Impaired standing balance:
Unraveling the underlying cause in elderly

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Contents

Part IV: General discussion and summary

Part V: Appendices

Chapter 1

General introduction

Falls are one of the leading causes of morbidity and mortality in the elderly [1]. One in three elderly aged above 65 years old falls at least once a year and one in ten elderly even falls twice or more per year [2]. Ten percent of falls among community-dwelling elderly result in serious injuries, like hip fractures (1-2%), other fractures (3-5%) and head injuries (5%), which have a major impact on the independence of elderly. These falls can also result in death [3]; two-third of accidental deaths are due to falls [4]. The risk on falling increases with age [5]. Together with the increasing population of elderly and the increased average life expectancy, this will result in an increase of the burden on the health care system causing high economic costs [6].

To prevent falls, we have to start by detecting the underlying cause of falling. One of the main causes and risk factors of falls is impaired standing balance [7], which is a common problem in the elderly [8;9]. Besides an increased risk of falling, impaired balance associates with mobility limitations and reduced quality of life [10;11]. To apply target interventions to improve standing balance, it is important to know the underlying and primary cause. However, several underlying systems are involved in standing balance, i.e. the muscles, the neural system, the cardiovascular system and the sensory systems (vision, proprioception and vestibular system) interacting with each other in a closed loop to maintain standing balance, resulting in an interrelation between cause and effect. These underlying systems deteriorate with age, diseases and medication use [12-15] and can correct for each other's deterioration by using compensation strategies. This makes it difficult to distinguish cause and effect and therefore to detect the underlying cause of impaired standing balance.

Current clinical balance tests, such as the Short Physical Performance Battery and Berg Balance Scale [16;17], assess the ability to maintain standing balance during a specific time period and task, e.g. eyes open or closed and/or a specific foot position. Other tests, like the Sensory Organization Test, assess the amount of sway by measuring Center of Pressure (CoP) movement and/or Center of Mass (CoM) movement during a specific time period, task and/or disturbance of the underlying sensory systems [18-20] indicating the quality of standing balance. Current balance tests lack in the identification of cause-and-effect relations, primary deterioration and compensation strategies, and primarily the quality of the underlying systems. This means that using current balance tests no specific diagnosis can be given and therefore it is difficult to apply targeted interventions to improve standing balance.

To overcome aforementioned drawbacks, a new engineering approach is required to assess standing balance [21-23]. In this approach the interrelation of cause and effect is taken into account by applying unpredictable, well-known disturbances of the underlying systems, e.g. movement of a visual scene or movement of the underground, during standing balance, which ‘open’ the closed loop. The relation between the disturbances and the reaction of the human body, represented by the body sway and ground reaction forces and moments, are identified by system identification techniques. Physiological meaning is given to the found relation using a model of the balance system, describing the underlying systems involved in standing balance. Therefore, this method gives insight in the underlying systems and their contribution to maintain standing balance, which will allow for early failure detection and will give opportunities for targeted interventions and disease management.

Aim and outline of this thesis

The aim of this thesis is to investigate the role of underlying systems in impaired standing balance in a heterogeneous population of community-dwelling elderly referred to a geriatric outpatient clinic, to assess the implementation of current balance tests in clinical practice and to validate a new engineering approach for early and differential diagnosis of impaired balance in elderly.

In *Chapter 2* we outlined the clinical need for a new engineering approach to assess standing balance and to detect the underlying deteriorations in standing balance. In part I, we investigated the association between several underlying systems and standing balance in a population of elderly outpatients, a heterogeneous population with several underlying causes of impaired balance. In *Chapter 3*, we investigated the association of muscle characteristics, in *Chapter 4* of cognitive status and in *Chapter 5* of blood pressure with standing balance.

Part II outlined the use of current balance tests in clinical practice. In *Chapter 6*, it is investigated whether CoP movement can be used to detect age-related differences in standing balance. In *Chapter 7*, the associations between several measures of impaired standing balance, i.e. ability to maintain standing balance, CoP movement, self-reported impaired standing balance and self-reported history of falls, are investigated in elderly outpatients resulting in a recommendation for their use in geriatric care.

In part III, we introduced system identification techniques to detect the underlying cause of impaired balance at an early stage. *Chapter 8* shows the possibilities to identify the use of proprioceptive information of the left and right leg independently in healthy young adults. In *Chapter 9* we studied if it is possible to detect differences in the use of proprioceptive information with age and specific diseases by system identification techniques. In *Chapter 10* a custom-made device, the Balance test Room (BalRoom), is introduced to apply well-known disturbances during standing balance giving the possibility to unravel the contribution of the sensory systems and the inter segmental coupling between the ankle and hip joint in standing balance. This chapter reports the reliability of the measures obtained with the BalRoom and system identification techniques to assess standing balance in healthy old adults.

In *Chapter 11* the key findings of this thesis are summarized with a reflection, and recommendations are provided to implement system identification techniques for diagnosis of impaired standing balance in clinical practice and for future research.

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Chapter 2

Impaired standing balance:

the clinical need for closing the loop

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Abstract

Impaired balance may limit mobility and daily activities, and plays a key role in the elderly falling. Maintaining balance requires a concerted action of the sensory, nervous and motor systems, whereby cause and effect mutually affect each other within a closed loop. Aforementioned systems and their connecting pathways are prone to chronological age and disease-related deterioration. System redundancy allows for compensation strategies, e.g. sensory reweighting, to maintain standing balance in spite of the deterioration of underlying systems. Once those strategies fail, impaired balance and possible falls may occur.

Targeted interventions to prevent falling require knowledge of the quality of the underlying systems and the compensation strategies used. As current clinical balance tests only measure the ability to maintain standing balance and cannot distinguish between cause and effect in a closed loop, there is a clear clinical need for new techniques to assess standing balance. A way to disentangle cause-and-effect relations to identify primary defects and compensation strategies is based on the application of external disturbances and system identification techniques, applicable in clinical practice.

This paper outlines the multiple deteriorations of the underlying systems that may be involved in standing balance, which have to be detected early to prevent impaired standing balance. An overview of clinically used balance tests shows that early detection of impaired standing balance and identification of causal mechanisms is difficult with current tests, thereby hindering development of well-timed and target-oriented interventions as described next. Finally, a new approach to assess standing balance and to detect the underlying deteriorations is proposed.

