure 2.5 Multi-Kinect v2 (gray lines) and Optotrak (black lines) time series of the left (panels B and D) and right (panels A and C) ankle in the anterior-posterior (AP; detrended) and mediolateral (ML) direction for a part of a comfortable walking speed trial, including between-systems agreement assessed with the intraclass correlation coefficient for consistency ($ICC_{(C,1)}$) and absolute agreement ($ICC_{(A,1)}$).

Agreement of time to walk 10 meters

Mean values of the time to walk 10 meters for CWS and MWS conditions are presented in Figure 2.6. There was a high level of agreement between the measurement systems according to the $ICC_{(A,1)}$ for both conditions. For the multi-Kinect v2 set-up and the Optotrak system, $ICC_{(A,1)}$ values were excellent for CWS ($ICC_{(A,1)}$ = 0.998) and MWS ($ICC_{(A,1)}$ = 0.999), with biases being smaller than one sample (CWS: -0.01 s, MWS: -0.01 s) and narrow limits of agreement (CWS: [-0.11 0.09] s, MWS: [-0.07 0.06] s). The comparison between the multi-Kinect v2 set-up and the stopwatch also revealed excellent $ICC_{(A,1)}$ values (CWS: 0.988, MWS: 0.989), but biases were greater (CWS: -0.09 s, MWS: -0.08 s) and limits of agreement wider (CWS: [-0.23 0.05] s, MWS: [-0.21 0.06] s). The same was true for the comparison between the Optotrak system and the stopwatch: excellent $ICC_{(A,1)}$ values (CWS: 0.987, MWS: 0.990) but biases were approximately two samples (CWS: -0.08 s, MWS: -0.07 s) and limits of agreement were again wider (CWS: [-0.26 0.11] s, MWS: [-0.21 0.07] s).

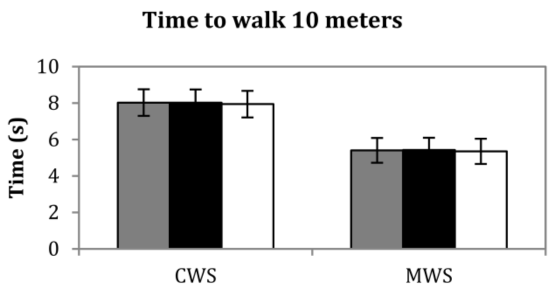

Figure 2.6 Time to walk 10 meters for CWS and MWS conditions. Bars represent average time to walk 10 meters for the multi-Kinect v2 set-up (gray bars), the Optotrak motion-registration system as the gold-standard reference (black bars) and the stopwatch as the clinical standard (white bars).

Discussion

In the current study, we evaluated a multi-Kinect v2 set-up for quantitative gait assessment during the 10MWT by determining between-systems agreement for body point’s time series, for spatiotemporal gait parameters and for the time to walk 10 meters. Performance of the multi-Kinect v2 set-up was compared to the Optotrak system (i.e., the gold-standard reference) to validate 3D full-body kinematical data of the just-released Kinect v2 sensor. We observed a good to excellent agreement between the two motion-registration systems for raw data (i.e., relevant body point's time series), spatiotemporal gait parameters and the time to walk 10 meters.

To the best of our knowledge, this study is the first to statistically compare unfiltered body point's time series stemming from a multi-Kinect v2 set-up to a gold-standard reference. Covering the entire measurement volume with a marker-based motion-registration system was quite difficult and required many cameras to avoid marker occlusion. In fact, the number of excluded body point's time series due to excessive missing values was substantially larger for the marker-based gold standard in 3D measurement accuracy (17 excluded time series, average percentage of missing values was 6.8%) than for the multiple-Kinect v2 set-up (no excluded time series, average percentage of missing values was 5.0%). For the remaining 2377 time series, $ICC_{(C,1)}$ values were generally exceeding 0.60 for all directions, indicating a good to excellent between-systems agreement. Nevertheless, some time series only demonstrated a poor to fair between-systems agreement, especially time series exhibiting a small range of motion. Note that the ICC is constructed using models that assume equal variance between two variables [24]. With a small range of motion (i.e., with low signal power and hence low true within-system variation), the noisier Kinect v2 data may have caused the error-variances of the two motion-registration systems to differ, with consequently a lower between-systems agreement. This is supported by results of a previous study [28], showing that larger movements of Parkinson's disease patients were better tracked by a Kinect v1 sensor than smaller movements. Thus, as long as body points are moving (i.e., high signal power), the resultant time series of Kinect v2 match well with those stemming from a gold standard in 3D measurement accuracy. Furthermore, low-pass filtering time series may also increase the between-systems agreement.

In the current study, all spatiotemporal gait parameters were derived from body point's time series with high (for the ML time series of the right ankle) or excellent levels of agreement (for all other time series; see Table 2.1, bold values). This resulted in excellent between-systems agreement (high $ICC_{(A,1)}$ values) of the from these time series derived spatiotemporal gait parameters walking speed, cadence, step length, stride length, step time and stride time. These spatiotemporal gait parameters can be accurately obtained with the multi-Kinect v2 set-up, as testified by negligible biases and narrow limits of agreement (Table 2.2). Step width was the only gait parameter that demonstrated good instead of excellent absolute agreement (Table 2.2). The deviant findings for step width may be due to systematic within-subject differences in ML ankle position time series between the two motion-registration systems. An example of such a systematic positional difference is presented in Figure 2.5. The left ML ankle position obtained with the multi-Kinect v2 set-up was about 3 to 4 centimeters more lateral compared to Optotrak's left ML ankle position (Figure 2.5D) while the right ML ankle positions matched well between the two systems (Figure 2.5C), resulting in a substantial bias of 3.6 cm in step width for this specific subject. This systematic between-systems mismatch for the left ML ankle position was confirmed by a clear difference between ICC values for consistency and absolute agreement ($ICC_{(C,1)}$ = 0.830, $ICC_{(A,1)}$ = 0.405; Figure 2.5D), whereas for the right ML ankle positions the ICC values were similar ($ICC_{(C,1)}$ = 0.818, $ICC_{(A,1)}$ = 0.783; Figure 2.5C). Note that this positional mismatch in ankle time series was not consistent among subjects in terms of its size, sign and side, which may explain the relatively larger between-subjects variation in the between-systems difference for step width (i.e., relatively wider limits of agreement in Table 2.2).

Kitsunezaki et al. [29] also assessed the possibility of instrumenting the 10MWT with multiple Kinect sensors. Specifically, they used two temporally integrated Kinect v1 sensors that were positioned at the 2-meter and 8-meter lines of a 10-meter walkway to determine the walking time of the intermediate 6 meters of the 10MWT. The mean difference in walking times obtained with the clinical standard (i.e., stopwatch) and the two Kinect v1 sensors was 0.15 seconds, which led the authors to conclude that a Kinect-based assessment was acceptable for practical use [29]. In the current study we quantified the time to walk 10 meters with a multi-Kinect v2 set-up, a gold-standard motion-registration system and a stopwatch. Despite examining walking time over a greater walking distance than Kitsunezaki et al. [29], we found smaller differences between the three measurement systems (≤ 0.09 s), especially between the multi-Kinect v2 set-up and the gold-standard motion-registration system (0.01 s). Noteworthy is that the agreement between these two motion-registration systems –in terms of $ICC_{(A,1)}$, biases and limits of agreement– was better than the agreement of either one with the clinical standard (i.e., stopwatch). To put these findings in perspective, the between-systems differences in the time to walk 10 meters were about 30 to 300 times smaller than the within-system differences between CWS and MWS conditions. Moreover, the meaningful change in walking speed of 5 cm/s according to Perera et al. [30] is at least twice as large as the between-systems differences in walking speed observed in the current study (i.e., after transforming the time to walk 10 meters to walking speed, ≤ 2.5 cm/s).

A multi-Kinect v2 set-up, such as the one described in the current study, may in practice be employed to automate the assessment of the 10MWT. An advantage of this set-up is that the 10MWT and quantitative gait assessment can be conducted simultaneously to reduce the time needed for a comprehensive assessment of walking ability. This could be beneficial for clinical applications, especially in view of our observation that the set-up can provide reliable estimates of the time to walk 10 meters and commonly used spatiotemporal gait parameters in a very quick, unobtrusive and patient-friendly manner. Other advantages of the Kinect v2 sensor are that 3D positional data of 25 body points (of up to six persons!) are tracked and available in real time, without markers, and not requiring time-consuming pre-registration calibration and post-registration labeling/tracking. Considering these assets, one may consider a multi-Kinect v2 set-up as a serious alternative for quantitative gait assessments.

A limitation of the multi-Kinect v2 set-up is the relatively low sampling frequency of 30 Hz. Although a good agreement between the multi-Kinect v2 set-up and the Optotrak system was found for almost all outcome measures of the current study, other outcome measures of interest may require higher sampling rates (e.g., the analysis of stride-to-stride fluctuations in stride times; [31]). Another limitation of the study was that the between-systems agreement was only assessed for healthy subjects. Before implementing the multi-Kinect v2 walkway in the clinic, gait parameters for the patient groups of interest should be validated first. Moreover, one can imagine that in a clinical context an accompanying person such as a therapist wants to walk along with a patient for safety reasons. Because 3D positional data of body points of up to six persons can be tracked with a Kinect v2 sensor, each being allocated with a unique body identification number, it is important to ensure the correct allocation of data to a specific person when tracking multiple persons with multiple Kinects (e.g., using minimization of 3D positional data when moving from one camera's field of view to another). Therefore, gait parameters need to be validated in various patient groups both with and without an accompanying person. As in healthy controls, good human-pose estimation is to be expected for patients. Clark et al. [32], for example, recently concluded that gait parameters of stroke patients derived from Kinect v1 data were highly reliable and could provide valuable additional information for gait analysis alongside the 10WMT. They stated that their findings provide support for implementing Kinect-based gait assessments in clinical settings [32]. With the development and validation of the multi-Kinect v2 instrumented 10-meter walkway, the current study may help pave the way to fulfill that premise.

Conclusion

Body point's time series obtained with a multi-Kinect v2 set-up match well with those derived with a gold standard in 3D measurement accuracy, particularly so for body points in motion. The excellent absolute agreements with the gold standard observed for time to walk 10 meters, walking speed, cadence, step length, stride length, step time and stride time emphasize that those parameters can be reliably obtained with the multi-Kinect v2 set-up. Future studies are recommended to test the clinical utility of the multi-Kinect v2 set-up to automate 10MWT assessments, thereby complementing the time to walk 10 meters with reliable spatiotemporal gait parameters obtained objectively in a quick, unobtrusive and patient-friendly manner.

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Supplement 2.1

Table S2.1 Overview of the body points obtained with the multi-Kinect v2 set-up and the Optotrak system. For the latter, anterior-posterior, mediolateral and vertical position time series were computed from virtual markers and/or smart markers. In case of a single virtual marker or smart marker, the time series of that specific marker were taken as the time series of the associated body point. In case of multiple virtual markers and/or smart markers, the associated marker positions were averaged in all three directions for each time sample.

Kinect body point	Smart Marker Rigid Body position	Virtual marker position	Smart marker position
Head	Head	Nasion, inion and left and right ear	-
Neck	-	-	-
Spine shoulder	-	-	Sternum
Spine mid	-	-	-
Spine base	Lower abdomen	Left and right anterior superior and posterior superior iliac spine	-
Shoulders	Upper arms	Head of the humurus	-
Elbows	Upper arms	Medial and lateral epicondyles	-
Wrists	Forearms	Distal heads of the radius and ulna	-
Hands	-	-	Back of the hand
Hand tips	-	-	-
Thumbs	-	-	-
Hips	Upper legs	Trochantor major	-
Knees	Upper legs	Medial and lateral condyles	-
Ankles	Lower legs	Medial and lateral malleoli	-
Feet	Feet	Calcaneus	Head of the distal phalanx of the hallux

Supplement 2.2

Video of body point's time series obtained with the multi-Kinect v2 set-up and the Optotrak system of a single representative trial during the comfortable walking speed condition of the 10-meter walking test. This video is available at https://doi.org/10.1371/journal.pone.0139913.s004.

Supplement 2.3

Data of body point's time series in the anterior-posterior, mediolateral and vertical direction for the multi-Kinect v2 set-up and the Optotrak system. This data is available at https://doi.org/10.1371/journal.pone.0139913.s001.

Supplement 2.4

Bland-Altman plots for the spatiotemporal gait parameters for comfortable walking speed and maximum walking speed conditions.

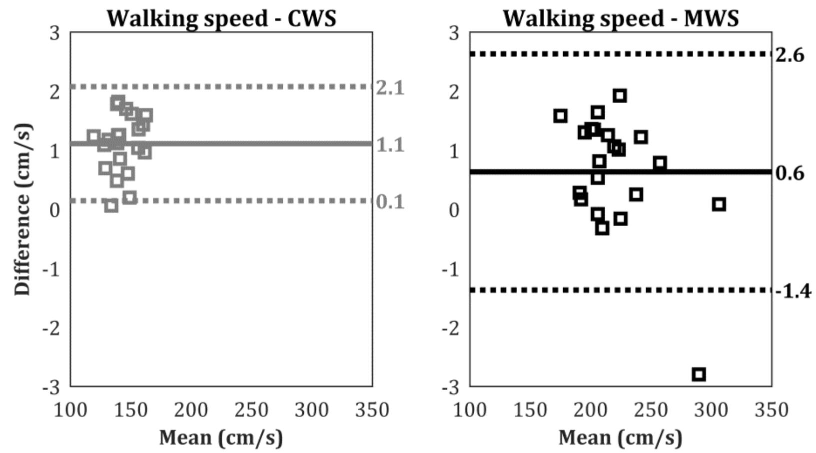

Figure S2.1 Bland-Altman plots for walking speed during the comfortable walking speed (CWS) and maximum walking speed (MWS) condition. Solid lines represent biases between the two motion registration systems. Dashed lines represent the 95% limits of agreement.

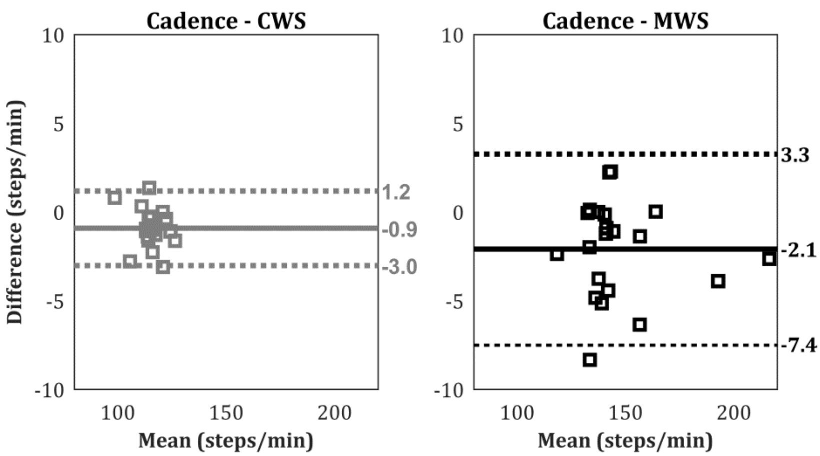

Figure S2.2 Bland-Altman plots for cadence during the comfortable walking speed (CWS) and maximum walking speed (MWS) condition. Solid lines represent biases between the two motion registration systems. Dashed lines represent the 95% limits of agreement.

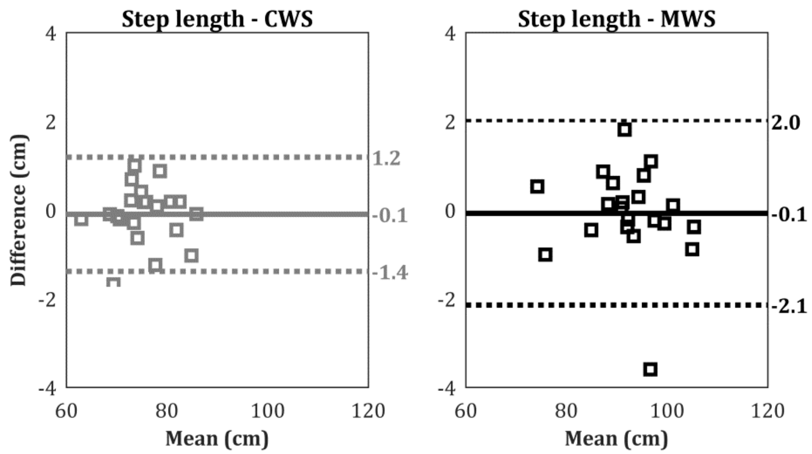

Figure S2.3 Bland-Altman plots for step length during the comfortable walking speed (CWS) and maximum walking speed (MWS) condition. Solid lines represent biases between the two motion registration systems. Dashed lines represent the 95% limits of agreement.

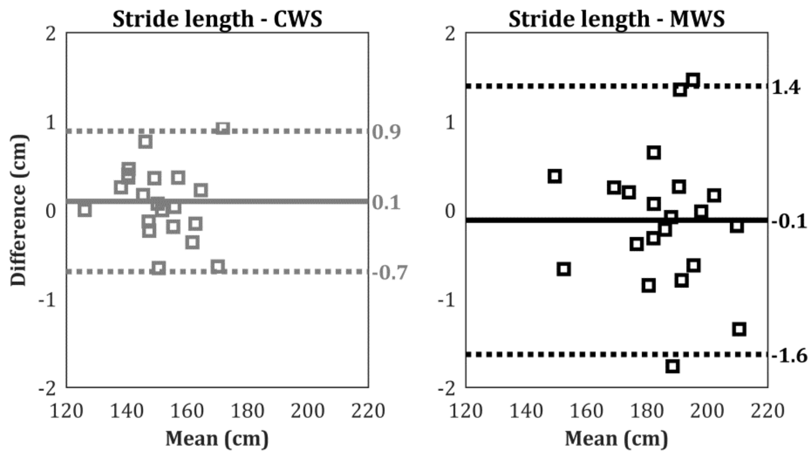

Figure S2.4 Bland-Altman plots for stride length during the comfortable walking speed (CWS) and maximum walking speed (MWS) condition. Solid lines represent biases between the two motion registration systems. Dashed lines represent the 95% limits of agreement.

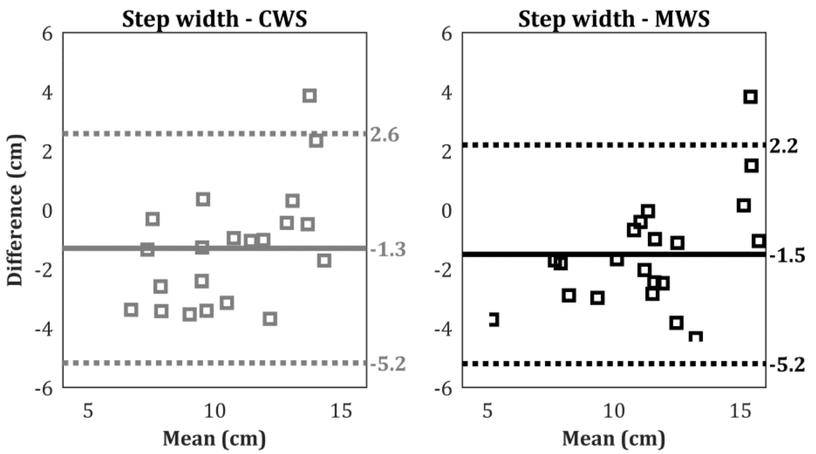

Figure S2.5 Bland-Altman plots for step width during the comfortable walking speed (CWS) and maximum walking speed (MWS) condition. Solid lines represent biases between the two motion registration systems. Dashed lines represent the 95% limits of agreement.

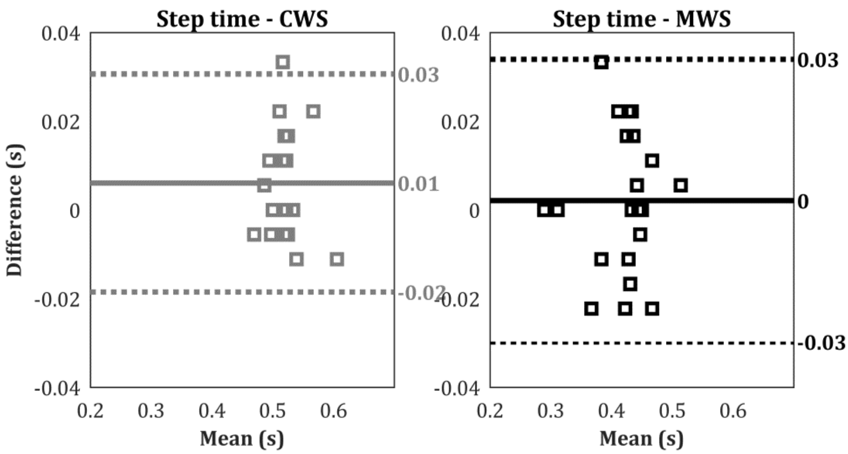

Figure S2.6 Bland-Altman plots for step time during the comfortable walking speed (CWS) and maximum walking speed (MWS) condition. Solid lines represent biases between the two motion registration systems. Dashed lines represent the 95% limits of agreement.

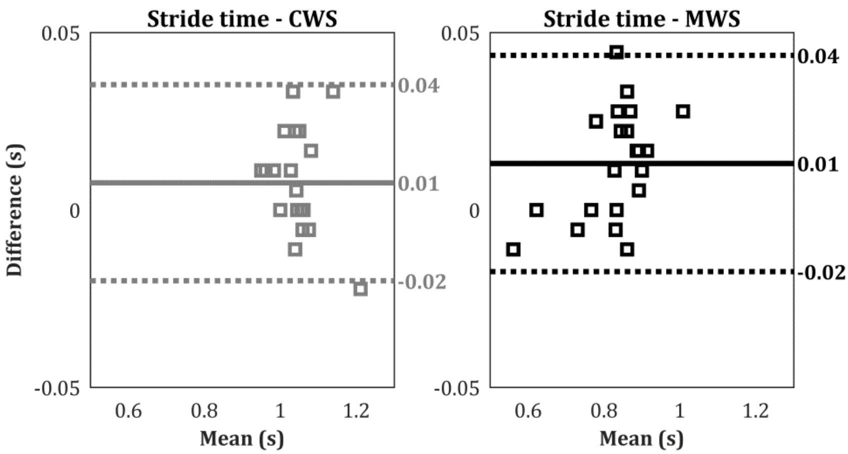

Figure S2.7 Bland-Altman plots for stride time during the comfortable walking speed (CWS) and maximum walking speed (MWS) condition. Solid lines represent biases between the two motion registration systems. Dashed lines represent the 95% limits of agreement.

Chapter 3

Walking-adaptability assessments with the Interactive Walkway: between-systems agreement and sensitivity to task and subject variations

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Published in Gait & Posture 2017;54:194-201

The ability to adapt walking to environmental circumstances is an important aspect of walking, yet difficult to assess. The Interactive Walkway was developed to assess walking adaptability by augmenting a multi-Kinect-v2 10-meter walkway with gait-dependent visual context (stepping targets, obstacles) using real-time processed markerless full-body kinematics. In this study we determined Interactive Walkway's usability for walking-adaptability assessments in terms of between-systems agreement and sensitivity to task and subject variations. Under varying task constraints, 21 healthy subjects performed obstacle-avoidance, sudden-stops-and-starts and goal-directed-stepping tasks. Various continuous walking-adaptability outcome measures were concurrently determined with the Interactive Walkway and a gold-standard motion-registration system: available response time, obstacle-avoidance and sudden-stop margins, step length, stepping accuracy and walking speed. The same holds for dichotomous classifications of success and failure for obstacle-avoidance and sudden-stops tasks and performed short-stride versus long-stride obstacle-avoidance strategies. Continuous walking-adaptability outcome measures generally agreed well between systems (high intraclass correlation coefficients for absolute agreement, low biases and narrow limits of agreement) and were highly sensitive to task and subject variations. Success and failure ratings varied with available response times and obstacle types and agreed between systems for 85-96% of the trials while obstacle-avoidance strategies were always classified correctly. We conclude that Interactive Walkway walking-adaptability outcome measures are reliable and sensitive to task and subject variations, even in high-functioning subjects. We therefore deem Interactive Walkway walking-adaptability assessments usable for obtaining an objective and more task-specific examination of one's ability to walk, which may be feasible for both high-functioning and fragile populations since walking adaptability can be assessed at various levels of difficulty.

Introduction

An important aspect of walking is one's ability to adapt walking to environmental circumstances [1-3]. Walking adaptability includes the ability to avoid obstacles, make sudden stops and starts and accurately place the feet to environmental context [1]. Most walking-related falls result from inadequate interactions with environmental context, leading to balance loss due to a trip, slip or misplaced step [4-6]. Walking adaptability thus seems to be an important determinant of fall risk, yet a comprehensive well-tested objective assessment of walking adaptability is lacking [1].

We try to fill this lacuna with the Interactive Walkway (IWW), a 10-meter walkway augmented with projected gait-dependent visual context, such as obstacles suddenly appearing at the position one would step next, demanding a step adjustment under time pressure. The basis of the IWW is an integrated multi-Kinect v2 set-up for markerless registration of 3D full-body kinematics during walking [7], which was recently validated over the entire 10-meter walkway against a gold standard in 3D measurement accuracy for both kinematics and derived gait parameters [7,8]. We have now equipped this set-up with a projector to augment the entire walkway with visual context, such as obstacles, sudden-stop-and-start cues and stepping targets, based on real-time processed integrated Kinect data. The so-elicited gait-environment interactions potentially allow for assessing various walking-adaptability aspects (e.g., the ability to avoid obstacles, suddenly stop or start, perform accurate goal-directed steps) as well as subject-specific variations and adaptations affecting walking-adaptability performance (e.g., adopting a slower walking speed to enhance goal-directed stepping accuracy).

The objective of this study is to determine the usability of the IWW for walking-adaptability assessments in a group of healthy adults in terms of between-systems agreement and sensitivity to task and subject variations. Walking-adaptability tasks and associated outcome measures are selected for their proven ability to distinguish between persons who vary in adaptive-walking limitations [2,3,9-12]. To determine the between-systems agreement, IWW-based walking-adaptability outcome measures are compared to those concurrently derived with a gold standard. The sensitivity to task variation is assessed by comparing walking-adaptability performance as a function of context variations, including different obstacle sizes and sequences of stepping targets. Sensitivity to subject variation is explored by quantifying speed-performance trade-offs between self-selected walking speed and adaptive stepping performance (success rates, safety margins). We expect that walking-adaptability outcomes agree well between systems and are sensitive to task and subject variations.

Methods

Subjects

A heterogeneous group of 21 healthy subjects (mean [range]: age 30 [19-63] years, height 176 [158-190] cm, weight 70 [53-83] kg, 11 males) without severe visual deficits or any medical condition that would affect walking participated. The local ethics committee approved the study. All subjects gave written informed consent prior to participation.

Experimental set-up and procedure

Full-body kinematics for walking over the entire 10-meter walkway was obtained with the IWW using four spatially and temporally integrated Kinect v2 sensors (Figure 3.1A) and the Optotrak system (Northern Digital Inc., Waterloo, Canada) for 19 matched body points as in [7; see also Supplement 3.1]. IWW and Optotrak data were sampled at 30 Hz (using custom-written software utilizing the Kinect-for-Windows Software Development Kit [SDK 2.0]) and 60 Hz (using First Principles data acquisition software), respectively. The IWW was equipped with a projector (Vivitek D7180HD, ultra-short-throw Full HD projector) to augment the entire 10-meter walkway with visual context for three sorts of walking-adaptability tasks: obstacle avoidance, sudden stops-and-starts and goal-directed stepping (Figure 3.1).

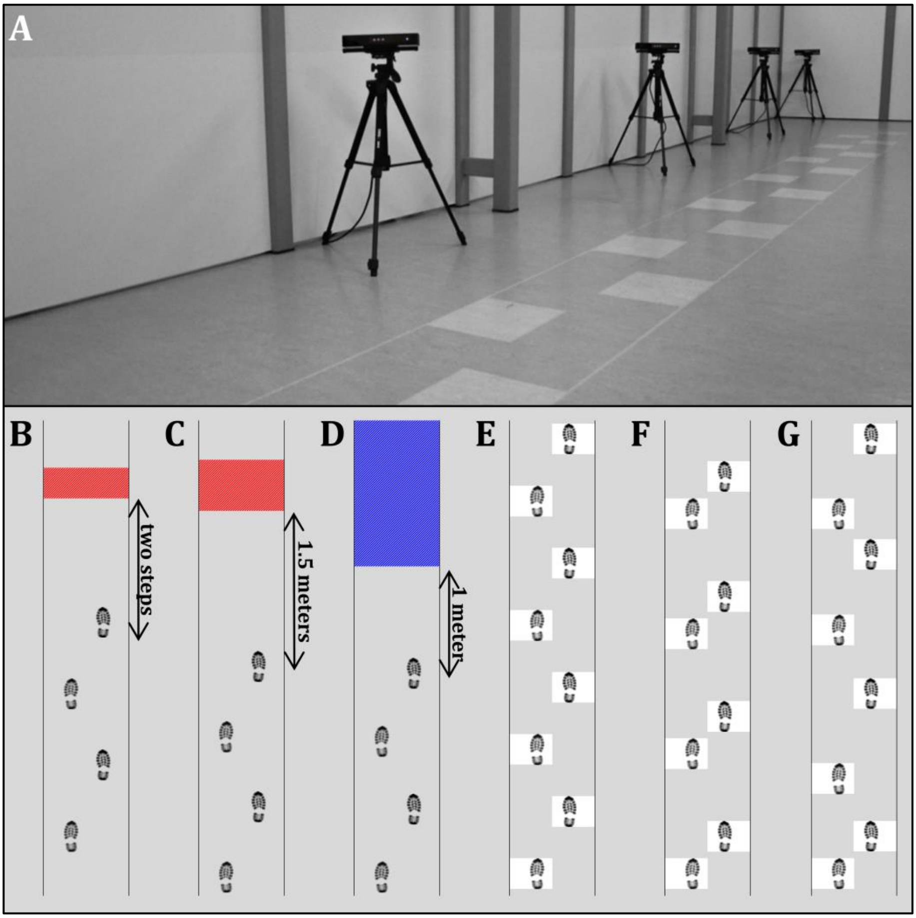

Figure 3.1 The set-up of the Interactive Walkway with visual context projected on the walkway (A). The four Kinect v2 sensors were positioned on tripods at a height of 0.75 meters alongside a walkway of 10 by 0.5 meters. The sensors were placed frontoparallel (i.e., with an angle of 70 degrees relative to the walkway direction) with a distance of 0.5 meters from the left border of the walkway. The first sensor was positioned at 4 meters from the start of the walkway and the other sensors were placed at inter-sensor distances of 2.5 meters. Schematics of the walking-adaptability tasks: obstacle avoidance with gait-dependent (B) and position-dependent obstacles (C), sudden stops-and-starts (D) and goal-directed stepping with symmetric stepping stones (E), asymmetric stepping stones (F) and variable stepping stones (G).

The obstacle-avoidance task consisted of 25 trials with one or two obstacles (a projected red rectangle) per trial. In total, 40 obstacles were presented, including 20 gait-dependent obstacles (obstacle at predicted foot-placement position appearing two steps ahead; Figure 3.1B) and 20 position-dependent obstacles (obstacle at an unpredictable predefined position appearing when a subject's ankle was within 1.5 meters from that obstacle; Figure 3.1C). Gait-dependent obstacles were 0.5 (width of the walkway) by 0.3 meters. Position-dependent obstacles were larger (0.5×0.5 meters) to increase the need for making step adjustments. Subjects were instructed to avoid suddenly appearing obstacles while walking at self-selected comfortable speeds.

The sudden-stops-and-starts task (Figure 3.1D) consisted of 25 trials with in total 40 cues (i.e., one or two sudden-stop-and-start cues per trial) to assess one's ability to suddenly stop and start walking. The cue was a big blue rectangle with a width of 0.5 meters that filled the walkway from an unpredictable predefined position till its end and appeared as soon as a subject's ankle was within 1 meter from this position, triggering the subject to stop walking. After a random period between 5 and 10 seconds, the rectangle disappeared, triggering the subject to start walking again. Subjects were instructed to walk at self-selected comfortable speeds and to stop behind the cue and to start walking as soon as the cue disappeared.

The goal-directed-stepping task consisted of symmetric-stepping-stones (SSS; Figure 3.1E), asymmetric-stepping-stones (ASS; Figure 3.1F) and variable-stepping-stones (VSS; Figure 3.1G) conditions. Subjects were instructed to step as accurately as possible onto the white shoe-size-matched stepping targets at a self-selected comfortable walking speed. For SSS, seven different imposed step-length trials ranging from 30 to 90 cm in steps of 10 cm were performed, all with three repetitions, yielding a total of 21 trials. For ASS, stride length remained 90 centimeters while left (L) and right (R) imposed step lengths were varied in separate trials from 15 to 75 centimeters in steps of 15 centimeters yielding five different imposed stepping asymmetries (L/R: *15/75*, *30/60*, *45/45*, *60/30*, *75/15*), all with three repetitions, yielding 15 trials. For VSS, imposed step lengths varied within each trial on a step-to-step basis randomly between 30 and 90 centimeters. Ten different VSS trials were performed, consisting of 21 stepping stones each.

The walking-adaptability tasks were block-randomized and preceded by a familiarization trial. Four ankle-to-shoe calibration trials, in which the subject was standing in two shoe-size-matched targets at different positions on the walkway, were also included to determine the average distance between shoe edges and the ankle for both systems. This calibration was needed to determine several walking-adaptability outcome measures (see below).

Data pre-processing and analysis

Data pre-processing followed established procedures [7]; details about the procedure and pre-processed data are presented as supplementary material (see Supplements 3.1 and 3.2). Due to excessive missing data, 62 out of 2,016 trials were excluded from further analysis, mainly for the gold-standard motion-registration system (i.e., marker occlusion and/or orientation issues) and concerning one subject.

The continuous walking-adaptability outcome measures were available response time (ART) and margins of the trailing and leading limb during obstacle crossing for the obstacle-avoidance task, ART and margin to the stop cue for the sudden-stops-and-starts task, step length, stepping accuracy and walking speed for SSS and VSS, and left and right step lengths, stepping accuracy and walking speed for ASS. These continuous outcome measures were calculated from specific body points' time series, estimates of foot contact and foot off and step locations, as detailed in Table 3.1, for both measurement systems alike in an aligned coordinate system, including the coordinates of obstacles, sudden-stop cues and targets. For all continuous outcome measures, statistical analyses were performed over averages over trials. For dichotomous outcome measures, step locations were extrapolated to the actual shoe dimensions based on the ankle-to-shoe calibration to determine whether or not obstacle-avoidance and sudden-stop trials were successfully performed, from which success rates were deduced. Successful gait-dependent obstacle-avoidance maneuvers were classified as short-stride or long-stride strategies [13].

Statistical analysis

Between-systems agreement was determined for continuous outcome measures using intraclass correlation coefficients for absolute agreement ($ICC_{(A,1)}$; [14]), with values above 0.60 and 0.75 representing good and excellent agreement, respectively; [15]. This analysis of between-systems agreement was complemented by mean differences and precision values obtained with a Bland-Altman analysis (i.e., the bias and the limits of agreement, respectively; [16]). For dichotomous outcome measures we report the percentage of non-matched ratings.

Sensitivity to task variation was examined using repeated-measures ANOVAs on continuous outcome measures of obstacle-avoidance and goal-directed-stepping tasks. For ART and obstacle-avoidance margins, a System (IWW, Optotrak) by Obstacle (gait-dependent, position-dependent) by Limb (trailing, leading) repeated-measures ANOVA was conducted. For step length, stepping accuracy and walking speed of SSS, a System by Imposed step length (*30*, *40*, *…, 90*) repeated-measures ANOVA was conducted. For left and right step lengths, stepping accuracy and walking speed of ASS, a System by Imposed step-length asymmetry (L/R: *15/75*, *30/60*, *45/45*, *60/30, 75/15*) repeated-measures ANOVA was conducted. For step length, stepping accuracy and walking speed of VSS, a System by Trial repeated-measures ANOVA was conducted. For the average stepping accuracy of the three goal-directed-stepping conditions, a System by Condition (SSS, ASS, VSS) repeated-measures ANOVA was conducted. One subject was excluded from the analyses of the goal-directed-stepping tasks due to multiple trials with excessive missing values.

Table 3.1 Calculation methods of continuous walking-adaptability outcome measures.

	Outcome measure	Unit	Calculation
Obstacle-avoidance	**Available response time**	s	The distance of the nearest anterior shoe edge to the border of the obstacle at the moment of its appearance divided by the average walking speed over the second before its appearance.
	Obstacle-avoidance margins	cm	The distance of the anterior shoe edge (trailing limb) and posterior shoe edge (leading limb) of the step locations to corresponding obstacle borders during obstacle crossing. Step locations were determined as the median anterior-posterior position of the ankle joint during the single-support phase (i.e., between foot off and foot contact of the contralateral foot) [7]. Estimates of foot contact and foot off were defined as the maxima and minima of the anterior-posterior time series of the ankles relative to that of the spine base [7,17].
Sudden-stops-and-starts	**Available response time**	s	The distance of the nearest anterior shoe edge to the border of the sudden-stop cue at the moment of its appearance divided by the average walking speed over the second before its appearance.
	Sudden-stop margin	cm	The minimum distance of the anterior shoe edge to the corresponding sudden-stop cue border during the period in which the cue was visible.
Goal-directed-stepping	**Step length**	cm	The median of the differences in the anterior-posterior direction of consecutive step locations.
	Stepping accuracy	cm	The standard deviation over the signed deviations between the center of the foot and the center of the target at step locations, as defined in step length. Stepping accuracy was determined over step locations that were identified for both systems to ensure a fair comparison. The center of the foot was determined using the average distance between the ankle and the middle of the shoe-size-matched targets of the calibration trials.
	Walking speed	cm/s	The distance travelled between the start and the 10-meter line of the walkway divided by the time, using the data of the spine shoulder.

The assumption of sphericity was checked according to Girden [18]. If Greenhouse-Geisser's epsilon exceeded 0.75, the Huynh-Feldt correction was applied; otherwise the Greenhouse-Geisser correction was used. Main effects were examined with a Least Significant Difference post-hoc test for factors with three levels and contrast analyses for factors with more than three levels. Paired-samples *t*-tests were used for significant interactions. Effect sizes were quantified with η_p^2.

Sensitivity to subject variation was examined by exploring speed-performance trade-offs. We determined Pearson's correlations between self-selected walking speed and stepping accuracy for all goal-directed-stepping tasks and between the speed-dependent ART and margins for obstacle-avoidance and sudden-stop tasks (i.e., significant positive correlations signal speed-performance trade-offs). We also assessed the influence of obstacle-avoidance and sudden-stop ratings on ART using a System by Rating (success, failure) repeated-measures ANOVA. In addition, obstacle-avoidance success rates were compared with a System by Obstacle repeated-measures ANOVA.

Results

Between-systems agreement

Excellent between-systems agreement was observed for ART and margins for obstacle-avoidance and sudden-stops-and-starts tasks, walking speed for all goal-directed-stepping conditions (SSS, ASS and VSS) and step length and stepping accuracy of VSS, supported by very high $ICC_{(A,1)}$ values, small biases and narrow limits of agreement (Table 3.2). The between-systems agreement for stepping accuracy of SSS and step lengths and stepping accuracy for ASS was overall good to excellent (Table 3.2). Between-systems statistics were ambiguous for step length of SSS (low $ICC_{(A,1)}$ values, negligible biases and very narrow limits of agreement; Table 3.2). Significant between-system biases, indicated in Table 3.2, all corresponded to significant System effects of associated outcome measures in the ANOVAs for the analysis of sensitivity to task and subject variations.

Success rates of gait-dependent and position-dependent obstacles were (mean ± SD) 94.7 ± 12.8% and 92.1 ± 15.6% for the IWW and 96.8 ± 6.5% and 93.2±12.1% for the gold standard, respectively. The percentage of non-matched ratings was 3.7% for gait-dependent obstacles (3.0% false negatives) and 5.1% for position-dependent obstacles (3.1% false negatives). Given the uneven distribution of ratings over categories (~95% success vs. ~5% failure), we also determined the percentages of specific agreement [19] for obstacle-avoidance successes (97.7%) and failures (61.5%), suggesting that the agreement for failures was considerably lower. The systems matched perfectly for classified avoidance strategies (0% non-matched ratings), with an overall preference for the long-stride strategy in avoiding gait-dependent obstacles (80.5 ± 15.3%). Success rates for sudden stops were 58.1 ± 23.5% for the IWW and 49.5 ± 22.0% for the gold standard, with 14.8% between-systems dis-matches (11.7% false positives).

Sensitivity to task variation

A significant Obstacle ($F(1,20) = 7.98$, $p = 0.010$, $\eta_p^2 = 0.285$) effect was found for ART, with longer ARTs for position-dependent obstacles (0.834 ± 0.016 s) than for gait-dependent obstacles (0.784 ± 0.011 s). Significant Obstacle ($F(1,20) = 508.73$, $p < 0.001$, $\eta_p^2 = 0.962$) and Limb ($F(1,20) = 29.40$, $p < 0.001$, $\eta_p^2 = 0.595$) effects were found for obstacle-avoidance margins, as well as a significant Obstacle×Limb interaction ($F(1,20) = 99.95$, $p < 0.001$, $\eta_p^2 = 0.833$). While margins were overall greater for gait-dependent obstacles and for the trailing limb, the interaction revealed that the difference between trailing and leading limbs was only evident for gait-dependent obstacles (27.7 ± 5.3 cm vs. 12.2 ± 5.3 cm) and not for position-dependent obstacles (11.4 ± 2.9 cm vs. 9.4 ± 4.9 cm).

Table 3.2 Mean values, between-subjects standard deviations (SD) and agreement statistics (bias, limits of agreement [95% LoA] and intraclass correlation coefficient for absolute agreement [$ICC_{(A,1)}$]) for the continuous outcome measures of the obstacle-avoidance, sudden-stops-and-starts and goal-directed-stepping tasks (symmetric-stepping-stones, asymmetric-stepping-stones and variable-stepping-stones conditions).

			Interactive Walkway mean ± SD	Optotrak system mean ± SD	Bias (95% LoA)	$ICC_{(A,1)}$
Obstacle-avoidance task						
Available response time (s)	**Gait-dependent**		0.792 ± 0.050	0.777 ± 0.049	-0.015* [-0.032 0.002]	0.945
	Position-dependent		0.834 ± 0.075	0.834 ± 0.076	0.000 [-0.023 0.024]	0.988
Margins (cm)	**Gait-dependent**	**Trailing limb**	27.68 ± 5.53	27.65 ± 5.06	-0.03 [-2.17 2.12]	0.980
		Leading limb	11.68 ± 5.45	12.78 ± 5.26	1.11* [-1.35 3.56]	0.954
	Position-dependent	**Trailing limb**	11.27 ± 3.08	11.54 ± 2.90	0.26 [-2.18 2.71]	0.913
		Leading limb	8.97 ± 4.91	9.82 ± 4.87	0.85* [-1.39 3.09]	0.960
Sudden-stops-and-starts task						
Available response time (s)			0.497 ± 0.067	0.490 ± 0.070	-0.007* [-0.035 0.021]	0.997
Margins (cm)			8.32 ± 7.29	8.35 ± 6.70	0.30 [-6.96 7.02]	0.876
Symmetric-stepping-stones						
Step length (cm)	**30**		29.95 ± 0.14	29.97 ± 0.32	0.02 [-0.55 0.58]	0.339
	40		39.96 ± 0.18	40.00 ± 0.28	0.04 [-0.61 0.68]	0.034
	50		50.06 ± 0.29	50.02 ± 0.35	-0.04 [-1.04 0.96]	-0.276
	60		60.02 ± 0.38	59.89 ± 0.48	-0.13 [-1.21 0.95]	0.189
	70		69.99 ± 0.25	69.91 ± 0.57	-0.07 [-1.05 0.90]	0.376
	80		79.89 ± 0.28	79.76 ± 0.48	-0.13 [-1.10 0.84]	0.210
	90		89.84 ± 0.37	89.81 ± 0.33	-0.03 [-0.82 0.76]	0.367

Table 3.2 Continued.

		Interactive Walkway mean ± SD	Optotrak system mean ± SD	Bias (95% LoA)	$ICC_{(A,1)}$
Stepping accuracy (cm)	**30**	1.77 ± 0.41	1.87 ± 0.38	0.10 [-0.55 0.75]	0.635
	40	1.80 ± 0.37	1.93 ± 0.45	0.13 [-0.66 0.92]	0.503
	50	1.81 ± 0.37	2.00 ± 0.47	0.20* [-0.49 0.88]	0.609
	60	1.91 ± 0.46	1.91 ± 0.52	0.00 [-0.77 0.78]	0.686
	70	1.91 ± 0.41	1.99 ± 0.49	0.08 [-0.64 0.80]	0.675
	80	1.88 ± 0.54	2.02 ± 0.53	0.15 [-0.89 1.19]	0.498
	90	2.02 ± 0.55	2.12 ± 0.56	0.10 [-0.59 0.78]	0.798
Walking speed (cm/s)	**30**	73.23 ± 12.95	72.89 ± 12.66	-0.34* [-1.03 0.35]	0.999
	40	86.93 ± 13.42	86.37 ± 13.04	-0.57* [-1.48 0.35]	0.999
	50	101.14 ± 14.11	100.42 ± 13.73	-0.72* [-1.67 0.23]	0.998
	60	112.28 ± 13.83	111.19 ± 13.28	-1.09* [-2.57 0.39]	0.995
	70	124.40 ± 13.38	123.24 ± 12.89	-1.16* [-2.59 0.26]	0.995
	80	136.70 ± 12.49	134.97 ± 12.07	-1.73* [-3.00 -0.46]	0.989
	90	145.07 ± 12.07	143.43 ± 11.67	-1.64* [-3.10 -0.19]	0.989
Asymmetric-stepping-stones					
Step length left (cm)	**15/75**	21.38 ± 3.66	19.75 ± 3.92	-1.63* [-4.30 1.03]	0.859
	30/60	34.23 ± 2.39	33.55 ± 2.71	-0.68 [-3.65 2.29]	0.803
	45/45	44.72 ± 1.17	44.50 ± 1.76	-0.22 [-3.03 2.59]	0.546
	60/30	55.44 ± 2.35	56.34 ± 2.82	0.90* [-2.03 3.83]	0.793
	75/15	67.44 ± 2.96	69.88 ± 3.58	2.45* [-0.96 5.86]	0.677

Step length right (cm)	**15/75**	68.57 ± 3.84	70.16 ± 3.96	1.60* [-1.41 4.61]	0.854
	30/60	55.76 ± 2.58	56.45 ± 2.84	0.69 [-2.48 3.86]	0.803
	45/45	45.37 ± 1.24	45.39 ± 1.87	0.01 [-2.85 2.88]	0.588
	60/30	34.62 ± 2.20	33.63 ± 2.66	-0.99* [-3.74 1.76]	0.777
	75/15	22.80 ± 2.89	19.96 ± 3.56	-2.83* [-6.37 0.71]	0.615
Stepping accuracy (cm)	**15/75**	3.87 ± 1.77	3.37 ± 1.58	-0.50* [-1.75 0.75]	0.891
	30/60	2.87 ± 1.13	2.65 ± 1.08	-0.21 [-1.54 1.11]	0.806
	45/45	1.73 ± 0.38	1.88 ± 0.46	0.14 [-0.59 0.88]	0.584
	60/30	3.02 ± 1.03	2.79 ± 1.03	-0.23 [-1.20 0.74]	0.869
	75/15	4.36 ± 1.36	3.34 ± 1.49	-1.02* [-2.35 0.31]	0.709
Walking speed (cm/s)	**15/75**	90.87 ± 12.05	90.33 ± 11.81	-0.54* [-1.34 0.25]	0.998
	30/60	92.01 ± 13.61	91.46 ± 13.35	-0.55* [-1.43 0.34]	0.999
	45/45	91.73 ± 14.14	91.20 ± 13.96	-0.53* [-1.34 0.28]	0.999
	60/30	89.23 ± 14.18	88.75 ± 13.92	-0.47* [-1.24 0.29]	0.999
	75/15	87.84 ± 13.51	87.31 ± 13.25	-0.53* [-1.33 0.26]	0.999
Variable-stepping-stones					
Step length (cm)		45.54 ± 0.82	45.49 ± 0.85	-0.05 [-0.96 0.86]	0.852
Stepping accuracy (cm)		2.60 ± 0.68	2.53 ± 0.65	-0.08 [-0.59 0.44]	0.920
Walking speed (cm/s)		97.89 ± 13.88	97.25 ± 13.56	-0.64* [-1.51 0.23]	0.998

* Significant between-systems difference ($p < 0.05$).

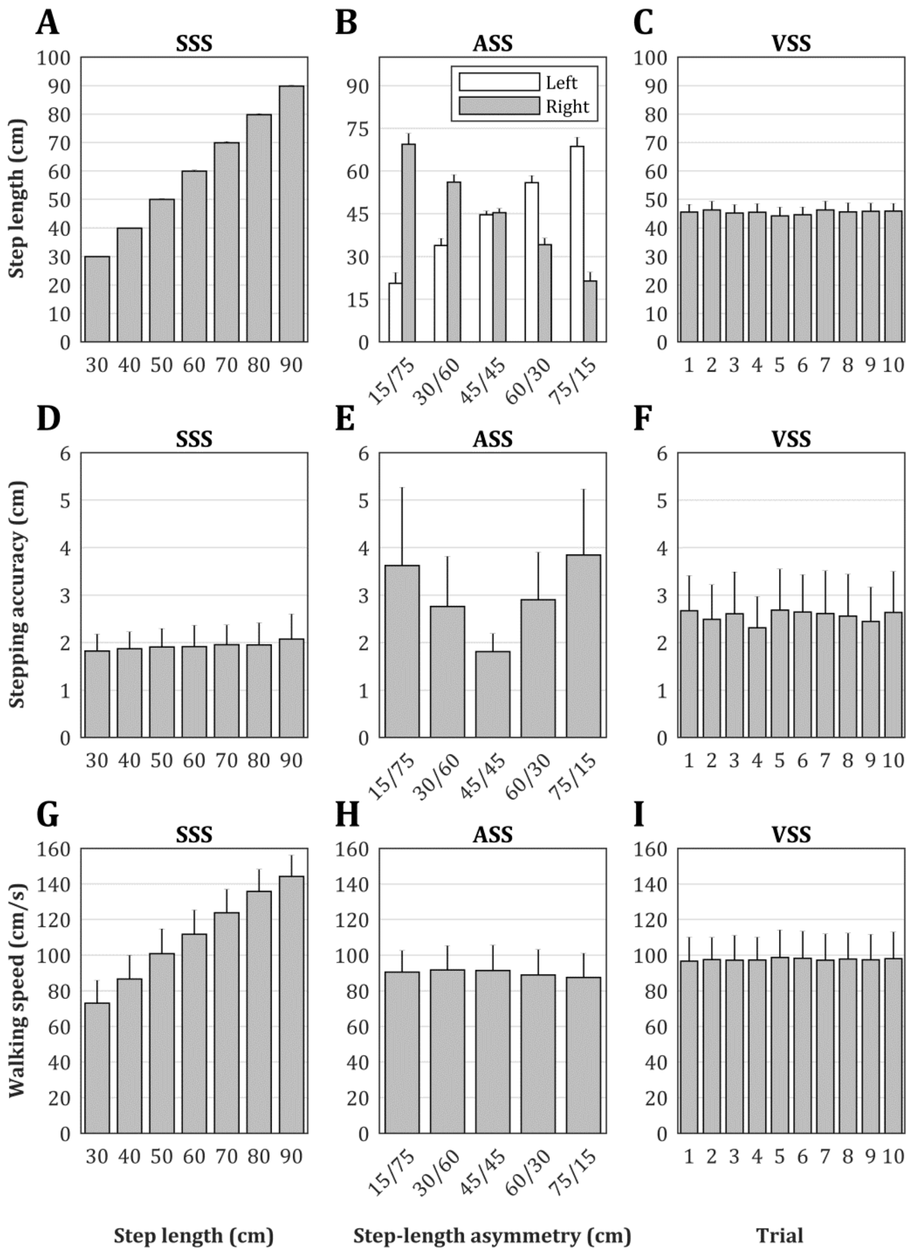

Figure 3.2 Step length (A, B and C), stepping accuracy (D, E and F) and walking speed (G, H and I) for the symmetric-stepping-stones (SSS; A, D and G), the asymmetric-stepping-stones (ASS; B, E and H) and the variable-stepping-stones (VSS; C, F and I) of the goal-directed-stepping task.

Subjects were well able to adjust their foot placement to the presented goal-directed-stepping targets (Table 3.2 and Figure 3.2). This was confirmed by very strong effects of Imposed step lengths on performed step lengths for SSS ($F(4.2,79.0) = 162327.08$, $p < 0.001$, $\eta_p^2 = 1.000$; Figure 3.2A) and ASS (left: $F(1.2,22.6) = 936.64$, $p < 0.001$, $\eta_p^2 = 0.980$; right: $F(1.2,22.7) = 913.62$, $p < 0.001$, $\eta_p^2 = 0.980$; Figure 3.2B). Stepping accuracy varied significantly with Imposed step-length asymmetry ($F(2.4,45.7) = 20.63$, $p < 0.001$, $\eta_p^2 = 0.521$), with significant quadratic ($F(1,19) = 53.99$, $p < 0.001$, $\eta_p^2 = 0.740$) and fourth-order ($F(1,19) = 18.83$, $p < 0.001$, $\eta_p^2 = 0.498$) contrasts (Figure 3.2E); no significant main or interaction effects were found on stepping accuracy for SSS (Figure 3.2D) or VSS (Figure 3.2F). Walking speed varied with step-length manipulations for SSS ($F(2.7,50.6) = 607.50$, $p < 0.001$, $\eta_p^2 = 0.970$; with significant linear [$F(1,19) = 1189.66$, $p < 0.001$, $\eta_p^2 = 0.984$] and quadratic [$F(1,19) = 9.29$, $p = 0.007$, $\eta_p^2 = 0.328$] contrasts; Figure 3.2G) and ASS ($F(2.7,50.6) = 4.72$, $p = 0.007$, $\eta_p^2 = 0.199$; with a significant linear contrast [$F(1,19) = 13.67$, $p = 0.002$, $\eta_p^2 = 0.418$]; Figure 3.2H). Average stepping accuracy varied significantly over goal-directed-stepping conditions ($F(1.5,28.3) = 36.80$, $p < 0.001$, $\eta_p^2 = 0.659$); stepping accuracy improved from ASS (2.99 ± 0.21 cm) to VSS (2.57 ± 0.15 cm) to SSS (1.93 ± 0.08 cm), with significant differences between all conditions.

Sensitivity to subject variation

Self-selected walking speed affects the available response time for obstacle-avoidance and sudden-stop tasks on the IWW, and thereby the difficulty of these walking-adaptability tasks. For sudden stops the overall success rate was 53.8 ± 22.4%, with a clear influence of rating on ART ($F(1,20) = 172.88$, $p < 0.001$, $\eta_p^2 = 0.896$); ARTs were longer for successful stops (0.536±0.012 s) than for failed stops (0.416 ± 0.012 s). In Figure 3.3 sudden-stop success and failure rates are depicted as a function of ART, showing a steady increase in stopping successes (and hence a decrease in stopping failures) with longer ARTs. A speed-performance trade-off was also found on margins to the stopping cue, with longer ARTs being associated with larger margins, for both systems alike (IWW: $r(20) = 0.597$, $p = 0.004$; gold standard: $r(20) = 0.698$, $p < 0.001$).

The influence of obstacle-avoidance ratings on ART could not be determined because of a ceiling effect; overall success rate was 94.2 ± 11.3%, with slightly higher success rates for gait-dependent obstacles (95.8 ± 2.1%) than for position-dependent obstacles (92.6 ± 2.9%; main Obstacle effect, $F(1,20) = 7.05$, $p = 0.015$, $\eta_p^2 = 0.261$). Obstacle-avoidance margins were not associated with ART (i.e., no speed-performance trade-off; $r(20) = [-0.115\ 0.211]$, $p > 0.359$).

Clear speed-performance trade-offs were observed for goal-directed stepping, with faster walking speeds being associated with poorer stepping accuracy, as evidenced by significant positive correlations between self-selected walking speed and stepping accuracy for SSS, ASS and VSS, for both systems alike (IWW: $r(20) = 0.722$, $p < 0.001$, $r(20) = 0.715$, $p < 0.001$ and $r(20) = 0.637$, $p < 0.001$, respectively; gold standard: $r(20) = 0.523$, $p = 0.018$, $r(20) = 0.668$, $p = 0.001$ and $r(20) = 0.569$, $p < 0.001$, respectively).

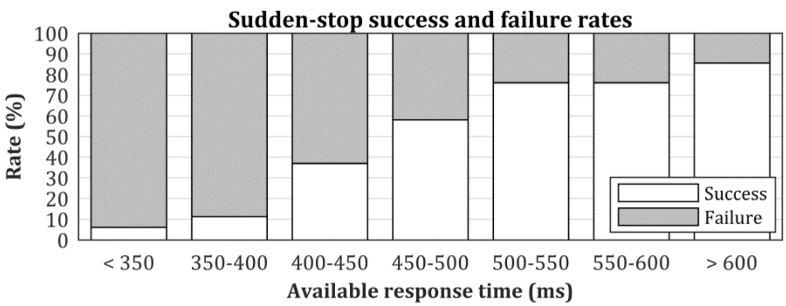

Figure 3.3 Sudden-stop success and failure rates for different available response times.

Discussion

We determined the usability of IWW walking-adaptability assessments in a group of healthy adults in terms of between-systems agreement and sensitivity to task and subject variations. We expected that walking-adaptability outcome measures agreed well between systems and were sensitive to task and subject variations. The results were in line with our expectations, which led us to conclude that the IWW is usable for walking-adaptability assessments.

First, the between-systems agreement for continuous walking-adaptability outcomes proved to be good to excellent, with high ICC values, small biases and narrow limits of agreement (Table 3.2). For the SSS conditions of goal-directed stepping, however, ICC values for step length were considerably lower, suggesting a poor between-systems agreement, which stood in stark contrast with excellent Bland-Altman agreement statistics (negligible biases and narrow limits of agreement; Table 3.2). This discrepancy was likely due to a lack of subject heterogeneity in step lengths since these were experimentally imposed with stepping targets, yielding minimal between-subject variance (see also Figure 3.2A) and hence arbitrarily low ICC values [20]. This discrepancy illustrates the importance of a complementary set of agreement statistics instead of relying solely on ICC as the measure for between-systems agreement [20]. The between-systems agreement for dichotomous walking-adaptability outcomes varied, ranging from 100% overall agreement for obstacle-avoidance strategies to 85.2% for successes and failures in sudden stops. The specific agreement for obstacle-avoidance failures was lower (~60%), yet based on a limited number of observations. Future research may exploit IWW's possibility to vary task difficulty to achieve a similar distribution of obstacle-avoidance successes and failures to properly quantify their between-systems agreement.

Second, continuous walking-adaptability outcomes were sensitive to task and subject variations. With goal-directed stepping, task variations led to different step lengths, stepping accuracies and walking speeds (Figure 3.2) while ARTs and margins of the trailing limb varied with obstacle type. This testifies to the power of projected visual context in modifying gait and in eliciting (sudden) step adjustments, in line with previous studies exploring the same concept during treadmill walking [3,21-23], as well as to the sensitivity of continuous walking-adaptability outcomes. Success rates differed between obstacle types, although differences were very small in the vicinity of a ceiling effect. Future studies may increase obstacle-avoidance difficulty with the IWW by reducing ART, projecting larger obstacles, and/or adding attention-demanding secondary tasks [24]. Varying task difficulty with ART manipulations seems particularly effective, since in the present study ART had a prominent effect on sudden-stop success rates (Figure 3.3) and in other studies on obstacle-avoidance success rates [12,25]. Sensitivity to subject variation was further demonstrated by speed-performance trade-offs in goal-directed stepping (subjects who walked faster stepped less accurately onto targets) and sudden stops (subjects with shorter ARTs had smaller margins to the stop cue). Revealing such context-dependent interactions by objectively quantifying a complementary set of outcome measures can be considered one of the strengths of the IWW, which may prove useful in identifying fallers [26] and designing tailored interventions to reduce fall risk [1].

Taken together, our results confirmed that IWW walking-adaptability outcome measures are reliable (albeit that obstacle-avoidance failure rates have to be considered with caution) and sensitive to task and subject variations, even in high-functioning subjects. Sensitivity to task and subject variations is important for walking-adaptability assessments in relatively high-functioning groups (such as community-dwelling older adults), where ceiling effects are a common concern in fall-risk assessments [27]. The same holds for floor effects in relatively fragile groups (such as fall-prone populations). The IWW potentially allows for walking-adaptability assessments that are feasible for both high-functioning and fragile populations since task difficulty can be varied. IWW assessments are also relatively safe (e.g., visual instead of physical obstacles), unobtrusive (markerless data) and hence time-efficient and patient-friendly. The premise is that persons at risk of falling during walking may be better identified with task-specific assessments attuned to common causes and circumstances of falls [4-6], such as IWW walking-adaptability tasks. Future studies are warranted to determine which walking-adaptability tasks and associated outcomes are good indicators of safe walking and accurate predictors of falls during walking.

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Supplement 3.1

Data pre-processing

The Kinect for Windows Software Development Kit (SDK 2.0, www.microsoft.com) provides 3D time series of 25 body points using inbuilt and externally validated human-pose estimation algorithms [1-5]. These body points are: head, neck, spine shoulder, spine mid, spine base and left and right shoulder, elbow, wrist, hand, thumb, hand tip, hip, knee, ankle and foot (Figure S3.1B). For offline data analysis, the 3D positional data for these body points were first pre-processed per Kinect sensor separately. Body points labelled as inferred (i.e., Kinect's human-pose estimation software infers positions when segments are partially occluded for example) were treated as missing values. The body point's time series were linearly interpolated using Kinect's time stamps to ensure a constant sampling frequency of 30 Hz, without filling in the parts with missing values. We removed data points from the time series when they did not meet our stringent requirements for valid human-pose estimation (e.g., a minimum of 15 out of the 25 possible body points should be labeled as tracked, including the head and at least one foot and ankle, without outliers in segment lengths). Subsequently, data of the four Kinect sensors were combined by taking for each sample the 3D positions of the body points of a validly estimated human pose. If, for a given sample, more than one sensor contained valid human pose data, the associated body point's 3D positions were averaged for that specific sample. Note that the online integration process of multiple Kinect v2 data was similar to this offline integration process, except for the linear interpolation based on time stamps.

For motion registration with the Optotrak system (Northern Digital Inc., Waterloo, Canada), Smart Marker Rigid Bodies (Northern Digital Inc., Waterloo, Canada) were attached to the head, upper arms, forearms, lower abdomen, upper legs, lower legs and feet, allowing for 6 degrees of freedom tracking of body segments (Figure S3.1A). In addition, 30 anatomical landmarks were digitized using a 3-marker digitizing probe to define various body point positions (so-called virtual markers) on abovementioned body segments. Smart markers were also placed on the sternum, hands and feet. Body point's time series of the Optotrak system were computed from the virtual markers and/or smart markers to resemble corresponding Interactive Walkway (IWW) body points (see Table S3.1). In case of a single virtual marker or smart marker, the time series of that specific marker was taken as the time series of the associated body point (e.g., sternum data representing the spine shoulder body point of the IWW). In case of multiple virtual markers and/or smart markers, the associated marker positions were averaged in all three directions for each time sample. Positions of the neck, spine mid, thumbs and hand tips body points were not tracked with the Optotrak system due to the limited number of available smart markers, rendering a total of 19 out of aforementioned 25 matched body points.

The coordinate systems of the IWW (3D body points and projector pixels) and the Optotrak system were spatially aligned to a common coordinate system using a spatial calibration grid. Optotrak data were down-sampled to 30 Hz. Subsequently, the cross-covariance and time lag were determined for paired time series in the mediolateral and vertical direction of the elbows, wrists and hands during the synchronization movement (i.e., ab- and adduction of both arms). These time series were first interpolated with a spline algorithm in case of missing data. The median of the time lags was used to temporally align the time series of the two motion-registration systems. Body point's time series with more than 50% of missing values were excluded from further analyses. The missing values of the remaining data were interpolated with a spline algorithm. The so-obtained time series were used for the calculation of the walking-adaptability outcome measures. In the current study, only the time series of the spine shoulder, spine base and left and right ankle in the anterior-posterior direction were needed for the calculation of the walking-adaptability outcome measures (Figure S3.2).

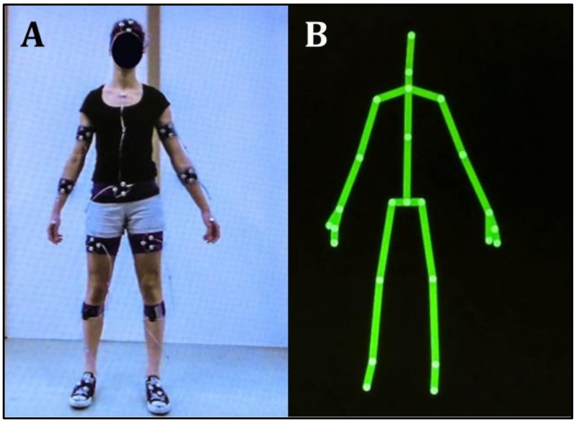

Figure S3.1 Body point determination with the Optotrak system and the Interactive Walkway. (A) Subject with all markers of the Optotrak system; (B) Snapshot of available Interactive Walkway body points of the same subject (derived with established human-pose estimation algorithms of Kinect v2).

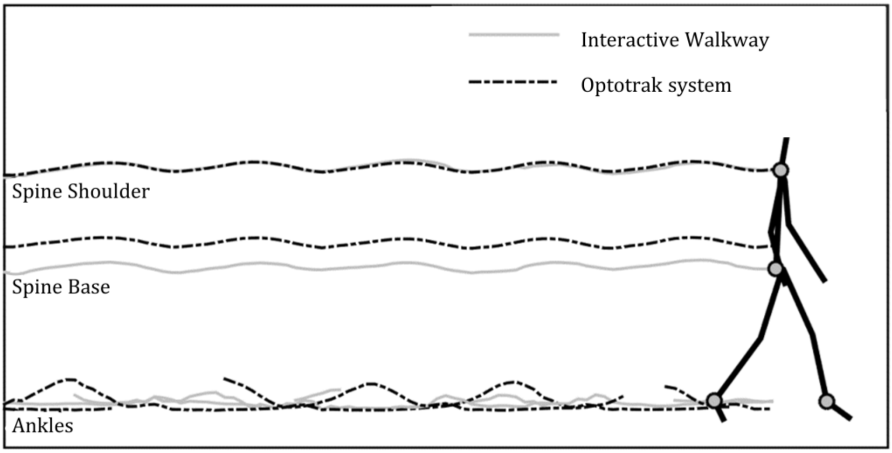

Figure S3.2 Raw time series of the two systems for the body points of interest to the current study. Note the missing values in the ankle data for the Optotrak time series.

Table S3.1 Overview of Optotrak marker data for deriving body points resembling Interactive Walkway body points.

Interactive Walkway body points	Smart Marker Rigid Body position	Virtual marker position	Smart marker position
Head	Head	Nasion, inion and left and right ear	-
Neck	-	-	-
Spine shoulder	-	-	Sternum
Spine mid	-	-	-
Spine base	Lower abdomen	Left and right anterior superior and posterior superior iliac spine	-
Shoulders	Upper arms	Head of the humurus	-
Elbows	Upper arms	Medial and lateral epicondyles	-
Wrists	Forearms	Distal head of the radius and ulna	-
Hands	-	-	Back of the hand
Hand tips	-	-	-
Thumbs	-	-	-
Hips	Upper legs	Trochantor major	-
Knees	Upper legs	Medial and lateral condyles	-
Ankles	Lower legs	Medial and lateral malleoli	-
Feet	Feet	Calcaneus	Head of the distal phalanx of the hallux

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Supplement 3.2

Data of body point's time series in the anterior-posterior, mediolateral and vertical direction for the Interactive Walkway and the Optotrak system. This data is available at: https://ars.els-cdn.com/content/image/

- 1-s2.0-S0966636217300553-mmc2.zip
- 1-s2.0-S0966636217300553-mmc3.zip
- 1-s2.0-S0966636217300553-mmc4.zip
- 1-s2.0-S0966636217300553-mmc5.txt

Chapter 4

Validation of foot placement locations from ankle data of a Kinect v2 sensor

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Published in Sensors 2017;17(10):E2301

The Kinect v2 sensor may be a cheap and easy to use sensor to quantify gait in clinical settings, especially when applied in set-ups integrating multiple Kinect sensors to increase the measurement volume. Reliable estimates of foot placement locations are required to quantify spatial gait parameters. This study aimed to systematically evaluate the effects of distance from the sensor, side and step length on estimates of foot placement locations based on Kinect's ankle body points. Subjects (n = 12) performed stepping trials at imposed foot placement locations distanced 2 m or 3 m from the Kinect sensor (distance), for left and right foot placement locations (side), and for five imposed step lengths. Body points' time series of the lower extremities were recorded with a Kinect v2 sensor, placed frontoparallelly on the left side, and a gold-standard motion-registration system. Foot placement locations, step lengths, and stepping accuracies were compared between systems using repeated-measures ANOVAs, agreement statistics and two one-sided t-tests to test equivalence. For the right side at the 2 m distance from the sensor we found significant between-systems differences in foot placement locations and step lengths, and evidence for nonequivalence. This distance by side effect was likely caused by differences in body orientation relative to the Kinect sensor. It can be reduced by using Kinect's higher-dimensional depth data to estimate foot placement locations directly from the foot's point cloud and/or by using smaller inter-sensor distances in case of a multi-Kinect v2 set-up to estimate foot placement locations at greater distances from the sensor.

Introduction

Quantitative gait assessments are a major undertaking in clinical settings (e.g., calibration procedures, patient-preparation time) and are costly due to expensive equipment [1]. The Microsoft Kinect v2 sensor may be a cheaper and easier to use alternative. It entails a RGB-D camera to create a depth image of its surrounding. Using machine-learning algorithms, the high-dimensional depth data can be reduced to 25 lower-dimensional three-dimensional (3D) body points of up to six people simultaneously, thereby eliminating the need for markers and calibration procedures [2]. The Kinect v2 sensor, originally developed for the gaming industry [2], has increasingly been studied in terms of its usability for quantitative gait assessments [3–10]. These studies collectively revealed that the Kinect v2 sensor is a promising tool for measuring spatiotemporal gait parameters [3–10].

Spatial gait parameters, such as step length, are quantified from estimates of foot placement locations, which are approximated from 3D positional data of Kinect's ankle body points [3,6–9]. However, Kinect's estimate of the ankle position seems to gradually change during the gait cycle in the anterior-posterior direction when compared to a gold standard, a phenomena that we observed in our own studies [6,7] as well as in other studies [9,11]. The influence of this gradual change in the anterior-posterior ankle position, as depicted in Figure 4.1A, on approximated foot placement locations has never been systematically examined, which seems essential given that yet unknown effects of distance from the Kinect v2 sensor, side and step length may affect outcome measures of quantitative gait assessments.

The objective of this study is to systematically compare foot placement locations, as approximated from ankle body point data, and associated estimates of step length and stepping accuracy between the Kinect v2 sensor and a gold-standard motion-registration system. To this end, the effect of distance to the Kinect v2 sensor, left and right foot placement locations (side) and imposed step lengths will be examined. We expect that foot placement locations, step lengths, and stepping accuracies will agree well between systems, without systematic between-systems effects of distance, side and imposed step length.

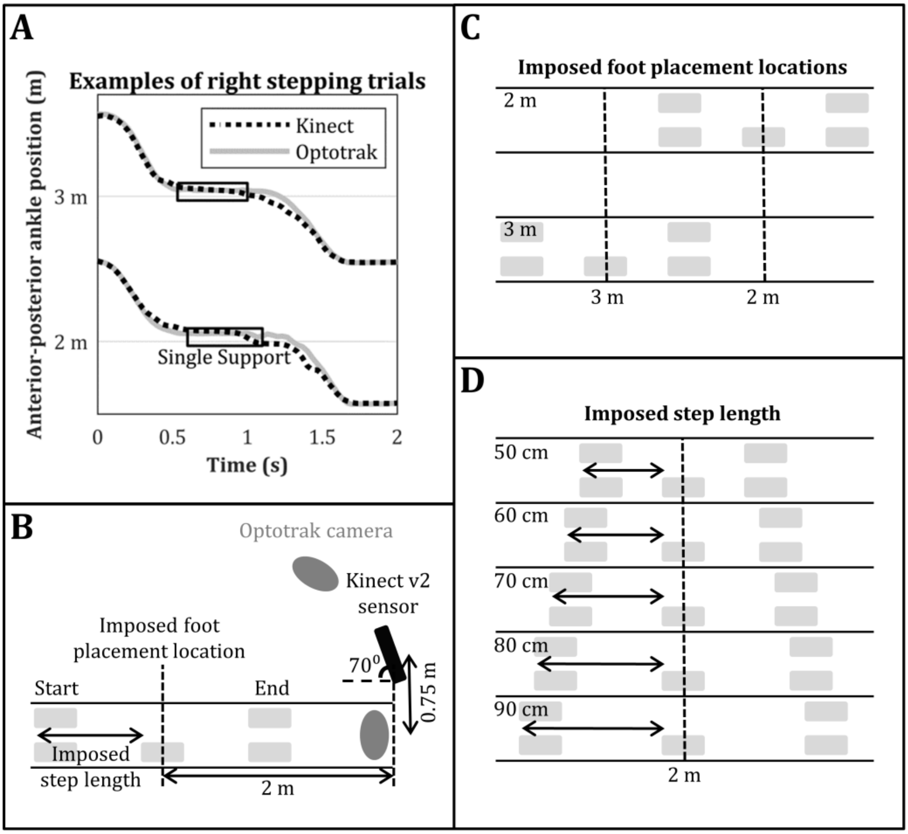

Figure 4.1 (A) Representative example of the right anterior-posterior ankle position for the Kinect v2 sensor (dotted black line) and a gold-standard Optotrak system (solid gray line) during two right stepping trials (at 2 m and 3 m distance from the sensor with the Kinect v2 sensor positioned at 0 m and walking direction towards the sensor). The single-support phase is indicated by the black boxes; (B) Schematic overview of the experimental set-up together with a right stepping trial at a 2 m distance from the sensor; (C) Schematic overview of the two imposed foot placement locations distanced 2 m (top) and 3 m (bottom) from the Kinect v2 sensor for right stepping trials; and, (D) Schematic overview of the different imposed step lengths for right stepping trials at a 2 m distance from the sensor.

Methods

Subjects

A group of 12 healthy subjects (mean [range]: age 28 [21 43] years, height 177 [158 190] cm, weight 74 [56 95] kg, 6 males) participated in this experiment. The Ethics Committee of the Department of Human Movement Sciences of the Vrije Universiteit Amsterdam (Amsterdam, The Netherlands) approved the study (ECB 2015-55). All of the subjects gave written informed consent prior to participation.

Experimental set-up and procedure

Body points' time series of the lower extremities were recorded with a Kinect v2 sensor and a gold-standard Optotrak system (Northern Digital Inc., Waterloo, ON, Canada). For the current study, the orientation and position of the Kinect sensor was in agreement with those of the Kinect sensors of a validated multi-Kinect v2 set-up for gait assessments (i.e., an angle of 70 degrees relative to the movement direction and a perpendicular distance of 0.75 meters to the center of the area of interest; [6,7]; Figure 4.1B). Multiple Kinect v2 sensors placed in a frontoparallel orientation (70 degrees) alongside a walkway allows for a larger measurement volume for quantitative gait assessments [6,7,9]. Two Optotrak cameras were needed to cover the same area as the Kinect sensor (see Figure 4.1B for a schematic overview). A spatial calibration grid was used to spatially align the coordinate systems of the two motion-registration systems to a common coordinate system, as detailed in [7].

As in [6,7], the Kinect for Windows Software Development Kit (SDK 2.0, www.microsoft.com) was used to obtain the 3D time series of 25 body points by means of inbuilt and externally validated human-pose estimation algorithms [3,6–9,12–14]. Kinect data were sampled at 30 Hz using custom-written software utilizing the SDK 2.0. For the Optotrak system, Smart Marker Rigid Bodies (Northern Digital Inc., Waterloo, ON, Canada) were attached to the body segments of the lower extremities (lower abdomen, upper legs, and lower legs) and virtual markers were assigned to these rigid bodies using a 3-marker digitizing probe using First Principles data acquisition software (see Supplement 4.1). The positions of the virtual markers were 14 anatomical landmarks chosen to match the body points of the Optotrak system with the body points of the lower body of the Kinect system (see Supplement 4.1). The positions of these virtual markers were averaged in all directions for each sample to obtain the positions of seven matched body points (see Supplement 4.1). Optotrak data were sampled at 60 Hz.

Subjects performed multiple stepping trials with foot placement locations being guided by five shoe-size-matched stepping stones (Figure 4.1B) presented using a projector (Vivitek D7180HD, ultra-short-throw Full HD projector), which was spatially aligned to the common coordinate system of the two motion-registration systems. The center of the middle stepping stone was positioned at two different imposed foot placement locations, distanced at either 2 m or 3 m from the Kinect sensor (Figure 4.1C). These distances ensure a high resolution of the depth data [15], and thus minimize the influence of depth resolution on the outcome measures. The middle stepping stone was either projected for the left or right foot depending on its mediolateral position. The position of the stepping stones indicating the starting and ending positions were determined based on the imposed step lengths (50 cm, 60 cm, 70 cm, 80 cm, or 90 cm; Figure 4.1D). Step width was set at 20 cm to ensure that the stepping stones did not overlap. Subjects were asked to stand as accurately as possible in the stepping stones indicating the starting position and then step with their left or right foot (depending on the imposed stepping pattern) in the middle stepping stone and end with both feet in the stepping stones indicating the ending position, thereby making a stepping movement. All of the trials were performed twice, yielding a total of 40 trials (i.e., at 2 m and 3 m distances, with the left and right side, at five imposed step lengths for two repetitions). Trials were block-randomized for distance and side.

Data pre-processing and analysis

Data pre-processing followed established procedures [6,7] using Matlab R2015a (The MathWorks Inc., Natick, MA, USA). Body points of the Kinect system classified as inferred (i.e., when Kinect's human-pose estimation software can only indirectly derive the position of the body point due to partial occlusion for instance) were removed from the time series. Body point's time series were linearly interpolated to ensure a constant sampling frequency of 30 Hz, without filling in the missing data points. Data points were removed from the time series when they did not meet our criteria for valid human pose estimation (e.g., a minimum of 15 out of the 25 possible body points should be labeled as tracked, including the head and at least one foot and ankle, without outliers in segment lengths). Optotrak body point's time series were down-sampled to 30 Hz. These data are available as supplementary material (see Supplement 4.2). Body point's time series of the spine base and left and right ankle in the anterior-posterior direction were interpolated with a spline algorithm and were used for the calculation of the outcome measures. Percentages of missing data for these body points' time series were on average 3.9% for the Kinect system and 0.6% for the Optotrak system, with maximum percentages of missing data of 21.4% and 20.1%, respectively.