Introduction

Impaired standing balance, defined as having difficulties maintaining an upright position in daily life activities, is a common problem among the elderly [1;2] and has a significant impact on the health and quality of life [1]. Impaired standing balance plays a key role in falls [3] and is a strong risk factor for falls [4]; one third of elderly persons aged 65 or older falls at least once a year [5-9]. Ten percent of falls among community-dwelling elderly persons result in serious injuries, such as hip fractures (1-2%), other fractures (3-5%) or head injuries (5%) [10]. A quarter of the deaths in home situations are the result of falls [11]. Furthermore, falls are related to psychosocial factors such as fear of falling and social isolation [12;13]; the resulting restricted mobility may further deteriorate standing balance [12;14]. Therefore, falls have a profound socioeconomic impact [15]. To prevent falling targeted interventions improving standing balance are needed which require knowledge of the underlying cause of impaired standing balance at an early stage.

The ability to maintain balance requires appropriate interaction of several key systems, i.e. the motor (muscles), nervous and sensory systems, connected via efferent and afferent signal pathways resulting in a closed loop in which cause and effect are interrelated. Aforementioned systems deteriorate with advanced age [16-18] and as a result of specific diseases and medication use [19]. System redundancy allows for compensation strategies to maintain balance and so it is only when those strategies fail, e.g. in cases of severe system deterioration, multiple system deterioration and/or environmental disturbances exceeding system resilience, that impaired balance and finally falling may occur. Impaired balance may thus go unnoticed until an advanced stage.

Current clinical balance tests, such as the Berg Balance Scale (BSS) and the Short Physical Performance Battery (SPPB), include an assessment of the ability to maintain standing balance during challenging standing conditions [20;21] by narrowing the base of support or closing the eyes. However, identification of cause-and-effect relations, primary deterioration and compensation strategies, and ultimately the quality of the underlying systems requires new technical approaches such as closed loop system identification techniques. This allows for early failure detection, so that there are no missed opportunities for targeted interventions and disease management.

The present paper outlines the clinical need for proper balance assessment, describes the available balance tests and proceeds to describe promising control engineering-based solutions and their applicability for clinical practice.

Deterioration of standing balance

Advanced age in combination with (multi) morbidity and the use of medication will result in a variety of deterioration patterns in the underlying systems involved in maintaining standing balance, which subsequently results in a widely heterogeneous pathophysiology of impaired standing balance among the elderly [16]. Changes in the sensory systems lead to conflicting and inaccurate sensory information about body position. Motor system changes comprise low muscle mass and strength, preventing correction for balance deviations in a proper and efficient way. Changes in the nervous system result in abnormal scaling and timing of corrective responses to internal disturbances, which include sensor and motor noise due to deterioration of the underlying systems, and external disturbances, which are caused by the environment, for example a slip or a push [16]. Due to system redundancy it is possible to compensate for those changes by selecting proper strategies to maintain balance.

Deterioration of the sensory systems

With advanced age, sensory systems deteriorate. Impaired proprioception is apparent from reduced vibration sense by the cutaneous receptors [22] or reduced joint position sense by the muscle spindles and the golgi tendon organs [23], due to axonal degeneration and decrease in the number and density of nerve fibers [22]. Reduced joint position sense can also be due to degenerating chrondrocytes in the cartilage surface of joints caused by degenerative joint disease [24]. Age-related diseases, such as diabetes, also result in impaired proprioception [25]. Visual impairment at an advanced age comprises a decline in visual acuity, contrast sensitivity, glare sensitivity, dark adaptation, accommodation and depth perception [16;17]. Cataract and macular degeneration mainly affect central vision, whereas chronic glaucoma reduce peripheral vision [26]. Vestibular impairment at an advanced age results from a reduced number of vestibular hair cells, Scarpa’s ganglion cells and nerve fibers [16;17;27;28]. Nerve conduction speed in afferent and efferent pathways slows down due to a decrease in the number of neurons, loss of myelination and other neural changes [17;27].

Deterioration of the motor system

With advanced age, muscle mass decreases, which can result in low muscle mass, i.e. sarcopenia [29]. Furthermore, muscle strength, the rate of force production and muscle power declines with age [30;31] due to age-related alterations in muscle architecture [32], muscle control [33;34], activation dynamics [35-37] and muscle fiber typing [38]. Tendon stiffness decreases with age due to an increase of non-reducible collagen cross-linking, a reduction in collagen fibril crimp angle, an increase in elastin content, a reduction of extracellular water content and an increase in type tube V collagen. This results in a lower velocity of shortening and a change in the length-tension relation, which causes a reduction of force production [39]. In addition, with age the tendon becomes thicker, hypoechogenic and more likely to tear [40]. Orthopedic pathologies (e.g. arthritis) can lead to restricted mobility; arthritis correlates with a decrease in range of motion in joints [41;42].

Deterioration of the nervous system

The sensory and motor system are linked by the nervous system. The nervous system has the adaptive capacity to compensate for the deterioration of the sensor and motor systems by selecting a compensation strategy to maintain balance. However, this capacity deteriorates with age and disease [16]. In the elderly, deficits in stimulus encoding, central processing and response initiation result in diminished transmission speed and a lower accuracy of sensory information and delayed muscle activation [16]. Impaired blood pressure regulation, as demonstrated by hypertension and orthostatic hypotension, could result in a decrease of cerebral blood flow [43;44] and therefore increase the risk of hypoperfusion of the brain, resulting in brain damage and impaired neural control. As with age cognitive control seems to become of increasing importance for standing balance [45;46], balance will also be negatively influenced by deteriorating cognitive function [47-49].

Compensation strategies to maintain standing balance

System deterioration may induce the selection of alternative compensation strategies. First, sensory reweighting implies that the nervous system will rely on more accurate as compared to less accurate and conflicting sensory information. The elderly are less capable of reweighting sensory information than young people [50;51]. Furthermore, in balance control the elderly rely more on visual information than do the young [52]. As a consequence, the elderly are less able to compensate in situations where visual information is disturbed or excluded by the environment. Second, the elderly rely more heavily on the hip strategy, i.e.

movement around the hip joint, to maintain standing balance compared to the young who rely more on the ankle strategy, i.e. pivot around the ankle joint during normal stance [53]. In response to more challenging conditions, e.g. altered sensory conditions in which vestibular or proprioceptive information is reduced, the young will change their balance strategy by relying more on the hip strategy [54]. As elderly already rely more heavily on the hip strategy, they are less able to adapt to environmental changes. Third, co-contraction is a commonly used strategy in the elderly when other compensation strategies cannot be used efficiently [55]. Co-contraction is energy-demanding and makes the body stiffer, reducing the range of motion. As a consequence, resilience to larger disturbances is reduced and stepping out strategies may be required to prevent falling [56]. Fourth, deterioration of underlying systems increases the attentional demands to maintain standing balance [57]. When attentional resources are limited, this could result in impaired standing balance or falls; if two tasks are performed simultaneously and they require more attentional demands than the total capacity, the performance on either or both tasks deteriorates depending on the difficulty of the tasks. One can compensate for the shortcoming of attention by task prioritization; one task is prioritized over another task to complete the most important task successfully [58;59].