The outcome measures were foot placement location, step length, and stepping accuracy. Foot placement locations were estimated from the anterior-posterior ankle position during the single-support phase (i.e., between foot off and foot contact of the contralateral foot; estimates of foot off and foot contact were defined as the minima and maxima of the anterior-posterior time series of the ankle relative to that of the spine base; [6,7,16]). Foot placement locations were transformed to center of the foot, using the ankle positions of the feet aligned with the stepping stones of the starting positions as a reference. To this end, the average distance of the left and right ankle to the center of the stepping stones was calculated over the episode of five samples before step initiation with the lowest amount of variation for each trial. Subsequently, foot placement locations were normalized to imposed foot placement locations (i.e., imposed foot placement location was subtracted from the measured foot placement location to correct for arbitrary effects in foot placement location as a function of the two imposed distances from the sensor). Step length was defined as the anterior-posterior distance between the starting position and the (non-normalized) foot placement location (see arrows in Figure 4.1D). Stepping accuracy was defined as the standard deviation over the signed normalized foot placement locations over step lengths and repetitions and was calculated per system, distance, and side.

Statistical analysis

One trial was accidentally not recorded with the Kinect system (experimenter forgot to start the recording without noticing it), resulting in missing data for foot placement location and step length for one participant (3 m distance, right side, 80 cm and repetition #2). Since missing data in a repeated-measures ANOVA will lead to the entire removal of that participant from the analysis, we decided to use this single observation for this participant and to average over the two repetitions for all other conditions and participants, yielding a single value for each combination of system, distance, side, and imposed step length for all of the participants. Two participants had to be excluded from further analyses due to displaced cluster markers of the Optotrak system.

All outcome measures (foot placement location, step length, and stepping accuracy) were compared between systems using repeated-measures ANOVAs (IBM SPSS Statistics 24). For foot placement locations and step lengths, a System (Kinect, Optotrak) by Distance (2 m, 3 m) by Side (left, right foot placement locations) by Imposed step length (50 cm, 60 cm, 70 cm, 80 cm, 90 cm) repeated-measures ANOVA was conducted. For stepping accuracy, a System by Distance by Side repeated-measures ANOVA was conducted. The assumption of sphericity was verified according to Girden [17]. The Huynh-Feldt correction was applied if the Greenhouse-Geisser's epsilon exceeded 0.75;

otherwise, the Greenhouse-Geisser correction was used. The main effects were examined with a Least Significant Difference post-hoc test for factors with two levels and contrast analyses for factors with more than two levels. Paired-samples *t*-tests were used for significant interactions involving the factor System, focusing on between-systems comparisons. Effect sizes were quantified with η_p^2.

In addition to the ANOVAs testing between-systems differences, we also performed agreement statistics to examine the agreement between the systems. The between-systems agreement was determined using intraclass correlation for absolute agreement ($ICC_{(A,1)}$) and consistency ($ICC_{(C,1)}$; [18]) using Matlab R2015a, with values above 0.60 and 0.75, representing good and excellent agreement, respectively [19]. Both types of ICCs were used in order to determine the influence of a potential systematic between-systems bias in the agreement. The ICCs were complemented by mean differences and precision values obtained with a Bland–Altman analysis (i.e., the bias [Kinect-Optotrak] and the limits of agreement [LoA], respectively; [20]).

In view of the low between-subject variation due to the imposed foot placement locations and step lengths, which may hinder the reliability of the ICCs [21], the outcome measures were also analyzed for between-systems equivalence using two one-sided *t*-tests (TOST; utilizing the TOSTER module in jamovi 0.7.3.2; [22]). For this analysis, the 90% confidence interval of the between-systems difference should be within pre-determined equivalence bounds for which the systems can be deemed equivalent. These bounds were conservatively set based on the LoA intervals found in [7]. That is, for foot placement locations and step lengths, the equivalence bounds were set at ± 2.145 cm (i.e., the smallest LoA interval of the obstacle-avoidance margins, which were similarly based on estimates of a single foot placement location; [7]). For stepping accuracies, the smallest LoA interval was used of the stepping accuracies obtained for precision-stepping trials to a sequence of regularly spaced stepping stones with imposed step lengths of 50 cm, 60 cm, 70 cm, 80 cm, and 90 cm ([7]; same step lengths as in the current study), resulting in equivalence bounds of ± 0.685 cm.

Results

Table 4.1 shows the data of all outcome measures together with the agreement statistics (bias, 95% LoA, $ICC_{(A,1)}$ and $ICC_{(C,1)}$) and TOST statistics.

Foot placement locations

A significant main effect of System ($F(1,9) = 5.87$, $p = 0.038$, $\eta_p^2 = 0.395$) was found on foot placement locations. Kinect estimated foot placement locations 0.76 cm posterior as compared to the Optotrak system. No other main or interaction effects were found, although there was a trend towards significant System×Imposed step length ($F(2.6,23.4) = 2.83$, $p = 0.067$, $\eta_p^2 = 0.239$) and System×Distance×Side ($F(1,9) = 4.66$, $p = 0.059$, $\eta_p^2 = 0.341$) interactions. There seemed to be a larger between-systems difference for the right foot placement location at 2 m when compared to the other conditions (see top panels in Figure 4.2). Regarding the equivalence tests, right foot placement locations at 2 m were found to be nonequivalent for 80 cm ($p = 0.072$) and 90 cm ($p = 0.110$), while all other foot placement locations were found to be equivalent ($p <$ 0.045). Note that in some cases the systems can be considered equivalent, as their 90% confidence intervals do not cross the equivalence bounds (i.e., no meaningful effect), and at the same time be statistically different in a *t*-test because the confidence intervals of the between-systems differences do not include zero (e.g., right foot placement locations at the 2 m distance for imposed step lengths of 50 cm, 60 cm, and 70 cm; Table 4.1, Figure 4.2).

Table 4.1 Mean values, between-subjects standard deviations (SD), agreement statistics (bias, limits of agreement [95% LoA] and intraclass correlation coefficients for absolute agreement [$ICC_{(A,1)}$] and consistency [$ICC_{(C,1)}$]) and results of the two one-sided *t*-tests (TOST) for foot placement locations, step lengths and stepping accuracies for all combinations of the independent variables Distance (2 m, 3 m), Side (left, right) and Imposed Step Length (50 cm, 60 cm, 70 cm, 80 cm, 90 cm).

				Kinect v2 mean ± SD	Optotrak mean ± SD	Bias [95% LoA]	$ICC_{(A,1)}$	$ICC_{(C,1)}$	TOST *p*-value
Foot placement location (cm)	**2 m**	**Left**	**50 cm**	−0.02 ± 0.87	−0.48 ± 1.33	0.46 [−1.93 2.85]	0.403	0.413	<0.001
			60 cm	−0.04 ± 1.24	−0.51 ± 1.67	0.47 [−2.06 3.00]	0.608	0.615	<0.001
			70 cm	0.02 ± 0.84	−0.61 ± 1.30	0.62 [−2.10 3.35]	0.178	0.193	0.004
			80 cm	0.47 ± 0.96	−0.29 ± 1.10	0.76 [−1.84 3.36]	0.147	0.174	0.005
			90 cm	0.01 ± 1.06	−0.73 ± 1.03	0.75 [−1.95 3.45]	0.115	0.135	0.005
		Right	**50 cm**	0.34 ± 1.35	−0.95 ± 1.03	1.28 * [−0.46 3.03]	0.471	0.727	0.007
			60 cm	0.68 ± 1.77	−0.77 ± 1.18	1.45 * [−0.79 3.70]	0.493	0.709	0.045
			70 cm	1.32 ± 1.17	−0.22 ± 0.79	1.54 * [−0.33 3.41]	0.254	0.544	0.038
			80 cm	0.57 ± 1.21	−1.04 ± 0.68	1.61 * [−0.48 3.69]	0.182	0.414	0.072 **
			90 cm	0.65 ± 1.52	−0.94 ± 1.04	1.59* [−1.02 4.20]	0.282	0.478	0.110 **
	3 m	**Left**	**50 cm**	−0.22 ± 1.16	−0.80 ± 1.13	0.58 [−1.69 2.85]	0.458	0.493	0.001
			60 cm	−0.10 ± 1.09	−0.44 ± 1.30	0.34 [−2.38 3.07]	0.334	0.325	0.001
			70 cm	−0.55 ± 1.57	−1.25 ± 1.50	0.70 [−2.89 4.29]	0.275	0.284	0.017
			80 cm	−0.00 ± 1.96	−0.79 ± 1.91	0.79 [−3.02 4.60]	0.480	0.495	0.027
			90 cm	−0.62 ± 1.51	−1.07 ± 1.82	0.45 [−2.92 3.83]	0.477	0.469	0.006
		Right	**50 cm**	−0.49 ± 1.48	−0.63 ± 1.64	0.14 [−2.84 3.11]	0.550	0.526	0.001
			60 cm	0.28 ± 1.59	0.02 ± 1.85	0.26 [−1.71 2.22]	0.836	0.831	<0.001
			70 cm	0.54 ± 1.34	0.04 ± 1.62	0.51 [−1.47 2.48]	0.744	0.770	<0.001

			80 cm	0.25 ± 1.42	−0.00 ± 2.13	0.25 [−2.39 2.89]	0.736	0.723	<0.001
			90 cm	0.04 ± 1.32	−0.57 ± 1.33	0.61 [−1.13 2.35]	0.717	0.777	<0.001
Step length (cm)	**2 m**	**Left**	**50 cm**	49.19 ± 1.38	50.32 ± 1.46	−1.13 * [−3.05 0.80]	0.590	0.761	0.005
			60 cm	59.32 ± 1.41	60.46 ± 1.50	−1.14 * [−3.36 1.08]	0.546	0.696	0.010
			70 cm	69.09 ± 0.94	70.20 ± 1.27	−1.12 * [−3.18 0.95]	0.380	0.554	0.006
			80 cm	79.45 ± 1.09	80.13 ± 1.40	−0.68 [−3.04 1.67]	0.492	0.542	0.002
			90 cm	90.06 ± 0.98	91.25 ± 1.38	−1.19 * [−3.95 1.58]	0.213	0.304	0.030
		Right	**50 cm**	49.02 ± 1.73	51.33 ± 1.37	−2.31 * [−3.59 −1.03]	0.439	0.913	0.773 **
			60 cm	58.73 ± 1.44	61.05 ± 1.30	−2.32 * [−3.77 −0.87]	0.353	0.854	0.762 **
			70 cm	67.50 ± 1.66	69.98 ± 1.39	−2.49 * [−4.64 −0.33]	0.325	0.744	0.825 **
			80 cm	79.52 ± 1.03	81.17 ± 1.25	−1.65 * [−2.97 −0.32]	0.411	0.827	0.022
			90 cm	89.49 ± 1.61	91.24 ± 1.72	−1.75 * [−3.41 −0.10]	0.566	0.871	0.089 **
	3 m	**Left**	**50 cm**	50.66 ± 1.35	50.73 ± 1.16	−0.06 [−1.92 1.80]	0.737	0.717	<0.001
			60 cm	60.18 ± 1.50	60.28 ± 1.38	−0.10 [−2.69 2.49]	0.605	0.581	<0.001
			70 cm	69.92 ± 1.91	70.78 ± 1.82	−0.85 [−5.72 4.02]	0.110	0.112	0.067 **
			80 cm	78.81 ± 2.14	80.02 ± 1.78	−1.21 [−5.81 3.38]	0.258	0.289	0.120 **
			90 cm	89.64 ± 1.99	90.74 ± 1.78	−1.11 [−5.60 3.38]	0.242	0.266	0.093 **
		Right	**50 cm**	50.79 ± 2.00	50.41 ± 2.10	0.39 [−2.77 3.55]	0.699	0.690	0.004
			60 cm	59.53 ± 1.97	59.65 ± 2.15	−0.12 [−2.60 2.36]	0.826	0.812	<0.001
			70 cm	69.60 ± 1.22	69.59 ± 1.54	0.01 [−2.61 2.62]	0.568	0.542	<0.001
			80 cm	79.44 ± 1.43	79.43 ± 2.29	0.00 [−3.52 3.53]	0.582	0.556	0.002
			90 cm	89.69 ± 1.32	89.63 ± 1.78	0.06 [−2.72 2.84]	0.615	0.590	<0.001

Table 4.1 Continued.

			Kinect v2 mean ± SD	Optotrak mean ± SD	Bias [95% LoA]	$ICC_{(A,1)}$	$ICC_{(C,1)}$	TOST *p*-value
Stepping accuracy(cm)	**2 m**	**Left**	1.33 ± 0.29	1.28 ± 0.33	0.05 [−0.24 0.33]	0.892	0.892	<0.001
		Right	1.30 ± 0.30	1.21 ± 0.26	0.08 [−0.18 0.35]	0.855	0.884	<0.001
	3 m	**Left**	1.52 ± 0.54	1.57 ± 0.61	−0.05 [−0.51 0.41]	0.922	0.917	<0.001
		Right	1.43 ± 0.47	1.48 ± 0.54	−0.05 [−0.78 0.68]	0.745	0.729	<0.001

* Significant between-systems difference ($p < 0.05$); ** Non-significant two one-sided *t*-tests, indicating nonequivalence (TOST $p > 0.05$).

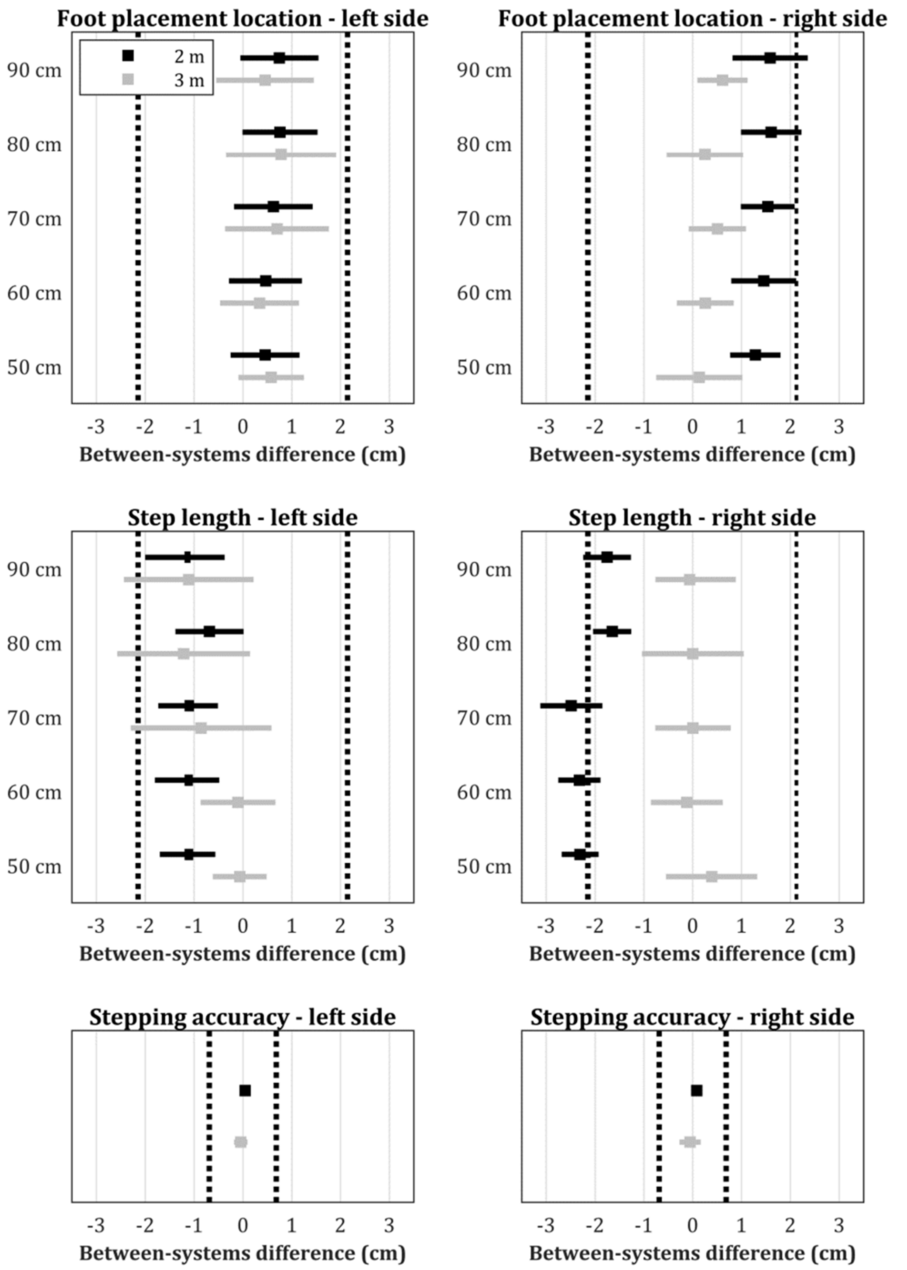

Figure 4.2 Results of the two one-sided *t*-tests, showing the between-systems differences and the 90% confidence intervals of all conditions for foot placement location, step length, and stepping accuracy.

Step length

A main effect of System was found on step length ($F(1,9) = 12.24$, $p = 0.007$, $\eta_p^2 = 0.576$). On average, Kinect underestimated step length with 0.94 cm as compared to the Optotrak system, a finding in line with abovementioned between-systems difference in foot placement locations. There was also a very strong effect of imposed step length on performed step length ($F(2.8,25.0) = 8167.28$, $p < 0.001$, $\eta_p^2 = 0.999$; with significant linear [$F(1,9) = 23285.32$, $p < 0.001$, $\eta_p^2 = 1.000$] and quadratic [$F(1,9) = 11.73$, $p = 0.008$, $\eta_p^2 = 0.566$] contrasts); step lengths increased with increasing imposed step lengths.

Furthermore, significant System×Distance ($F(1,9) = 13.12$, $p = 0.006$, $\eta_p^2 = 0.593$) and System×Distance×Side ($F(1,9) = 12.26$, $p = 0.007$, $\eta_p^2 = 0.577$) interactions were observed. The significant between-systems bias was only found at the 2 m distance and more strongly so for right step lengths (Figure 4.3), indicated by the significantly larger between-systems difference for the right step length at 2 m ($t(9) = 3.51$, $p = 0.007$). In addition, Distance×Imposed step length ($F(4,36) = 5.45$, $p = 0.002$, $\eta_p^2 = 0.377$; with significant linear by linear [$F(1,9) = 18.31$, $p = 0.002$, $\eta_p^2 = 0.670$] and linear by fourth order [$F(1,9) = 13.35$, $p = 0.005$, $\eta_p^2 = 0.597$] contrasts) and System×Distance×Imposed step length ($F(2.8,25.1) = 4.35$, $p = 0.015$, $\eta_p^2 = 0.326$) interactions were found; significant between-systems differences were again only found at the 2 m distance, with the smallest between-systems bias for 80 cm (Table 4.1, Figure 4.4).

Step lengths were generally found to be equivalent (most $p < 0.030$) with some exceptions for the right step length at 2 m, in agreement with the System×Distance×Imposed step length interaction, and the left step length at 3 m due to a relatively large between-subject variation (Figure 4.2).

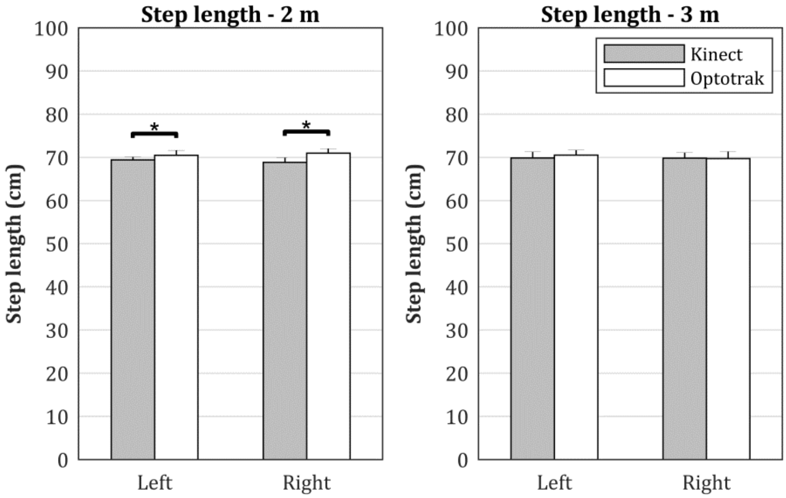

Figure 4.3 Visual representation of the interaction effect of System, Distance, and Side. The significant between-systems bias in step length was only found at the 2 m distance (indicated by the asterisks) and more strongly so for right step lengths (indicated by the significantly larger between-systems difference for the right step length).

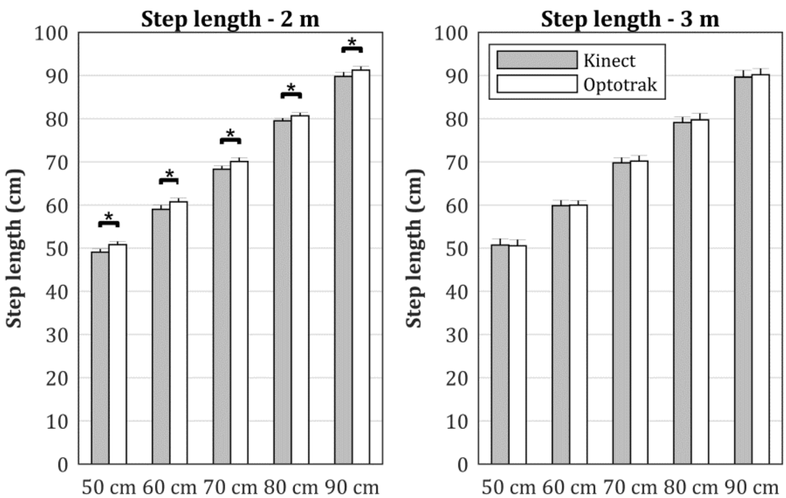

Figure 4.4 Visual representation of the interaction effect of System, Distance and Imposed step length. Significant between-systems differences in step length were only found at 2 m, with larger biases for larger imposed step lengths.

Stepping accuracy

For stepping accuracy, no significant main or interaction effects were found (all $p > 0.089$, all $\eta_p^2 < 0.287$). There was a trend towards significance for the System×Distance ($F(1,9) = 3.62$, $p = 0.089$, $\eta_p^2 = 0.287$) interaction. Kinect seemed to slightly underestimate stepping accuracy at the 2 m distance, and to slightly overestimate stepping accuracy at the 3 m distance (i.e., see the non-significant positive and negative biases in Table 4.1, respectively). Nevertheless, stepping accuracy was found to be equivalent between the systems ($p < 0.001$; Figure 4.2).

Discussion

The objective of this study was to systematically compare foot placement locations, as approximated from ankle body point data, and associated estimates of step length and stepping accuracy between the Kinect v2 sensor and a gold-standard Optotrak system. We expected that foot placement locations, step lengths, and stepping accuracies all agreed well between systems, without systematic between-systems effects of distance from the sensor, side and imposed step length. However, our results revealed a small but significant between-systems difference in foot placement locations and step lengths; Kinect estimated foot placement locations on average 0.76 cm posterior and consequently underestimated step length by 0.94 cm when compared to the Optotrak system. Note that these biases were predominantly found for the 2 m distance and were more pronounced for the right side. Nevertheless, stepping accuracies and estimates of foot placement locations and step lengths were generally statistically equivalent (i.e., no statistically meaningful between-systems bias, as evidenced by a statistically significant TOST), with a few nonequivalent exceptions in foot placement locations and step lengths mostly for the right side at the 2 m distance (Table 4.1, Figure 4.2). Two factors may have mediated the larger between-systems differences for the right side at the 2 m distance: 1) depth occlusion and 2) body orientation relative to the Kinect sensor. Since the Kinect sensor was positioned frontoparallelly on the left side of the participant, the right leg could be partially occluded by the swinging left leg during the stepping movement, and more strongly so nearby the sensor, which may have affected the outcomes. In the supplementary material (see Supplement 4.3) we describe an additional analysis aimed at examining the role of occlusion (and associated interpolation of the missing data) as a factor mediating the larger between-systems differences found for the foot placement locations of the right side at the 2 m distance. Based on the results we can conclude that depth occlusion did not cause the larger between-systems bias.

Could the second factor, body orientation relative to the Kinect sensor, then explain the between-systems differences for the right side at 2 m distance from the sensor? As can be seen in Figure 4.5, the orientation relative to the Kinect sensor changes with distance from the sensor and body side: from quite frontally for the left side at the 3 m distance to a more frontoparallel orientation for the right side at the 2 m distance. Orientation relative to the sensor likely affects the depth image of shank and foot segments due to orientation-based differences in self-occlusion of those body segments, which might influence the estimation of the position of the ankles from the point clouds by the machine-learning algorithm (cf. Figure 5B in [9]), and as such estimates of foot placement locations. Indeed, Wang et al. [23] showed that the positional error in body point estimates increases with deviations from a frontal orientation relative to the Kinect v2 sensor, especially so for body points of the body side that was turned away from the sensor. The turned-away body side was the right side in the current study, with the greatest deviations from a frontal orientation at the 2 m distance. This was also the condition with a meaningful between-systems bias in estimated foot placement locations, making body orientation relative to the sensor a very likely cause for the observed between-systems differences.

Knowing that body orientation relative to the sensor affects body point estimation, we will now discuss ways to minimize orientation biases in (multi-) Kinect set-ups for measuring gait with (a) sensor(s) placed alongside a walkway. A first recommendation could be to use sensors on both sides of a walkway in order to average out side-dependent orientation biases. Müller et al. [9] recently compared one-sided and two-sided multi-Kinect v2 set-ups to a gold-standard motion-registration system. They found superior between-systems agreement in step widths for the two-sided set-up, suggesting that mediolateral orientation biases, which are opposite in direction for the two sides, can indeed be successfully averaged out. Unfortunately, a two-sided set-up will not help to solve anterior-posterior orientation biases because these biases are similar in direction for both sides, with greater biases closer to the sensor. A second recommendation could be to use Kinect's higher-dimensional depth data to estimate foot placement locations directly from the foot's point cloud instead of approximating it from the lower-dimensional ankle body points' time series. Point clouds are robust, richer in information, and are likely less prone to orientation errors. Previous studies indeed found superior results for outcome measures (i.e., stride durations, stride lengths, and step asymmetries) derived from Kinect's higher-dimensional point clouds than for their counterparts derived from Kinect's lower-dimensional body points' time series [24-26]. As point clouds contain more information about the foot, they may additionally allow for finer-grained foot-related gait parameters, which seem particularly useful in clinical populations with gait deviations and foot deformations. Although point clouds may thus be a very useful alternative for determining foot placement locations, the higher dimensionality of the point clouds place greater demands on data handling. This is not much of a concern for post-processing, but will be a burden for real-time processing of gait data from multiple Kinect sensors for gait-dependent event control (e.g., suddenly projecting an obstacle at the location where one will step next; [7]). A more parsimonious solution, therefore, seems to be to collect body point data at greater distances from the sensor, for which we have shown that they are less prone to orientation biases. In the case of a multi-Kinect v2 set-up, this implies smaller inter-sensor distances to create more overlap between the measurement volumes of the sensors. Consequently, body point data nearby the sensor, which suffers from orientation biases, can be ignored because the same body points are already detected by the more distant sensor whose data is minimally affected by orientation biases.

A limitation of this study was that the effect of distance to the sensor was assessed in a rather coarse-grained manner (i.e., 2 levels, at 2 m and 3 m from the sensor). As a consequence, the precise cut-off for ignoring nearby data to circumvent orientation biases remains unknown. Another limitation is that two participants had to be excluded due to displaced cluster markers of the Optotrak system during the experiment, resulting in a relatively small sample size. The sample consisted of healthy adults without gait deviations, whose gait may not be representative for the gait of various patient groups. Nevertheless, there is no reason to expect inferior depth images or body point estimation of the lower extremities for persons with gait deviations [4], so the same recommendations apply for negating orientation biases when the Kinect v2 sensor is used for quantitative gait assessments in clinical populations.

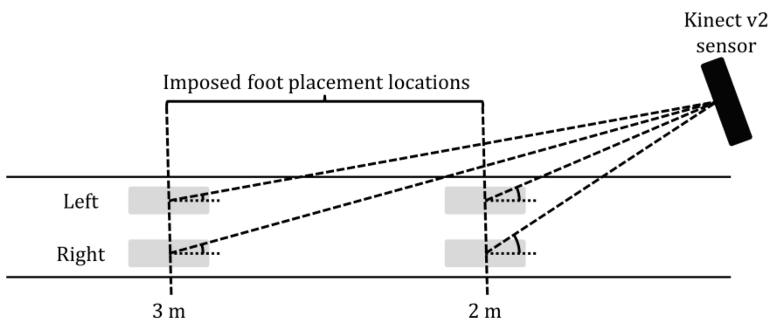

Figure 4.5 An overview of the influence of distance from the sensor and body side on body orientation relative to the Kinect sensor.

Conclusions

There is a meaningful between-systems difference in foot placement locations, albeit only nearby the sensor and exclusively for the body side turned away from the sensor (in our study the right side at a 2 m distance). This distance by side between-systems effect is not mediated by depth occlusion through the contralateral swinging leg, but is likely caused by body orientation differences relative to the sensor. Such orientation effects might be reduced by using the higher-dimensional depth data to estimate foot placement locations directly from the foot's point cloud and/or by using smaller inter-sensor distances in the case of a multi-Kinect v2 set-up, allowing for foot placement estimations at greater distances from the sensor.

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Supplement 4.1

Marker set-up of the Optotrak system.

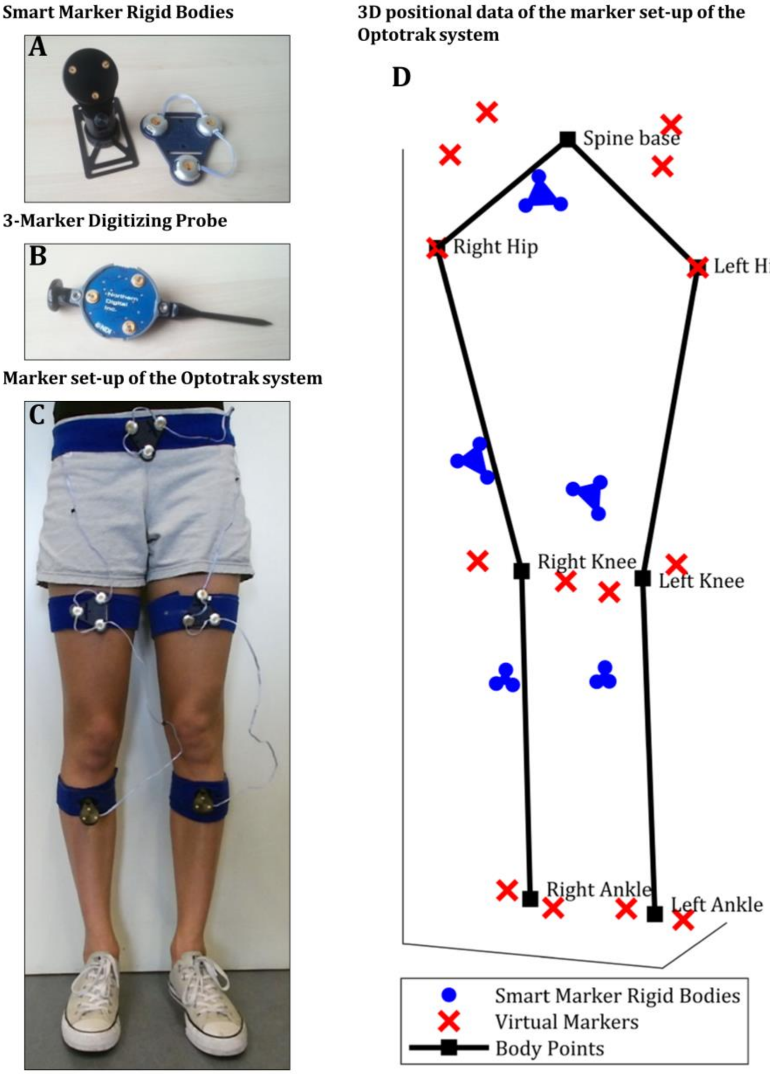

Figure S4.1 (A) Smart Marker Rigid Bodies of the Optotrak system. (B) 3-marker digitizing probe for assigning virtual markers to the Smart Marker Rigid Bodies. (C) Overview of the marker set-up of the Optotrak system. (D) Schematic overview of the 3D positional data of the marker set-up of the Optotrak system. Smart Marker Rigid Bodies (presented in blue) were attached to the body segments of the lower abdomen, upper legs, and lower legs. Virtual markers (red crosses) were assigned to these rigid bodies using a 3-marker digitizing probe. The positions of the virtual markers were 14 anatomical landmarks chosen to match the body points of the Optotrak system with the body points of the Kinect system (Table S4.1). The positions of these virtual markers were averaged in all directions for each sample to obtain the positions of seven matched body points (Table S4.1; black squares).

Table S4.1 Overview of Optotrak marker data for deriving body points resembling Kinect body points.

Kinect body points	Smart Marker Rigid Body position	Virtual marker position
Spine base	Lower abdomen	Left and right anterior superior and posterior superior iliac spine
Hips	Upper legs	Trochantor major
Knees	Upper legs	Medial and lateral condyles
Ankles	Lower legs	Medial and lateral malleoli

Supplement 4.2

Data of body points' time series in the anterior-posterior, mediolateral and vertical direction for the Kinect v2 sensor and the Optotrak system. Data is available at https://www.mdpi.com/1424-8220/17/10/2301/s1.

Supplement 4.3

In this supplementary material we describe an additional analysis aimed at examining the role occlusion (and the associated interpolation of missing data) may have played in the larger between-systems differences observed for the right side at the 2 m distance. First, we compared the amount of occlusion in the Kinect v2 data between distances and sides during the single-support phase. Second, we introduced occlusion (i.e., based on observed occlusion for the right side) to the data of the typically unoccluded left side to examine its effect on estimates of foot placement locations. If these foot placement locations are systematically affected by the introduced occlusion at the 2 m distance only, occlusion (and the associated interpolation of missing data) likely caused the observed between-systems differences for the 2 m distance for right foot placements.

Methods

Data analysis

The first step in the analysis was to compare the amount of occlusion (i.e., missing data) in the Kinect v2 data between distances and sides. Therefore, raw Kinect v2 body point's time series of the ankles without interpolation of the missing data points were used. The amount of occlusion was determined during the single-support phase (i.e., between foot off and foot contact of the contralateral foot), since foot placement locations were estimated using the anterior-posterior ankle position during this phase. Estimates of foot off and foot contact were calculated as detailed in the main text. Within this single-support phase, the samples representing missing data were identified and the percentage occlusion during the single-support phase was calculated. The distribution of occlusion over the single-support phase was visualized with a histogram presenting the percentage of all trials with occlusion during a specific part of the time-normalized single-support phase in bins of 5%.

The next step in the analysis was to introduce occlusion (i.e., based on observed occlusion for the right side) to the data of the typically unoccluded left side to examine the effect of occlusion (and the associated interpolation of missing data) on estimates of foot placement locations. This was done by using the observed occlusion during the right single-support phase of matched trials (i.e., in terms of distance and imposed step length). Subsequently, the so-obtained 'occluded' time series of the left ankle were interpolated with a spline algorithm before calculating foot placement locations and determining between-systems differences.

Statistical analysis

The amount of occlusion was assessed using a Distance (2 m, 3 m) by Side (left foot placement location, right foot placement location) repeated-measures ANOVA. The assumption of sphericity was checked according to Girden [1]. If Greenhouse–Geisser's epsilon exceeded 0.75, the Huynh–Feldt correction was applied; otherwise the Greenhouse–Geisser correction was used. Main effects were examined with a Least Significant Difference post hoc test. Paired-samples t-tests were used in case of a significant interaction. Effect sizes were quantified with η_p^2.

The between-systems differences for the foot placement locations of the left stepping trials were compared between original and 'occluded' data with a paired-samples t-test for each distance by imposed step length combination.

Results

The amount of occlusion differed significantly between distances (2 m: 11.60 ± 0.71%, 3 m: 9.60 ± 0.71%; $F(1,9) = 6.41$, $p = 0.032$, $\eta_p^2 = 0.416$) and sides (left: 0.07 ± 0.07%, right: 21.13 ± 1.16%; $F(1,9) = 339.17$, $p < 0.001$, $\eta_p^2 = 0.974$). Furthermore, there was a significant Distance×Side interaction ($F(1,9) = 6.21$, $p = 0.034$, $\eta_p^2 = 0.408$), revealing that the significant difference between the two distances was only evident for the right side with a significantly larger amount of occlusion for the 2 m distance (2 m: 23.11 ± 4.40%, 3 m: 19.15 ± 4.48%; $t(9) = 2.51$, $p = 0.033$). In Figure S4.2, the amount and distribution of occlusion during the single-support phase in the left and right ankle data are depicted, presented separately for the two distances. As can be appreciated from the figure (right panel), occlusion in the single-support phase for the right ankle occurred earlier for the 2 m distance than for the 3 m distance, which may have contributed to the significant difference in the amount of occlusion between these two distances.

The original and 'occluded' data of the left ankle during the single-support phase are presented in Figure S4.3, separately for the 2 m and 3 m distance. The introduced missing data has little to no effect on the presented time series for both distances. This was confirmed by the results of the foot placement locations presented in Table S4.2. The bias in the between-systems differences of the foot placement locations calculated with the original and 'occluded' data were not present (i.e., identical values for the foot placement locations calculated with the original data and the 'occluded' data) or negligible (i.e., submillimeter biases with low amount of variation). These biases, if any, were not significant for both distances.

Conclusion

Occlusion in the Kinect v2 data cannot explain the more pronounced between-systems differences seen for foot placement locations and consequently step lengths for the right side at the 2 m distance. Whereas the amount and timing of occlusion during the right single-support phase slightly differed between the 2 m and 3 m distance, the foot placement locations calculated with the 'occluded' data of the left ankle demonstrated negligible biases compared to the foot placement locations calculated with the original data, for both distances alike.

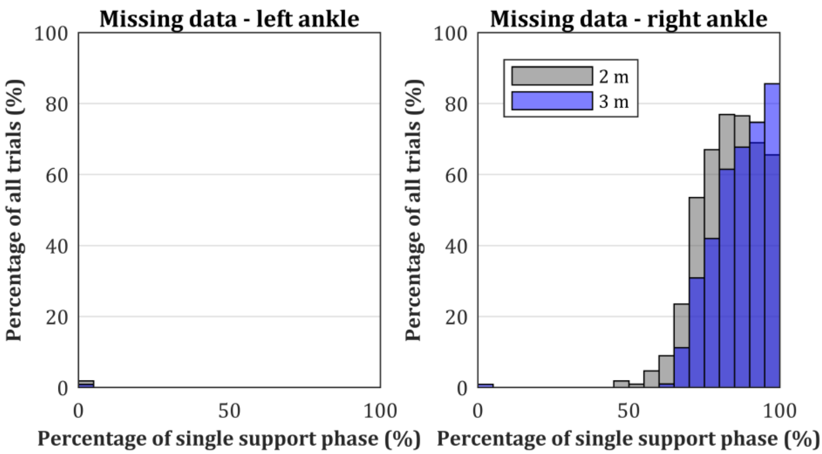

Figure S4.2 The amount and distribution of occlusion over the single-support phase, presented as the percentage of all trials with occlusion during a specific part of the time-normalized single-support phase in bins of 5%, for the left and right ankle (left and right panel, respectively), presented separately for the 2 m (gray) and 3 m (blue) distance.

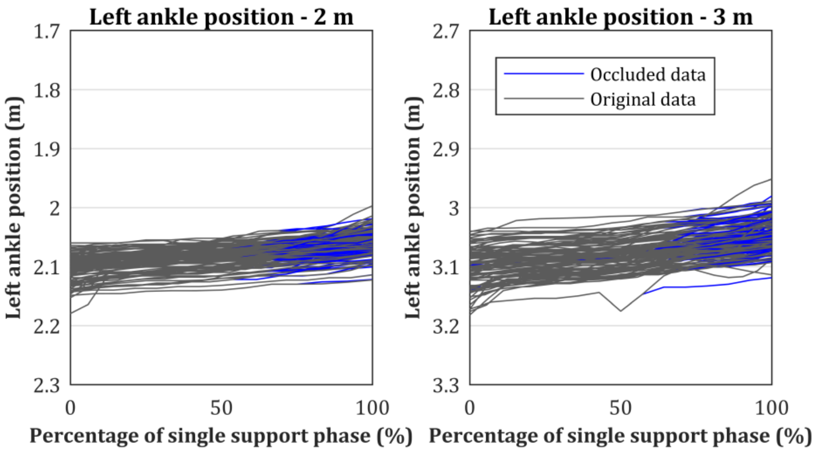

Figure S4.3 The original (gray) and 'occluded' (blue) time series of the left ankle in the anterior-posterior direction during the single-support phase, presented for the 2 m and 3 m distance (left and right panel, respectively).