Current standing balance assessment

Clinical balance tests

Clinical balance tests are developed to assess physical performance, such as the Tinetti Balance Test [60], the Functional Reach Test [61], the Berg Balance Scale (BBS) [62], the Clinical balance test of Sensory Interaction and Balance (CTSIB) [63], the Short Physical Performance Battery (SPPB) [64], the Balance Error Scoring System (BESS) [65], the Star Excursion Balance Test (SEBT) [66] and the Romberg's test [67]. As daily activities require balance and balance is hard to detect during these activities, in those tests the ability to maintain balance is dichotomously assessed and scored in specific standing and/or dynamic balance conditions, possibly combined with walking.

Clinical balance tests are practical in use because of their low cost, simple equipment and time efficiency. Furthermore, the tests have a good inter-rater and intra-rater reliability [20;21;68-71]. Due to the dichotomous assessment of the ability to maintain standing balance, clinical balance tests only detect impaired balance when compensation strategies fail [68;72]. Often, active people can maintain standing balance without any problem despite severe system deterioration due to an efficient compensation by selection of proper strategies [72].

This may hamper the use of clinical balance tests in active elderly people or at an early stage of deterioration (i.e. ceiling effect). In addition, clinical balance tests do not provide information about the underlying systems involved in maintaining standing balance and the compensation strategies used. Therefore, the underlying cause of impaired standing balance cannot be detected.

Posturography

Posturography is an alternative method to assess standing balance using a continuous scale [73]. Static posturography comprises assessment of the Center of Mass (CoM) and/or Center of Pressure (CoP) movement during an unperturbed stance. CoM movement represents movement of the body, while CoP movement is a reflection of balance control to keep CoM within the base of support [74]. CoM and CoP movement are interrelated but reflect different aspects of balance control, which shows the necessity to measure both entities simultaneously. CoM movement can be measured using inertial sensors [54;75-77] or position tracking systems [78;79], which measure body segment displacement with respect to a local or global coordinate system. CoP movement can be measured using force plates [80-82] or in-shoe pressure assessment devices [83;84] which measure ground reaction forces. Inertial sensors and in-shoe pressure assessment devices are less expensive and can be used outside the laboratory. Deterioration detection of a specific sensory system can be facilitated by manipulation of standing conditions, i.e. several foot positions (changes in base of support), with eyes open or eyes closed (elimination of vision), or on a firm or compliant surface (disturbance of proprioception) [73]. The Sensory Orientation Test (SOT) uses six sensory conditions in which the information of three main sensory systems is alternately eliminated or disturbed. Ratios between conditions give more insight into the quality of the underlying sensory systems [85]. In contrast to static posturography, dynamic posturography comprises CoM or CoP movement assessment during external disturbances applied by platform movement or disturbances applied to upper body parts.

Posturography is easily applicable, but a major disadvantage is the high intrasubject variability preventing individual assessment of standing balance [73]. A main source of variability is the use of different compensation strategies depending on age, disease and test condition [86-88]. The reliability depends on the population of interest, time of measurement and number of trials. To reach a good reliability, it is recommended to measure CoP and/or CoM movement more than once and during a time period of 90 seconds [88;89], which is less feasible in clinical practice and in an elderly population. The results of posturography are also inherently difficult to interpret. Increased CoP or CoM movement is generally assumed to reflect a deterioration of balance control; this may however not be the case [90-92]. As the underlying systems are interrelated, selection of another compensation strategy could induce either increased or diminished CoP and/or CoM movement, in fact reflecting optimal balance control. Furthermore, changes in CoM and/or CoP movement can be multicausal, i.e. caused by deterioration of several underlying systems. In addition, CoP and/or CoM movement are influenced by training, such as ballet training. Ballet dancers show a better stability compared with untrained controls [93;94], but have an increased CoP and/or CoM movement in specific sensory conditions compared with untrained controls due to different use of sensory information [95;96]. As a result, posturography cannot distinguish between the various underlying systems and the compensation strategies used and it therefore fails to reveal the details of the underlying pathophysiology of impaired standing balance [92].

Interventions to improve standing balance

Individually targeted multifactorial intervention, including individual risk assessment, is shown to be the most effective with a significant and beneficial effect on the rate of falling [97]. However, due to the lack of clinical tests that can make a distinction between underlying causes of impaired standing balance, nowadays general fall prevention interventions are used, comprising exercising, environmental modification, medication optimization, education, or a combination. To reduce the risk of falling, exercising seems to be the best to use in the elderly [97-99]. Exercising, either balance, resistance or cognitive-motor training [100;101] could also be prescribed to improve standing balance in the elderly in particular [102].

For traditional balance training there are hardly any scientific guidelines regarding contents, optimal duration and intensity. The American College of Sports Medicine (ACSM) recommends exercises that include 1) standing conditions with increasing difficulty caused by gradually reducing the base of support (e.g. semi-tandem stance, tandem stance, one-leg stance); 2) dynamic movements that disturb the CoM (e.g. tandem walk, circle turns); 3) stressing muscle groups involved in standing balance (e.g. heel stands, toe stands); and 4) reducing sensory input (e.g. standing with eyes closed) [103]. Perturbation-based balance training concentrates on compensation strategies to recover from unexpected disturbances using exercises matching real life conditions [104]. Multitask balance training focuses on balance control during dual task activities, as instability increases when shared attention is needed [105]. Perturbation-based and multitask balance training are shown to be more effective than traditional balance training [106]. However, a drawback of all aforementioned training types is the lack of a clear dose-response relationship and the unknown effects on the underlying systems and the compensation strategies used [107].

Resistance training is used to improve the motor system, i.e. muscle function. It comprises strength training [108;109] and power training [110;111] to increase muscle strength and velocity of force production respectively. High intensity strength training appears to be more effective than low intensity training. However, the effect on standing balance is less clear [112]. Power training has been shown to be more effective in improving standing balance than strength training [113]. Low intensity power training seems to be better than high or medium intensity power training [114]. However, the most effective intensity of resistance training is still under debate.

Cognitive-motor training focuses on the attentional demands needed to perform standing balance conditions. Three types of cognitive or cognitive-motor trainings are proposed. First, cognitive rehabilitation intervention has as goal to maximize the cognitive functioning and/or to reduce the risk of cognitive decline, e.g. by mental imagery training on standing balance. Second, cognitive-motor interventions are interventions combining cognitive tasks with physical tasks, e.g. balancing with a current mental task like memorizing words. Third, computerized interventions use biofeedback or virtual reality to improve standing balance. In the first case, feedback is given on the balance task, e.g. by visual feedback about the CoP movement. In the second case, environments are created in which subjects interact with images and virtual objects in a virtual environment, such as computer games. Previous research showed that cognitive and cognitive-motor training are effective to improve standing balance. However, more research is needed to get more evidence on the effectiveness of cognitive or cognitive-motor training [101].

Despite the generally positive effect of balance training, resistance training and cognitive-motor training on standing balance, it remains unclear which intervention (i.e. content, duration and intensity) can best be prescribed to improve standing balance in any specific case. This requires identification of the underlying cause and primary deterioration in impaired standing balance and the proper compensation strategy to be trained to improve standing balance. This is not possible with the current clinical assessment tools, preventing goal directed and time efficient therapy.

A new method to identify the underlying cause of impaired standing balance

As with current clinical balance tests and posturography it is difficult to identify and to distinguish the primary deterioration of the various underlying systems and the used compensation strategies which are needed to prescribe targeted interventions, there is a clear clinical need for novel techniques to assess standing balance.

Balance control: a closed loop

The underlying systems involved in balance control interact within a closed loop (Figure 1). When the body is disturbed by internal and/or external disturbances, it has to react to these disturbances. Changes in body position are perceived by the three main sensory systems: central and peripheral [115;116] vision, proprioception and the vestibular system [117]. This sensory information is combined and integrated by the nervous system with a specific time delay. Subsequent motor system action in the form of corrective, stabilizing joint torques is generated. This changes body position, which is again perceived by the sensory systems. Thus, in daily life cause and effect are interrelated in a continuous process (Figure 1) within a closed loop [118].

Externally applied disturbances and closed loop system identification techniques

One way to "break open" the loop of balance control and disentangle cause-and-effect relations is to apply precise external disturbances and record how the system reacts. The relation between the disturbances and the response can be described in the frequency domain by a frequency response function (FRF); per applied disturbance frequency the amplitude ratio and time delay between input and output is described. FRFs can be compared between or within subjects to identify changes in the balance control across different disturbance conditions. An additional step is to translate those FRFs to parameters, which makes it possible to describe the underlying systems involved in balance control. The experimental FRFs are compared with a model of the balance control describing the underlying systems mathematically. Using optimization methods, the parameters are estimated, so that they will represent the experimental data the best. The estimated parameters give a physiological meaning to the FRFs [119].

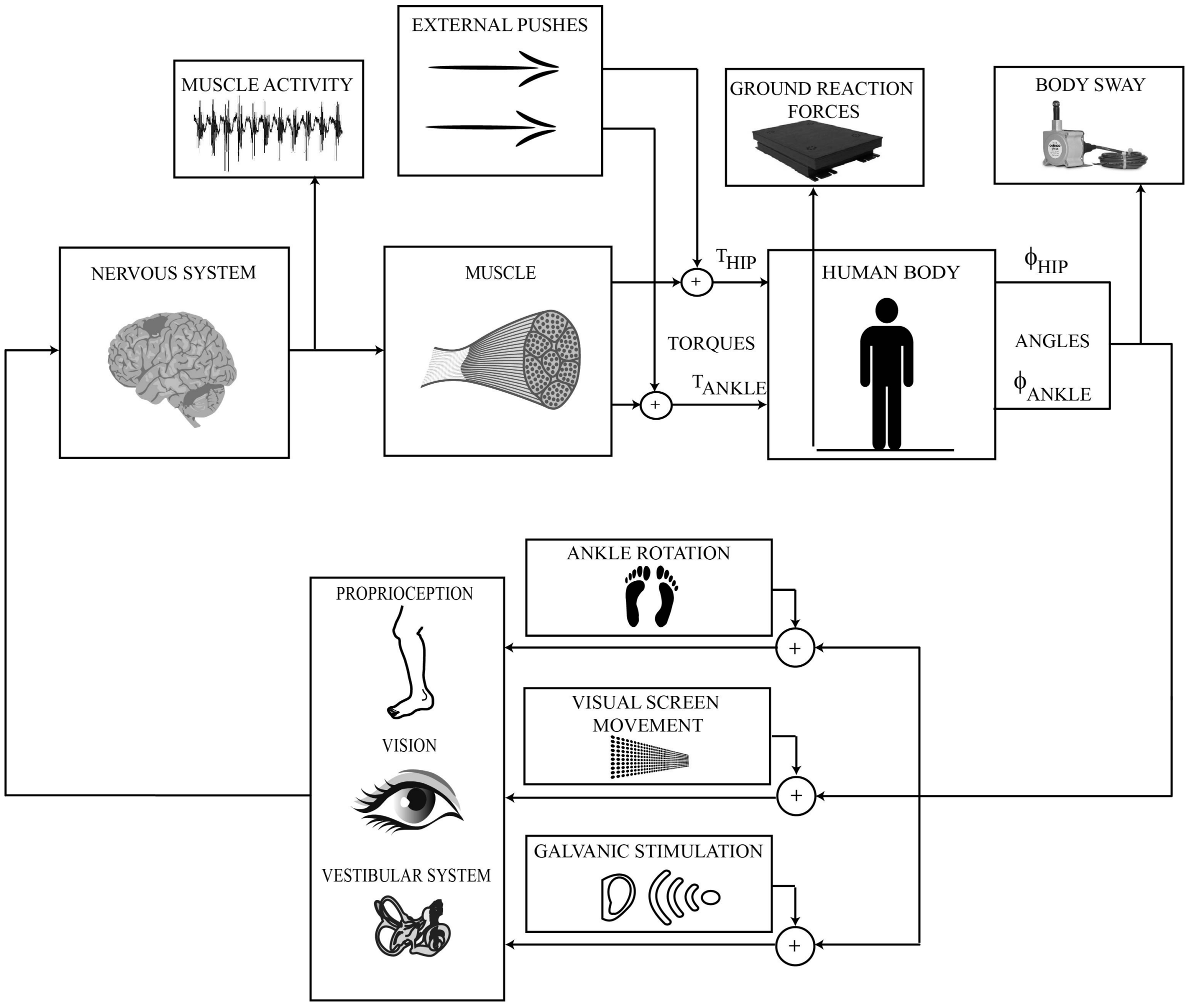

Figure 1. Balance control represented as a closed loop. The position of the human body is perceived by the sensory systems (i.e. proprioceptive, visual and vestibular system). The sensory information is sent to the central nervous system. Here, the information is combined and a command is sent to the muscles (i.e. the motor system), which will contract and change the body position. Using external disturbances the balance control can be disturbed at different places in the loop (e.g. by external pushes, ankle rotations, visual scene movement or galvanic stimulation) and the reaction to the disturbances can be established in different places by measuring muscle activity, ground reaction forces (i.e. Center of Pressure movement) and body sway (i.e. Center of Mass movement).