Table S4.2 Mean values and between-subjects standard deviations (SD) of the between-systems differences (in cm) for foot placement locations calculated with the original and 'occluded' data of the left ankle, bias in between-systems differences and *t*-statistics.

			Between-systems difference				
			Original	'Occluded'	Bias		
Foot placement location (cm)			**mean ± SD**	**mean ± SD**	**mean ± SD**	***t*(9)**	***p***
	2 m	**50 cm**	0.458 ± 1.220	0.464 ± 1.224	0.006 ± 0.019	1.00	0.343
		60 cm	0.468 ± 1.290	0.468 ± 1.290	0 ± 0*	-	-
		70 cm	0.625 ± 1.390	0.625 ± 1.390	0 ± 0*	-	-
		80 cm	0.762 ± 1.326	0.762 ± 1.326	0 ± 0*	-	-
		90 cm	0.747 ± 1.378	0.747 ± 1.378	0 ± 0*	-	-
	3 m	**50 cm**	0.579 ± 1.156	0.579 ± 1.156	0 ± 0*	-	-
		60 cm	0.344 ± 1.392	0.344 ± 1.392	0 ± 0*	-	-
		70 cm	0.699 ± 1.833	0.699 ± 1.833	0 ± 0*	-	-
		80 cm	0.786 ± 1.944	0.801 ± 1.950	0.015 ± 0.046	1.00	0.343
		90 cm	0.453 ± 1.723	0.405 ± 1.647	-0.048 ± 0.218	0.70	0.504

* Identical values for the foot placement locations calculated with the original and 'occluded' data of the Kinect v2 system.

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Chapter 5

Assessing walking adaptability in stroke patients

Geerse DJ, Roerdink M, Marinus J, van Hilten JJ

Under review

Purpose. The ability to adapt walking is important for safe ambulation. Assessments of impairments in walking adaptability with the Interactive Walkway (IWW) may aid in the development of individualized therapy strategies of stroke patients. The IWW is an overground walkway with Kinect v2 sensors for a markerless registration of full-body kinematics which can be augmented with (gait-dependent) visual context to assess walking adaptability. This study aims to evaluate the potential of the IWW as a new technology for assessing walking adaptability in stroke patients. Materials and methods. 30 stroke patients and 30 controls performed clinical tests, quantitative gait assessments and various walking-adaptability tasks on the IWW. Outcome measures were compared between stroke patients and controls to examine known-groups validity. Pearson's correlation coefficients were calculated to assess the relationship between and within clinical test scores, spatiotemporal gait parameters and walking-adaptability outcome measures. Results. Good known-groups validity for walking-adaptability tasks was demonstrated. In addition, walking-adaptability tasks complemented clinical tests and spatiotemporal gait parameters and addressed different aspects of walking ability and walking adaptability. Conclusion. The IWW allows for a quick, unobtrusive and comprehensive quantitative assessment of walking adaptability with potential for monitoring recovery after stroke and informing neurologic therapy strategies.

Introduction

Walking speed assessed over short distances (e.g., 10-meter walking test), spatiotemporal gait parameters (e.g., step length) and clinical tests (e.g., Timed Up-and-Go test) are frequently used outcome measures of walking ability in stroke patients [1]. However, these outcome measures mainly reflect only two of the three aspects of walking ability, that is, the abilities to generate repetitive stepping and to maintain balance while walking. The third aspect of walking ability, the ability to adjust steps to one's surrounding, is largely left unaddressed, which is unfortunate as it is essential for safe and independent ambulation [2]. Walking adaptability is defined as the ability to adapt walking to meet behavioral task goals and demands of the environment [2] and includes, among others, the ability to avoid obstacles, make sudden stops, place feet accurately in a cluttered environment and walk while performing a dual task [2]. Laboratory studies showed that stroke patients generally have a reduced ability to adapt walking to environmental circumstances [3-6]. This reduced walking adaptability makes these patients more susceptible to walking-related falls due to trips, slips or misplaced steps [7-9]. Assessing walking adaptability thus seems essential to better understand and treat walking limitations. Unfortunately, there is no comprehensive clinical test of walking adaptability [2] and laboratory studies have thus far typically focused on specific aspects of walking adaptability, mainly obstacle avoidance [3-6,10,11]. As a consequence, we lack a thorough understanding of walking adaptability after stroke.

The Interactive Walkway (IWW; Figure 5.1) may help fill this void. It is an overground walkway equipped with multiple Kinect v2 sensors for markerless 3D full-body motion registration [12]. The IWW is augmented with (gait-dependent) visual context, such as suddenly appearing obstacles and stop cues (based on real-time processed gait data), to assess walking adaptability [13]. Furthermore, attention-demanding secondary tasks, such as serial-3 subtractions [11] or an auditory Stroop task [4,10], can be added to assess dual-task walking.

The aim of this study is to evaluate the potential of the IWW as a new technology for assessing walking adaptability in stroke patients. To this end, we will 1) evaluate the known-groups validity of IWW outcome measures by comparing them between stroke patients and healthy controls, 2) relate these outcome measures to clinical test scores and spatiotemporal gait parameters of unconstrained walking, and 3) examine to what extent the various walking-adaptability tasks address different aspects of walking adaptability.

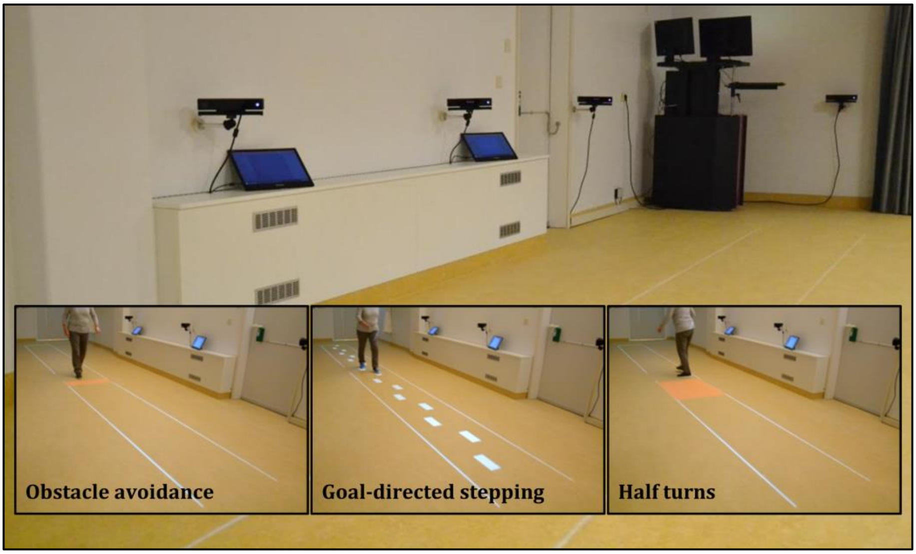

Figure 5.1 The set-up of the Interactive Walkway with various walking adaptability tasks (insets).

Methods

Subjects

In total, 30 stroke patients and 30 age- and sex-matched healthy controls (mean±std: 62.5 ± 10.1 vs. 62.9 ± 10.3 years, respectively; 18 males and 12 females) were included in this study. Stroke patients were recruited from the outpatient clinic of the Leiden University Medical Center and from a list of patients who were discharged from the Rijnlands Rehabilitation Center. Controls were recruited via advertisement. Subjects had to be 18 years or older and should have command of the Dutch language. Stroke patients had to experience residual motor dysfunction (Fugl-Meyer Assessment lower extremity score < 34), but had to be able to stand unsupported for more than 20 seconds and walk independently. Stroke patients were permitted to use walking aids, including quad canes (n = 3), canes (n = 4), ankle foot orthoses (n = 11) and functional electrical stimulation (n = 1). Controls had to have unimpaired gait, normal cognitive function (Montreal Cognitive Assessment score ≥ 23; [14]) and normal or corrected to normal vision. Exclusion criteria were (additional) neurological diseases and/or other problems interfering with gait function. Stroke patients were excluded if they were less than 12 weeks post-stroke. Stroke patients were 7.9 ± 7.3 years post-stroke, had a Fugl-Meyer Assessment lower extremity score of 19.7 ± 7.4 (possible range 0-34; higher scores indicate better motor function) and a Montreal Cognitive Assessment score of 24.4 ± 4.1 (possible range 0-30; higher scores indicate better cognitive abilities), which was not assessed in four stroke patients due to (severe) aphasia. Healthy controls had a significantly higher Montreal Cognitive Assessment score of 27.7 ± 1.4 (p < 0.001). Data was collected within the Technology in Motion project (protocol registered as NL54281.058.15; www.toetsingonline.nl). All subjects gave written informed consent, and the study was approved by the local medical ethics committee (P15.232).

Experimental set-up and procedure

Clinical gait and balance tests were administered. Two gait tests were included to assess mobility: the Timed-Up-and-Go test [15,16] and the 10-meter walking test at comfortable and maximum walking speed [15,17]. Longer completion times indicate worse mobility. The Tinetti Balance Assessment [18,19] has two sections that evaluate gait and balance performance, of which the combined score was used in this study (possible range 0-28; higher scores indicate better performance). Two balance tests were administered (with higher scores indicating a better balance): the 7-item Berg Balance Scale [20], to measure static and dynamic balance during specific movement tasks (possible range 0-14), and the Functional Reach Test [21,22], to determine the maximal distance one can reach forward from a standing position.

Unconstrained walking and walking adaptability were assessed on the IWW using four spatially and temporally integrated Kinect v2 sensors to obtain full-body kinematics. The IWW set-up was based on a validated IWW set-up used in Geerse et al. [12,13], with improved inter-sensor distances following recommendations of Geerse et al. [23] (Figure 5.1). The sensors were positioned at a height of 0.95 m alongside a walkway of 8 by 0.75 m. The first three sensors were placed frontoparallel (i.e., with an angle of 70 degrees relative to the walkway direction) with a distance of 1.2 m from the left border of the walkway. The last sensor was positioned frontally at the end of the walkway, since this will minimize orientation-based biases [24]. The first sensor was positioned at 3 m from the start of the walkway and the other sensors were placed at inter-sensor distances of 2.1 m. The IWW was equipped with a projector (EPSON EB-585W, ultra-short-throw 3LCD projector) to augment the entire 8-meter walkway with visual context for the walking-adaptability tasks. The coordinate systems of the sensors and projector were spatially aligned to a common coordinate system using a spatial calibration grid. IWW data were sampled at 30 Hz using custom-written software utilizing the Kinect-for-Windows Software Development Kit (SDK 2.0).

Subjects performed unconstrained walking and various walking-adaptability tasks on the IWW (Figure 5.2; see Table 5.1 for more details and Supplement 5.1 for a video of the tasks). Unconstrained walking was assessed with an 8-meter walking test. Walking adaptability was broadly assessed with the following tasks: obstacle avoidance, sudden stops-and-starts, goal-directed stepping (with symmetric and irregular stepping stones), narrow walkway, speed adjustments (speeding up and slowing down), slalom, turning (half and full turns in both directions) and dual-task walking (plain and augmented). Dual-task walking was assessed by adding an auditory Stroop task [25] in which the words high and low (in Dutch) were pronounced at a high or low pitch (i.e., congruent and incongruent stimuli) to both the plain 8-meter walking test and the augmented obstacle-avoidance task, respectively. The subject had to respond with the pitch of the spoken word. The IWW assessment comprises a total of 35 trials (Table 5.1). All tasks were performed at a self-selected walking speed.

Half of the subjects started with the block of clinical tests, the other half with the IWW assessment. With regard to the latter, subjects always started with the 8-meter walking test, which enabled us to adjust the settings of the walking-adaptability tasks to one's own gait characteristics in an attempt to obtain a similar level of difficulty for each subject (see Table 5.1). For example, available response times for suddenly appearing obstacles were controlled by self-selected walking speed during the 8-meter walking test and available response distance (ARD in Figure 5.2). Subsequently, the 8-meter walking test was performed with the dual task (i.e., plain dual-task walking), preceded by a familiarization trial in which the auditory Stroop task was practiced while sitting. The remaining IWW tasks were randomized in blocks (Table 5.1), with rest breaks in between to prevent fatigue.

Data pre-processing and analysis

Data pre-processing followed Geerse et al. [12,13], as detailed in Supplement 5.2. In total, 91 trials (4.2% of all trials) were excluded since some subjects (i.e., five stroke patients) were not able to perform the tasks or the trials were not recorded properly (i.e., incorrect recording or not all Kinect sensors were able to track the subject). The outcome measures of the IWW tasks were calculated from specific body points' time series, estimates of foot contact and foot off and step locations, as detailed in Table 5.1 and Supplement 5.2. The average over trials per task per subject was calculated for all outcome measures.

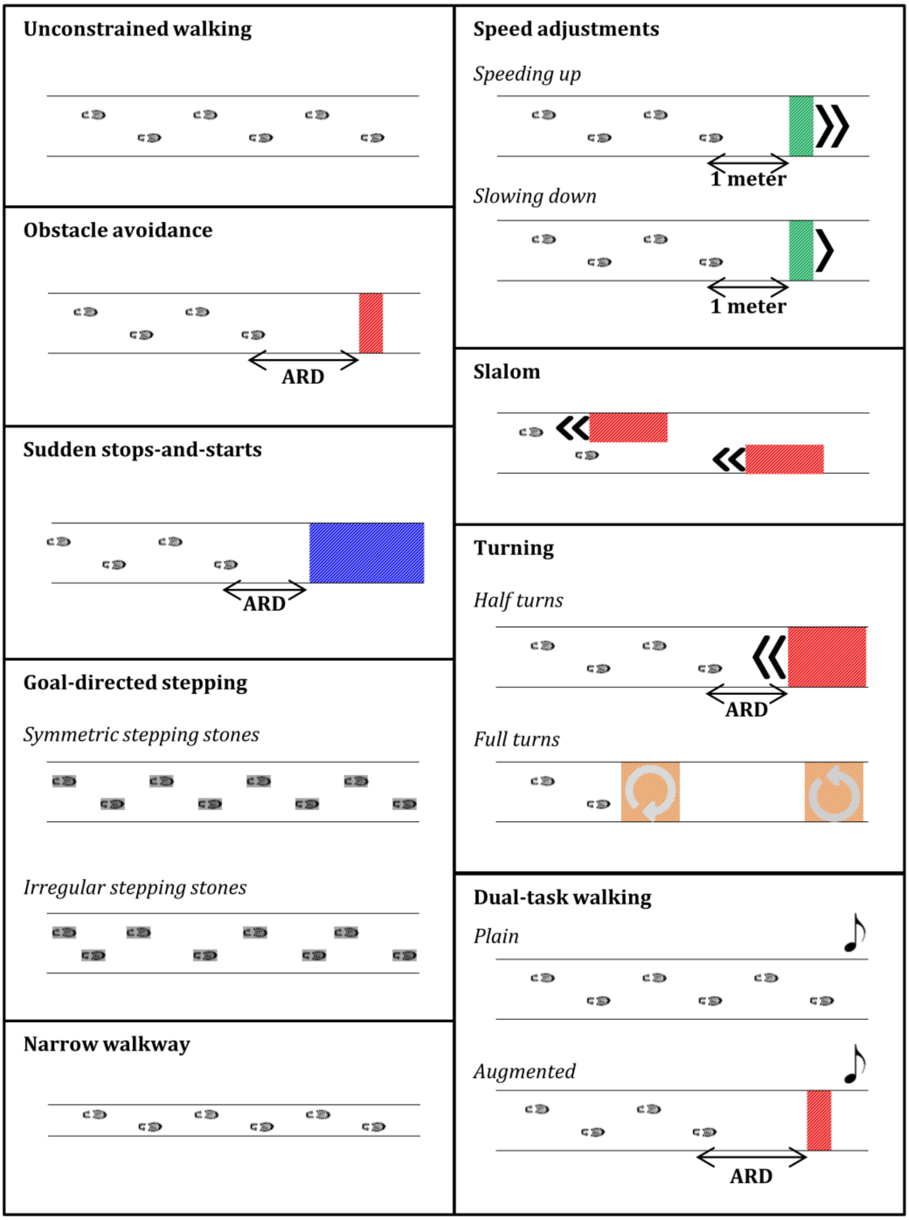

Figure 5.2 Schematics of unconstrained walking and walking-adaptability tasks on the Interactive Walkway. The available response distance (ARD) of the suddenly appearing obstacles and cues varied over subjects depending on their own gait characteristics.

Table 5.1 Interactive Walkway tasks and outcome measures of unconstrained walking and walking adaptability.

Tasks	n	Level of difficulty	Characteristics	Outcome measure	Unit	Calculation
Unconstrained walking						
8-meter walking test	2		Walking at self-selected walking speed.	Walking speed	cm/s	The distance travelled between the 0-meter and 8-meter line on the walkway divided by the time, using the data of the spine shoulder.
				Step length	cm	The median of the differences in the anterior-posterior direction of consecutive step locations.
				Stride length	cm	The median of the differences in anterior-posterior direction of consecutive ipsilateral step locations.
				Step width	cm	The median of the absolute mediolateral difference of consecutive step locations.
				Cadence	steps/min	Calculated from the number of steps in the time interval between the first and last estimate of foot contact.
				Step time	s	The median of the time interval

						between two consecutive instants of foot contact.
				Stride time	s	The median of the time interval between two consecutive ipsilateral instants of foot contact.
				Symmetry step length	%	Smallest step length (i.e., left or right) divided by the largest step length times 100%.
				Symmetry step time	%	Shortest step time (i.e., left or right) divided by the longest step time times 100%.
Walking adaptability						
Obstacle avoidance	5	ART = 1 s (three trials) ART = 0.75 s (two trials)	Avoiding suddenly appearing obstacles.	Obstacle-avoidance margins	cm	The distance of the anterior shoe edge (trailing limb) and posterior shoe edge (leading limb) of the step locations to corresponding obstacle borders during obstacle crossing.
				Success rate	%	Number of successfully avoided obstacles divided by the number of obstacles presented times 100%.

Table 5.1 Continued.

Tasks		n	Level of difficulty	Characteristics	Outcome measure	Unit	Calculation
Sudden stops-and-starts		5	ART = 1 s (three trials) ART = 0.75 s (two trials)	Stopping behind the suddenly appearing stop cues and start walking as soon as the cues disappear.	Sudden-stop margins	cm	The minimum distance of the anterior shoe edge to the corresponding stop cue border during the period in which the cue was visible.
					Success rate	%	Number of successful stops divided by the number of stop cues presented times 100%.
					Initiation time	s	The time between disappearance of the stop cue and the moment of first foot contact.
Goal-directed stepping	**SSS**	3	Average SL 75% average SL 125% average SL	Stepping as accurately as possible onto the shoe-size-matched stepping stones.	Stepping accuracy	cm	The standard deviation over the signed deviations between the center of the stepping target and the center of the foot at corresponding step locations. The center of the foot was determined using the average distance between the ankle and the middle of the shoe-size-matched targets of
	ISS	2	25% variation in SL left and right 50% variation in SL left and right				

							the calibration trials.
					Normalized walking speed	%	Walking speed divided by SSWS times 100%.
Narrow walkway		2	WW = 1.5*SW+FW WW = SW+FW	Walking between the lines of the walkway.	Success rate	%	Number of steps inside the walkway divided by the total number of steps taken times 100%.
					Normalized walking speed	%	Walking speed divided by SSWS times 100%.
					Normalized step width	%	Step width divided by the imposed step width times 100%.
Speed adjustments	**SU**	2	120% SSWS 140% SSWS	Start walking and when a speed cue appears one meter in front of the subjects it has to be followed at the imposed speed.	Success rate	%	The percentage of the time spend walking faster (or slower) than the imposed speed minus (or plus) 20% during the period in which the speed cue was visible.
	SD	2	80% SSWS 60% SSWS				
					Normalized walking speed	%	Walking speed divided by the imposed walking speed times 100%.

Table 5.1 Continued.

Tasks		n	Level of difficulty	Characteristics	Outcome measure	Unit	Calculation
Slalom		2	Symmetric distance between obstacles Variable distance between obstacles	Walking around the moving obstacles that approach the subjects with a speed of 50% SSWS.	Success rate	%	Number of successfully avoided obstacles divided by the number of obstacles presented times 100%.
					Normalized walking speed	%	Walking speed divided by SSWS times 100%.
Turning	**HT**	2	ART = 3 s ART = 2 s	Start walking and when a turning cue approaches the subject with a speed of 100% SSWS, the subject has to turn and walk back to the start.	Success rate	%	Number of successful half turns divided by the number of half turns times 100%.
					Turning time	s	Time within the turning square (for full turns) or time from appearance of the turning cue till moment walking direction was reversed (for half turns), using the data of the spine shoulder.
	FT	1		In the two presented squares the subject has to make a full turn as fast and safe as possible in the direction of the arrow.			

Dual-task walking	**PDT**	2		Walking while also performing a dual task. The dual task was an auditory Stroop task.	Normalized walking speed	%	Walking speed divided by SSWS times 100%.
	ADT	5	ART = 1 s (three trials) ART = 0.75 s (two trials)	Avoiding suddenly appearing obstacles while also performing a dual task. The dual task was an auditory Stroop task.	Normalized success rate	%	Obstacle avoidance success rate divided by success rate of the obstacle avoidance task times 100%, excluding subjects that had an obstacle-avoidance success rate of 0% at baseline.
					Success rate dual task	%	Number of correct responses divided by the number of stimuli given times 100% (excluding subjects that had an obstacle-avoidance success rate of 0% at baseline for ADT).
Total trials		**35**					

Abbreviations: SSS = symmetric stepping stones; ISS = irregular stepping stones; SU = speeding up; SD = slowing down; HT = half turns; FT = full turns; PDT = plain dual-task walking (8-meter walking test with dual task); ADT = augmented dual-task walking (obstacle avoidance with dual task); ART = available response time; SL = step length; WW = walkway width; SW = step width; FW = foot width; SSWS = self-selected walking speed of unconstrained walking.

Statistical analysis

The known-groups validity of clinical test scores, spatiotemporal gait parameters and IWW walking-adaptability outcome measures was evaluated by comparing them between stroke patients and healthy controls using independent-samples t-tests. We computed r ($r = \sqrt{t^2/(t^2 + df)}$) to quantify the effect sizes, where values between 0.100-0.299 were regarded as small, between 0.300-0.499 as medium and above 0.500 as large effect sizes [26].

Pearson's correlation coefficients were determined only for stroke patients and calculated between and within the various types of walking-ability assessments (i.e., clinical tests, unconstrained walking and IWW walking adaptability). Absolute correlations between 0-0.499, 0.500-0.699, 0.700-0.899 and 0.900-1.000 were regarded as low, moderate, high and very high, respectively [27]. SPSS version 24 (IBM© SPSS©, Armonk, New York, United States) was used to perform the statistical analyses. Alpha was set at 0.05. No adjustment for multiple comparisons was made due to the exploratory nature of this study.

Results

Known-groups validity

Stroke patients performed significantly worse on all clinical tests compared to healthy controls ($p \leq 0.001$; Table 5.2). This was also seen for the spatiotemporal gait parameters: all outcome measures showed values associated with lower walking speeds, wider step widths and less symmetric steps for stroke patients ($p < 0.001$; Table 5.2). Furthermore, stroke patients performed significantly worse than healthy controls on all IWW walking-adaptability outcome measures, except stepping accuracy on irregular stepping stones, normalized walking speed of speeding up trials, turning time of half turns and normalized success rate during augmented dual-task walking (Table 5.2).

Relations between the three types of walking-ability assessments

First, correlation coefficients were determined between clinical tests scores and spatiotemporal gait parameters (second block in top row in Figure 5.3). Of the 54 possible correlations, 45 (83.3%) were significant, out of which 28 (51.9%) were high, 13 (24.1%) were moderate and 4 (7.4%) were low. Next, correlation coefficients were determined between clinical test scores and IWW walking-adaptability outcome measures (third block in top row in Figure 5.3). Of the 156 possible correlations, 56 (35.9%) were significant, out of which 2 (1.3%) were very high, 4 (2.6%) were high, 31 (19.9%) were moderate and 19 (12.2%) were low. Lastly, correlation coefficients were determined between spatiotemporal gait parameters and IWW walking-adaptability outcome measures (third block of center row in Figure 5.3). Of the 234 possible correlations, 70 (29.9%) were significant, out of which 15 (6.4%) were high, 32 (13.7%) were moderate and 23 (9.8%) were low.

Relations within each type of walking-ability assessments

Considerable redundancy was found for the clinical tests in stroke patients (top left block in Figure 5.3). All 15 possible correlations were significant (100.0%), out of which 3 (20.0%) were very high, 6 (40.0%) were high, 2 (13.3%) were moderate and 4 (26.7%) were low. The spatiotemporal gait parameters were also highly correlated (second block along the diagonal in Figure 5.3). Of the 36 possible correlations, 34 (94.4%) were significant, out of which 7 (19.4%) were very high, 8 (22.2%) were high, 10 (27.8%) were moderate and 9 (25.0%) were low. For IWW walking-adaptability outcome measures, a lower percentage of significant correlations was found (bottom right block in Figure 5.3). Of the 325 possible correlations, only 57 (17.5%) were significant, out of which 1 (0.3%) was very high, 6 (1.8%) were high, 19 (5.8%) were moderate and 31 (9.5%) were low.

Table 5.2 Means, standard deviations and between-groups statistics of outcome measures of clinical tests, unconstrained walking and walking adaptability tasks on the Interactive Walkway for stroke patients and healthy controls.

			Stroke mean ± SD	Control mean ± SD	*t*-value	*p*-value	*r*-value
Clinical test							
Timed-Up-and-Go test	**Time (s)***		17.3 ± 11.4	7.4 ± 2.2	$t_{31.1}$ = -4.62	<0.001	0.638
10-meter walking test	**Time (s)***	**CWS**	16.6 ± 13.2	7.3 ± 1.0	$t_{29.3}$ = -3.83	0.001	0.577
	Time (s)*	**MWS**	13.5 ± 11.3	5.3 ± 0.8	$t_{29.3}$ = -3.94	<0.001	0.588
Tinetti Balance Assessment	**Score***		21.1 ± 5.0	27.7 ± 0.5	$t_{29.6}$ = 7.19	<0.001	0.797
7-item Berg Balance Scale	**Score***		10.0 ± 2.5	13.3 ± 1.3	$t_{43.8}$ = 6.50	<0.001	0.701
Functional Reach Test	**Reaching distance (cm)***		22.3 ± 7.2	29.9 ± 5.6	t_{58} = 4.60	<0.001	0.517
Unconstrained walking							
8-meter walking test	**Walking speed (cm/s)***		83.0 ± 34.6	134.3 ± 1.0	$t_{45.0}$ = 7.11	<0.001	0.727
	Step length (cm)*		52.4 ± 14.2	74.5 ± 9.4	$t_{50.3}$ = 7.10	<0.001	0.707
	Stride length (cm)*		105.3 ± 28.7	149.9 ± 18.7	$t_{49.8}$ = 7.13	<0.001	0.711
	Step width (cm)*		17.3 ± 5.5	11.1 ± 2.8	$t_{43.3}$ = -5.55	<0.001	0.645
	Cadence (steps/min)*		94.0 ± 20.5	112.3 ± 7.5	$t_{36.7}$ = 4.57	<0.001	0.602
	Step time (s)*		0.669 ± 0.184	0.526 ± 0.038	$t_{31.4}$ = -4.15	<0.001	0.595
	Stride time (s)*		1.335 ± 0.378	1.047 ± 0.074	$t_{31.2}$ = -4.10	<0.001	0.591
	Symmetry step length (%)*		85.5 ± 15.0	96.6 ± 2.3	$t_{30.3}$ = 4.03	<0.001	0.591
	Symmetry step time (%)*		78.7 ± 13.8	96.1 ± 2.9	$t_{31.5}$ = 6.80	<0.001	0.771

Walking adaptability							
Obstacle avoidance	**Margins trailing limb (cm)***		9.0 ± 8.4	19.9 ± 7.3	t_{58} = 5.38	<0.001	0.577
	Margins leading limb (cm)*		2.3 ± 6.8	12.1 ± 6.1	t_{58} = 5.88	<0.001	0.611
	Success rate (%)*		45.1 ± 32.4	88.2 ± 11.3	$t_{35.9}$ = 6.88	<0.001	0.754
Sudden stops-and-starts	**Sudden-stop margins (cm)***		-1.8 ± 7.2	5.4 ± 9.2	t_{57} = 3.33	0.002	0.403
	Success rate (%)*		56.5 ± 25.9	76.8 ± 18.5	$t_{50.7}$ = 3.46	0.001	0.437
	Initiation time (s)*		1.653 ± 0.462	1.338 ± 0.235	$t_{41.3}$ = -3.28	0.002	0.455
Goal-directed stepping	**Stepping accuracy (cm)***	**SSS**	3.7 ± 1.7	2.5 ± 0.7	$t_{35.6}$ = -3.48	0.001	0.504
	Normalized walking speed (%)*	**SSS**	78.5 ± 18.9	96.0 ± 16.5	t_{56} = 3.77	<0.001	0.449
	Stepping accuracy (cm)	**ISS**	4.8 ± 2.1	3.9 ± 1.0	$t_{40.4}$ = -1.97	0.056	0.296
	Normalized walking speed (%)*	**ISS**	77.7 ± 18.4	96.0 ± 15.7	t_{57} = 4.11	<0.001	0.478
Narrow walkway	**Success rate (%)***		68.7 ± 27.4	84.3 ± 17.4	t_{57} = 2.62	0.011	0.328
	Normalized walking speed (%)*		80.4 ± 17.3	99.0 ± 11.9	t_{57} = 4.83	<0.001	0.539
	Normalized step width (%)*		66.8 ± 30.2	37.7 ± 16.1	t_{57} = -4.64	<0.001	0.523
Speed adjustments	**Success rate (%)***	**SU**	58.5 ± 13.9	69.7 ± 10.1	$t_{47.0}$ = 3.46	0.001	0.450
	Normalized walking speed (%)	**SU**	87.8 ± 9.9	90.2 ± 6.7	$t_{44.8}$ = 1.07	0.291	0.158
	Success rate (%)*	**SD**	72.3 ± 6.8	79.1 ± 5.2	t_{55} = 4.24	<0.001	0.496
	Normalized walking speed (%)*	**SD**	102.9 ± 4.1	99.4 ± 2.3	$t_{40.1}$ = -3.94	<0.001	0.528
Slalom	**Success rate (%)***		43.3 ± 21.1	55.3 ± 23.0	t_{54} = 2.03	0.048	0.266
	Normalized walking speed (%)*		79.8 ± 15.5	94.7 ± 9.6	$t_{40.5}$ = 4.23	<0.001	0.554
Turning	**Success rate (%)***	**HT**	11.1 ± 25.3	65.0 ± 35.1	$t_{52.6}$ = 6.69	<0.001	0.678
	Turning time (s)	**HT**	1.533 ± 0.285	1.435 ± 0.251	t_{55} = -1.38	0.174	0.182
	Turning time (s)*	**FT**	6.164 ± 4.508	2.149 ± 0.961	$t_{28.1}$ = -4.53	<0.001	0.650

Table 5.2 Continued.

			Stroke mean ± SD	Control mean ± SD	*t*-value	*p*-value	*r*-value
Dual-task walking	**Normalized walking speed (%)***	**PDT**	79.7 ± 14.2	87.7 ± 9.5	$t_{56} = 2.54$	0.014	0.321
	Success rate dual task (%)*	**PDT**	77.4 ± 21.6	94.9 ± 12.2	$t_{43.9} = 3.80$	<0.001	0.498
	Normalized success rate (%)	**ADT**	80.8 ± 69.3	97.2 ± 23.9	$t_{27.4} = 1.11$	0.277	0.208
	Success rate dual task (%)*	**ADT**	68.3 ± 24.8	91.6 ± 9.2	$t_{28.1} = 4.38$	<0.001	0.637

Abbreviations: CWS = comfortable walking speed; MWS = maximum walking speed; SSS = symmetric stepping stones; ISS = irregular stepping stones; SU = speeding up; SD = slowing down; HT = half turns; FT = full turns; PDT = plain dual-task walking (8-meter walking test with dual task); ADT = augmented dual-task walking (obstacle avoidance with dual task).

*Significant between-groups difference ($p < 0.05$).

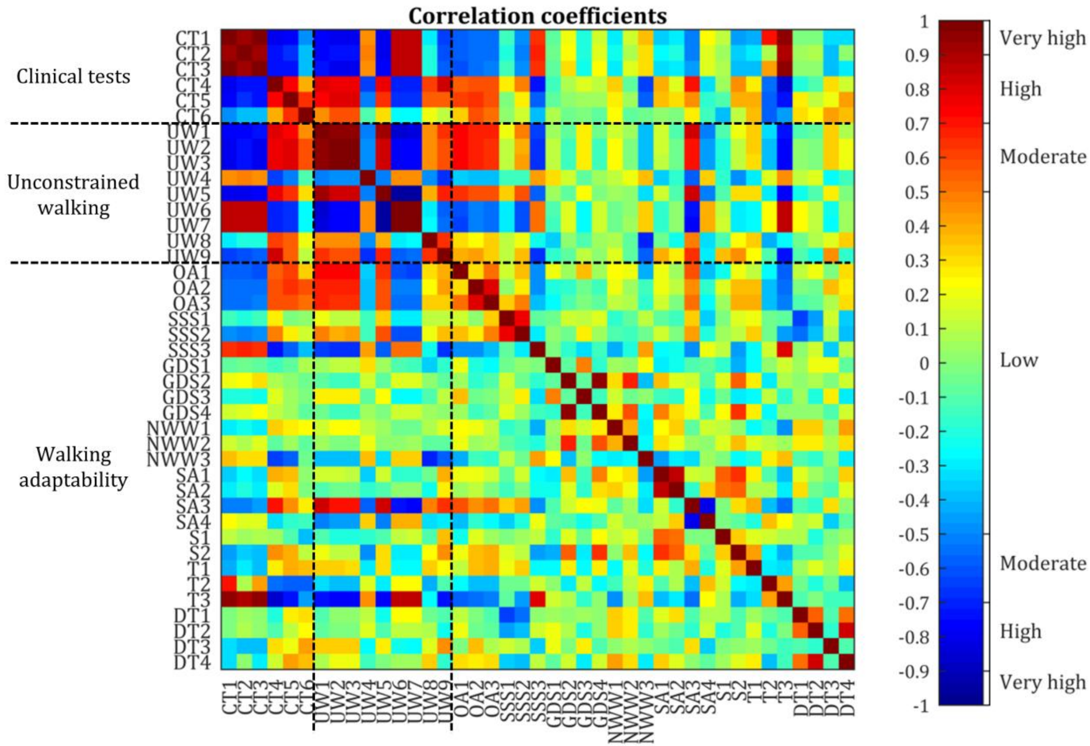

Figure 5.3 Overview of the correlation coefficients between (i.e., outer boxes) and within (i.e., boxes around the diagonal) the various types of walking-ability assessments (i.e., clinical tests [CT1-6], unconstrained walking [UW1-9] and walking adaptability [OA1-4, SSS1-4, GDS1-4, NWW1-3, SA1-4, S1-2, T1-4, DT1-15]) in stroke patients. The order of the outcome measures on the axes is in agreement with Table 5.2. The dotted black lines separate the three types of walking-ability assessments.

Discussion

A stroke may result in impaired walking adaptability and affect the ability to negotiate environmental challenges, thus potentially contributing to the high fall risk seen in this population [9]. Assessments of walking adaptability may guide gait rehabilitation programs or contribute to the design of future targeted and individualized interventions directed at improving safe community ambulation after stroke. However, currently available assessments of walking ability after stroke hardly take walking adaptability into account [2]. We therefore evaluated the potential of the IWW as a new technology for a quick, unobtrusive and comprehensive quantitative assessment of walking adaptability in stroke patients.

As a first step, we evaluated its known-group validity. As expected, for almost all outcome measures stroke patients performed significantly worse than healthy controls (Table 5.2). Group differences for spatiotemporal gait parameters measured with the IWW were as expected [28-30] and in line with the results of an earlier study showing that the Kinect v2 sensor can measure spatiotemporal gait parameters with considerable accuracy in stroke patients [31]. Also in accordance with the findings of previous studies, IWW outcome measures of the various walking-adaptability tasks revealed that stroke patients have problems avoiding obstacles [3,5,6], making sudden step adjustments [32,33], making full turns [34] and combining walking with secondary tasks [10,30]. Besides, normalized walking speeds were significantly lower for stroke patients, indicating that they adjusted their walking speed more than controls when walking in complex environments. These results emphasize the importance of assessing walking adaptability in an overground setting, which allows stroke patients to lower their walking speed depending on their ability to meet environmental demands [11]. In the current study, only stepping accuracy of the irregular stepping stones, normalized walking speed of speeding up trials, turning time of half turns and normalized success rate of augmented dual-task walking did not exhibit significant group differences.

Nonetheless, medium and large effect sizes were found for all other IWW outcome measures with differences occurring in the expected direction. Therefore, the results of this study suggest good known-groups validity for IWW walking-adaptability tasks, similar to that of clinical tests and spatiotemporal gait parameters.

Previous studies have indicated that there is a need for a more comprehensive clinical evaluation of walking ability, addressing all of its three key aspects (i.e., abilities to generate repetitive stepping, maintain balance while walking and adapt walking to environmental demands; [1,2]). Interesting in that regard is our observation of high to very high correlations between clinical tests and spatiotemporal gait parameters, which both mainly seem to address stepping and balance aspects of walking ability. IWW walking-adaptability tasks appeared to complement these tests, as evidenced by the relatively few significant correlations between walking-adaptability outcome measures and those pertaining to clinical tests and unconstrained walking (Figure 5.3). Moreover, the significant correlations were mostly low or moderate in magnitude, suggesting that the walking-adaptability tasks had added value by focusing especially on the third walking-ability aspect, that is, the ability to adjust walking to environmental circumstances [2].

We assessed walking adaptability quite broadly with, as it turned out, some redundancy in the outcome measures. Hence, not all of the assessed tasks need to be included for a comprehensive assessment of walking adaptability. That is, IWW tasks whose outcome measures do not exhibit group differences or are highly correlated with currently used tests can be excluded because they add little information. In this study this concerned sudden starts, speed adjustments, full turns and augmented dual-task walking tasks.

For a comprehensive assessment of walking ability, we recommend to include unconstrained walking (to identify gait impairments during steady-state walking) and some complementary IWW walking-adaptability tasks. With regard to unconstrained walking, assessing it with the IWW provides more detailed information than clinical test scores. In addition, the outcome measures may be more sensitive to changes over time as was suggested by Vernon et al. [35] for outcome measures of the Kinect-instrumented Timed Up-and-Go test. With regard to complementary IWW walking-adaptability tasks, various candidate tasks seem capable to address different aspects of walking adaptability. This was evidenced by the few significant correlations among outcomes of the various walking-adaptability tasks (bottom right block in Figure 5.3), in contrast to outcomes pertaining to clinical tests and unconstrained walking, which were highly interrelated and hence somewhat redundant with one another. Performing multiple clinical tests is therefore not only time-consuming, but also does not provide more insight into a patient's walking ability, in contrast to the addition of some complementary and discriminative IWW walking-adaptability tasks, such as obstacle avoidance, goal-directed stepping, narrow walkway and plain dual-task walking.