Identifying deterioration in the nervous system and changes in strategies requires mechanical disturbances. Measuring separately the generated activity of each leg (i.e. the CoP movement) and the CoM movement, makes it possible to identify the contribution of each leg to the stabilization of standing balance [120]. By applying mechanical disturbances at ankle and hip level, the inter-segmental stabilizing mechanisms which represent the contribution of the ankle and hip strategy to the control of standing balance can be identified. Furthermore, the movements of the two joints influence each other. This coupling between the joints can be expressed by relating the joint torques to the joint angles [121].

Quantifying the contribution of the sensory systems requires disturbances of a specific sensory system, e.g. visual scene movement disturbing vision or ankle rotations disturbing proprioception. The contribution of each sensory system in maintaining standing balance can subsequently be expressed by a weighting factor [122]. A distinction can be made in the contribution of the proprioceptive information of the left and the right leg to detect asymmetries [123]. Sensory reweighting strategies can be assessed by increasing sensory disturbance amplitudes [122] as this scales down the contribution of a sensory system, and thus lowers its weighting factor. The quality of the sensory systems can be determined by estimating the noise level [124].

Applying precise external disturbances makes it possible to identify the quality of each underlying system. Simultaneous disturbances of different sensory systems allow for assessment of sensory reweighting and together with mechanical disturbances aimed at different joints, hip and ankle strategies can be identified. The use of random multisine disturbances consisting of specific frequencies prevents anticipation and allows for assessment of the bandwidth of system quality. As the goal is to identify the balance control and not to identify the limits of the balance control, sub maximal amplitudes which can the participant withstand, are used to disturb the system.

Clinical relevance

The use of externally applied disturbances and closed loop system identification techniques makes it possible to detect a deterioration in the underlying systems and the compensation strategies used by elderly persons with impaired standing balance. Using this knowledge a physician can diagnose the underlying and primary cause of impaired standing balance, which makes it possible to prescribe targeted interventions. This method may also be applicable to detect deterioration of balance control at an early stage in elderly persons without impaired standing balance, i.e. who do not show deterioration of balance control using current clinical balance tests. Furthermore, the described method is time and cost effective since it allows for simultaneous application of several external disturbances with different frequency contents. The external disturbances are sub maximal, which makes the method safe for the patient. However, before this method can be clinically applied, further research has to investigate sensitivity and specificity of the method to identify impaired standing balance and risk of falling in the population of interest. As such, prototypes are currently implemented and evaluated in clinical practice.

Conclusion

There is a clinical need for new techniques to assess standing balance that can detect the underlying cause and primary deterioration in impaired standing balance at an early stage. Externally applied disturbances in combination with closed loop system identification techniques may fill the void, which makes it possible to intervene in impaired standing balance, at an early stage, with targeted interventions.

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Part I

The role of underlying systems in standing balance


balance
disturbances
compensation
control
deterioration
impaired
sensory
strategies
stepping
training
used
systems
movement
assessment
information
elderly
cognitive
underlying
proprioception
interventions
clinical
nervous
identification
possible
tests
increase
motor
joint
reduced
measure
combined
different
techniques
activities
age
result
external
effect
loop
needed
task
quality
specific
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force
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changes
improve
preventing
identify
decrease
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simultaneous
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sensitivity
amplitudes
difficulty
processing
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technique
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optimization
contraction
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ability
decline
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allows
subsequently
position
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elimination
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Chapter 3

Muscle strength rather than muscle mass is associated with standing balance in elderly outpatients

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Abstract

Assessment of the association of muscle characteristics with standing balance is of special interest as muscles are a target for potential intervention, i.e. by strength training.

This cross-sectional study included 197 community-dwelling elderly outpatients (78 males, 119 females, mean age 82 years) referred to a geriatric outpatient clinic. Muscle characteristics included handgrip and knee extension strength, appendicular lean mass divided by height squared (ALM/height^2), and lean mass as percentage of body mass. Two aspects of standing balance were assessed: the ability to maintain balance and the quality of balance measured by Center of Pressure (CoP) movement during ten seconds of side-by-side, semi-tandem and tandem stance, with both eyes open and eyes closed. Logistic and linear regression models were adjusted for age, and additionally for height, body mass, cognitive function and multimorbidity.

Handgrip and knee extension strength, adjusted for age, were positively related to the ability to maintain balance with eyes open in side-by-side ($p=0.011$; $p=0.043$), semi-tandem ($p=0.005$; $p=0.021$) and tandem stance ($p=0.012$; $p=0.014$), and with eyes closed in side-by-side ($p=0.004$; $p=0.004$) and semi-tandem stance (not significant; $p=0.046$). Additional adjustments affected the results only slightly. ALM/height^2 and lean mass percentage were not associated with the ability to maintain standing balance, except for an association between ALM/height^2 and tandem stance with eyes open ($p=0.033$) that disappeared after additional adjustments. Muscle characteristics were not associated with CoP movement.

Muscle strength rather than muscle mass was positively associated with the ability to maintain standing balance in elderly outpatients. Assessment of CoP movement was not of additional value.

Introduction

Among 37 million elderly aged over 65 years, 7 million reported impaired standing balance in the past 12 months in the National Health Interview Survey in 2008 [1]. Standing balance is dependent on integrated functioning of the sensory systems (vestibular, visual, and proprioceptive system), neural control, and muscle characteristics. These systems degenerate with increasing chronological age, by cumulative tissue damage, specific diseases and medication use [2-6]. Muscle characteristics are of special interest, as recent evidence suggests that strength training can improve muscle strength and muscle mass, even in elderly [7-9]. To develop targeted interventions for impaired standing balance in elderly outpatients, it is important to understand the contribution of muscle strength and muscle mass to standing balance.

In healthy elderly it was shown that muscle strength is associated with the ability to maintain standing balance [10;11]. Quadriceps muscle mass has also been associated with the ability to maintain standing balance in healthy elderly [12]. Besides the ability to maintain standing balance, the quality of balance can be assessed additionally by measuring the Center of Pressure (CoP) movement. In healthy elderly, muscle mass [12;13] but not muscle strength has been associated with CoP movement [14-16].

It remains unknown if associations between muscle characteristics and standing balance are present in elderly outpatients, while this group is obviously of clinical interest. These outpatients are more likely to suffer from multimorbidity and deterioration in more than one system involved in standing balance [11;17;18]. Only few studies describe the association between muscle characteristics and standing balance in elderly with mobility difficulties, often applying exclusion criteria for co-morbidity or severe mobility limitations [19;20]. We assessed the association between muscle characteristics and two aspects of standing balance, the ability to maintain balance as well as the CoP movement, in community-dwelling elderly referred to a geriatric outpatient clinic.