One of the limitations of this study was that clinical tests, unconstrained walking and walking adaptability were only assessed in a single session. Future studies should examine their test-retest reliability to estimate minimal detectable change scores that are essential for monitoring progress in gait rehabilitation. We further noticed that the available response times were significantly lower for stroke patients on some walking-adaptability tasks, which were caused by a higher self-selected walking speed in those tasks than in the preceding unconstrained walking task. This could have negatively influenced the outcome measures on these tasks and as such have amplified group differences. In future studies the available response times should therefore be based on a real-time indication of walking speed, which is quite feasible with the IWW. Another limitation could be that the IWW currently only uses 2D projections to evoke step responses, which do not actually pose a physical risk for the patient. This was clearly demonstrated in the study of Timmermans et al. [36]. Cognitive-motor interference did not differ between walking over physical or projected obstacles in stroke patients, although motor performance was prioritized more when walking over physical obstacles. Nevertheless, walking-adaptability tasks with 2D projections appeared effective, since outcome measures did demonstrate differences between groups with overall medium to large effect sizes.

Conclusions

The benefit of a broad assessment of walking adaptability is that it may reveal the specific aspects of walking adaptability that are most severely impaired, which could then be targeted in individualized training programs [37]. Van Swigchem et al. [5] found that even in mildly affected stroke patients walking adaptability may be reduced, possibly increasing their risk of falling. Training of walking adaptability, overground or on a treadmill, has shown to be effective in improving walking ability in stroke patients [4,9,38,39] and in reducing risk of falling [9]. The IWW assessment may thus contribute to a more optimized and individualized gait training program to improve safe community ambulation and reduce the risk of walking-related falls by adjusting the training content and difficulty level to the specific needs and competences of the patient.

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Supplement 5.1

Video of Interactive Walkway tasks of unconstrained walking and walking adaptability in a patient with stroke. This video is available at https://youtu.be/nV9tGvlPogs.

Supplement 5.2

Data pre-processing

The Kinect for Windows Software Development Kit (SDK 2.0, www.microsoft.com) provides 3D time series of 25 body points using inbuilt and externally validated human-pose estimation algorithms [1-5]. These body points are: head, neck, spine shoulder, spine mid, spine base and left and right shoulder, elbow, wrist, hand, thumb, hand tip, hip, knee, ankle and foot. For offline data analysis, the 3D positional data for these body points were first pre-processed per Kinect sensor separately. Body points labelled as inferred (i.e., Kinect's human-pose estimation software infers positions when segments are partially occluded for example) were treated as missing values. The body point's time series were linearly interpolated using Kinect's time stamps to ensure a constant sampling frequency of 30 Hz, without filling in the parts with missing values. We removed data points from the time series when they did not meet our stringent requirements for valid human-pose estimation (e.g., a minimum of 15 out of the 25 possible body points should be labeled as tracked, including the head and at least one foot and ankle, without outliers in segment lengths). In addition, a manual check of the data was added to remove errors of the algorithm due to depth occlusion of the right leg by the left leg. Subsequently, data of the four Kinect sensors were combined by taking for each sample the 3D positions of the body points of a validly estimated human pose. If, for a given sample, more than one sensor contained valid human pose data, the associated body point's 3D positions were averaged for that specific sample.

Body point's time series with more than 50% of missing values were excluded from further analyses. However, percentages of missing data for both groups did not exceed 23.1% with an average of 4.7 ± 2.2% for the body points' time series of interest (i.e., ankles, spine base and spine shoulder). The missing values were interpolated with a spline algorithm. The so-obtained time series were used for the calculation of the Interactive Walkway outcome measures of unconstrained walking and walking adaptability.

The outcome measures of the Interactive Walkway assessment were calculated from specific body points' time series, estimates of foot contact and foot off and step locations, as detailed in Table 5.1. Estimates of foot contact and foot off were defined as the maxima and minima of the anterior–posterior time series of the ankles relative to that of the spine base [3,6,7]. Step locations were determined as the median anterior–posterior and mediolateral position of the ankle joint during the single-support phase (i.e., between foot off and foot contact of the contralateral foot; [3,6]). Shoe edges and center of the foot were also needed to calculate several outcome measures. Ankle-to-shoe calibration trials, in which the subject was standing in two shoe-size-matched targets at a position on the walkway in front of the last Kinect, were included to determine the average distance between shoe edges and the ankle.

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Chapter 6

Assessing walking adaptability in Parkinson's disease: "The Interactive Walkway"

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Published in Frontiers in Neurology 2018;9:1096

Introduction. In patients with Parkinson's disease (PD) many aspects of walking ability deteriorate with advancing disease. Clinical tests typically evaluate single aspects of walking and to a lesser extent assess more complex walking tasks involving a combination of the three key aspects of walking ability (i.e., generating stepping, maintaining postural equilibrium, adapting walking). The Interactive Walkway allows for assessing more complex walking tasks to address features that are relevant for daily life walking of patients, including adaptive walking and dual-task walking. Methods. To evaluate the expected added value of Interactive Walkway assessments in PD patients, we first evaluated its known-groups validity for outcome measures of unconstrained walking, adaptive walking and dual-task walking. Subsequently, these outcome measures were related to commonly used clinical test scores. Finally, we evaluated the expected added value of these outcomes over clinical tests scores in discriminating PD patients with and without freezing of gait. Results. Interactive Walkway outcome measures showed significant differences between freezers, non-freezers and healthy controls, in expected directions. Most Interactive Walkway outcome measures were not or at best moderately correlated with clinical test scores. Finally, Interactive Walkway outcome measures of adaptive walking slightly better discriminated freezers from non-freezers than clinical tests scores. Conclusion. We confirmed the added value of Interactive Walkway assessments, which provides a comprehensive evaluation of walking ability incorporating features of its three key aspects. Future studies are warranted to examine the potential of the Interactive Walkway for the assessment of fall risk and informing on tailored falls prevention programs in PD patients and in other populations with impaired walking ability.

Introduction

Walking ability is a multifaceted construct which includes the ability to generate stepping, to maintain postural equilibrium, and to adjust walking to meet behavioral goals and environmental demands [1]. In Parkinson's disease (PD) these walking ability aspects all deteriorate to some extent with advancing disease. This is evidenced by an inability to generate effective stepping (e.g., freezing of gait [FOG]), a reduced ability to adapt walking to environmental circumstances, and a limited ability to combine walking with secondary tasks [2-5]. Such impairments in walking ability may contribute to an increased fall risk. This is clearly demonstrated in PD, where most falls are due to FOG, impaired adaptive walking resulting in trips, and limitations in dual-task walking [6,7]. Clinical tests to evaluate gait and balance disturbances in PD typically evaluate single aspects of walking ability (i.e., the ability to generate stepping or to maintain postural equilibrium) and to a lesser extent assess more complex walking tasks (i.e., adaptive walking and dual-task walking) involving a combination of the three key aspects of walking (stepping, equilibrium and adaptation). The Interactive Walkway (IWW; Figure 6.1) allows for assessing more complex walking tasks to address features that are relevant for daily life walking of patients, which could guide the management of clinical care.

This study aimed to evaluate the expected added value of IWW assessments in PD patients, which includes an assessment of more complex walking tasks. The IWW utilizes multiple external sensors for a validated quick markerless 3D full-body motion registration of unconstrained walking [8]. Moreover, the IWW can be used to assess adaptive walking by augmenting the walkway with visual context, such as suddenly appearing obstacles [9], whose location and timing can be controlled based on real-time processed full-body kinematics. Finally, the IWW may be used to assess the ability to combine walking tasks with a secondary task by quantifying dual-task costs of walking and adaptive walking [10]. In this study, we first examined the known-groups validity of IWW outcome measures of unconstrained walking, adaptive walking and dual-task walking to detect differences between PD patients with FOG, PD patients without FOG and healthy controls. Secondly, we compared IWW outcome measures to commonly used clinical tests of gait and balance impairment to identify redundancy and complementarity between tests. Thirdly, we examined the expected added value of the IWW over clinical tests in discriminating PD patients with and without FOG.

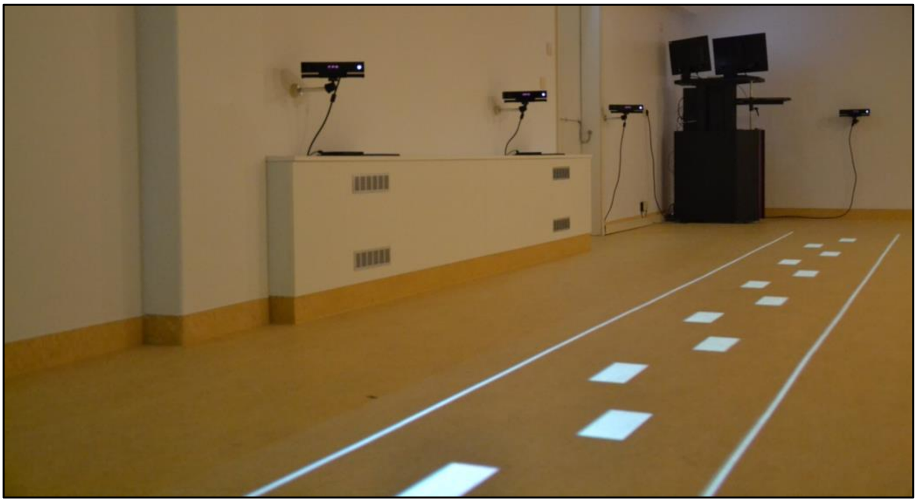

Figure 6.1 Set-up of the Interactive Walkway with visual context projected on the walkway.

Methods

Subjects

Walking ability was assessed in 30 PD patients and 30 age- and sex-matched healthy controls (Table 6.1). PD patients and controls were recruited from the outpatient clinic of the Leiden University Medical Center and via advertisement, respectively. PD patients had to meet the UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria [11] and have a Hoehn and Yahr stage of 1-4 [12]. In addition, subjects had to be 18 years or older, have command of the Dutch language, be able to stand unsupported for more than 20 seconds and walk independently. PD patients were evaluated using the Movement Disorder Society version of the Unified Parkinson's Disease Rating Scale motor score [13]. The New Freezing of Gait Questionnaire [14] was used to classify PD patients with and without FOG (i.e., based on a score greater than or equal to zero, respectively), leading to the classification of 14 freezers and 16 non-freezers. The Scales for Outcomes in Parkinson's disease – Cognition [15] was administered to assess cognitive abilities, since this scale is sensitive to PD-specific cognitive deficits. PD patients were measured in the ON state. Controls did not suffer from neurological or orthopedic diseases interfering with gait, had normal cognitive function (Montreal Cognitive Assessment score ≥ 23; [16]) and (corrected to) normal vision. All subjects gave written informed consent, and the study was approved by the local medical ethics committee (P15.232).

Experimental set-up and procedure

We used clinical tests of gait and balance impairment that have previously been suggested or recommended for use in PD patients [17]. Two tests assessed mobility: the Timed-Up-and-Go test and the 10-meter walking test at comfortable and maximum walking speed. Longer completion times indicate poorer mobility. The Tinetti Balance Assessment has two sections that evaluate gait and balance performance of which the combined score was used in this study (higher scores indicate a better performance). Two other balance tests were administered: the 7-item Berg Balance Scale, to measure static and dynamic balance, and the Functional Reach Test, to determine the maximal reaching distance (higher scores indicating a better balance). The order of these clinical tests was randomized.

Table 6.1 Group characteristics of Parkinson's disease patients (all, freezers and non-freezers) and healthy controls.

		Parkinson's disease	Freezer (n = 14)	Non-freezer (n = 16)	Control
Age (years)	**mean ± SD**	63.1 ± 10.0	61.8 ± 9.6	64.2 ± 10.5	62.9 ± 10.3
Sex	**male/female**	18/12	10/4	8/8	18/12
Disease duration (years)	**mean ± SD**	12.2 ± 6.7	14.3 ± 6.8	10.3 ± 6.3	-
Levodopa equivalent daily dose (mg)[a]	**mean ± SD**	939 ± 771	1258 ± 947	661 ± 441	-
SCOPA-COG [0-43]*	**mean ± SD**	30.4 ± 7.1	28.9 ± 8.0	31.8 ± 6.3	-
MDS-UPDRS motor score [0-132]**	**mean ± SD**	36.9 ± 18.0	41.4 ± 20.3	32.9 ± 15.3	-
Hoehn and Yahr stage [1-5][**,a]	**mean ± SD**	2.3 ± 0.7	2.6 ± 0.7	2.0 ± 0.5	-
NFOGQ [0-24]**	**mean ± SD**	-	19.9 ± 5.0	0	-
MOCA [0-30]*	**mean ± SD**	-	-	-	27.7 ± 1.4

Abbreviations: SCOPA-COG = Scales for Outcomes in Parkinson's disease – Cognition; MDS-UPDRS = Movement Disorder Society version of the Unified Parkinson's Disease Rating Scale; NFOGQ = New Freezing of Gait Questionnaire; MOCA = Montreal Cognitive Assessment.

*Higher scores represent better outcomes.

**Higher scores represent worse outcomes.

[a]Significant difference between freezers and non-freezers ($p < 0.05$).

The IWW was used to assess unconstrained walking, adaptive walking and dual-task walking (cf. Figure 6.2; see Supplement 6.1 and Table 6.2 for more details). Full-body kinematics was obtained using four spatially and temporally integrated Kinect v2 sensors, which allows for a quick markerless assessment of walking. The sensor set-up was based on a validated IWW set-up [8,9], with improved inter-sensor distances following recommendations of Geerse et al. [18] (Figure 6.1). The sensors were positioned at a height of 0.95 m alongside a walkway of 8 by 0.75 m. The first three sensors were placed frontoparallel (i.e., with an angle of 70^0 relative to the walkway direction) with a distance of 1.2 m from the left border of the walkway. The last sensor was positioned frontally at the end of the walkway, since this will minimize orientation-based biases. The first sensor was positioned at 3 m from the start and the other sensors were placed at inter-sensor distances of 2.1 m (Figure 6.1). The IWW was equipped with a projector (EPSON EB-585W, ultra-short-throw 3LCD projector) to augment the entire walkway with visual context. The coordinate systems of the sensors and the projector were spatially aligned using a spatial calibration grid. IWW data were sampled at 30 Hz using custom-written software utilizing the Kinect-for-Windows Software Development Kit (SDK 2.0). Unconstrained walking was assessed with an 8-meter walking test. Adaptive walking was assessed with obstacle avoidance, sudden stops-and-starts, goal-directed stepping (symmetric and irregular stepping stones), narrow walkway (entire walkway and sudden narrowing), speed adjustments (speeding up and slowing down), slalom and turning (half and full turns). Dual-task walking was assessed in plain and augmented walking environments by adding an auditory Stroop task in which the words high and low were pronounced at a high or low pitch (i.e., congruent and incongruent stimuli) to the 8-meter walking test and obstacle-avoidance task, respectively. Subjects had to respond with the pitch of the spoken word. The IWW assessment contained 36 trials (Table 6.2). Subjects were instructed to complete each trial at a self-selected walking speed, while also responding to the Stroop stimuli in case of dual-task walking. Figure 6.2 presents a schematic representation of the IWW assessment.

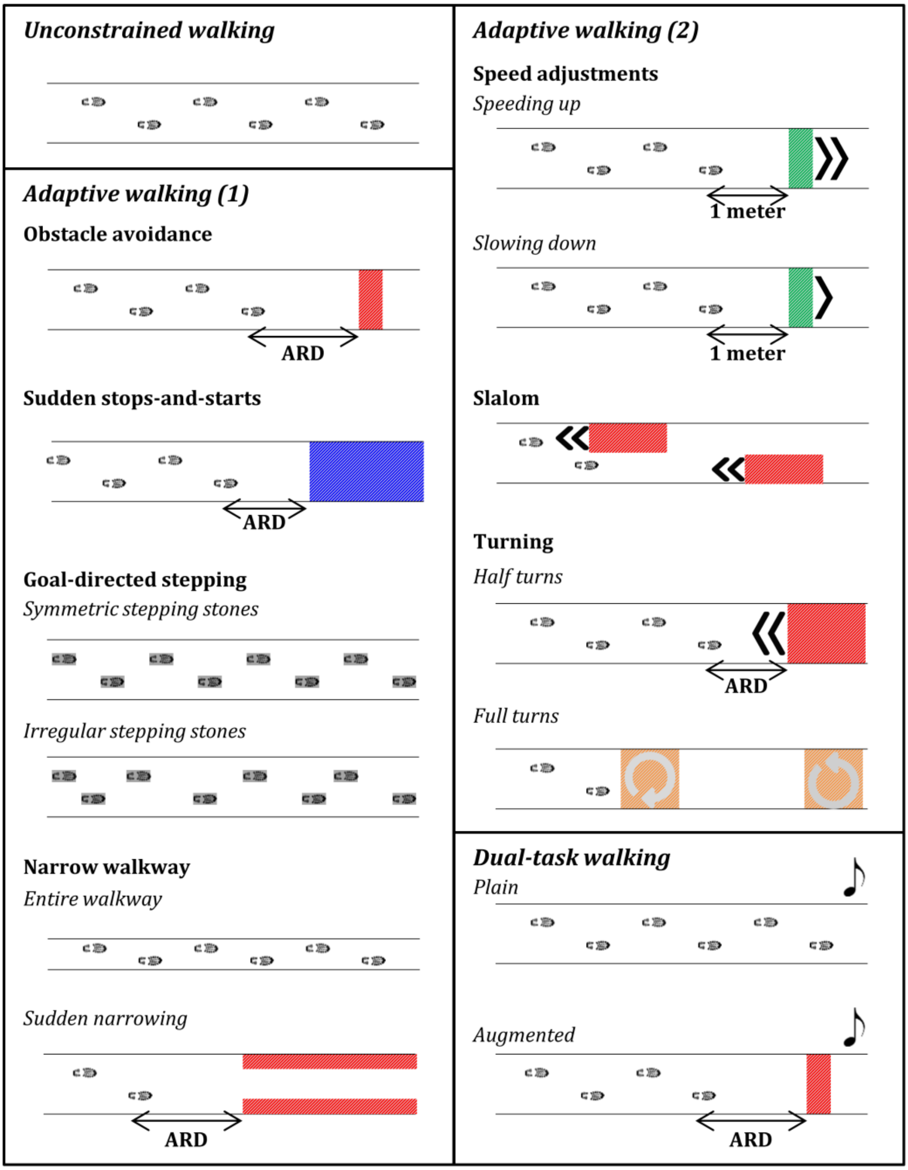

Figure 6.2 Schematic representation of the Interactive Walkway assessment, including unconstrained walking, adaptive walking and dual-task walking. The available response distance (ARD) of the suddenly appearing obstacles and cues was patient-tailored to yield a similar response time.

Half of the subjects started with the block of clinical tests, the other half with the IWW assessment. With regard to the latter, subjects always started with the 8-meter walking test, allowing us to adjust the settings of the adaptive walking tasks to one's own gait characteristics in an attempt to obtain a similar level of difficulty for each subject (see Table 6.2). For example, available response times for suddenly appearing obstacles were controlled by self-selected walking speed during the 8-meter walking test and available response distance (ARD in Figure 6.2). Subsequently, plain dual-task walking was performed, preceded by a familiarization trial in which the dual task was practiced while sitting. The remaining IWW tasks were randomized in blocks (Table 6.2).

Data pre-processing and analysis

Data pre-processing followed Geerse et al. [8,9], as detailed in Supplement 6.2. In total, 12 trials (1.1% of all trials) were excluded since subjects were not able to perform the tasks or trials were not recorded properly (i.e., incorrect recording or not all sensors were able to track the subject). These trials only concerned PD patients. The IWW outcome measures of unconstrained walking, adaptive walking and dual-task walking were calculated from specific body points' time series, estimates of foot contact and foot off, and step locations, as detailed in Table 6.2 and Supplement 6.2. The average over trials per IWW task per subject was calculated for all outcome measures (Table 6.2).

Statistical analysis

IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, N.Y., USA) was used to perform the statistical analyses. With regard to the known-groups validity we examined the effect of group (i.e., freezer, non-freezer or control) on clinical test scores and IWW outcome measures of unconstrained walking, adaptive walking and dual-task walking using one-way ANOVAs or the Kruskal-Wallis test if the assumption of normality was violated (i.e., significant Shapiro-

Wilk test). For one-way ANOVAs, the assumption of homogeneity of variance was checked using the Levene's test. If significant, the Welch test was used and main effects were examined using Games-Howell post hoc tests. Otherwise, main effects were examined with Least Significant Difference post hoc tests. For the Kruskal-Wallis test, main effects were examined using multiple Mann-Whitney tests. Effect sizes were quantified with omega squared (ω^2) for one-way ANOVAs and eta squared (η^2) for Kurskal-Wallis tests. There was no correction for multiple comparisons due to the explorative character of the study and given the dependency between the outcome measures.

Pearson's correlation coefficients were determined between clinical test scores and IWW outcome measures for PD patients only. Absolute correlations between 0-0.499, 0.500-0.699, 0.700-0.899 and 0.900-1.000 were regarded as low, moderate, high and very high correlations, respectively [19].

Stepwise discriminant analyses were conducted to determine the added value of IWW outcome measures over clinical test scores in discriminating freezers from non-freezers, using Wilks' lambda method (entry = 3.84 and removal = 2.71) in four different models. Predictor variables were clinical test scores (model 1), IWW gait characteristics of unconstrained walking (model 2), IWW outcome measures of adaptive walking (model 3) and IWW outcome measures of dual-task walking (model 4; Table 6.2). Subjects were only included if they had values for all possible predictor variables. Three not highly correlated predictor variables with the highest effect sizes for the comparison between freezers and non-freezers were selected per model. All models were cross-validated using the leave-one-out method (i.e., each subject is classified by a discriminant function which is based on all subjects except itself; [20]). The accuracy (i.e., proportion of correctly classified freezers and non-freezers) of discriminant models and cross-validated discriminant models was determined. Furthermore, exact McNemar's tests were performed to establish if one model significantly outperformed the others.

Table 6.2 Interactive Walkway tasks and outcome measures of unconstrained walking, adaptive walking and dual-task walking.

	n	Level of difficulty	Characteristics	Outcome measure	Unit	Calculation
Unconstrained walking						
8-meter walking test	2		Walking at self-selected walking speed.	Walking speed	cm/s	The distance travelled between the 0-meter and 8-meter line on the walkway divided by the time, using the data of the spine shoulder.
				Step length	cm	The median of the differences in the anterior-posterior direction of consecutive step locations.
				Stride length	cm	The median of the differences in anterior-posterior direction of consecutive ipsilateral step locations.
				Step width	cm	The median of the absolute mediolateral difference of consecutive step locations.
				Cadence	steps/min	Calculated from the number of steps in the time interval between the first and last estimate of foot contact.
				Step time	s	The median of the time interval between two consecutive instants

						of foot contact.
				Stride time	s	The median of the time interval between two consecutive ipsilateral instants of foot contact.
Adaptive walking						
Obstacle avoidance	5	ART = 1 s (three trials) ART = 0.75 s (two trials)	Avoiding suddenly appearing obstacles.	Obstacle-avoidance margins	cm	The distance of the anterior shoe edge (trailing limb) and posterior shoe edge (leading limb) of the step locations to corresponding obstacle borders during obstacle crossing.
				Success rate	%	Number of successfully avoided obstacles divided by the number of obstacles presented times 100%.
Sudden stops-and-starts	5	ART = 1 s (three trials) ART = 0.75 s (two trials)	Stop behind the suddenly appearing stop cues and start walking as soon as the cues disappear.	Sudden-stop margins	cm	The minimum distance of the anterior shoe edge to the corresponding stop cue border during the period in which the cue was visible.
				Success rate	%	Number of successful stops divided by the number of stop cues presented times 100%.

Table 6.2 Continued.

		n	Level of difficulty	Characteristics	Outcome measure	Unit	Calculation
					Initiation time	s	The time between disappearance of the stop cue and the moment of first foot contact.
Goal-directed stepping	**SSS**	3	Average SL 75% average SL 125% average SL	Stepping as accurately as possible onto the shoe-size-matched stepping stones.	Stepping accuracy	cm	The standard deviation over the signed deviations between the center of the stepping target and the center of the foot at corresponding step locations. The center of the foot was determined using the average distance between the ankle and the middle of the shoe-size-matched targets of the calibration trials (Supplement 6.2).
	ISS	2	25% variation in SL left and right 50% variation in SL left and right				
					Normalized walking speed	%	Walking speed divided by SSWS times 100%.
Narrow walkway	**EW**	2	WW = 1.5*SW+FW WW = SW+FW	Walking between the lines of the walkway or between the blocks of the suddenly narrowing walkway.	Success rate	%	Number of steps inside the walkway or the sudden narrowing walkway divided by the total number of steps taken times 100%.
	SN	1	ART = 1 s, WW = 1.5*SW+FW				
					Normalized	%	Walking speed divided by SSWS

					walking speed		times 100%.
					Normalized step width	%	Step width divided by the imposed step width times 100%.
Speed adjustments	**SU**	2	120% SSWS 140% SSWS	The subject has to follow a speed cue appearing one meter in front of the subject at the imposed speed.	Success rate	%	The percentage of the time spend walking faster (or slower) than the imposed speed minus (or plus) 20% during the period in which the speed cue was visible.
	SD	2	80% SSWS 60% SSWS				
					Normalized walking speed	%	Walking speed divided by the imposed walking speed times 100%.
Slalom		2	Symmetric distance between obstacles Variable distance between obstacles	Walking around the moving obstacles that approach the subjects with a speed of 50% SSWS.	Success rate	%	Number of successfully avoided obstacles divided by the number of obstacles presented times 100%.
					Normalized walking speed	%	Walking speed divided by SSWS times 100%.
Turning	**HT**	2	ART = 3 s ART = 2 s	When a turning cue approaches the subject with a speed of 100% SSWS, the subject has to turn and walk back to the start.	Success rate	%	Number of successful half turns divided by the number of half turns times 100%.

Table 6.2 Continued.

	n	Level of difficulty	Characteristics	Outcome measure	Unit	Calculation
FT	1		In the two presented squares the subject has to make a full turn as fast and safe as possible in the direction of the arrow.	Turning time	s	Time within the turning square (for full turns) or time from appearance of the turning cue till moment walking direction was reversed (for half turns), using the data of the spine shoulder.
Dual-task walking						
Plain	2		Walking at self-selected walking speed while also performing a dual task. The dual task was an auditory Stroop task.	Normalized walking speed	%	Walking speed divided by SSWS times 100%.
Augmented	5	ART = 1 s (three trials) ART = 0.75 s (two trials)	Avoiding suddenly appearing obstacles and while also performing a dual task. The dual task was an auditory Stroop task.	Normalized success rate	%	Obstacle avoidance success rate divided by success rate of the obstacle avoidance task times 100%, excluding subjects that had an obstacle-avoidance success rate of 0% at baseline.
				Success rate dual task	%	Number of correct responses divided by the number of stimuli given times 100% (excluding subjects that had an obstacle-

		avoidance success rate of 0% at baseline for augmented dual-task walking).
Total trials	**36**	

Abbreviations: SSS = symmetric stepping stones; ISS = irregular stepping stones; EW = entire walkway; SN = sudden narrowing; SU = speeding up; SD = slowing down; HT = half turns; FT = full turns; ART = available response time; SL = step length; WW = walkway width; SW = step width; FW = foot width; SSWS = self-selected walking speed of unconstrained walking.

Table 6.3 Means, standard deviations and between-groups statistics of clinical test scores and Interactive Walkway outcome measures of unconstrained walking, adaptive walking and dual-task walking for freezers, non-freezers and controls.

			Freezers mean ± SD	Non-freezers mean ± SD	Control mean ± SD	Between-groups statistics	*p*-value	Effect size
Clinical tests								
Timed-Up-and-Go test	**Time (s)**[b]		12.3 ± 6.9	8.5 ± 3.2	7.4 ± 2.2	$H_2 = 6.02$	0.049	0.102
10-meter walking test	**Time (s)**[a,b]	**CWS**	9.3 ± 2.0	8.0 ± 1.7	7.3 ± 1.0	$H_2 = 9.77$	0.008	0.166
	Time (s)[b,c]	**MWS**	6.9 ± 2.0	6.1 ± 1.2	5.3 ± 0.8	$H_2 = 8.66$	0.013	0.147
Tinetti Balance Assessment	**Score [0-28]**[a,b,c]		23.8 ± 3.5	26.1 ± 2.3	27.7 ± 0.5	$H_2 = 30.69$	<0.001	0.520
7-item Berg Balance Scale	**Score [0-14]**[b]		10.6 ± 3.1	12.3 ± 2.7	13.3 ± 1.3	$H_2 = 10.54$	0.005	0.179
Functional Reach Test	**Reaching distance (cm)**[b,c]		22.0 ± 9.2	25.7 ± 6.3	29.9 ± 5.6	$F_{2,57} = 6.98$	0.002	0.166
Unconstrained walking								
8-meter walking test	**Walking speed (cm/s)**[b]		111.7 ± 26.5	121.4 ± 22.8	134.3 ± 19.0	$F_{2,57} = 5.46$	0.007	0.129
	Step length (cm)[b]		62.8 ± 13.4	70.1 ± 11.1	74.5 ± 9.4	$F_{2,57} = 5.57$	0.006	0.132
	Stride length (cm)[b]		126.1 ± 26.7	140.9 ± 21.9	149.9 ± 18.7	$H_2 = 7.90$	0.019	0.134
	Step width (cm)		10.7 ± 2.9	9.3 ± 3.1	11.1 ± 2.8	$F_{2,57} = 2.05$	0.138	0.034
	Cadence (steps/min)		112.1 ± 6.9	108.9 ± 13.5	112.3 ± 7.5	$F_{2,27.8} = 0.42$	0.659	-0.020
	Step time (s)		0.524 ± 0.036	0.551 ± 0.068	0.526 ± 0.038	$F_{2,27.4} = 0.97$	0.391	-0.001
	Stride time (s)		1.052 ± 0.074	1.098 ± 0.140	1.047 ± 0.074	$F_{2,27.0} = 0.91$	0.415	-0.003
Adaptive walking								
Obstacle avoidance	**Margins trailing limb (cm)**		15.0 ± 8.0	19.1 ± 8.4	19.9 ± 7.3	$F_{2,57} = 1.95$	0.151	0.031
	Margins leading limb (cm)[b,c]		3.9 ± 9.7	6.3 ± 8.0	12.1 ± 6.1	$F_{2,57} = 6.70$	0.002	0.160

	Success rate (%)[b,c]		56.4 ± 39.7	67.6 ± 32.0	88.2 ± 11.3	$H_2 = 8.59$	0.014	0.146
Sudden stops-and-starts	**Sudden-stop margins (cm)**		-0.9 ± 9.1	4.9 ± 6.2	5.4 ± 9.2	$F_{2,57} = 2.79$	0.070	0.056
	Success rate (%)		62.3 ± 22.2	71.5 ± 13.5	76.8 ± 18.5	$H_2 = 4.99$	0.083	0.085
	Initiation time (s)		1.522 ± 0.330	1.281 ± 0.108	1.338 ± 0.235	$H_2 = 5.17$	0.076	0.088
Goal-directed stepping	**Stepping accuracy (cm)[a,c]**	**SSS**	2.5 ± 1.0	3.2 ± 1.0	2.5 ± 0.7	$F_{2,57} = 4.29$	0.018	0.099
	Normalized walking speed (%)[b]	**SSS**	83.6 ± 17.1	90.6 ± 16.4	96.0 ± 16.5	$H_2 = 6.23$	0.044	0.106
	Stepping accuracy (cm)	**ISS**	4.1 ± 1.9	4.8 ± 1.9	3.9 ± 1.0	$H_2 = 3.22$	0.200	0.055
	Normalized walking speed (%)	**ISS**	84.0 ± 20.5	88.2 ± 18.8	96.0 ± 15.7	$H_2 = 4.77$	0.092	0.081
Narrow walkway	**Success rate (%)**	**EW**	78.3 ± 25.6	77.2 ± 21.8	84.3 ± 17.4	$H_2 = 1.60$	0.448	0.028
	Normalized walking speed (%)	**EW**	86.7 ± 27.8	94.4 ± 11.0	99.0 ± 11.9	$F_{2,23.1} = 1.64$	0.216	0.021
	Normalized step width (%)	**EW**	47.5 ± 22.4	40.4 ± 19.9	37.7 ± 16.1	$F_{2,55} = 0.80$	0.455	-0.007
	Success rate (%)	**SN**	87.1 ± 25.6	83.4 ± 32.0	94.2 ± 13.7	$H_2 = 1.21$	0.547	0.020
	Normalized walking speed (%)	**SN**	87.9 ± 21.7	90.5 ± 12.1	92.8 ± 11.8	$H_2 = 0.31$	0.858	0.005
Speed adjustments	**Success rate (%)[b]**	**SU**	61.6 ± 11.5	63.0 ± 15.0	69.7 ± 10.1	$H_2 = 6.39$	0.041	0.110
	Normalized walking speed (%)	**SU**	86.8 ± 7.0	87.7 ± 7.8	90.2 ± 6.7	$F_{2,56} = 1.27$	0.288	0.009
	Success rate (%)	**SD**	76.5 ± 4.1	78.7 ± 5.3	79.1 ± 5.2	$F_{2,56} = 1.24$	0.297	0.008
	Normalized walking speed (%)	**SD**	99.3 ± 3.1	97.3 ± 10.2	99.4 ± 2.3	$H_2 = 0.54$	0.764	0.009
Slalom	**Success rate (%)**		53.5 ± 16.6	61.7 ± 23.3	55.3 ± 23.0	$F_{2,56} = 0.63$	0.539	-0.013
	Normalized walking speed (%)		86.6 ± 24.0	97.1 ± 11.6	94.7 ± 9.6	$F_{2,23.1} = 1.04$	0.370	0.001
Turning	**Success rate (%)**	**HT**	42.3 ± 40.0	46.9 ± 38.6	65.0 ± 35.1	$H_2 = 4.18$	0.124	0.072
	Turning time (s)	**HT**	1.532 ± 0.449	1.453 ± 0.277	1.435 ± 0.251	$H_2 = 0.04$	0.980	0.001
	Turning time (s)[b,c]	**FT**	4.841 ± 2.899	3.322 ± 2.243	2.149 ± 0.961	$H_2 = 14.82$	0.001	0.256

Table 6.3 Continued.

		Freezers	Non-freezers	Control	Between-groups statistics		
		mean ± SD	**mean ± SD**	**mean ± SD**		***p*-value**	**Effect size**
Dual-task walking							
Plain	**Normalized walking speed (%)**	88.5 ± 11.8	79.1 ± 20.0	87.7 ± 9.5	$H_2 = 1.93$	0.380	0.033
	Success rate dual task (%)	81.6 ± 23.4	94.0 ± 10.1	94.9 ± 12.2	$H_2 = 3.92$	0.141	0.068
Augmented	**Normalized success rate (%)**	83.7 ± 50.0	98.0 ± 31.4	97.2 ± 23.9	$H_2 = 2.08$	0.353	0.038
	Success rate dual task (%)	72.2 ± 26.8	86.1 ± 18.8	91.6 ± 9.2	$H_2 = 3.94$	0.139	0.072

Abbreviations: CWS = comfortable walking speed; MWS = maximum walking speed; SSS = symmetric stepping stones; ISS = irregular stepping stones; EW = entire walkway; SN = sudden narrowing; SU = speeding up; SD = slowing down; HT = half turns; FT = full turns.

[a]Significant difference between freezers and non-freezers ($p < 0.05$).

[b]Significant difference between freezers and controls ($p < 0.05$).

[c]Significant difference between non-freezers and controls ($p < 0.05$).

Results

Known-groups validity

As expected, freezers performed significantly worst, non-freezers performed in-between, and matched controls performed best on almost all assessments (i.e., clinical tests, unconstrained walking and adaptive walking; Table 6.3). There was one exception; freezers had significantly better stepping accuracies than non-freezers on the goal-directed stepping task with symmetric stepping stones. No significant group differences were found for IWW outcome measures of dual-task walking.

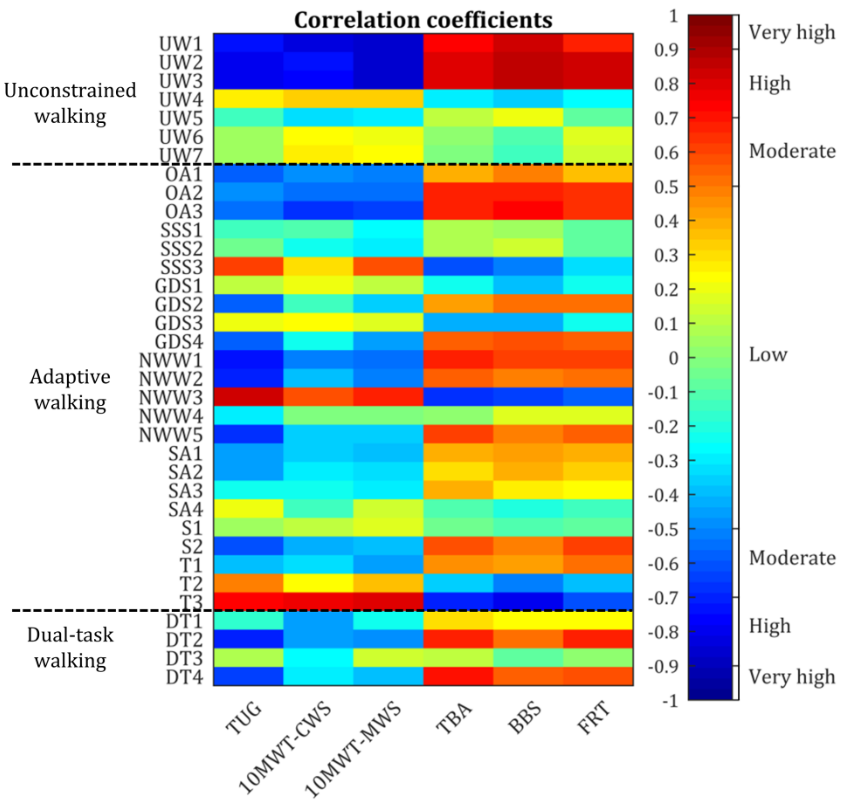

Figure 6.3 Pearson's correlation coefficients between clinical test scores (x-axis; i.e., Timed-Up-and-Go test [TUG], 10-meter walking test at comfortable and maximum walking speed [10MWT-CWS, 10MWT-MWS], Tinetti Balance Assessment [TBA], 7-item Berg Balance Scale [BBS] and

Functional Reach Test [FRT]) and Interactive Walkway outcome measures (y-axis; i.e., gait characteristics of unconstrained walking [UW1-7], outcome measure of adaptive walking [OA1-3, SSS1-3, GDS1-4, NWW1-3, SA1-4, S1-2, T1-3], and outcome measures of dual-task walking [DT1-4]) in patients with Parkinson's disease. The order of the outcome measures on the x-axes is in agreement with Table 6.3. The dotted black lines separate the three types of Interactive Walkway tasks (i.e., unconstrained walking, adaptive walking and dual-task walking). The colorbar provides a visualization of the strength and direction of the correlation.

Correlations between outcome measures

Of the 42 possible correlations between clinical test scores and IWW gait characteristics, 18 (42.9%) were significant, out of which 17 (40.5%) were high and 1 (2.4%) was moderate (Figure 6.3). Significant correlations were only found for walking speed, step length and stride length. For IWW outcome measures of adaptive walking, 88 (61.1%) of the possible 144 correlations were significant. Nevertheless, only 9 (6.3%) were high, while 45 (31.3%) were moderate and 34 (23.6%) were low (Figure 6.3). High correlations were mainly found for turning time of full turns. For IWW outcome measures of dual-task walking, 11 (45.8%) out of the possible 24 correlations were significant, out of which 1 (4.2%) was high, 7 (29.2%) were moderate and 3 (12.5%) were low (Figure 6.3).

Discriminant analyses of freezers and non-freezers

For model 1 (clinical tests), group membership (i.e., freezer or non-freezer) was predicted using only the 10-meter walking test at comfortable walking speed (p = 0.025, Wilks' lambda = 0.791, Canonical correlation = 0.457), the sole predictor variable contributing significantly to the model. 5 of 10 freezers (50.0%) and 13 of 14 non-freezers (92.9%) were correctly classified. The accuracy of model 1 and its cross validation were both 75.0%. For model 2 (IWW gait characteristics), none of the predictor variables contributed significantly to the model. For model 3 (IWW outcome measures of adaptive walking), group membership was predicted using stepping accuracy on symmetric stepping stones of the goal-directed stepping task and turning time of full turns (p = 0.005, Wilks' lambda = 0.598, Canonical correlation = 0.634) such that 7 of 10 freezers (70.0%) and 12 of 14 non-freezers (85.7%) were correctly classified, with an accuracy of 79.2%. The accuracy of the cross-validated model was 70.8%. For model 4 (IWW outcome measures of dual-task walking), none of the predictor variables contributed significantly to the model. The results of an exact McNemar's test demonstrated that there was no statistical significant difference in the proportion of freezers and non-freezers identified with models 1 and 3 (p = 0.688).

Discussion

This study aimed to examine the expected added value of IWW assessments in PD patients, focusing on known-groups validity, relations with clinical test scores and discriminating freezers from non-freezers.

On all clinical tests, freezers scored worst, non-freezers scored in-between and controls scored best (Table 6.3). These known-groups differences were also found for IWW gait characteristics (Table 6.3); freezers had significantly lower walking speeds and smaller step and stride lengths than controls, which is in agreement with findings of others using marker-based motion registration systems or the Kinect v2 sensor [21,22]. Significant group differences in expected directions were also observed for IWW outcome measures of adaptive walking (Table 6.3). As in Caetano et al. [3], both freezers and non-freezers had more difficulty adapting walking to suddenly appearing obstacles than controls as reflected by lower obstacle-avoidance success rates. In line with other studies [23,24], margins of the leading limb were smaller in freezers and non-freezers, which probably increases their risk of tripping in real life. Furthermore, group differences were found for the goal-directed stepping, speed adjustments and full turns tasks. In general, freezers scored worst, non-freezers in between, and controls best. An interesting exception was stepping accuracy on symmetric stepping stones, where freezers had significantly better stepping accuracies than non-freezers. Irregular stepping stones showed the same trend, although this did not reach significance possibly due to the larger within-groups variations for this task (Table 6.3). It is well known that visual cues may lead to considerable improvement in walking of freezers [25]. This is likely mediated by a better visual exploration of freezers than non-freezers in terms of gaze fixations to task-relevant information [26], which is known to result in a better stepping performance [27]. No significant group differences were found for the sudden stops-and-starts, narrow walkway and slalom tasks. Reasons for the null effect for the narrow walkway tasks could be that step width and tandem gait are typically preserved in PD patients [28], which was corroborated by an absence of between-groups differences in step width in our study. For the other tasks, the cueing effect of the visual context may have confounded potential group differences. Hence, one could consider removing these tasks from adaptive walking assessments in PD patients. For dual-task walking, also no significant group differences were found. An explanation could be that task prioritization varied among subjects, leading to large within-groups variations for the outcome measures of dual-task walking which reduced the likelihood of finding significant between-groups differences. Note that other studies have also demonstrated that there were no differences in dual-task interference for gait characteristics and cognitive tasks between PD patients and controls [29]. The added value of dual-task walking in a walking ability assessment in PD is therefore questionable (see also Gaßner et al. [30] and Smulders et al. [10]). Our study not only confirmed these results, but also showed that quantifiable differences between groups are particularly evident for other aspects of adaptive walking (e.g., obstacle avoidance and goal-directed stepping).

The group differences found for the IWW tasks of unconstrained walking, obstacle avoidance, goal-directed stepping, speed adjustments and full turns imply that these tasks could be used in a comprehensive walking ability assessment with the IWW, incorporating the three key aspects of walking ability. Usually, a combination of the three key walking-ability aspects (i.e., stepping, equilibrium and adaptation) is needed for a successful task performance. Indeed, for most IWW tasks a combination was required strongly tapping into the aspect of walking adaptability, while adaptation was not or only moderately targeted by commonly-used clinical tests that mainly measure steady-state gait and static balance as evidenced by the low correlations (Figure 6.3). While high correlations between tests suggest redundancy in information content, low or no correlations suggest that tests contain complementary information. IWW gait characteristics and turning time of full turns correlated highly with clinical tests, addressing mainly aspects of stepping and equilibrium. PD patients seem to experience problems when having to deviate from their normal gait pattern [3], which requires dynamic balance control. Balance problems in PD patients and especially freezers are evident in the current study, demonstrated by large effect sizes for balance tests and full turns. Clinicians mainly focus on gait impairments [31], although dynamic balance control is also of great importance during challenging walking tasks. Therefore, in order to obtain a more comprehensive characterization of a subject's walking ability, both unconstrained and adaptive walking should be assessed, for example with obstacle-avoidance and goal-directed stepping.

This study also aimed to determine the expected added value of the IWW over clinical tests in discriminating freezers from non-freezers. We indeed found that IWW adaptive walking tasks discriminated better than clinical tests, although the added value was somewhat limited and the proportion of freezers and non-freezers identified with model 3 did not differ significantly from model 1. Clinical tests performed slightly worse compared to adaptive walking tasks with regard to the percentage of freezers correctly classified (50.0% vs. 70.0%, respectively). The percentage of non-freezers correctly classified was high for both models (92.9% and 85.7%, respectively). IWW gait characteristics and IWW outcome measures of dual-task walking did not contribute significantly to the discriminant analysis. Although we could discriminate freezers from non-freezers, the freezing phenomenon itself was rarely observed. IWW tasks elicited FOG episodes in only 12 out of 466 (2.6%) trials, concerning five freezers and mostly during tasks that included turning (in agreement with literature; [32]). Explanations for the limited amount of FOG episodes could be the focused attention due to the specific instructions of the IWW tasks, cueing effects of visual content and the fact that we assessed PD patients during the ON state, while the occurrence of FOG episodes increases during the OFF state.

The latter is also a limitation of this study, since medication may improve gait impairments and could therefore lead to smaller group differences in walking ability. However, we still found significant between-groups differences, which may indicate that the IWW is a sensitive evaluation tool of walking ability. Another limitation is the relatively small sample size of the discriminant analyses (i.e., 10 freezers and 14 non-freezers). We therefore needed to pre-select predictor variables for the models to prevent overfitting, since the smallest group needs to exceed the number of predictor variables. Finally, the significant difference between freezers and non-freezers in disease severity (i.e., Hoehn and Yahr stage; Table 6.1) might have influenced the results of this study by increasing the group differences of walking-ability outcome measures.

In conclusion, the IWW assessment exhibited expected differences between freezers, non-freezers and healthy controls, with most IWW outcome measures reflecting combinations of stepping, equilibrium and adaptation; key aspects of walking that are addressed separately in most clinical tests. IWW adaptive walking tasks also contributed to a slightly better discrimination of freezers from non-freezers. Hence, it seems fair to conclude that the IWW is of added value in PD patients when assessing walking ability. The IWW tasks of adaptive walking evaluate more complex gait in comparison with clinical tests, which fits an assessment of walking ability in the early stages of PD where ceiling effects can occur. Future studies should examine the responsiveness of the IWW outcome measures on an individual level and in response to levodopa treatment (i.e., by examining differences in walking ability between the ON and

OFF state). In addition, since the impairments in walking ability evaluated with the IWW are linked to walking-related falls, future studies are warranted to examine the clinical potential of the IWW for assessing fall risk and informing on tailored falls prevention programs in PD patients or other populations prone to declines in walking ability (e.g., elderly, stroke). Note that the current study is helpful in that regard, by informing on the subtasks and associated outcome measures providing complementary information with a decent between-groups contrast.

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Supplement 6.1

Video of Interactive Walkway tasks of unconstrained walking, adaptive walking and dual-task walking in a person with Parkinson's disease with dyskinesia. The subject had consented to the making of the video for publication purposes. This video is available at https://youtu.be/p1a07lL9veM.

Supplement 6.2

Data pre-processing

The Kinect for Windows Software Development Kit (SDK 2.0, www.microsoft.com) provides 3D time series of 25 body points using inbuilt and externally validated human-pose estimation algorithms [1-5]. These body points are: head, neck, spine shoulder, spine mid, spine base and left and right shoulder, elbow, wrist, hand, thumb, hand tip, hip, knee, ankle and foot. For offline data analysis, the 3D positional data for these body points were first pre-processed per Kinect sensor separately. Body points labelled as inferred (i.e., Kinect's human-pose estimation software infers positions when segments are partially occluded for example) were treated as missing values. The body point's time series were linearly interpolated using Kinect's time stamps to ensure a constant sampling frequency of 30 Hz, without filling in the parts with missing values. We removed data points from the time series when they did not meet our stringent requirements for valid human-pose estimation (e.g., a minimum of 15 out of the 25 possible body points should be labeled as tracked, including the head and at least one foot and ankle, without outliers in segment lengths). In addition, a manual check of the data was added to remove errors of the algorithm due to occlusion of the right leg by the left leg. Subsequently, data of the four Kinect sensors were combined by taking for each sample the 3D positions of the body points of a validly estimated human pose. If, for a given sample, more than one sensor contained valid human pose data, the associated body point's 3D positions were averaged for that specific sample.

Body point's time series with more than 50% of missing values were excluded from further analyses. However, percentages of missing data for both groups did not exceed 27.2% with an average of 5.3 ± 1.6% for the body points' time series of interest (i.e., ankles, spine base and spine shoulder). The missing values were interpolated with a spline algorithm. The so-obtained time series were used for the calculation of the Interactive Walkway (IWW) outcome measures of unconstrained walking, adaptive walking and dual-task walking.

The outcome measures of the IWW assessments were calculated from specific body points' time series, estimates of foot contact and foot off and step locations, as detailed in Table 6.2. Estimates of foot contact and foot off were defined as the maxima and minima of the anterior–posterior time series of the ankles relative to that of the spine base [3,6,7]. Step locations were determined as the median anterior–posterior and mediolateral position of the ankle joint during the single-support phase (i.e., between foot off and foot contact of the contralateral foot; [3,6]). Shoe edges and center of the foot were also needed to calculate several outcome measures. Ankle-to-shoe calibration trials, in which the subject was standing in two shoe-size-matched targets at a position on the walkway in front of the last Kinect, were included to determine the average distance between shoe edges and the ankle.

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Chapter 7

Walking adaptability for targeted fall-risk assessments

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Published in Gait & Posture 2019;70:203-210

Background. Most falls occur during walking and are due to trips, slips or misplaced steps, which suggests a reduced walking adaptability. The objective of this study was to evaluate the potential merit of a walking-adaptability assessment for identifying prospective fallers and risk factors for future falls in a cohort of stroke patients, Parkinson's disease patients, and controls (n = 30 for each group). Research question. Does an assessment of walking-adaptability improve the identification of fallers compared to generic fall-risk factors alone? Methods. This study comprised an evaluation of subject characteristics, clinical gait and balance tests, a quantitative gait assessment and a walking-adaptability assessment with the Interactive Walkway. Subjects' falls were registered prospectively with falls calendars during a 6-month follow-up period. Generic and walking-related fall-risk factors were compared between prospective fallers and non-fallers. Binary logistic regression and Chi-square Automatic Interaction Detector analyses were performed to identify fallers and predictor variables for future falls. Results. In addition to fall history, obstacle-avoidance success rate and normalized walking speed during goal-directed stepping correctly classified prospective fallers and were predictors of future falls. Compared to the use of generic fall-risk factors only, the inclusion of walking-related fall-risk factors improved the identification of prospective fallers. Significance. If cross-validated in future studies with larger samples, these fall-risk factors may serve as quick entry tests for falls prevention programs. In addition, the identification of these walking-related fall-risk factors may help in developing falls prevention strategies.

Introduction

The incidence of falls increases with age, but is particularly high in patients with neurological disorders, such as stroke and Parkinson's disease (PD) [1,2]. Falls can occur as a result of both intrinsic factors (i.e., subject characteristics and gait impairments) and extrinsic factors (e.g., slippery floor, uneven walking surface) [3]. For the latter, it is important to be able to adapt walking to the environment, an aspect of walking that is difficult to assess with clinical tests [4]. Most falls occur during walking and are due to trips, slips or misplaced steps [5-7], suggesting a reduced walking adaptability. An evaluation of walking adaptability could potentially improve the identification of fallers and may help in developing falls prevention strategies [8]. The Interactive Walkway (IWW; Figure 7.1) can be used to perform quick and unobtrusive quantitative gait assessments [9] and to quantify various aspects of walking adaptability [10].

The aim of this study is to evaluate the potential merit of the IWW for identifying prospective fallers and risk factors for future falls in a composite cohort with stroke patients, PD patients and controls. First, we will examine differences in walking ability between fallers and non-fallers. Second, two methods will be used to identify fallers and risk factors for future falls; one extensive method and one easily interpretable method fit for use in the clinic. We expect that walking-adaptability assessments improve the classification of prospective fallers compared to generic fall-risk factors alone (i.e., subject characteristics, clinical gait and balance tests, quantitative gait assessments) and that a poor walking adaptability is a risk factor for future falls.

Methods

Subjects

30 stroke patients, 30 PD patients and 30 controls participated in this study (Table 7.1). Groups were age- and sex-matched. Patients were recruited from the outpatient clinics of neurology and rehabilitation medicine of the Leiden University Medical Center and from a list of patients who were discharged from

the Rijnlands Rehabilitation Center. Controls were recruited via advertisement. Subjects were 18 years or older and had command of the Dutch language. Patients had to be able to stand unsupported for more than 20 seconds and walk independently. Stroke patients had to be more than 12 weeks post stroke. PD patients had to fulfill clinical diagnostic criteria according to the UK Parkinson's Disease Society Brain Bank [11] and could have a Hoehn and Yahr stage of 1-4 [12]. PD patients were measured in the ON state. Controls had to have unimpaired gait, normal cognitive function (Montreal Cognitive Assessment score ≥ 23; [13]) and normal or corrected to normal vision. Exclusion criteria were (additional) neurological diseases and/or problems interfering with gait function. All subjects gave written informed consent, and the study was approved by the local medical ethics committee (P15.232).

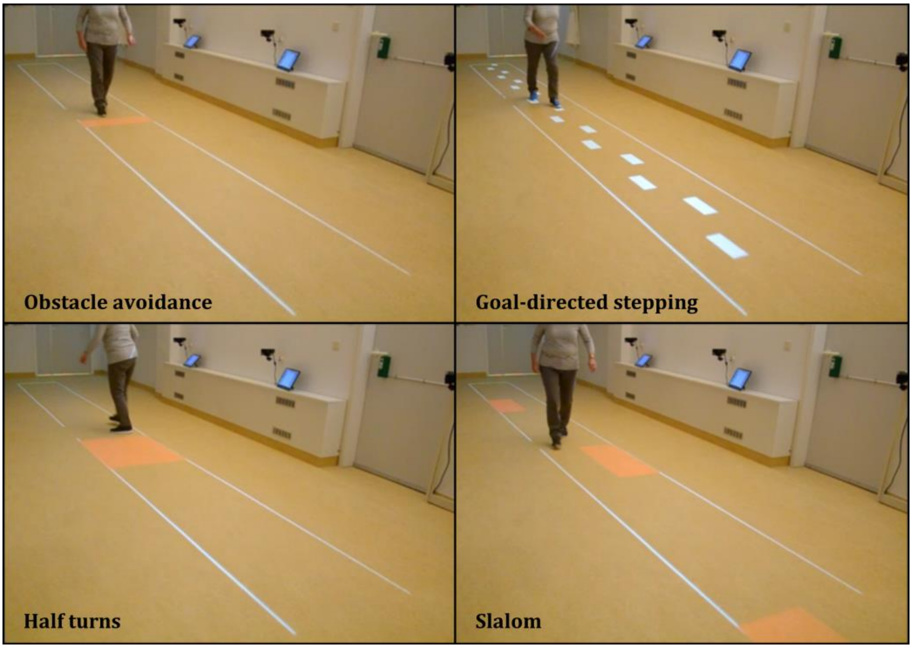

Figure 7.1 The Interactive Walkway for an assessment of walking adaptability, which may unveil potential fall-risk factors.

Table 7.1 Group characteristics of stroke patients, Parkinson's disease patients and controls.

		Stroke	Parkinson's disease	Control
Age (years)	**mean ± SD**	62.5 ± 10.1	63.1 ± 10.0	62.9 ± 10.3
Sex	**male/female**	18/12	18/12	18/12
MOCA [0-30]*	**mean ± SD**	22.5 ± 6.3	-	27.7 ± 1.4
FMA lower extremity [0-34]*	**mean ± SD**	19.7 ± 7.4	-	-
Bamford classification	**PACS/TACS/ POCS/LACS/unk**	16/2/2/8/1	-	-
SCOPA-COG [0-43]*	**mean ± SD**	-	30.4 ± 7.1	-
MDS-UPDRS motor score [0-132]**	**mean ± SD**	-	36.9 ± 18.0	-
Hoehn and Yahr stage [1-5]**	**mean ± SD**	-	2.3 ± 0.7	-

Abbreviations: MOCA = Montreal Cognitive Assessment; FMA = Fugl-Meyer Assessment; PACS = partial anterior circulation stroke; TACS = total anterior circulation stroke; POCS = posterior circulation syndrome; LACS = lacunar syndrome; unk = unknown; SCOPA-COG = Scales for Outcomes in Parkinson's Disease – Cognition; MDS-UPDRS = Movement Disorder Society version of the Unified Rating Scale for Parkinson's disease.

* Higher scores represent better outcomes.

** Higher scores represent worse outcomes.

Experimental set-up and procedure

Before performing the experimental tasks, the Montreal Cognitive Assessment [14] and Scales for Outcomes in Parkinson's Disease – Cognition [15] were administered to assess cognitive abilities. In stroke patients, sensorimotor impairment was assessed using the Fugl-Meyer Assessment - lower extremity [16]. Higher scores on these clinical tests reflect better outcomes (Table 7.1). In PD patients, the Movement Disorder Society version of the Unified Rating Scale for Parkinson's disease [17] and Hoehn and Yahr stage [12] were administered to assess disease severity, with higher scores reflecting worse outcomes (Table 7.1). All subjects completed the Falls Efficacy Scale - International [18] to assess fear of falling, the Modified Survey of Activities of Fear of Falling in the Elderly Scale [19] to assess activity avoidance due to fear of falling (higher scores indicate more fear of falling) and were asked about their fall history in the year prior to the experiment.

Commonly-used clinical gait and balance tests included the Timed-Up-and-Go test and the 10-meter walking test at comfortable and maximum walking speed to assess mobility (longer completion times indicate worse mobility), the Tinetti Balance Assessment for an evaluation of gait and balance performance of which the combined score of the two sections was used in this study (higher scores indicate better performance), the 7-item Berg Balance Scale to measure static and dynamic balance during specific movement tasks (lower outcome indicates worse balance) and the Functional Reach Test to determine the maximal distance one can reach forward from a standing position (smaller distance indicates worse balance). The order of these commonly-used clinical tests was randomized.

The validated IWW [9,10,20] was used for quantitative gait and walking-adaptability assessments. The IWW set-up, using multiple Kinect sensors for markerless 3D motion registration, is described in detail in Supplement 7.1. The quantitative gait assessment was performed using an 8-meter walking test. In addition, subjects performed various walking-adaptability tasks under varying levels of difficulty: obstacle avoidance, sudden stops-and-starts, goal-directed stepping (symmetric and irregular stepping stones), narrow walkway (entire walkway and sudden narrowing), speed adjustments (speeding up and slowing down), slalom, turning (half and full turns) and dual-task walking (plain and augmented), yielding a total of 36 trials (Figure 7.2; see Supplement 7.1 for more details and Supplement 7.2 for a video). Dual-task walking was assessed using an auditory Stroop task in which the words high and low were pronounced at a high or low pitch (i.e., congruent and incongruent stimuli) simultaneously with the 8-meter walking test (plain dual-task walking) and obstacle-avoidance task (augmented dual-task walking), respectively. Subjects had to respond with the pitch of the spoken word, which was different from the spoken word in case of an incongruent stimulus. Stimuli were presented with a fixed interval of 2 s. Subjects were instructed to complete each trial at a self-selected walking speed, while also responding to the Stroop stimuli in case of dual-task walking.

Half of the subjects in each group started with the clinical tests, the other half with the IWW assessment. With regard to the latter, subjects always started with the 8-meter walking test, which enabled us to adjust the settings of the walking-adaptability tasks to one's own gait characteristics in an attempt to obtain a similar level of difficulty for each subject (see Supplement 7.1). For example, available response times for suddenly appearing obstacles were controlled by self-selected walking speed during the 8-meter walking test and available response distance (ARD in Figure 7.2). Subsequently, the 8-meter walking test was performed with the dual task (i.e., plain dual-task walking), preceded by a familiarization trial in which the auditory Stroop task was practiced while sitting. The remaining IWW tasks (as specified in Table 7.2) were randomized in blocks.

After the experiment, subjects were asked to register falls during a 6-month follow-up period using a falls calendar. Subjects had to report every day whether they had fallen. A fall was defined as an unexpected event in which the subject comes to rest on the ground, floor, or lower level [21]. Subjects were asked to send back their falls calendar every month and were contacted on a monthly basis to ask about the falls that occurred.

Data pre-processing and analysis

Data pre-processing followed Geerse et al. [9,10], as reproduced in more detail in Supplement 7.1. 111 trials (3.4% of all trials) were excluded since subjects did not perform the tasks or trials were not recorded properly (i.e., incorrect recording or inability of sensors of the IWW to track the subject). These excluded trials only concerned stroke and PD patients. IWW outcome measures were calculated from specific body points' time series, estimates of foot contact and foot off and step locations, as detailed in Table 7.2 and Supplement 7.1. Outcome measures of dual-task performance were success rate, response time and a composite score that represents the trade-off between these two outcome measures (Table 7.3; [22-24]). The average over trials per IWW task per subject was calculated for all outcome measures.

Falls calendars were used to classify subjects as prospective faller (i.e., those reporting at least one fall during the follow-up period) or non-faller. In the literature, fallers are classified using both retrospective and prospective falls. Therefore, non-fallers were defined as subjects that did not report a fall in the follow-up period or in the year prior to the experiment. Only walking- or balance-related falls were taken into account. A total of 88 subjects completed the entire 6-month follow-up period. One PD patient stopped prematurely with the falls calendar as it took too much time, but was not excluded from the analyses since this patient was already identified as a prospective faller based on the received falls calendars. One stroke patient who did not fill in a single falls calendar was excluded. In total, 33 (37.1%; 37.9% of stroke patients, 50.0% of PD patients and 23.3% of controls) subjects reported at least one fall in the follow-up period (i.e., prospective fallers), of which 24 (72.7% of prospective fallers; 27.0% of total) also had a history of falling. In the sample of 56 (62.9%) subjects without a prospective fall, 47 (83.9%; 52.8% of total) were actual non-fallers according to our definition; consequently, 9 (16.1%; 10.1% of total) subjects were excluded since they had a history of falling without prospective falls.

Statistical analysis

Outcome measures of prospective fallers (n = 33) and non-fallers (n = 47) were compared using chi-squared tests for categorical data and independent-samples *t*-tests for continuous variables to examine differences in walking ability. We computed *r* to quantify the effect sizes of continuous variables [25], where values between 0.10-0.29 were regarded as small, between 0.30-0.49 as medium and above 0.50 as large effect sizes [25].

Binary logistic regression analyses (forward method, Wald test) were performed on four models (Table 7.3) to identify prospective fallers and predictor variables for future falls. Model 1 included only subject characteristics (e.g., age, fall history, group) as potential predictor variables. For model 2, clinical test scores were added to subject characteristics. Model 3 consisted of subject characteristics, clinical test scores and spatiotemporal gait parameters. For model 4, also IWW walking-adaptability outcome measures were added. We calculated the sensitivity (i.e., percentage correctly classified prospective fallers), specificity (i.e., percentage correctly classified non-fallers) and overall accuracy (i.e., percentage of correctly classified prospective fallers and non-fallers) for each prediction model. We also inspected the sign and size of the coefficients (i.e., describing the relationship between predictor variable and outcome) to determine the direction of the association with falls and the relevance of a predictor variable. Receiver operating characteristic curve analyses were used to assess the predictive accuracy of each model by estimating the area under the curve (AUC). AUCs of more than 0.70, 0.80 and 0.90 are considered acceptable, excellent and outstanding, respectively [26]. Multiple imputation was performed to handle missing data (1.4%, 69 complete cases) in 23 out of 48 potential predictor variables. Five imputations were performed using chained equations including all potential predictor variables of model 4 and the outcome variable (i.e., prospective faller or non-faller).

We also used the Chi-square Automatic Interaction Detector (CHAID) analysis to identify significant predictors for inclusion in a prediction model based on a decision tree. Potential predictor variables included in our model were subject characteristics, clinical test scores, spatiotemporal gait parameters and IWW walking-adaptability outcome measures. In our model, we imposed a minimum of one subject per node, a significance level of 0.05 (with a Bonferroni correction) and a division on a maximum of two levels to keep the decision tree as simple as possible. Sensitivity, specificity and overall accuracy were calculated.

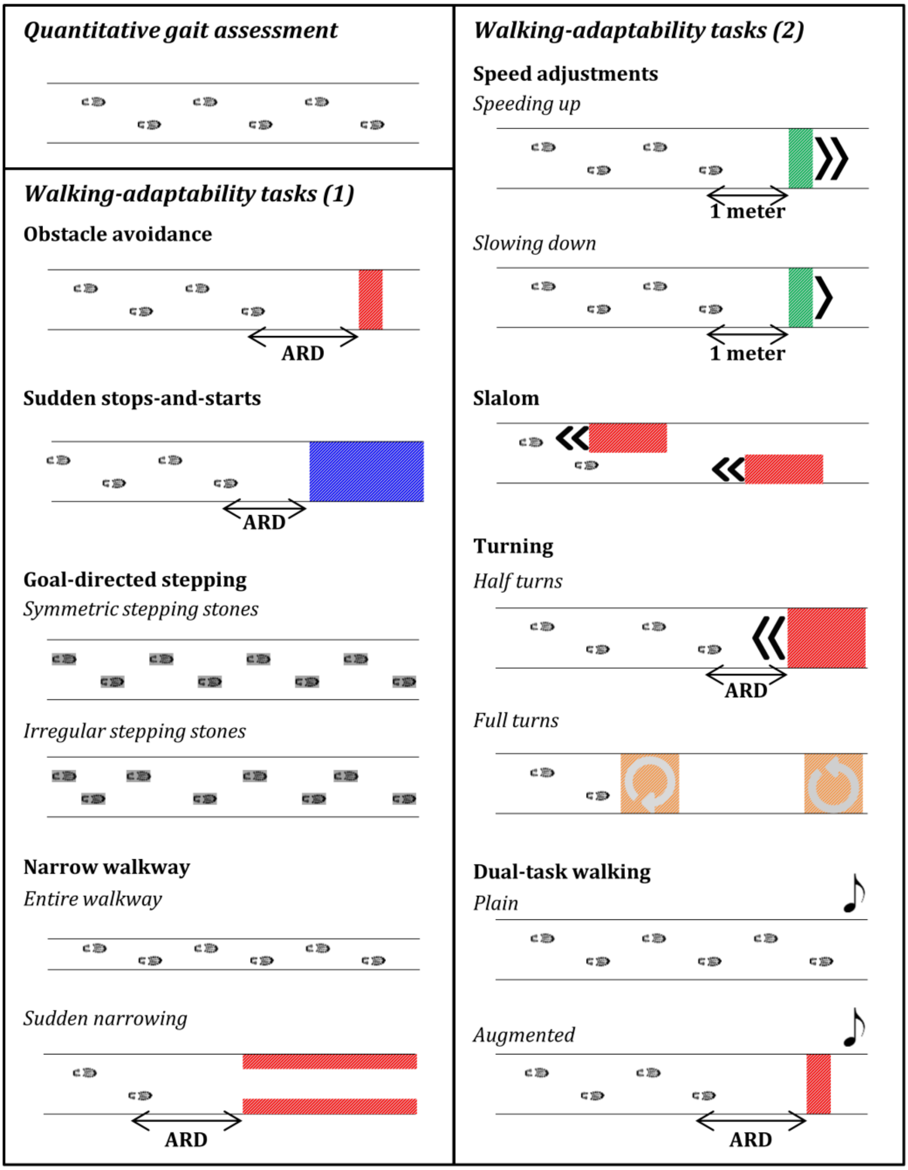

Figure 7.2 Schematic of the quantitative gait assessment and walking-adaptability tasks on the Interactive Walkway, as detailed in the main text.

Table 7.2 Outcome measures of the quantitative gait assessment and walking-adaptability tasks of the Interactive Walkway.

	Outcome measure	Unit	Calculation
Quantitative gait assessment			
8-meter walking test	Walking speed	cm/s	The distance travelled between the 0-meter and 8-meter line on the walkway divided by the time, using the data of the spine shoulder.
	Step length	cm	The median of the differences in the anterior-posterior direction of consecutive step locations.
	Stride length	cm	The median of the differences in anterior-posterior direction of consecutive ipsilateral step locations.
	Step width	cm	The median of the absolute mediolateral difference of consecutive step locations.
	Cadence	steps/min	Calculated from the number of steps in the time interval between the first and last estimate of foot contact.
	Step time	s	The median of the time interval between two consecutive instants of foot contact.
	Stride time	s	The median of the time interval between two consecutive ipsilateral instants of foot contact.
Walking-adaptability tasks			
Obstacle avoidance	Obstacle-avoidance margins	cm	The distance of the anterior shoe edge (trailing limb) and posterior shoe edge (leading limb) of the step locations to corresponding obstacle borders during obstacle crossing.
	Success rate	%	Number of successfully avoided obstacles divided by the number of obstacles presented times 100%.

Sudden stops-and-starts		Sudden-stop margins	cm	The minimum distance of the anterior shoe edge to the corresponding stop cue border during the period in which the cue was visible.
		Success rate	%	Number of successful stops divided by the number of stop cues presented times 100%.
		Initiation time	s	The time between disappearance of the stop cue and the moment of first foot contact.
Goal-directed stepping	**SSS** **ISS**	Stepping accuracy	cm	The standard deviation over the signed deviations between the center of the stepping target and the center of the foot at corresponding step locations. The center of the foot was determined using the average distance between the ankle and the middle of the shoe-size-matched targets of the calibration trials (see Supplement 7.1).
		Normalized walking speed	%	Walking speed divided by walking speed of the 8MWT times 100%.
Narrow walkway	**EW** **SN**	Success rate	%	Number of steps inside the walkway or the sudden narrowing walkway divided by the total number of steps taken times 100%.
		Normalized walking speed	%	Walking speed divided by walking speed of the 8MWT times 100%.
		Normalized step width	%	Step width divided by the imposed step width by the entire walkway times 100%.
Speed adjustments	**SU** **SD**	Success rate	%	The percentage of the time spend walking faster (or slower) than the imposed speed minus (or plus) 20% during the period in which the speed cue was visible.
		Normalized walking speed	%	Walking speed divided by the imposed walking speed times 100%.

Table 7.2 Continued.

		Outcome measure	Unit	Calculation
Slalom		Success rate	%	Number of successfully avoided obstacles divided by the number of obstacles presented times 100%.
		Normalized walking speed	%	Walking speed divided by walking speed of the 8MWT times 100%.
Turning	**HT** **FT**	Success rate	%	Number of successful half turns divided by the number of half turns times 100%.
		Turning time	s	Time within the turning square (for full turns) or time from appearance of the turning cue till moment walking direction was reversed (for half turns), using the data of the spine shoulder.
Dual-task walking	**PDT**	Normalized walking speed	%	Walking speed divided by walking speed of the 8MWT times 100%.
	ADT	Normalized success rate	%	Obstacle avoidance success rate divided by success rate of the obstacle-avoidance task times 100%, excluding subjects that had an obstacle-avoidance success rate of 0% at baseline.
		Success rate dual task	%	Number of correct responses divided by the number of stimuli given times 100%. No response was classified as an incorrect response.
		Response time	s	Average time between stimulus onset and response onset.
		Composite score dual task	%	Success rate dual task divided by the response time.

Abbreviations: SSS = symmetric stepping stones; ISS = irregular stepping stones; EW = entire walkway; SN = sudden narrowing; SU = speeding up; SD = slowing down; HT = half turns; FT = full turns; PDT = plain dual-task walking (8-meter walking test with dual task); ADT = augmented dual-task walking (obstacle avoidance with dual task); 8MWT = 8-meter walking test.

Results

Prospective fallers had significantly more fear of falling (i.e., higher score on the Falls Efficacy Scale) and more often avoided activities due to fear of falling (i.e., higher score on the Modified Survey of Activities of Fear of Falling in the Elderly Scale; Table 7.3) than non-fallers. In addition, prospective fallers performed overall worse on clinical tests (significantly for the Timed-Up-and-Go test, Tinetti Balance Assessment and 7-item Berg Balance Scale) and IWW tasks (significantly for the obstacle-avoidance, sudden-stops-and-starts, goal-directed-stepping and turning tasks) and walked slower and with smaller steps than non-fallers (Table 7.3).

Binary logistic regression models

Model 1 included fall history (B = 23.11) and age (B = 0.08) as best predictor variables for prospective falls, models 2 and 3 also only included fall history and age, while model 4 included fall history (B = 24.16), obstacle-avoidance success rate (B = -0.07) and reaching distance on the Functional Reach Test (B = 0.20). Sensitivity increased from 72.7% (models 1-3) to 78.8% (model 4), specificity increased from 97.9% to 100.0% and overall accuracy increased from 87.5% to 91.3%. AUC increased from 0.926 (95% CI = [0.858 0.995]; models 1-3) to 0.943 (95% CI = [0.886 1.000]; model 4).

CHAID analysis

The CHAID analysis identified three significant predictors for prospective falls (Figure 7.3). Subjects were initially dichotomized by fall history, with retrospective falls classifying 24 of 80 subjects as prospective faller of which all were actual prospective fallers. The remaining 56 subjects without a fall history (i.e., falls-naïve cohort, including 9 prospective fallers) were split by obstacle-avoidance success rate (> 77.8% and ≤ 77.8%). 35 subjects with a success rate > 77.8% were classified as non-fallers, of which 33 subjects were non-fallers. The remaining 21 subjects with an obstacle-avoidance success rate ≤ 77.8%

were finally split by normalized walking speed during goal-directed stepping on symmetric stepping stones (> 91.9% and ≤ 91.9% or missing). The 6 subjects with a normalized walking speed > 91.9% were classified as prospective fallers, of which 5 subjects were prospective fallers. The sensitivity of this model was 87.9% (29 out of 33 prospective fallers correctly identified), while the specificity was 97.9% (46 out of 47 non-fallers correctly identified), with an overall accuracy of 93.8%.

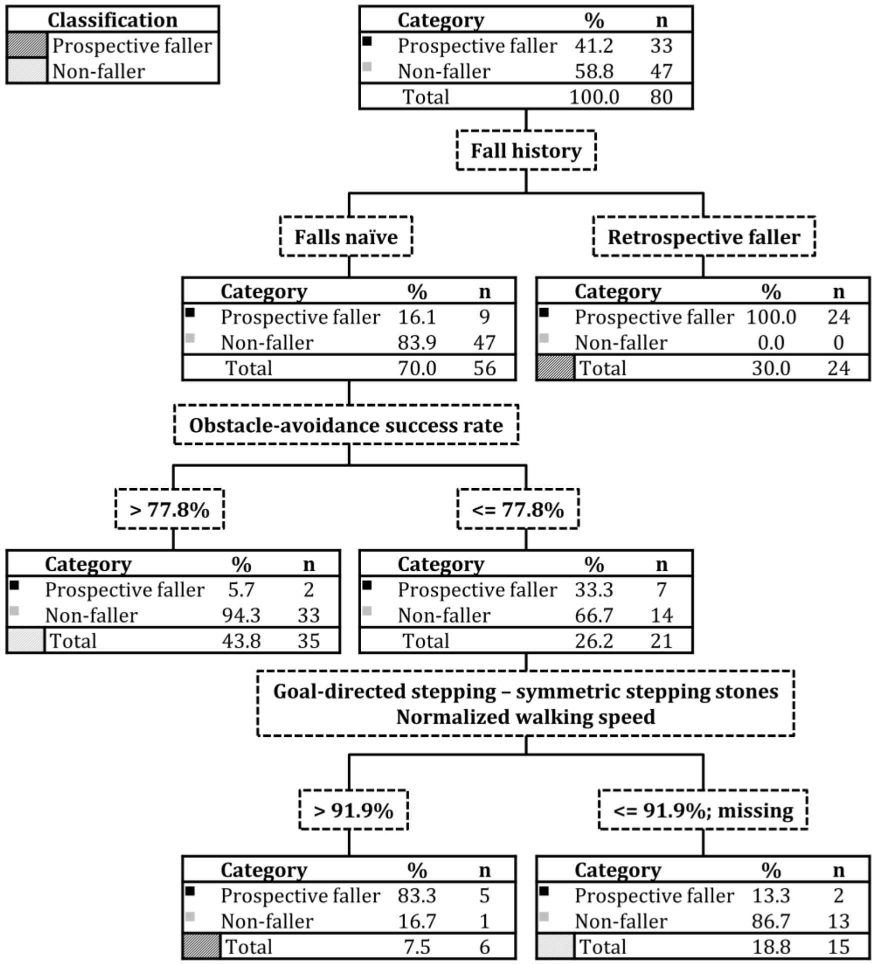

Figure 7.3 Decision tree of the CHAID analysis.

Table 7.3 Means, standard deviations and between-groups statistics of subject characteristics, clinical tests, the quantitative gait assessment and the walking-adaptability tasks for prospective fallers and non-fallers.

			Prospective faller n = 33 mean ± SD	Non-faller n = 47 mean ± SD		*p*-value	*r*-value
Subject characteristics							
Group	**S/PD/C**		11/15/7	13/13/21	$\chi^2_2 = 5.01$	0.082	-
Gender	**male/female**		18/15	31/16	$\chi^2_2 = 1.06$	0.302	-
Age	**Age (years)**		64.8 ± 10.5	60.5 ± 9.2	$t_{78} = -1.94$	0.056	0.215
Falls Efficacy Scale	**Score [0-64]***		9.5 ± 7.1	4.6 ± 6.0	$t_{61.7} = -3.27$	0.002	0.385
mSAFFE	**Score [17-51]***		24.4 ± 6.2	20.7 ± 5.6	$t_{78} = -2.80$	0.006	0.302
Clinical tests							
Timed-Up-and-Go test	**Time (s)***		14.1 ± 11.4	9.8 ± 6.1	$t_{78} = -2.15$	0.035	0.236
10-meter walking test	**Time (s)**	**CWS**	13.4 ± 12.7	9.3 ± 5.0	$t_{39.1} = -1.76$	0.087	0.271
10-meter walking test	**Time (s)**	**MWS**	10.4 ± 11.0	7.1 ± 4.3	$t_{78} = -1.83$	0.072	0.203
Tinetti Balance Assessment	**Score [0-28]***		23.4 ± 4.5	25.8 ± 4.1	$t_{78} = 2.50$	0.015	0.272
7-item Berg Balance Scale	**Score [0-14]***		10.8 ± 2.9	12.4 ± 2.3	$t_{78} = 2.80$	0.006	0.302
Functional Reach Test	**Reaching distance (cm)**		24.2 ± 8.2	27.5 ± 6.6	$t_{78} = 1.95$	0.055	0.216
Quantitative gait assessment							
8-meter walking test	**Walking speed (cm/s)***		100.1 ± 32.5	121.0 ± 34.5	$t_{78} = 2.74$	0.008	0.296
	Step length (cm)*		60.0 ± 15.4	68.9 ± 14.8	$t_{78} = 2.60$	0.011	0.283
	Stride length (cm)*		120.7 ± 30.9	138.5 ± 29.7	$t_{78} = 2.60$	0.011	0.282

Table 7.3 Continued.