Methods

Setting

This cross-sectional study included 207 community-dwelling elderly who were referred to a geriatric outpatient clinic in a middle-sized teaching hospital (Bronovo Hospital, The Hague, Netherlands) for a comprehensive geriatric assessment (CGA) between March 2011 and

January 2012. CGA was performed during a two hour visit including questionnaires and physical and cognitive measurements. All tests were performed by trained nurses or medical staff. Medical charts were retrospectively evaluated. The study was reviewed and approved by the institutional review board of the Leiden University Medical Center (Leiden, the Netherlands). Because this research is based on regular patient care, the need for individual informed consent was waived. In the present analyses, 10 elderly outpatients (4.8%) were excluded due to missing data on standing balance, leaving 197 outpatients for analyses.

Elderly outpatient characteristics

Questionnaires included information on marital status, current smoking, alcohol use and living arrangements. Anthropometric data included assessment of body mass, height and body mass index. Information on diseases and use of medication was extracted from medical records. Multimorbidity was rated as the presence of two or more diseases, including chronic obstructive pulmonary disease, heart failure, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson's disease, (osteo)arthritis, transient ischemic attack and stroke. The Hospital Anxiety and Depression scale (HADS) was used to detect depressive symptoms [21]. A score higher than 8 out of 21 points indicated depressive symptoms. Global cognitive function was assessed using the Mini Mental State Examination (MMSE) [22]. Physical functioning was self-reported in a questionnaire with questions on experienced falls during the last 12 months, walking difficulties, impaired standing balance and use of walking aids. Physical functioning was assessed with a 10 meter walking test at usual pace in steady state, and with the short physical performance battery (SPPB) [23]. The SPPB comprises the ability to maintain balance in three different standing positions with eyes open, a timed four meter walk, and a timed sit-to-stand test.

Standing balance

The ability to maintain standing balance

The ability to maintain standing balance was tested in different standing conditions. Elderly outpatients, wearing non slip socks, were instructed to maintain balance for 10 seconds in each standing condition. Three different standing positions characterized by a progressive narrowing of the base of support were performed both with eyes open and eyes closed. During side-by-side stance, elderly outpatients were instructed to stand with the medial malleoli as close together as possible; during semi-tandem stance, elderly outpatients were standing with the medial side of the heel of one foot touching the big toe of the other foot; during tandem stance, elderly outpatients were standing with both feet in line while the heel of one foot touched the toes of the other. Standing positions were first assessed with eyes open as part of the SPPB [23]. Subsequently, all standing positions were repeated with eyes closed. The elderly outpatients were allowed three trials if standing balance was lost prematurely. When the elderly outpatients could not complete a standing position, consecutive positions were not performed. Six elderly outpatients did not attempt the standing positions with eyes closed due to lack of time or lack of motivation, leaving 191 outpatients for analyses of standing balance conditions with eyes closed.

Center of Pressure movement

All standing conditions were performed on a triangular six degrees of freedom force plate (Forcelink B.V., Culemborg, The Netherlands) to measure CoP movement. Only successful trials, i.e. completion of 10 seconds of maintaining balance without stepping out in case of loss of balance, were considered for further analyses (i.e. n=183 were able to maintain balance in side-by-side stance). Because of missing data due to technical problems (n=18) and unknown reasons (n=29), CoP movement was available in 136 elderly outpatients (in side-by-side stance eyes open). Time series of CoP movement in medio-lateral and anterior-posterior direction were used to calculate single CoP parameters [24]. Direction specific CoP composite scores were calculated from standardized single CoP parameters (mean amplitude, amplitude variability, mean velocity, velocity variability and range), in anterior-posterior (AP) and medial-lateral (ML) direction [25]. As age related differences in CoP movement are most pronounced in ML direction [25], analyses are shown in ML direction. Analyses in AP direction are given in supplementary tables.

Muscle characteristics

Muscle strength

Handgrip strength was measured using an isometric hand dynamometer (JAMAR hand dynamometer, Sammons Preston, Inc., Bolingbrook, IL, USA). Outpatients were instructed to maintain an upright standing position with their arms along the side, while holding the dynamometer in one hand. The width of the dynamometer’s handle was adjusted to hand size such that the middle phalanx rested on the inner handle. Three trials were performed alternately for each hand. Outpatients were actively encouraged to squeeze with maximal strength. The best performance of all trials was used for analyses.

Isometric knee extension strength was measured in a seated position with hips and knees in 90 degrees by a force transducer mounted in a chair (Forcelink B.V., Culemborg, The Netherlands). Outpatients were asked to push with maximal effort against a cuff positioned just above the talocrural joint. Holding on to the armrest of the chair or leaning backward was allowed, but not rising from the seating. This was checked by the investigator and corrected if necessary. Three trials were performed for each leg. The best performance of all trials was used for analyses. Structural measurement of knee extension strength was added to the CGA in May 2011.

Muscle mass

Body composition was measured using a direct segmental multi-frequency bioelectrical impedance analysis (BIA, InBody 720, Biospace Co., Ltd, Seoul, Korea). This technique has been shown to be a valid tool for the assessment of whole body composition and segmental lean measurements [26]. The elderly outpatients wore normal indoor clothing and were instructed to stand barefoot on the machine platform holding a sensor in each hand. Two formulas were used to represent muscle mass. ALM/height^2 was calculated as the sum of lean mass in all four limbs (appendicular lean mass (ALM)) divided by the height squared [4]. Lean mass percentage was calculated as total lean mass as percentage of total body mass [27].

In case of inability to stand on the machine platform without assistance for two minutes (n=5), wearing compressive stockings (n=22), having a pacemaker (n=15), or unknown reasons (n=14), BIA was not assessed. After exclusion of data due to technical problems (n=9) valid BIA data were available in 132 elderly outpatients.

Statistical analyses

Continuous variables with Gaussian distribution are presented as mean and standard deviation, otherwise as median and interquartile range or number and percentage. All muscle characteristics were standardized into sex-specific z-scores. The association between standardized muscle characteristics and the ability to maintain standing balance was analyzed using logistic regression with adjustment for age. Additional adjustment models included body mass, height, MMSE score and multimorbidity. The association between muscle characteristics and CoP movement was studied using linear regression with the same adjustment models. Statistical analyses were performed using SPSS for Windows (SPSS Inc, Chicago, USA), version 20. P values <0.05 were considered statistically significant.

Results

Elderly outpatient characteristics

The characteristics of elderly outpatients are presented in Table 1. Mean age was 81.9 years. 64.5 Percent of the elderly outpatients had at least one fall incident in the 12 months prior to the visit to the outpatient clinic.

Standing balance

Ability to maintain standing balance

The percentage of elderly outpatients able to maintain balance in different standing conditions is shown in Figure 1. In more difficult standing conditions, less elderly outpatients were able to maintain standing balance. In the standing positions with eyes open 183 elderly outpatients (92.9%) were able to maintain side-by-side stance, 164 (83.2%) semi-tandem stance and 66 (33.5%) tandem stance. In standing positions with eyes closed 152 elderly outpatients (79.6%) were able to maintain side-by-side stance, 90 (47.1%) semi-tandem stance and 4 (2.1%) tandem stance.