			Prospective faller n = 33 mean ± SD	Non-faller n = 47 mean ± SD		*p*-value	*r*-value
	Step width (cm)		13.5 ± 5.2	12.4 ± 5.3	t_{78} = -0.94	0.348	0.106
	Cadence (steps/min)		101.6 ± 18.7	108.0 ± 15.0	t_{78} = 1.71	0.092	0.190
	Step time (s)		0.609 ± 0.174	0.560 ± 0.097	t_{78} = -1.59	0.117	0.177
	Stride time (s)		1.216 ± 0.357	1.118 ± 0.196	t_{78} = -1.58	0.119	0.176
Walking-adaptability tasks							
Obstacle avoidance	**Margins trailing limb (cm)**		13.4 ± 8.8	17.0 ± 9.2	t_{78} = 1.74	0.085	0.194
	Margins leading limb (cm)*		3.9 ± 9.8	9.1 ± 6.7	$t_{52.5}$ = 2.66	0.010	0.345
	Success rate (%)*		49.6 ± 37.7	77.9 ± 23.8	$t_{49.6}$ = 3.82	<0.001	0.476
Sudden stops-and-starts	**Sudden-stop margins (cm)***		0.0 ± 7.6	4.3 ± 9.2	t_{77} = 2.19	0.031	0.242
	Success rate (%)*		59.8 ± 23.6	73.7 ± 20.1	t_{77} = 2.82	0.006	0.306
	Initiation time (s)		1.521 ± 0.357	1.383 ± 0.320	t_{77} = -1.81	0.074	0.202
Goal-directed stepping	**Stepping accuracy (cm)***	**SSS**	3.4 ± 1.6	2.7 ± 1.1	$t_{51.9}$ = -2.42	0.019	0.319
	Normalized walking speed (%)	**SSS**	89.0 ± 15.8	90.4 ± 16.8	t_{77} = 0.39	0.697	0.045
	Stepping accuracy (cm)*	**ISS**	4.7 ± 1.8	3.9 ± 1.0	$t_{46.3}$ = -2.07	0.044	0.291
	Normalized walking speed (%)	**ISS**	87.7 ± 18.6	90.1 ± 15.8	t_{78} = 0.63	0.531	0.071
Narrow walkway	**Success rate (%)**	**EW**	76.9 ± 25.8	78.6 ± 22.3	t_{77} = 0.32	0.752	0.036
	Normalized walking speed (%)	**EW**	89.1 ± 19.9	92.7 ± 16.5	t_{77} = 0.87	0.390	0.098
	Normalized step width (%)	**EW**	52.4 ± 26.4	46.8 ± 29.0	t_{77} = -0.86	0.390	0.098
	Success rate (%)	**SN**	88.0 ± 21.9	90.0 ± 23.2	t_{74} = 0.38	0.705	0.044

	Normalized walking speed (%)	**SN**	90.8 ± 16.0	92.1 ± 11.6	t_{74} = 0.42	0.675	0.049
Speed adjustments	**Success rate (%)**	**SU**	62.3 ± 14.6	65.5 ± 12.3	t_{75} = 1.06	0.294	0.121
	Normalized walking speed (%)	**SU**	87.9 ± 8.7	89.2 ± 7.6	t_{75} = 0.73	0.466	0.084
	Success rate (%)	**SD**	75.5 ± 6.0	77.7 ± 6.4	t_{75} = 1.57	0.121	0.178
	Normalized walking speed (%)	**SD**	100.4 ± 4.0	99.4 ± 6.6	t_{75} = -0.77	0.443	0.089
Slalom task	**Success rate (%)**		56.3 ± 24.0	50.9 ± 21.2	t_{75} = -1.04	0.301	0.119
	Normalized walking speed (%)		87.3 ± 20.3	91.5 ± 13.1	$t_{46.9}$ = 1.02	0.311	0.148
Turning task	**Success rate (%)**	**HT**	32.3 ± 37.7	50.0 ± 40.8	t_{75} = 1.93	0.058	0.217
	Turning time (s)	**HT**	1.513 ± 0.303	1.459 ± 0.309	t_{75} = -0.77	0.445	0.088
	Turning time (s)*	**FT**	5.304 ± 4.587	3.058 ± 2.038	$t_{39.8}$ = -2.59	0.013	0.380
Dual-task walking	**Normalized walking speed (%)**	**PDT**	84.0 ± 13.8	82.9 ± 15.0	t_{75} = -0.31	0.759	0.036
	Success rate dual task (%)	**PDT**	86.7 ± 18.0	88.6 ± 19.6	t_{75} = 0.42	0.679	0.048
	Response time (s)*	**PDT**	1.108 ± 0.161	0.986 ± 0.150	t_{75} = -3.41	0.001	0.139
	Composite score dual task (%)	**PDT**	81.1 ± 24.6	92.0 ± 25.0	t_{75} = 1.90	0.062	0.214
	Success rate (%)	**ADT**	91.6 ± 67.2	92.0 ± 31.8	$t_{31.6}$ = 0.03	0.977	0.005
	Success rate dual task (%)	**ADT**	77.5 ± 24.8	84.0 ± 19.9	t_{69} = 1.22	0.228	0.145
	Response time (s)	**ADT**	1.102 ± 0.147	1.040 ± 0.131	t_{69} = -1.84	0.070	0.216
	Composite score dual task (%)	**ADT**	71.7 ± 25.3	81.7 ± 21.3	t_{69} = 1.77	0.081	0.209

Abbreviations: S = stroke patient; PD = Parkinson's Disease patient; C = control; mSAFFE = Modified Survey of Activities of Fear of Falling in the Elderly Scale; CWS = comfortable walking speed; MWS = maximum walking speed; SSS = symmetric stepping stones; ISS = irregular stepping stones; EW = entire walkway; SN = sudden narrowing; SU = speeding up; SD = slowing down; HT = half turns; FT = full turns; PDT =plain dual-task walking (8-meter walking test with dual task); ADT = augmented dual-task walking (obstacle avoidance with dual task).

* Significant difference between prospective fallers and non-fallers ($p < 0.05$).

Discussion

This study evaluated the potential merit of the IWW for identifying fallers and risk factors for future falls in a composite cohort with stroke patients, PD patients and controls. Prospective fallers experienced more fear of falling, a well-known fall-risk factor [8,21,27]. Fallers also more often reported fear-induced activity avoidance than non-fallers. In addition, prospective fallers walked slower and with smaller steps, and had a poorer performance on clinical gait and balance tests. As anticipated, prospective fallers performed worse on various walking-adaptability tasks, including the obstacle-avoidance, sudden-stops, goal-directed-stepping and full-turn tasks. Since tripping is considered one of the most common causes of falls in everyday life [5-7], smaller margins of the leading limb during obstacle avoidance were expected. Overall, the ability to make step adjustments, either under time pressure demands or during goal-directed stepping, was impaired in prospective fallers and was associated with falls in [28,29]. This may point at specific underlying gait impairments that can be targeted in falls prevention strategies to reduce fall risk. No differences were found between prospective fallers and non-fallers for dual-task walking, except for response time during plain dual-task walking (Table 7.3). An explanation for this might be between-subject variation in task prioritization in both groups. In the study of Timmermans et al. [30] the amount of cognitive-motor interference did not differ between obstacle avoidance over physical obstacles compared to projected obstacles, while task prioritization did. In Timmermans et al. [30] and in the current study, subjects were instructed to perform both tasks as well as possible, affording differences in task prioritization. This likely increased between-subject variation in the performance of the walking task and the cognitive task, which might explain the lack of a clear effect of the dual task (Table 7.3). Note that response time during augmented dual-task walking and the composite scores showed trends towards poorer dual-task performance in fallers.

We performed two different analyses to identify prospective fallers and predictor variables for future falls, namely the binary logistic regression and CHAID analysis, which both performed very well in terms of overall accuracy. The results of the CHAID analysis are easier to interpret and implement in daily practice [31]. On the other hand, binary logistic regression models are more informative on the relevance of a predictor variable (i.e., size of coefficient). Both analyses identified fall history and obstacle-avoidance success rate as predictor variables. The CHAID analysis additionally identified normalized walking speed during goal-directed stepping on symmetric stepping stones as predictor variable, whereas age and reaching distance on the Functional Reach Test both significantly increased fall risk (i.e., positive coefficients) in the binary logistic regression models. Group (i.e., stroke, Parkinson's disease, control) was not identified as a significant predictor variable for prospective falls. This suggests that the presence of a neurological disorder does not automatically increase fall risk, a finding in line with another study on fall-risk assessments [32]. Notably, controls without specific disorders also experienced falls (23.3%). A decreased walking ability in older adults compared to younger adults has been demonstrated [33], both in steady-state walking and walking adaptability. Assessing limitations in walking ability, regardless of their cause (e.g., neurological disorders, ageing), thus likely provides a better indication of someone's fall risk. In accordance with previous studies, fall history was the best sole predictor of future falls in our study [27,34]. All subjects classified as prospective faller in models 1-3 had a history of falling and the coefficients for fall history in the models were high. The addition of obstacle-avoidance success rate and reaching distance led to the correct classification of two more fallers and one non-faller. Using the CHAID analysis, we subsequently evaluated risk factors of first falls in the falls-naïve cohort. It appeared that subjects who poorly performed the obstacle-avoidance task and who did not substantially lower their walking speed during goal-directed stepping are most at risk of falling (i.e., 5 out of 9 fallers correctly classified). Reminiscent of a speed-accuracy trade-off, subjects seem to maintain their normal walking speed (i.e., no significant group difference in normalized walking speed), at the expense of stepping accuracy (i.e., significantly less accurate in prospective fallers). However, the latter seems more important when walking in the community. There thus appears to be a discrepancy between their perceived and actual walking ability, which may be a factor contributing to falls [35]. The amount of misjudgment has been emphasized to be useful to include in fall-risk assessments [36] and allows for better personalized interventions [35]. This was confirmed by the study of Butler et al. [37]; subjects that took higher risks than their physical ability allowed were more likely to experience a fall in the upcoming year. Assessing walking adaptability in addition to asking about falls in the previous year thus seems of added value when assessing fall risk. Besides, identification of these walking-related fall-risk factors may lead to more targeted, personalized and possibly more effective falls prevention programs.

A limitation of this study was the sample size. Although 90 subjects were included and followed prospectively for falls, this was still relatively small when the distribution of fallers and non-fallers and the type of analysis are taken into account. This limits cross-validation of the models and the risk of overfitting must be considered. This study should therefore be regarded as a first step in evaluating the proposed comprehensive fall-risk assessment including generic and walking-related factors. The results, when confirmed by a larger sample, provide indications for a strategy to identify subjects that are at a high risk of falling. First, subjects should be asked about their fall history and subjects with a history of walking-related falls may be advised to follow a falls prevention program, aimed at improving balance, walking and walking adaptability. Second, subjects that are falls-naïve should perform an assessment of about five minutes, including the obstacle-avoidance and goal-directed stepping tasks and a baseline walk (to determine normalized walking speed) to identify potential fallers. Subjects with poor walking adaptability who do not reduce their walking speed accordingly, may also be advised to follow a falls prevention program. Given these walking-related predictor variables, such a program should be geared towards improving (sudden) step adjustments and creating awareness about a subject's ability to adapt walking in order to reduce their walking-related fall risk.

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Supplement 7.1

Experimental set-up and procedure

The quantitative gait assessment and walking-adaptability assessment were performed on the Interactive Walkway (IWW; Figure S7.1) using four spatially and temporally integrated Kinect v2 sensors to obtain full-body kinematics. The IWW set-up was based on a validated IWW set-up used in Geerse et al. [1,2], with improved inter-sensor distances following recommendations of Geerse et al. [3]. The sensors were positioned at a height of 0.95 m alongside a walkway of 8 by 0.75 m. The first three sensors were placed frontoparallel (i.e., with an angle of 70 degrees relative to the walkway direction) with a distance of 1.2 m from the left border of the walkway. The last sensor was positioned frontally at the end of the walkway, since this will minimize orientation-based biases [4]. The first sensor was positioned at 3 m from the start of the walkway and the other sensors were placed at inter-sensor distances of 2.1 m. The IWW was equipped with a projector (EPSON EB-585W, ultra-short-throw 3LCD projector) to augment the entire 8-meter walkway with visual context for the walking-adaptability tasks. The coordinate systems of the sensors and projector were spatially aligned to a common coordinate system using a spatial calibration grid. IWW data were sampled at 30 Hz using custom-written software utilizing the Kinect-for-Windows Software Development Kit (SDK 2.0). Details about the experimental tasks performed on the IWW can be found in Table S7.1.

Data pre-processing and analysis

The Kinect for Windows Software Development Kit (SDK 2.0, www.microsoft.com) provides 3D time series of 25 body points using inbuilt and externally validated human-pose estimation algorithms [1,5-8]. These body points are: head, neck, spine shoulder, spine mid, spine base and left and right shoulder, elbow, wrist, hand, thumb, hand tip, hip, knee, ankle and foot. For offline data analysis, the 3D positional data for these body points were first pre-processed per Kinect sensor separately. Body points labelled as inferred (i.e., Kinect's human-pose estimation software infers positions when segments are partially occluded for example) were treated as missing values. The body point's time series were linearly interpolated using Kinect's time stamps to ensure a constant sampling frequency of 30 Hz, without filling in the parts with missing values. We removed data points from the time series when they did not meet our stringent requirements for valid human-pose estimation (e.g., a minimum of 15 out of the 25 possible body points should be labeled as tracked, including the head and at least one foot and ankle, without outliers in segment lengths). In addition, a manual check of the data was added to remove errors of the algorithm due to depth occlusion of the right leg by the left leg. Subsequently, data of the four Kinect sensors were combined by taking for each sample the 3D positions of the body points of a validly estimated human pose. If, for a given sample, more than one sensor contained valid human pose data, the associated body point's 3D positions were averaged for that specific sample.

Body point's time series with more than 50% of missing values were excluded from further analyses. However, percentages of missing data for all three groups did not exceed 27.3% with an average of 5.0 ± 2.1% for the body points' time series of interest (i.e., ankles, spine base and spine shoulder). The missing values of the remaining data were interpolated with a spline algorithm. The so-obtained time series were used for the calculation of the spatiotemporal gait parameters and walking-adaptability outcome measures.

The outcome measures of the IWW assessment were calculated from specific body points' time series, estimates of foot contact and foot off and step locations, as detailed in Table 7.2. Estimates of foot contact and foot off were defined as the maxima and minima of the anterior–posterior time series of the ankles relative to that of the spine base [1,2,9]. Step locations were determined as the median anterior–posterior and mediolateral position of the ankle joint during the single-support phase (i.e., between foot off and foot contact of the contralateral foot; [1,2]). Shoe edges and center of the foot were also needed to calculate several outcome measures. Ankle-to-shoe calibration trials, in which the subject was standing in two shoe-size-matched targets at a position on the walkway in front of the last Kinect, were included to determine the average distance between shoe edges and the ankle.

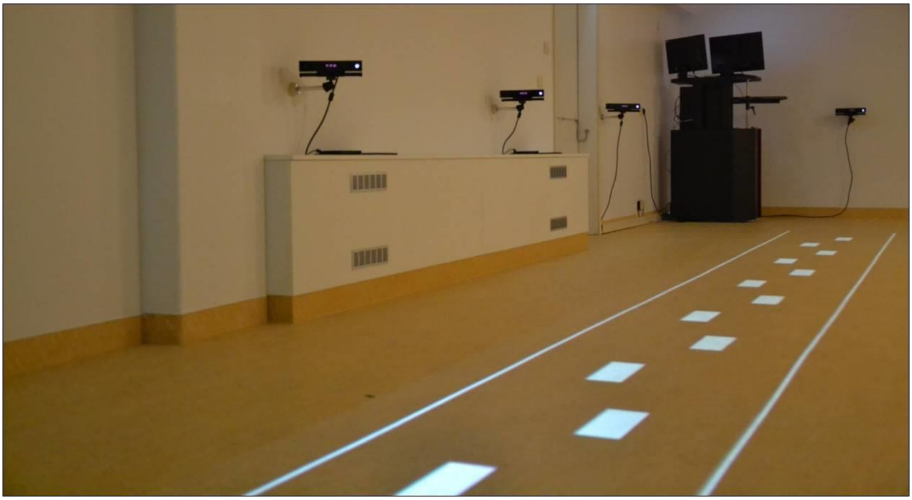

Figure S7.1 Set-up of the Interactive Walkway with visual context projected on the walkway.

Table S7.1 Quantitative gait assessment and walking-adaptability tasks on the Interactive Walkway.

Assessments		n	Level of difficulty	Characteristics
Quantitative gait assessment				
8-meter walking test		2		Walking at self-selected walking speed.
Walking-adaptability tasks				
Obstacle avoidance		5	ART = 1 s (three trials) ART = 0.75 s (two trials)	Avoiding suddenly appearing obstacles.
Sudden stops-and-starts		5	ART = 1 s (three trials) ART = 0.75 s (two trials)	Stopping behind the suddenly appearing stop cues and start walking as soon as the cues disappear.
Goal-directed stepping	**SSS**	3	Average SL 75% average SL 125% average SL	Stepping as accurately as possible onto the shoe-size-matched stepping stones.
	ISS	2	25% variation in SL left and right 50% variation in SL left and right	
Narrow walkway	**EW**	2	WW = 1.5*SW+FW WW = SW+FW	Walking between the lines of the walkway or between the blocks of the suddenly narrowing walkway.
	SN	1	ART = 1 s, WW = 1.5*SW+FW	
Speed adjustments	**SU**	2	120% SSWS 140% SSWS	When a speed cue appears one meter in front of the subjects it has to be followed at the imposed speed.
	SD	2	80% SSWS 60% SSWS	

Slalom		2	Symmetric distance between obstacles Variable distance between obstacles	Walking around the moving obstacles that approach the subjects with a speed of 50% SSWS.
Turning	**HT**	2	ART = 3 s ART = 2 s	When a turning cue approaches the subject with a speed of 100% SSWS, the subject has to turn and walk back to the start.
	FT	1		In the two presented squares the subject has to make a full turn as fast and safe as possible in the direction of the arrow.
Dual-task walking	**PDT**	2		Walking while also performing a dual task. The dual task was an auditory Stroop task.
	ADT	5	ART = 1 s (three trials) ART = 0.75 s (two trials)	Avoiding suddenly appearing obstacles while also performing a dual task. The dual task was an auditory Stroop task.
Total trials		**36**		

Abbreviations: SSS = symmetric stepping stones; ISS = irregular stepping stones; EW = entire walkway; SN = sudden narrowing; SU = speeding up; SD = slowing down; HT = half turns; FT = full turns; PDT =plain dual-task walking (8-meter walking test with dual task); ADT = augmented dual-task walking (obstacle avoidance with dual task); ART = available response time; SL = step length; WW = walkway width; SW = step width; FW = foot width; SSWS = self-selected walking speed of unconstrained walking.

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Supplement 7.2

Video of assessments on the Interactive Walkway in a patient with stroke. This video is available at https://youtu.be/k7O2kc5R-K8.

Chapter 8

Summary, general discussion and future perspectives

Summary

Neurological disorders may impair various aspects of walking ability that are needed for safe and independent walking (cf. Balasubramanian et al. [1]), therefore requiring different rehabilitation strategies. A comprehensive assessment addressing the key components of walking ability may help to tailor management strategies to the individual needs of each patient. The Interactive Walkway (IWW) is a promising, unobtrusive and low-cost assessment tool of walking ability in daily practice. Nevertheless, it is unclear if 1) this approach can provide a valid assessment of walking ability and, if so, 2) if it has clinical potential in the assessment of walking ability and fall risk in patients with stroke and Parkinson's Disease (PD). The aim of this thesis was to gain insight into these two aspects.

Part 1: Can the IWW be used for a valid comprehensive assessment of walking ability?

The most commonly used outcome measure of walking ability is walking speed assessed over short distances, for example using the 10-meter walking test. Using the IWW, this 10-meter walking test can be expanded with quantitative gait assessments, performed in a quick, unobtrusive and patient-friendly manner. In doing so, standard clinical tests are complemented with additional information about gait and balance impairments derived from 3D kinematics during walking. The study described in **Chapter 2** aimed to validate the IWW for markerless quantitative gait assessments in terms of 3D full-body kinematics and associated spatiotemporal gait parameters against a gold-standard marker-based motion-registration system in a group of 21 healthy subjects. The 10-meter walking test was conducted at comfortable and maximum walking speed, while 3D full-body kinematics was concurrently recorded with the IWW and the Optotrak system (i.e., the gold standard). The results demonstrated that 3D kinematics agreed well between the motion-registration systems, particularly so for body points in motion. Moreover,

spatiotemporal gait parameters also matched well between systems. The results of Chapter 2 thus indicated that quantitative gait assessments can reliably be performed with the IWW.

In addition to measuring steady-state walking, the IWW also allows for assessing walking adaptability by projecting interactive visual context onto the walkway in the form of, for example, stepping targets and obstacles. In **Chapter 3**, the between-systems agreement and sensitivity to task and subject variations for various walking-adaptability assessments on the IWW was addressed. Under varying task constraints, 21 healthy subjects performed obstacle-avoidance, sudden-stops-and-starts and goal-directed-stepping tasks. The results demonstrated that walking-adaptability outcome measures, such as obstacle-avoidance margins, generally agreed well between the IWW and Optotrak system. Second, walking-adaptability outcomes were sensitive to task and subject variations. With goal-directed stepping, task variations led to different step lengths, stepping accuracies and walking speeds while available response times and obstacle-avoidance margins varied with obstacle type. This testifies to the power of projected visual context to modify gait and to elicit (sudden) step adjustments, in line with previous studies exploring the same concept during treadmill walking [2-5]. Sensitivity to task and subject variations is important for walking-adaptability assessments in relatively high-functioning groups (such as community-dwelling older adults), where ceiling effects are a common concern [6]. The same holds for floor effects in relatively fragile patient groups. The IWW potentially allows for walking-adaptability assessments that are feasible for both high-functioning and fragile populations since task difficulty can be varied. In addition, IWW assessments are also relatively safe (e.g., visual instead of physical obstacles), unobtrusive (markerless data) and hence time-efficient and patient-friendly. The IWW walking-adaptability assessments were therefore deemed usable for obtaining an objective and more task-specific examination of one’s ability to walk, which warrants studies on its clinical potential as discussed in Chapters 5 to 7.

Based on the insights obtained in these two validation studies, another validation study of the Kinect v2 sensor of the IWW was performed. The study described in **Chapter 4** aimed to systematically evaluate the effects of distance to the sensor, body side (i.e., left or right) and step length on estimates of foot placement locations calculated using Kinect's ankle body points. Estimates of foot placement locations are required to quantify spatial gait parameters and outcome measures of walking adaptability. In total, 12 healthy subjects performed stepping trials with imposed foot placement locations at various distances from the Kinect sensor, for the left and right body side, and for multiple imposed step lengths, concurrently recorded with a Kinect v2 sensor and the Optotrak system. The results revealed a small but significant between-systems difference in foot placement locations and step lengths. These were likely caused by differences in body orientation relative to the Kinect sensor, whereby the ankle was estimated more posteriorly. This effect can be reduced by using smaller inter-sensor distances in the IWW set-up to estimate foot placement locations at greater distances from the sensor.

Taken together, it can be concluded that the IWW can be used to validly assess both steady-state walking (Chapter 2) and walking adaptability (Chapter 3) in a group of healthy adults. In doing so, it yields a more comprehensive assessment, addressing important components of the tripartite model of walking ability (i.e., the ability to generate stepping, to maintain postural equilibrium and to adapt walking to environmental demands). The results of Chapters 2 to 4 also led us to improve the IWW set-up by reducing inter-sensor distances. Subsequently, we set out to evaluate the clinical potential of the IWW as a tool for assessing walking ability and fall risk in patient groups, as will be discussed next.

Part 2: What is the clinical potential of the IWW for assessing walking ability and fall risk?

The aim of the study presented in **Chapter 5** was to evaluate the potential of the IWW as a new technology for assessing walking ability in stroke patients. Assessments of impairments in walking ability may aid in the development of individualized rehabilitation strategies. 30 stroke patients and 30 age- and sex-matched healthy controls performed clinical tests as well as quantitative 3D gait assessments and various walking-adaptability tasks using the IWW. The results of this study suggested good known-groups validity for IWW walking-adaptability tasks, similar to that of clinical tests and quantitative gait assessments. In addition, walking-adaptability tasks appeared to complement these assessments, as evidenced by the mainly low to moderate correlations between outcome measures of walking adaptability and those obtained from clinical tests and quantitative gait assessments. Our findings therefore suggested that using the IWW to evaluate steady-state walking and walking adaptability with obstacle avoidance and goal-directed stepping may provide a quick, unobtrusive and comprehensive quantitative assessment of walking ability with potential for monitoring recovery after stroke and informing rehabilitation strategies.

In **Chapter 6** steady-state walking (i.e., quantitative gait assessments), adaptive walking and dual-task walking were evaluated with the IWW in 14 PD patients with freezing of gait (FOG), 16 PD patients without FOG and 30 healthy controls. Similar to the results of the clinical tests, freezers scored worst, non-freezers scored in-between and controls scored best on most IWW tasks, suggesting good known-groups validity. PD patients especially experienced problems when having to deviate from their steady-state gait pattern, which requires dynamic balance control. Therefore, in order to obtain a more comprehensive characterization of a subject's walking ability, both steady-state and adaptive walking should be assessed, for example with obstacle avoidance and goal-directed stepping. It was demonstrated that these IWW tasks also provide additional information compared to clinical tests given the low to moderate correlations between these two types of assessment. Moreover, IWW outcome measures of adaptive walking slightly better discriminated freezers from non-freezers than clinical test scores. The IWW thus shows potential as a more comprehensive walking-ability assessment in PD, incorporating all its key aspects of which many may be linked to falls. The latter premise was explored in more detail in Chapter 7, as discussed next.

In **Chapter 7**, the potential merit of the IWW to identify prospective fallers and risk factors for future falls was evaluated in a composite cohort of stroke patients, PD patients and healthy controls. This study comprised an evaluation of subject characteristics, clinical gait and balance tests, and a quantitative gait assessment and walking-adaptability assessment on the IWW. Subjects' falls were registered with monthly falls calendars during a 6-month follow-up period to identify subjects as prospective fallers (i.e., experiencing at least one walking-related fall during the follow-up period) or non-fallers. Prospective fallers experienced more fear of falling and more fear-of-falling-related activity avoidance at baseline than non-fallers. In addition, prospective fallers walked slower and with smaller steps, and had a poorer performance on clinical gait and balance tests. As anticipated, prospective fallers also performed worse on various walking-adaptability tasks. In addition to fall history, obstacle-avoidance success rate and normalized walking speed during goal-directed stepping were identified as predictor variables for falls and these fall-risk factors improved the identification of fallers. It appears that subjects who performed worse on the obstacle-avoidance task without substantially lowering their walking speed during goal-directed stepping are most at risk of falling. Identification of these task-specific fall-risk factors may lead to more targeted, personalized and, possibly, more effective falls prevention programs. If validated in larger samples in future studies these measures hold promise as future entry tests for falls prevention programs.

Collectively, our findings show that the IWW contributes to the evaluation of walking ability in patients with stroke (Chapter 5) and PD (Chapter 6). Additionally, limitations in walking adaptability proved to be a risk factor for falls, which resulted in a better identification of prospective fallers (Chapter 7). The IWW thus seems to be a valuable option for a comprehensive assessment of walking ability and fall risk in stroke patients and PD patients.

General discussion

The overarching goal of this thesis was to examine if the IWW could provide a valid and comprehensive assessment of walking ability in various patient groups under the premise that this improves the identification of prospective fallers. The results showed that the IWW indeed allows for a valid and comprehensive assessment of walking ability, including the aspect of walking adaptability. Moreover, the IWW adds value to the evaluation of walking ability in stroke patients and PD patients, also uncovering limitations in walking adaptability that resulted in a better identification of prospective fallers. In the following sections, steps towards a more comprehensive fall-risk assessment are outlined by means of a roadmap (Figure 8.1). Furthermore, the broader implication of the insights obtained in this thesis are discussed for the IWW and beyond.

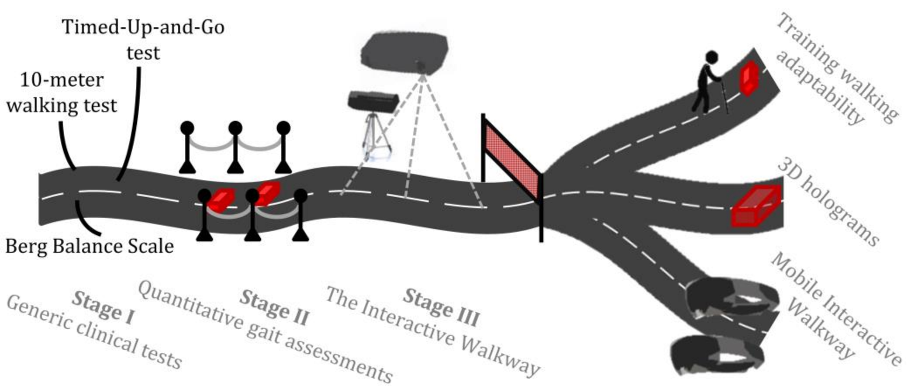

Figure 8.1 Roadmap of the steps towards a more comprehensive fall-risk assessment.

Towards a more comprehensive assessment of walking ability

Walking speed assessed over short distances, for example using the 10-meter walking test (stage I of the roadmap; Figure 8.1), is the most commonly used outcome measure of walking ability in the clinic. Furthermore, generic gait and balance assessments examining functional mobility and balance outcomes, such as the Timed-Up-and-Go test and the Berg Balance Scale, are also frequently used clinical tests (stage I of the roadmap; Figure 8.1). These clinical tests only give a single value as outcome of walking ability. More detailed insight into gait and balance impairments can be obtained using quantitative gait assessments (stage II of the roadmap; Figure 8.1). These clinical tests and assessments, however, do not account for the full repertoire of walking skills needed for safe walking. That is, they mainly address steady-state gait as seen on a 'red carpet' (stage II of the roadmap; Figure 8.1), which does not mimic the typically encountered real-life walking environments.

As mentioned in the General Introduction, walking ability is defined as the ability to walk independently and safely from one place (A) to the other (B) [7]. The environmental and situational context between A and B is inherently variable, placing different demands on walking [7]. With regard to the former, one can envision obstacles like doorsteps or other people. With regard to the latter, one may, for example, be distracted or in a hurry. The three components of the tripartite model of walking ability [1] comprehensively address such demands, comprising one's ability to 1) generate effective stepping, 2) maintain balance while walking and 3) adapt walking to environmental or situational context. Currently, the latter component of walking adaptability is typically not assessed in the clinic. One domain of walking adaptability, namely obstacle negotiation [1], has been examined using 3D kinematics when crossing real obstacles (stage II of the roadmap; Figure 8.1; [8-12]) and an impaired obstacle-avoidance performance was found in stroke patients and PD patients [8,11-15]. However, real obstacles are potential trip hazards and hence such assessments are relatively unsafe. Moreover, obstacle-avoidance tasks evaluate just a single domain of walking adaptability.

With the IWW, multiple domains of walking adaptability can be assessed (stage III in the roadmap; Figure 8.1). A projector is used to augment the walkway with (gait-dependent) visual context which allows for an assessment of various walking-adaptability domains (e.g., obstacle negotiation, postural transitions, maneuvering in traffic; [1]) in a safe manner. While quantitative gait assessments performed with the IWW predominantly address the stepping and balance components of the tripartite model, given the high correlations with clinical test scores in stroke patients (Chapter 5) and PD patients (Chapter 6), IWW tasks seemingly assess a complementary aspect of walking ability, namely the walking-adaptability aspect. Taken together, the IWW thus holds promise as a more comprehensive assessment of walking ability by addressing all key aspects of this motor function.

Walking ability and falls: moving to a task-specific assessment

Since most falls occur during walking [16-18], it seems useful to consider limitations in walking ability as potential risk factors for future falls. A comprehensive assessment of walking ability may therefore inform about factors that increase walking-related fall risk. Such assessments should be task-specific, meaning that they focus on functional tasks rather than impairments [19]. Examples of functional tasks are steady-state walking (stages I, II and III of the roadmap; Figure 8.1), specific movement tasks to test static and dynamic balance (i.e., Berg Balance Scale; stage I of the roadmap; Figure 8.1) and walking-adaptability tasks on the IWW (stage III of the roadmap; Figure 8.1). A task-specific assessment could help identify why people fall during walking and can help personalize treatments by targeting specific risk factors. Task-specific training, relearning a task by practicing that specific task, has been shown effective in gait rehabilitation [20,21]. In this thesis, important steps have been taken towards a task-specific assessment of fall risk. The IWW assessment presented in Chapters 5 to 7 included various walking-related tasks (i.e., steady-state walking and walking-adaptability tasks) to assess walking ability. As demonstrated in these chapters, some of these tasks usefully contribute to a comprehensive assessment of walking ability and fall risk, whereas others don't, which is helpful in shortening the assessment protocols (as described below).

The obstacle-avoidance and goal-directed stepping outcome measures were significantly different between stroke patients and controls (Chapter 5), between PD patients and controls (Chapter 6) and fallers and non-fallers (Chapter 7), in line with other studies [8,11-15,22,23]. In addition, goal-directed stepping differed between freezers and non-freezers, with better stepping accuracies for freezers. One earlier study [3], in which the C-Mill was used to assess walking adaptability in a group of amputees, showed the importance of obstacle-avoidance and goal-directed stepping tasks as informative tasks of walking ability. The C-Mill is a treadmill embedded with a force plate onto which gait-dependent visual context, such as obstacles and stepping targets, can be presented. The results demonstrated that obstacle avoidance and goal-directed stepping were unique, complementary aspects of walking ability given the low to moderate correlations with clinical tests. We confirmed and elaborated the findings of Houdijk et al. [3] to patients with stroke (Chapter 5) and PD (Chapter 6). Together, these results support the assumption that walking adaptability is not covered in clinical assessments of walking ability. Notably, obstacle-avoidance success rate and normalized walking speed during goal-directed stepping improved the identification of prospective fallers (Chapter 7). Poor obstacle avoidance or stepping performance has previously already been found to be associated with falls [22-25], emphasizing the merit of assessing walking adaptability for fall risk assessments.

Altogether, it is thus important to add task-specific factors associated with walking-related falls to an assessment of walking ability and fall risk, which can be done with the IWW. Since the obstacle-avoidance and goal-directed stepping tasks provide a valid assessment of walking adaptability and improve the identification of fallers, these tasks are advised to be included in a task-specific assessment of walking ability aimed at assessing fall risk.

Walking ability and falls: moving to a generic assessment

It is known that in most neurological disorders, fall incidence is higher than in the healthy population [26,27], which may be due to underlying gait and balance impairments. In fact, gait and balance disturbances significantly correlated with falls in patients with neurological disorders and were identified as risk factors for falls [26,27]. In addition, most fallers in this group of patients reported that they tripped over an obstacle [27], suggesting a reduced walking adaptability. A task-specific assessment of walking ability and fall risk focusses on limitations in walking of patients instead of on impairments associated with a particular disease or disorder itself. This task-specific approach therefore allows for a more generic fall-risk assessment, which could apply to various diseases and disorders. In this thesis, we have mainly focused on task-specific fall-risk factors (Chapter 7). Group (i.e., stroke, PD, control) was also included in the models of Chapter 7; as expected, group was not identified as a significant predictor variable for prospective falls. However, the sample size and the distribution of fallers and non-fallers across groups may have been too small to detect group differences. Nevertheless, in both groups, approximately half of the patients fell in the year prior to the assessment (Chapter 7). In addition, not all prospective fallers of the falls-naïve cohort in Chapter 7 belonged to the same group (i.e., three stroke patients, two PD patients and four healthy controls) and these fallers were classified by specific limitations in walking ability (i.e., suboptimal obstacle-avoidance success rates in combination with a maladaptive walking speed during precision stepping). As can be noticed, healthy controls without specific disorders also experienced falls. A decreased walking ability in older adults compared to younger adults has been demonstrated, both in steady-state walking and walking adaptability [28]. Age was also positively associated with the number of falls in patients with neurological disorders [26,27]. In Chapter 7, age did not differ significantly between prospective fallers and non-fallers, but was identified as a predictor variable for falls in the prediction models that did not include walking-adaptability outcome measures. Limitations in walking ability, regardless of their cause (e.g., neurological disorders, ageing), thus likely give a better indication of someone's fall risk, calling for a generic and task-specific fall-risk assessment.

Walking ability and falls: minimizing assessment time

As discussed in the previous two sections, it seems useful to assess fall risk in a task-specific and generic manner. From a more practical point of view, fall-risk assessments should also be concise. In an outpatient clinic a physician generally obtains a momentary impression of a patient's walking ability and fall risk. However, administering multiple clinical tests may imply redundancy, since several tests were highly interrelated, as demonstrated in Chapter 5, and thus only increase the burden for the patient. This is also the case when combining clinical tests with quantitative gait assessments. Given the high correlation between IWW quantitative gait assessments and clinical tests, a possibility could be to combine the IWW quantitative gait and walking-adaptability assessment to obtain the sought-after quick and comprehensive assessment of fall risk.

Previous studies have indicated that steady-state gait characteristics are associated with falls [27,29], while this is often not the case for clinical test scores due to potential ceiling effects [6]. This was however not confirmed by the results presented in Chapter 7. Nevertheless, significant differences were found between fallers and non-fallers for walking speed and step length, suggesting that a quantitative gait assessment might be informative in a fall risk assessment. Since gait parameters were highly correlated with conventional clinical test scores of gait and balance (Chapters 5 and 6), performing quantitative gait assessments with the IWW instead of clinical tests could therefore be a good option for a quick and comprehensive fall-risk assessment. A quantitative gait assessment with the IWW requires about the same time as the 10-meter walking test. The latter test only provides walking speed, while a quantitative gait assessment with the IWW provides more information, based on 3D kinematics of the whole body. A quantitative gait assessment and some complementary walking-adaptability tasks (i.e., obstacle-avoidance and goal-directed stepping as suggested above) on the IWW thus seems to be a good option for assessing walking ability in a quick (5-10 minutes) and comprehensive manner. However, removing clinical tests from the binary logistic regression models in Chapter 7 did not lead to the inclusion of spatiotemporal gait parameters as predictor variables and slightly worsened the classification of prospective fallers and non-fallers. Therefore, more research is needed to explore the feasibility of the IWW as a tool to quickly estimate fall risk.

The Interactive Walkway for a more comprehensive fall-risk assessment?

Though the task-specific and generic fall-risk assessment of the IWW seems promising, more research is needed to confirm its potential merit as a comprehensive fall-risk assessment. First of all, the fall prediction models presented in this thesis have to be cross-validated with an independent composite cohort of stroke patients, PD patients and healthy controls. Second, the responsiveness of IWW outcome measures to subtle changes over time has to be examined. In all studies of this thesis, assessments of walking ability were performed once. This will only provide the momentary status of a person. It is however important that IWW assessments can be used to validly monitor the effect of a disease or treatment on the walking ability and thus potentially also fall risk of a patient. Third, I have focused on assessing walking ability in two highly prevalent neurological disorders, namely stroke and PD. It is not yet known if the IWW can be used to asses walking ability validly in other patient populations. This is partly due to the fact that the Kinect v2 sensor best recognizes persons from a frontal view and occasionally fails to detect persons with an abnormal body posture. This could potentially be a problem in disorders like dystonia and cerebral palsy where body posture is severely affected. Future studies should therefore focus on a greater variety of patient groups to be able to determine for which disorders the IWW is best suited for fall-risk assessments.

	Positive	**Negative**
Internal	**Strengths** Markerless motion registration Assessment of sudden step adjustments Safe assessment of walking adaptability Overground assessment Individually tailored Comprehensive assessment	**Weaknesses** 2D projections Bound to a specific location Frontal view body recognition
External	**Opportunities** Entry point falls prevention program Personalized falls prevention programs	**Threats** Competition Discontinuation Kinect v2 sensor

Figure 8.2 Schematic of the SWOT analysis of the Interactive Walkway intended for use as a fall-risk assessment in the clinic.