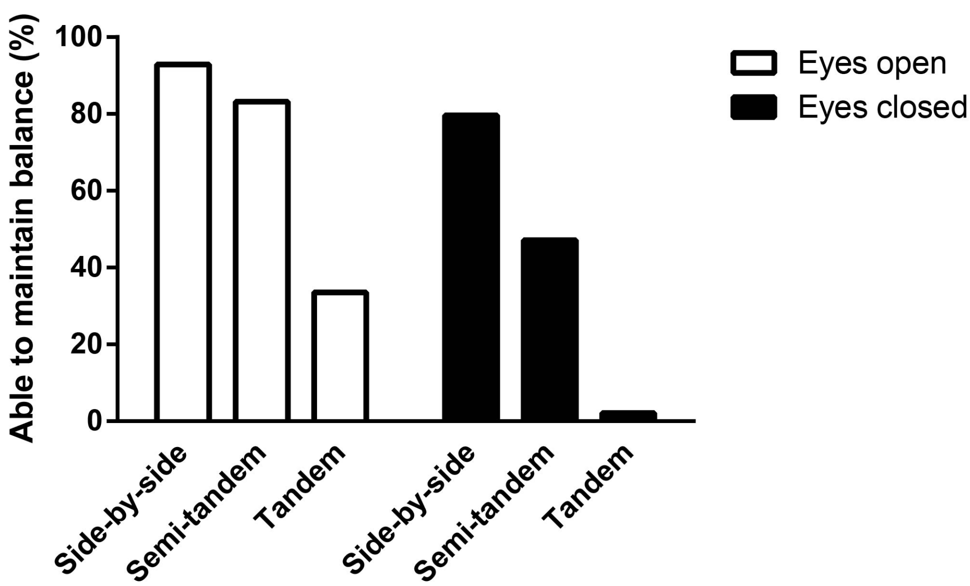

Figure 1. Percentage of elderly outpatients able to maintain balance in the different standing positions with eyes open and eyes closed.

Center of Pressure movement

Supplementary Table 1 shows the CoP movement represented by different CoP parameters used for calculating composite scores in anterior-posterior (AP) and medio-lateral (ML) direction. CoP parameters were higher in more difficult standing conditions.

Table 1. Elderly outpatient characteristics.

	All (n=197)	Male (n=78)	Female (n=119)
Socio-demographics			
Age, years	81.9 (7.1)	80.7 (6.8)	82.7 (7.2)
Widowed, n (%) [a]	80 (41.5)	17 (21.8)	63 (54.8)
Living arrangements, n (%) [a]			
Institutionalized	0 (0)	0 (0.0)	0 (0.0)
Sheltered	40 (20.6)	13 (16.9)	27 (23.1)
Independent	154 (79.4)	64 (83.1)	90 (76.9)
Current smoking, n (%) [b]	22 (16.2)	9 (16.1)	13 (16.3)
Excessive alcohol use, n (%) [#]	8 (4.1)	5 (6.4)	3 (2.5)
Anthropometry			
Body mass, kg	71.8 (15.5)	78.7 (12.1)	67.3 (15.8)
Height, cm	167 (10)	176 (7)	161 (6)
BMI, kg/m^2	25.8 (4.5)	25.5 (3.6)	25.9 (5.0)
Health characteristics			
Multimorbidity, n (%) [c, †]	95 (50.3)	43 (55.1)	52 (46.8)
Number of medication, median (IQR) [c]	5 (3-7)	6 (3-7)	5 (2-7)
Depressive symptoms, n (%) [d, ‡]	28 (23.1)	17 (30.9)	11 (16.7)
MMSE, points; median (IQR)	27 (24-29)	27 (25-29)	27 (24-29)
Physical functioning			
Gait speed, m/s	0.87 (0.29)	0.93 (0.31)	0.83 (0.27)
SPPB, points; median (IQR)	7 (5-10)	8 (6-10)	7 (5-9)
Self-reported, n (%)			
Fall incident previous 12 months	127 (64.5)	45 (57.7)	82 (68.9)
Walking difficulties [a]	143 (73.0)	52 (66.7)	91 (77.1)
Use of walking aid [a]	108 (55.1)	33 (42.9)	75 (63.0)
Impaired standing balance [a]			
Never	34 (17.4)	10 (12.8)	24 (20.5)
Sometimes	73 (37.4)	33 (42.3)	40 (34.2)
Regularly	57 (29.2)	24 (30.8)	33 (28.2)
Always	31 (15.9)	11 (14.1)	20 (17.1)
Muscle characteristics			
Handgrip strength, kg	26.1 (8.2)	33.7 (6.2)	21.1 (4.9)
Knee extension strength, N [b]	202 (96)	261 (108)	162 (60)
ALM/height^2, kg/m^2 [b]	7.14 (1.20)	7.82 (0.84)	6.63 (1.19)
Lean mass percentage, % [b]	63.8 (8.9)	69.6 (6.6)	59.6 (7.9)

All parameters are presented as mean with standard deviation unless indicated otherwise. Data available in [a] n=195, [b] n=132, [c] n=189 and [d] n=121. [#] Defined as > 14 units per week for females or > 21 units per week for males. [†] Present in case of two or more diseases, including chronic obstructive pulmonary diseases, heart failure, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson's disease, (osteo)arthritis, transient ischemic attack and stroke. [‡] Present with a depression subscore of > 8 on the Hospital Anxiety and Depression Scale. Abbreviations: IQR, inter quartile range; MMSE, Mini Mental State Examination; SPPB, Short Physical Performance Battery; ALM, appendicular lean mass.

Muscle characteristics and standing balance

Muscle strength

The association between muscle strength and the ability to maintain balance in different standing conditions is displayed in Table 2. Elderly outpatients with a higher handgrip strength or knee extension strength were significantly more likely to be able to maintain standing balance for ten seconds in all standing conditions, except for handgrip strength and semi-tandem stance with eyes closed. Further adjustments for body mass, height, MMSE score, and multimorbidity, attenuated the associations, but overall significance remained.

Handgrip strength and knee extension strength were not associated with CoP movement in ML (Table 3) and in AP (supplementary Table 2) direction.

Muscle mass

Table 2 displays the association between muscle mass and the ability to maintain standing balance in different standing conditions. There was no association between ALM/height^2 or lean mass percentage and the ability to maintain standing balance, except for a positive association between ALM/height^2 and tandem stance with eyes open that disappeared in the fully adjusted model.