SWOT analysis of the Interactive Walkway intended for use as a fall-risk assessment in the clinic

Currently, the IWW is still mostly a scientific tool and there are several steps to be made before it can be implemented into the clinic. A strengths, weaknesses, opportunities and threats (SWOT) analysis may help to determine where future research should focus on in order to implement the IWW as a fall-risk assessment tool in the clinic (Figure 8.2). The SWOT analysis has two main categories, namely internal and external factors. Internal factors are inherent to the product and dictate its strengths and weaknesses. External factors are the opportunities and threats presented by the environment external to the product. Below, these four SWOT categories are discussed for the IWW intended for use as a fall-risk assessment in the clinic.

Strengths

The studies presented in this thesis have emphasized several benefits of the IWW that are relevant for its intended use as a fall-risk assessment in the clinic. First of all, 3D full-body kinematics is obtained without markers by using the Kinect v2 sensor. Normally, full-body kinematics can be obtained using expensive, high-end, marker-based motion-registration systems. The Kinect sensor is a cheap and easy-to-use alternative. Using the Kinect sensor for motion registration also significantly reduces preparation time, which is more convenient for the patient. In addition, the movements of the patients are not restricted by markers and are therefore expected to be more natural. Another advantage of the Kinect sensor is that the data are available immediately and can be processed online. This makes the system usable for movement-dependent event control [30]. Walking adaptability has so far mostly been assessed with fixed obstacles or targets in laboratory studies [8,11,12] or with specific clinical tests (e.g., Dynamic Gait Index; [31]). On the IWW, movements of the subject may trigger the presentation of the visual context, therefore requiring adjustments under controllable time pressure demands. The IWW can thus assess walking adaptability to both expected (e.g., slalom, goal-directed stepping) and unexpected (e.g., sudden obstacle avoidance, sudden stops-and-starts) challenges in the environment.

The additional benefit of using projections instead of real obstacles is that it makes the assessment of walking adaptability safer since patients cannot physically trip as could be the case when trying to avoid real obstacles. Furthermore, interacting directly with meaningful visual context in an overground walking environment may also be seen as a strength. An assessment with projected visual context has previously been performed on the C-Mill, demonstrating that this is an effective and safe way of assessing walking adaptability [32-35]. However, natural responses, such as slowing down in a complex environment, cannot be assessed on a fixed-speed treadmill. Furthermore, tasks such as stopping and turning cannot be performed. These tasks are all well possible with the IWW, since it entails an overground assessment. However, a potential problem might be task prioritization. In a study of Timmermans et al. [36], cognitive-motor interference and task prioritization was assessed for obstacle avoidance, contrasting avoidance of real physical obstacles and projected visual obstacles. Although the amount of cognitive-motor interference did not differ between tasks, task prioritization did. Motor performance was prioritized in an environment characterized by physical context as compared to an environment with projected context. In the study of Timmermans et al. [36] and in the studies presented in Chapters 5 to 7, subjects were instructed to perform both the dual task and the obstacle avoidance task as well as possible. Task prioritization could therefore explain the lack of a clear effect of the dual task on obstacle-avoidance performance in Chapters 6 and 7.

Another strength of the IWW is that tasks can be individually tailored, meaning that the difficulty of the walking-adaptability tasks can be adjusted to the ability of the individual (e.g., amount of variation, available response distance) making it suitable for both healthy controls and various patient groups. A final strength of the IWW for use as a fall-risk assessment is that it comprised both steady-state walking and walking adaptability, providing a comprehensive assessment of walking ability. This yields information complementary to standard clinical assessments (Chapters 5 to 7), mainly information about a patient's walking adaptability. Considering these strengths, is seems fair to conclude that the IWW seems promising for use as a fall-risk assessment.

Weaknesses

Despite the benefits of a fall-risk assessment with the IWW, there is still room for improvement. Currently, the IWW only uses 2D projections to evoke step responses. In real life, obstacles or other objects we need to interact with are not always flat. In many studies, foot clearance during obstacle crossing [8,11,12,37-39] was found to be an important factor for successful obstacle-avoidance behavior to avoid falls. Moreover, age-related changes in obstacle-crossing strategies were found to depend on the specific characteristics of the obstacle, such as obstacle height [40]. Simply adding real 3D obstacles to the IWW is possible but not preferable, considering that it increases the risk of falls during a fall-risk assessment and it then becomes impossible to assess sudden step adjustments. Using 3D holographic obstacles may be a solution to address this weakness (see also future perspectives) and could potentially also improve the ability of the IWW to elicit FOG in PD patients, which was not possible with 2D visual context as was found in Chapter 6. Nevertheless, the obstacle-avoidance task with 2D projections appeared effective, since obstacle-avoidance success rate did demonstrate differences between groups and improved the identification of prospective fallers (Chapters 5 to 7).

Another weakness of the IWW for use as a fall risk assessment is that it is bound to a specific assessment space, comparable to other motion registration systems. This does however not need to be a big space, because the IWW has been optimized for use in a corridor. An additional instrumental weakness of the IWW set-up used in this thesis is that it is bound to measuring walking in one direction. The Kinect v2 sensor is trained to recognize persons from a frontal view. This means that the patient has to walk twice the distance, making the assessment twice as long. This can however be solved by using Kinect sensors on both sides. Another weakness of the IWW for use as a fall-risk assessment is that the Kinect sensor sometimes has difficulty recognizing patients (i.e., considering the 3.4% of removed trials in Chapter 7). It seems that this was caused by certain body postures, such as a body posture turned away from the sensor (e.g., as a result of a hemiplegic gait in stroke on the side opposite to the sensor placement) or a very stooped posture (e.g., in severely affected PD patients). This may reduce the quality of the 3D full-body kinematic data.

Opportunities

Instead of only being used to screen who is at risk of falling, IWW assessments of walking ability may provide specific entry points for fall prevention programs to target task-specific risk factors for reducing fall risk and improving walking ability. In Weerdesteyn et al. [25], a decrease in fall risk was associated with an improved obstacle-avoidance performance. Poor obstacle-avoidance success rate was also a risk factor for falls in Chapter 7. It thus seems imperative to train obstacle-avoidance in generic falls prevention programs. Furthermore, assessments of walking ability may be used to provide a more personalized falls prevention program. A personalized approach might increase adherence to the falls prevention program (i.e., by being challenging, but feasible for the patient) and foster lasting change (i.e., by targeting the right limitations in walking ability; [41,42]). The potential of the IWW to guide personalized therapy still needs to be examined, since the outcomes of the studies in Chapters 5 to 7 have only focused on comparing groups (i.e., patients vs. controls and prospective fallers vs. non-fallers) instead of looking into individual traits that increase fall risk. High-end machine learning techniques permit the individualization of fall-risk assessments [43]. These techniques require a large dataset that can be collected relatively easily with the IWW. In order to provide personalized therapy to patients, future studies should thus focus on IWW fall-risk assessments in a large group of patients with various disorders.

Threats

Finally, there are some threats that may jeopardize the use of the IWW for use as a fall-risk assessment. The biggest threat is the competitive field in which several fall-risk assessments are available. Further, many of these assessments have already been cross-validated in much larger patient groups [44,45]. Although our studies suggest that walking adaptability has additive value in a fall-risk assessment, more evidence is needed before the IWW assessment will be adopted in the clinic.

It is relevant to note that Microsoft has decided to discontinue the production of the Kinect v2 sensor. Although this is an unfortunate event, the principle of the IWW (i.e., using real-time processed markerless 3D data to interactively present visual context to evoke step responses and assess walking adaptability) remains. Other sensors may serve as input for the IWW (e.g., Orbec, SIMI), and Microsoft will soon release the Kinect v4 sensor, which can be regarded as an upgrade of the Kinect v2 sensor given the better specifications (e.g., increased depth resolution). These sensors may be examined for their potential to replace the Kinect v2 sensor, which would require new validation studies comparable to those presented in Chapters 2 to 4.

Future perspectives

In the SWOT analysis of the IWW as a fall-risk assessment tool for use in the clinic, some directions for future research were already mentioned. We have now reached the finish of the roadmap, as presented in Figure 8.1. This does not mean however that the development of the IWW ends here. I propose three future paths for the IWW: 1) moving from assessment to training, 2) moving from 2D to 3D context, and 3) moving from a location-bound to a mobile set-up (see crossroads in Figure 8.1), as will be discussed next.

The Interactive Walkway for training walking adaptability

The IWW can also potentially be used to train walking adaptability in a falls prevention program. Walking adaptability has already been trained on a treadmill using projected visual context (i.e., the C-Mill; [32-35]). Results of these studies demonstrated that walking ability improved after task-specific training with visual context [32-35]. In contrast to the C-Mill, the IWW allows for training of walking adaptability in an overground setting. This leaves room for natural responses to environmental context, such as slowing down or even stopping before crossing an obstacle, which is not possible on a fixed-speed treadmill. This makes training of walking adaptability with the IWW especially useful in fragile populations, who often slow down in complex environments [36]. In Chapter 5, it was shown that stroke patients lowered their walking speed relatively more in complex situations compared to healthy controls. In addition, overestimation of someone's walking ability (i.e., not substantially lowering walking speed when walking adaptability is limited) increases the risk of falling as demonstrated in Chapter 7. Training people to adopt a safer strategy when walking in a complex environment might therefore be useful. This is all well possible with the IWW, confirming its potential as a training tool in addition to an assessment tool of walking ability and fall risk.

The Interactive Walkway with 3D holograms

As already mentioned, the IWW uses 2D projections for an assessment of walking adaptability, which could be considered a weakness of the system although promising results of such an assessment have been obtained in this thesis and beyond (e.g., C-Mill studies; [32-35]). However, there are new techniques available that can be used to present 3D holographic context for an assessment or training of walking adaptability. The HoloLens (Figure 8.3) is a mixed-reality headset which uses multiple Kinect v3 sensors to scan the environment in order to present holograms at a fixed position in the real world. This could potentially be used in combination with the IWW in order to give an extra dimension to the presented visual context. In the study of Binaee & Diaz [46], illusionary 3D augmented reality obstacles produced realistic obstacle-avoidance behavior in terms of foot placement and foot clearance. In an unpublished pilot study conducted at the Department of Human Movement Sciences of the Vrije Universiteit Amsterdam using the HoloLens for 3D obstacle avoidance, it was demonstrated that scaling the obstacle height indeed also leads to scaling of the foot clearance of the leading limb during obstacle crossing. The holographic context presented with the HoloLens thus seems suitable for evoking step adjustments in 3D. Nevertheless, although people seem to step over the obstacle quite well with their leading limb, this is not always the case for their trailing limb (Figure 8.3). The limited field of view is often reported by participants as a drawback of the current version of the HoloLens. Hence, the presented obstacle is not entirely visible when a person steps over it, unless the person looks directly down. The field of view is supposed to increase with the newer version of the HoloLens, which could potentially improve the ecological validity of 3D holographic obstacle avoidance. Besides, it needs to be determined whether certain additions, such as providing (direct) feedback on performance, can improve the obstacle-avoidance performance and as such the potential of the HoloLens for use in fall-risk assessments and for training walking adaptability in falls prevention programs.

The mobile Interactive Walkway

Technology is always moving and develops fast. Within the time period of my PhD project, the Kinect sensor progressed from the v1 sensor with relatively poor depth resolution to the v2 sensor as used in this thesis to a mobile v3 sensor embedded in the HoloLens and soon a v4 sensor will be launched with even better technical specifications and extra options. The development of these new techniques (i.e., Kinect sensor, HoloLens) yields new possibilities for the assessment of walking ability and fall risk and for training of walking adaptability.

The IWW was developed and tested within the 'Technology in Motion' project (tim.lumc.nl). In this NWO-funded project, new emerging low-cost techniques, such as the Kinect v2 sensor, were used to quantify motor disorders in an unobtrusive and patient-friendly manner. The multi-Kinect based IWW fitted well within the aims of this project, as does the HoloLens. The HoloLens has the potential to be used as an extension of the IWW to move from 2D to 3D context as described above, but might potentially also be used as a stand-alone system to assess and train walking adaptability. The HoloLens is able to scan the environment in order to present holograms at a fixed position. In addition, this information can be used by the HoloLens to determine where someone is in that environment in order to present holograms in a movement-dependent manner. This would allow for a safe assessment of walking adaptability with 3D holograms, without being bound to a specific location as is the case for the IWW. Furthermore, head position data can be measured to calculate spatiotemporal gait parameters. Preliminary data demonstrated good agreement between the IWW and HoloLens for step length (absolute between-systems difference ≤ 0.87 cm), walking speed (absolute between-systems difference ≤ 1.72 cm/s) and cadence (absolute between-systems difference ≤ 2.02 steps/min). However, walking-adaptability outcome measures, such as obstacle-avoidance margins, require more detailed kinematics stemming from an external motion-registration system (such as a location bound IWW). Nevertheless, with the arrival of the Kinect v4 sensor for the HoloLens, it might be used as the desired motion registration system when worn by the assessor(s) looking at the patient. This could yield a more flexible way of performing quantitative gait assessments and walking-adaptability assessments in the clinic, without being bound to a particular location. Linking the HoloLenses of the patient and the assessor(s) further enables that they both can see the holograms. The envisioned mobile IWW, based on coupled HoloLenses, thus seems promising for assessment and training of walking ability and fall risk and is definitely a path worth exploring.

Figure 8.3 The HoloLens (A) and obstacle avoidance over a holographic obstacle presented with the HoloLens with the leading (B) and trailing (C) limb.

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Abbreviations

2D	Two-dimensional
3D	Three-dimensional
8MWT	8-meter walking test
10MWT	10-meter walking test
ADT	Augmented dual-task walking (obstacle avoidance with dual task)
AP	Anterior-posterior
ARD	Available response distance
ART	Available response time
ASS	Asymmetric stepping stones
C	Control
CI	Confidence interval
CWS	Comfortable walking speed
EW	Entire walkway
FMA	Fugl-Meyer Assessment
FOG	Freezing of gait
FT	Full turns
FW	Foot width
HT	Half turns

$ICC_{(A,1)}$	Intraclass correlation coefficient for absolute agreement
$ICC_{(C,1)}$	Intraclass correlation coefficient for consistency
ISS	Irregular stepping stones
IWW	Interactive Walkway
L	Left
MDS-UPDRS	Movement Disorder Society version of the Unified Rating Scale for Parkinson's disease
ML	Mediolateral
MOCA	Montreal Cognitive Assessment
mSAFFE	Modified Survey of Activities of Fear of Falling in the Elderly Scale
MWS	Maximum walking speed
NFOGQ	New Freezing of Gait Questionnaire
PD	Parkinson's disease (patient)
PDT	Plain dual-task walking (8-meter walking test with dual task)
R	Right
S	Stroke patient
SCOPA-COG	Scales for Outcomes in Parkinson's Disease – Cognition
SD	Slowing down
SL	Step length

SN	Sudden narrowing
SSS	Symmetric stepping stones
SSWS	Self-selected walking speed of unconstrained walking
SU	Speeding up
SW	Step width
SWOT	Strengths, weaknesses, opportunities and threats
V	Vertical
VSS	Variable stepping stones
WW	Walkway width

Videos

Overview of the videos that were published with this thesis.

Chapter 2 (Supplement 2.2)

Video of body point's time series obtained with the multi-Kinect v2 set-up and the Optotrak system of a single representative trial during the comfortable walking speed condition of the 10-meter walking test. This video is available at https://doi.org/10.1371/journal.pone.0139913.s004.

Chapter 5 (Supplement 5.1)

Video of Interactive Walkway tasks of unconstrained walking and walking adaptability in a patient with stroke. This video is available at https://youtu.be/nV9tGvlPogs.

Chapter 6 (Supplement 6.1)

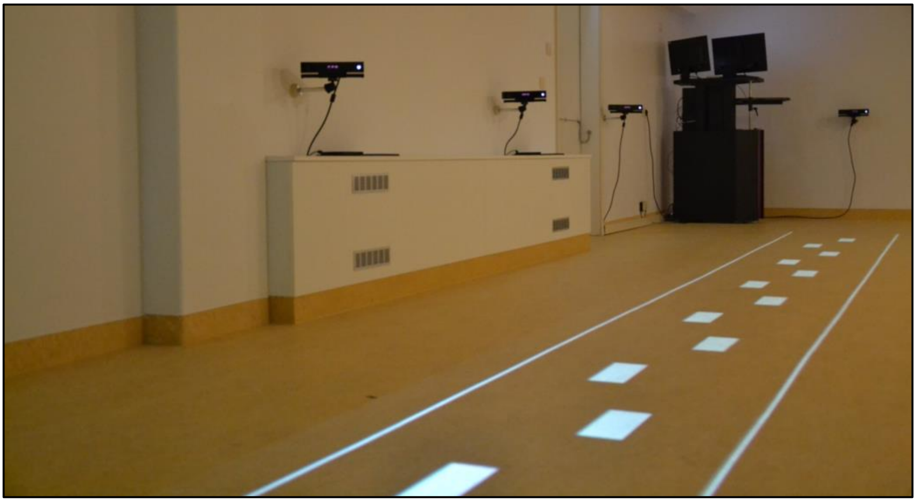
Video of Interactive Walkway tasks of unconstrained walking, adaptive walking and dual-task walking in a person with Parkinson's disease with dyskinesia. The subject had consented to the making of the video for publication purposes. This video is available at https://youtu.be/p1a07lL9veM.

Chapter 7 (Supplement 7.2)

Video of assessments on the Interactive Walkway in a patient with stroke. This video is available at https://youtu.be/k7O2kc5R-K8.

Nederlandse samenvatting

Neurologische aandoeningen kunnen een negatief effect hebben op verschillende aspecten van loopvaardigheid die nodig zijn om veilig en zelfstandig te kunnen lopen. Dit vraagt om uiteenlopende revalidatiestrategieën. Een uitgebreide en volledige beoordeling van de belangrijkste aspecten van loopvaardigheid zou kunnen helpen om deze strategieën beter af te stemmen op de individuele behoeften van de patiënt. De *Interactive Walkway* (figuur N1.1) lijkt een veelbelovend, patiëntvriendelijk en goedkoop meetinstrument voor loopvaardigheid in de dagelijkse praktijk. De *Interactive Walkway* bestaat uit meerdere Kinect v2-sensoren, waarmee het volledige gangbeeld -zonder markers op het lichaam- in 3D gemeten kan worden. De *Interactive Walkway* kan, naast het meten van het gangbeeld, mogelijk ook het zogenoemde loopspecifieke aanpassingsvermogen op een veilige manier in kaart brengen door het (plotseling) presenteren van visuele projecties op het looppad in de vorm van staptegels of obstakels (figuur N1.1). Dit lijkt waardevol omdat het lopen in het dagelijks leven vaak aangepast moet worden, bijvoorbeeld bij het oversteken van een straat of bij het ontwijken van scheefliggende stoeptegels. Een slecht aanpassingsvermogen wordt bovendien in verband gebracht met een hoger valrisico. Dit aspect van loopvaardigheid wordt doorgaans echter niet in klinische testen beoordeeld. De *Interactive Walkway* biedt nu de mogelijkheid om loopvaardigheid vollediger te meten door naast het gangbeeld ook het loopspecifieke aanpassingsvermogen in kaart te brengen. Het is alleen onduidelijk of 1) de *Interactive Walkway* loopvaardigheid valide kan meten en, zo ja, 2) of de *Interactive Walkway* nuttig is voor het bepalen van loopvaardigheid en valrisico in de kliniek bij patiënten met een beroerte en patiënten met de ziekte van Parkinson. Het doel van dit proefschrift was om inzicht te krijgen in deze twee aspecten.



Figuur N1.1 De *Interactive Walkway* met visuele projecties op het looppad.

Deel 1: Kan loopvaardigheid valide en volledig gemeten worden met de Interactive Walkway?

De meest gebruikte uitkomstmaat van loopvaardigheid is loopsnelheid over korte afstanden, bepaald met bijvoorbeeld de 10-meter looptest. Met de *Interactive Walkway* kan deze 10-meter looptest worden uitgebreid met een snelle, niet-invasieve en patiëntvriendelijke kwantitatieve gangbeeldanalyse. De 3D-kinematica geeft aanvullende informatie over loop- en balansproblemen, wat niet mogelijk is met standaard klinische testen. De studie beschreven in **Hoofdstuk 2** was gericht op het valideren van een kwantitatieve gangbeeldanalyse met de *Interactive Walkway* in een groep van 21 gezonde personen. De 10-meter looptest werd uitgevoerd op comfortabele en maximale loopsnelheid, terwijl 3D-kinematica van het hele lichaam gelijktijdig werd gemeten met zowel de *Interactive Walkway* als het Optotrak systeem (d.w.z. de gouden standaard). De resultaten lieten zien dat 3D-kinematica goed overeenkwam tussen deze bewegingsregistratiesystemen, vooral bij grote bewegingsuitslagen. Hetzelfde gold voor spatiotemporele gangparameters die uit 3D-kinematica kunnen worden afgeleid. De resultaten van Hoofdstuk 2 lieten dus zien dat een kwantitatieve gangbeeldanalyse valide uitgevoerd kan worden met de *Interactive Walkway*.

De *Interactive Walkway* kan, naast het meten van het gangbeeld, mogelijk ook het loopspecifieke aanpassingsvermogen in kaart brengen. Hiertoe worden visuele projecties (plotseling) op het looppad gepresenteerd in de vorm van staptegels of obstakels. In **Hoofdstuk 3** werd gekeken naar de overeenkomst tussen de *Interactive Walkway* en het Optotrak systeem, en de gevoeligheid voor taak- en tussenpersoonsvariatie van verschillende taken op de *Interactive Walkway* ter bepaling van het aanpassingsvermogen. In totaal voerden 21 gezonde personen meerdere *Interactive Walkway*-taken uit met verschillende moeilijkheidsgraden: obstakels ontwijken, plotseling stoppen en starten, en doelgerichte stappen. De resultaten lieten zien dat uitkomstmaten van het aanpassingsvermogen, zoals obstakel-ontwijkmarges, over het algemeen goed overeenkwamen. Daarnaast waren deze uitkomstmaten gevoelig voor taak- en tussenpersoonsvariatie. Variatie in doelgericht stappen resulteerde in verschillende staplengten, stapnauwkeurigheden en loopsnelheden, terwijl reactietijden en obstakel-ontwijkmarges verschilden per obstakeltype. Dit betekent dat het gebruik van de visuele projecties mogelijkheden biedt om het lopen te manipuleren en (plotselinge) stapaanpassingen uit te lokken, in overeenstemming met eerdere onderzoeken die eenzelfde concept onderzochten tijdens lopen op een loopband. Gevoeligheid voor taak- en tussenpersoonsvariatie is belangrijk ter bepaling van het aanpassingsvermogen van relatief goed functionerende groepen (zoals thuiswonende ouderen), waar plafondeffecten een veelvoorkomend probleem zijn. Hetzelfde geldt voor bodemeffecten bij relatief kwetsbare patiëntgroepen. De *Interactive Walkway* maakt een kwantitatieve bepaling van het aanpassingsvermogen mogelijk en is haalbaar voor zowel goed functionerende als kwetsbare populaties, aangezien de moeilijkheidsgraad van de taak kan worden aangepast. Bovendien is het vaststellen van het aanpassingsvermogen met de *Interactive Walkway* relatief veilig (visuele in plaats van fysieke obstakels), niet belastend (meten zonder markers op het lichaam), en daardoor tijdbesparend en patiëntvriendelijk. De *Interactive Walkway*-taken lijken daardoor bruikbaar voor het verkrijgen van objectieve en meer taakspecifieke informatie van iemands loopvaardigheid. Dit rechtvaardigt studies naar de klinische potentie, zoals is beschreven in de Hoofdstukken 5 tot en met 7.

De inzichten verkregen in de twee validatiestudies gaven aanleiding voor nog een derde validatiestudie. De studie beschreven in **Hoofdstuk 4** had als doel het systematisch onderzoeken van het effect van afstand van het lichaam tot de sensor, lichaamszijde (d.w.z. links of rechts) en staplengte op de voetplaatsingslocaties bepaald aan de hand van de geschatte enkelposities door de Kinect v2-sensor van de *Interactive Walkway*. De voetplaatsingslocaties zijn nodig voor het kwantificeren van spatiële gangparameters en verschillende uitkomstmaten van het aanpassingsvermogen. In totaal hebben 12 gezonde personen staptaken met opgelegde voetplaatsingslocaties op verschillende afstanden van de Kinect sensor uitgevoerd, voor zowel de linker- als de rechtervoet en met verschillende opgelegde staplengten. Deze staptaken werden gelijktijdig vastgelegd met de Kinect v2-sensor en het Optotrak systeem. Kleine maar significante verschillen tussen de systemen werden gevonden voor voetplaatsingslocaties en staplengte. Deze werden waarschijnlijk veroorzaakt door verschillen in lichaamsoriëntatie ten opzichte van de Kinect sensor, waardoor de enkelposities meer naar achteren werden geschat. Dit effect kan eenvoudig verminderd worden door de afstanden tussen de sensoren van de *Interactive Walkway*-opstelling te verkleinen, om zo voetplaatsingslocaties op grotere afstanden van de sensor te kunnen bepalen.

Uit deze drie validatiestudies kan worden geconcludeerd dat de *Interactive Walkway* gebruikt kan worden om zowel het gangbeeld (Hoofdstuk 2) als het loopspecifieke aanpassingsvermogen (Hoofdstuk 3) valide in kaart te brengen bij gezonde personen. Het biedt tevens de mogelijkheid voor een volledig(er) looponderzoek, waarbij alle onderdelen van het drieledig model van loopvaardigheid worden meegenomen, te weten het vermogen om 1) stappen te genereren, 2) de balans te bewaren en 3) het lopen aan te passen aan de omgeving. De resultaten van Hoofdstukken 2 tot en met 4 hebben ook tot een verbetering van de *Interactive Walkway*-opstelling geleid door het verkleinen van de afstand tussen de sensoren. De volgende stap was het bestuderen van de klinische potentie van de *Interactive Walkway* ter bepaling van loopvaardigheid en valrisico bij verschillende patiëntgroepen, zoals hierna zal worden besproken.

Deel 2: Is de Interactive Walkway nuttig voor het bepalen van loopvaardigheid en valrisico in de kliniek?

Het doel van de studie beschreven in **Hoofdstuk 5** was om te onderzoeken of de *Interactive Walkway* gebruikt kan worden ter bepaling van loopvaardigheid bij patiënten met een beroerte. Het in kaart brengen van beperkingen in loopvaardigheid kan helpen bij het ontwikkelen van geïndividualiseerde revalidatiestrategieën. Bij 30 patiënten met een beroerte en 30 gezonde controlepersonen van gelijke leeftijd en gelijk geslacht werden verschillende klinische testen afgenomen, evenals kwantitatieve 3D-gangbeeldanalyses en verschillende *Interactive Walkway*-taken. De resultaten van deze studie suggereren een goede *known-groups* validiteit voor *Interactive Walkway*-uitkomstmaten van het aanpassingsvermogen, vergelijkbaar met die van klinische testen en kwantitatieve gangbeeldanalyses. Bovendien bleken *Interactive Walkway*-taken aanvullende informatie te geven, gezien de overwegend lage tot middelmatig sterke correlaties tussen de uitkomstmaten van het aanpassingsvermogen, en die van klinische testen en kwantitatieve gangbeeldanalyses. Deze bevindingen suggereerden daarom dat het bepalen van het gangbeeld en het loopspecifieke aanpassingsvermogen, door middel van obstakels ontwijken en doelgericht stappen, met de *Interactive Walkway* een snel, niet-invasief en volledig kwantitatief beeld geeft van loopvaardigheid. Dit biedt mogelijkheden voor het monitoren van herstel na een beroerte en voor het individualiseren van revalidatiestrategieën.

In **Hoofdstuk 6** werden het gangbeeld (d.w.z. kwantitatieve gangbeeldanalyse), adaptief lopen en dubbeltaaklopen onderzocht met de *Interactive Walkway* bij 14 patiënten met de ziekte van Parkinson met *freezing of gait*, 16 patiënten met de ziekte van Parkinson zonder *freezing of gait* en 30 gezonde controlepersonen. Patiënten met *freezing of gait* scoorden het slechtst, patiënten zonder *freezing of gait* scoorden gemiddeld en controlepersonen scoorden het best op de meeste *Interactive Walkway*-taken, in overeenstemming met de resultaten van de klinische testen. Dit suggereert een goede *known-groups* validiteit voor de *Interactive Walkway*-taken. Patiënten met de ziekte van Parkinson ondervonden vooral problemen wanneer zij moesten afwijken van hun eigen looppatroon, waarbij een beroep moest worden gedaan op de dynamische balanscontrole. Om een goed beeld te krijgen van iemands loopvaardigheid moet daarom zowel het gangbeeld als het adaptief lopen worden onderzocht, bijvoorbeeld door middel van obstakels ontwijken en doelgericht stappen. In deze studie werd aangetoond dat deze *Interactive Walkway*-taken ook aanvullende informatie geven ten opzichte van klinische testen, gezien de lage tot middelmatig sterke correlaties tussen deze twee typen testen. Bovendien bleek classificatie van patiënten mét en zónder *freezing of gait* aan de hand van *Interactive Walkway*-uitkomstmaten van adaptief lopen iets beter dan classificatie op grond van klinische testscores. De *Interactive Walkway* heeft dus potentie om loopvaardigheid bij de ziekte van Parkinson volledig(er) te bepalen. Het maakt het mogelijke om belangrijke aspecten die mogelijk een verband hebben met valincidenten in kaart te brengen, zoals is onderzocht in Hoofdstuk 7.

In **Hoofdstuk 7** werd onderzocht of de *Interactive Walkway* gebruikt kan worden om toekomstige vallers en risicofactoren voor toekomstige valincidenten te identificeren in een gemengd cohort van patiënten met een beroerte, patiënten met de ziekte van Parkinson en gezonde personen. In deze studie werd gekeken naar persoonskarakteristieken, klinische loop- en balanstesten, een kwantitatieve gangbeeldanalyse en *Interactive Walkway*-

taken. Valkalenders werden gebruikt om gedurende zes maanden prospectief alle valincidenten te registeren. Zodoende konden personen als vallers (d.w.z. tenminste een loopgerelateerde val gedurende de vervolgperiode) of niet-vallers worden geïdentificeerd. Bij aanvang van de vervolgperiode hadden vallers meer angst om te vallen en vermeden ze meer activiteiten uit angst om te vallen dan niet-vallers. Daarnaast liepen vallers langzamer en met kleinere stappen en presteerden ze slechter op klinische loop- en balanstesten. Zoals verwacht presteerden vallers ook slechter op verschillende *Interactive Walkway*-taken. Naast valgeschiedenis werden het percentage succesvol ontweken obstakels en de genormaliseerde loopsnelheid tijdens doelgericht stappen geïdentificeerd als voorspellende variabelen van valincidenten, en toevoeging van deze risicofactoren verbeterde de identificatie van vallers. Personen die slecht scoorden op de obstakel-ontwijktaak en die hun loopsnelheid niet aanzienlijk verlaagden tijdens doelgericht stappen liepen het grootste risico om te vallen. Het identificeren van deze taakspecifieke valrisicofactoren kan leiden tot meer gerichte, gepersonaliseerde en mogelijke effectievere valpreventieprogramma's. Deze taken lijken, mits geverifieerd in een grotere groep, dus veelbelovende aangrijpingspunten voor toekomstige valpreventieprogramma's.

Gezamenlijk laten deze bevindingen zien dat de loopvaardigheid van patiënten met een beroerte (Hoofdstuk 5) en patiënten met de ziekte van Parkinson (Hoofdstuk 6) valide en volledig gemeten kan worden met de *Interactive Walkway*. Bovendien bleken beperkingen in het aanpassingsvermogen risicofactoren voor valincidenten, variabelen die ook bij kunnen dragen aan een betere identificatie van vallers (Hoofdstuk 7). De *Interactive Walkway* heeft dus potentie om de loopvaardigheid bij patiënten met een beroerte en patiënten met de ziekte van Parkinson valide en volledig in kaart te brengen, en is daarmee veelbelovend voor het inschatten van het valrisico.

Dankwoord

It is good to have an end to journey towards; but it is the journey that matters, in the end – Ursula K. Le Guin

Deze bijzondere reis, met dit proefschrift als eindresultaat, was niet mogelijk geweest zonder de hulp en steun van velen.

Melvyn, bedankt voor je vertrouwen in mij. Na mijn onderzoeksstage heb je mij de kans gegeven verder te gaan binnen het onderzoek met de *Interactive Walkway* en inmiddels hebben we de samenwerking voortgezet binnen een nieuw project. Ik wil je bedanken voor het feit dat je me regelmatig uit mijn comfortzone hebt gehaald. Zonder jou was de groei die ik heb doorgemaakt niet mogelijk geweest.

Han, je deur stond altijd open voor vragen met betrekking tot statistiek en methodologie. Bedankt voor je open houding en rustige uitleg.

Bob, je enthousiasme werkt aanstekelijk. Je hebt me uitgedaagd af en toe buiten de gebaande paden te denken en meer de mogelijkheden te zien in plaats van de moeilijkheden.

Linda, ik heb enorm veel van je geleerd. Bedankt voor je hulp bij mijn onderzoek en je vele adviezen.

Bert, bedankt voor je technische ondersteuning gedurende mijn promotieonderzoek.

Deelnemers van de verschillende studies, bedankt voor jullie deelname en enthousiasme! De betrokken studenten (**Detmar, Josine, Wietse en Ronald**), bedankt voor jullie hulp bij het opzetten en uitvoeren van de studies.

Collega's van de afdelingen Bewegingswetenschappen en Neurologie, en het *Technology in Motion* project, bedankt voor jullie interesse, input en de fijne samenwerking. Ik wil in het bijzonder **Elma** bedanken voor haar hulp bij de metingen met de patiënten.

Lieve familie, vrienden en teamgenoten, bedankt voor jullie steun, interesse in mijn onderzoek en de (zo af en toe erg gewenste) afleiding!

Papa, mama en Nicky, een geweldige basis om op terug te kunnen vallen. Bedankt dat jullie er altijd voor me zijn als ik dat nodig heb!

Lieske, het was vanaf het begin al duidelijk dat jij mijn paranimf zou zijn. Ook al woon je nu niet meer om de hoek, je bent me blijven steunen vanaf een afstand. Ik vind het super fijn om je aan mijn zijde te hebben en hoop dat dit nog lang zo zal zijn.

Erwin, jij hebt het hele proces van dichtbij meegemaakt. Als ik het een keer niet meer overzag zorgde jij er voor dat ik dingen weer op een rijtje kon zetten. Je was er voor me als ik een presentatie wilde oefenen of als ik gewoon een luisterend oor nodig had. Bedankt voor je steun, liefde en de rust die je me brengt. Ik ben ontzettend blij dat je ook tijdens mijn verdediging naast me zal staan.

Curriculum Vitae

Daphne Geerse (June 15th, 1990) was born in Haarlem, the Netherlands. In 2008, she completed her pre-university education (Schoter Scholengemeenschap, Haarlem) and started her study Human Movement Sciences at the Vrije Universiteit (VU) Amsterdam. She obtained her Bachelor's degree in 2011 and decided to continue her education at the VU Amsterdam with the Research Master Fundamental and Clinical Human Movement Sciences, from which she graduated cum laude in 2014. During her Master Research Internship, she examined the validity of the Kinect v1 sensor as motion registration system and explored the potential of the Interactive Walkway for an assessment of walking adaptability in stroke patients at Rehabilitation center Reade in Amsterdam. After this, she could continue working on the Interactive Walkway during her PhD project under the supervision of prof. dr. J.J. van Hilten and dr. J. Marinus (department of Neurology, Leiden University Medical Center [LUMC]) and dr. M. Roerdink (department of Human Movement Sciences, VU Amsterdam), which resulted in this thesis. Her PhD project was part of the NWO-funded research program Technology in Motion; a collaboration between the LUMC, VU Amsterdam and Delft University of Technology. The goal of this program was to develop low-cost, unobtrusive and objective assessments of motor performance in stroke and Parkinson's disease patients. Daphne focused on the Interactive Walkway as a novel assessment tool for walking and walking adaptability. During her PhD project, Daphne has supervised master students, assisted in courses, published in international peer-reviewed journals and presented her work at multiple international congresses. Her expertise and main research interest is on quantitative assessments of walking using new technologies. She is currently working as a post-doctoral researcher on Project HoloCue, a continued collaboration between the VU Amsterdam and LUMC funded by the Michael J. Fox Foundation, to examine the potential of the HoloLens for alleviating freezing of gait in Parkinson's disease patients.

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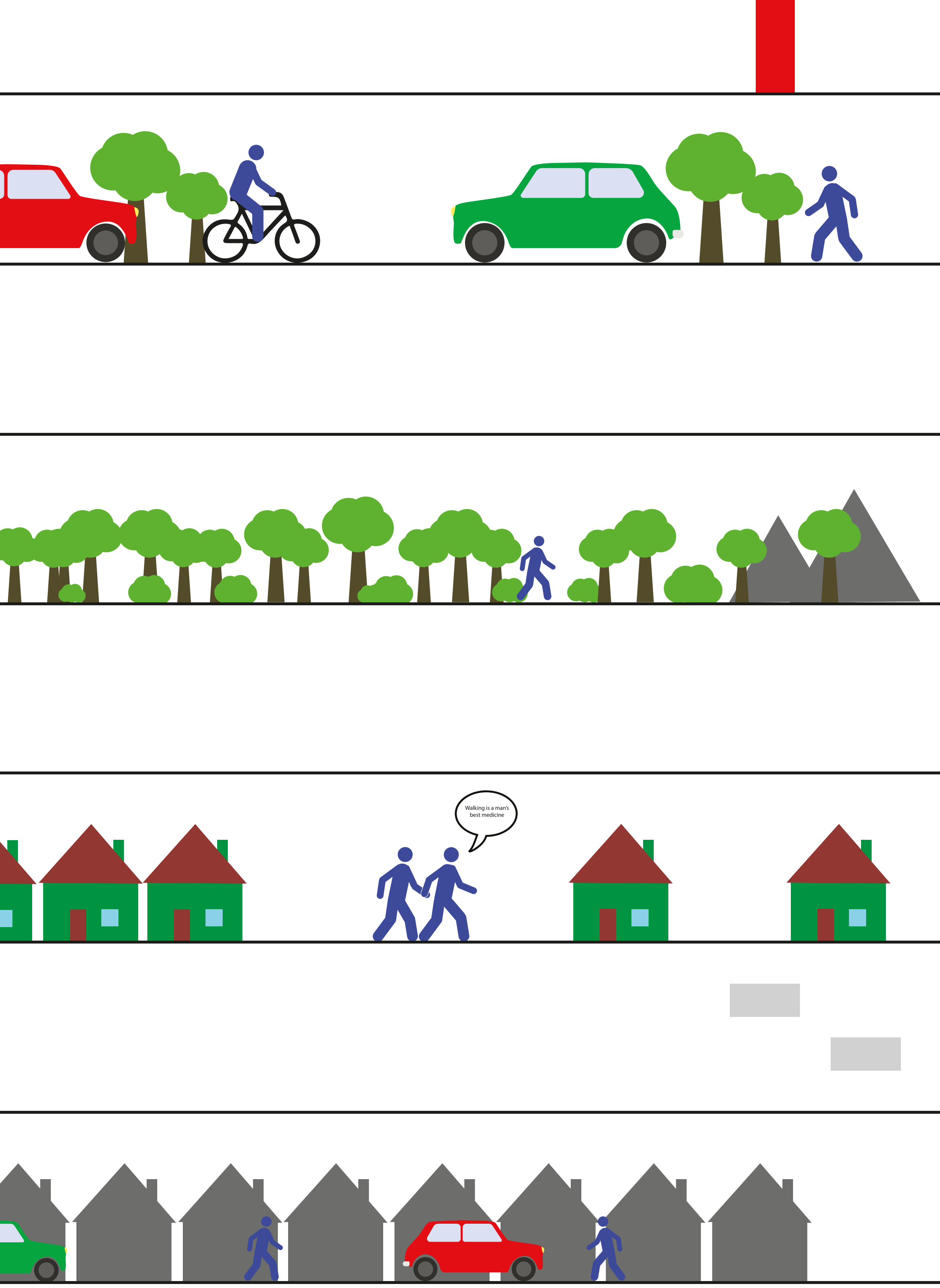
Walking is a man’s best medicine