Both indices of muscle mass, ALM/height^2 as well as lean mass percentage, were not associated with the CoP movement in ML (Table 3) and in AP (supplementary Table 2) direction.

Discussion

Muscle strength is positively associated with the ability to maintain standing balance in community-dwelling elderly referred to a geriatric outpatient clinic. Muscle mass did not associate with the ability to maintain standing balance in most balance conditions, although a positive association was found between ALM/height^2 and tandem stance with eyes open. Muscle strength and muscle mass were not associated with quality of balance as measured with CoP movement. This is the first study that examines different muscle characteristics in association with the ability to maintain standing balance as well as CoP movement during standing balance in a population of elderly outpatients without any exclusion criteria.

Table 2. Association between muscle characteristics and ability to maintain balance in different standing positions with eyes open and eyes closed.

	Side-by-side			Semi-tandem			Tandem		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Eyes open									
Handgrip strength									
Model 1	2.81	1.27-6.21	**0.011**	1.98	1.23-3.18	**0.005**	1.58	1.11-2.26	**0.012**
Model 2	2.17	0.89-5.33	0.09	1.78	1.07-2.95	**0.026**	1.59	1.09-2.31	**0.016**
Model 3	2.16	0.85-5.45	0.11	1.69	1.01-2.81	**0.046**	1.47	1.00-2.16	**0.050**
Knee extension strength									
Model 1	3.87	1.04-14.36	**0.043**	2.11	1.12-3.99	**0.021**	1.67	1.11-2.51	**0.014**
Model 2	5.33	1.14-24.96	**0.034**	2.38	1.21-4.68	**0.012**	1.78	1.16-2.74	**0.008**
Model 3	5.34	1.04-27.33	**0.045**	2.11	1.06-4.23	**0.035**	1.76	1.11-2.78	**0.016**
ALM/height²									
Model 1				0.81	0.48-1.35	0.41	1.57	1.04-2.39	**0.033**
Model 2†	n.a*			0.64	0.34-1.21	0.17	1.57	1.03-2.41	**0.038**
Model 3†				0.65	0.34-1.24	0.19	1.44	0.85-2.46	0.18
Lean mass percentage									
Model 1				1.24	0.69-2.20	0.47	0.96	0.66-1.40	0.82
Model 2‡	n.a*			1.26	0.70-2.26	0.45	0.95	0.65-1.39	0.78
Model 3‡				1.69	0.87-3.30	0.12	0.90	0.60-1.36	0.62
Eyes closed									
Handgrip strength									
Model 1	1.94	1.24-3.03	**0.004**	1.11	0.80-1.54	0.54			
Model 2	2.03	1.26-3.30	**0.004**	1.17	0.83-1.66	0.37	n.a*		
Model 3	2.00	1.22-3.27	**0.006**	1.19	0.83-1.71	0.34			
Knee extension strength									
Model 1	2.62	1.37-5.03	**0.004**	1.5	1.01-2.23	**0.046**			
Model 2	3.33	1.61-6.89	**0.001**	1.72	1.13-2.63	**0.012**	n.a*		
Model 3	2.95	1.40-6.18	**0.004**	1.74	1.11-2.73	**0.017**			
ALM/height²									
Model 1	0.99	0.60-1.62	0.95	0.87	0.59-1.29	0.50			
Model 2†	1.02	0.55-1.89	0.95	0.98	0.59-1.62	0.94	n.a*		
Model 3†	1.00	0.54-1.85	1.00	0.96	0.56-1.64	0.88			
Lean mass percentage									
Model 1	1.30	0.77-2.20	0.33	1.16	0.80-1.68	0.44			
Model 2‡	1.30	0.77-2.19	0.33	1.16	0.80-1.69	0.43	n.a*		
Model 3‡	1.41	0.80-2.48	0.23	1.23	0.83-1.83	0.31			

All muscle characteristics were standardized in sex-specific Z-scores. Ability to maintain standing balance: 0=unable, 1=able. * Not applicable, number of elderly outpatients able or unable to maintain the standing condition is less than 5. Model 1: adjusted for age, model 2: as model 1 and body mass and height, model 3: as model 2 and MMSE score and multimorbidity. † not adjusted for height. ‡ not adjusted for body mass. Abbreviations: MMSE, Mini Mental State Examination; ALM, appendicular lean mass.

Table 3. Association between muscle characteristics and Center of Pressure movement in medio-lateral direction in different standing positions with eyes open and eyes closed.

	Side-by-side			Semi-tandem			Tandem		
	Beta	SE	P	Beta	SE	P	Beta	SE	P
Eyes open (available)	*(n=136)*			*(n=120)*			*(n=56)*		
Handgrip strength									
Model 1	–0.08	0.08	0.33	0.02	0.09	0.86	–0.09	0.13	0.52
Model 2	–0.10	0.09	0.23	–0.03	0.09	0.78	–0.15	0.14	0.27
Model 3	-0.09	0.09	0.34	–0.03	0.10	0.78	–0.14	0.15	0.33
Knee extension strength									
Model 1	–0.02	0.08	0.77	0.03	0.07	0.64	0.04	0.14	0.78
Model 2	–0.01	0.09	0.92	0.07	0.07	0.31	0.01	0.14	0.95
Model 3	0.01	0.09	0.88	0.07	0.08	0.35	0.02	0.15	0.88
ALM/height²									
Model 1	0.06	0.09	0.54	-0.04	0.12	0.75	-0.12	0.12	0.30
Model 2†	0.06	0.12	0.64	-0.17	0.17	0.31	-0.25	0.16	0.14
Model 3†	0.10	0.12	0.42	-0.17	0.18	0.34	-0.19	0.17	0.28
Lean mass percentage									
Model 1	0.09	0.09	0.33	0.01	0.10	0.96	-0.06	0.10	0.55
Model 2‡	0.07	0.09	0.45	-0.03	0.10	0.78	-0.09	0.11	0.41
Model 3‡	0.10	0.10	0.31	-0.04	0.11	0.74	-0.07	0.11	0.51
Eyes closed (available)	*(n=119)*			*(n=75)*					
Handgrip strength									
Model 1	0.09	0.08	0.30	0.10	0.10	0.32			
Model 2	0.06	0.08	0.46	0.08	0.11	0.47			
Model 3	0.05	0.09	0.55	0.05	0.12	0.67			
Knee extension strength									
Model 1	0.14	0.10	0.15	0.23	0.12	0.06			
Model 2	0.17	0.10	0.08	0.27	0.13	0.033			
Model 3	0.14	0.10	0.16	0.17	0.14	0.23	n.a.*		
ALM/height²									
Model 1	0.06	0.11	0.60	0.04	0.17	0.82			
Model 2†	-0.10	0.15	0.53	-0.04	0.25	0.88			
Model 3†	-0.07	0.15	0.65	0.06	0.27	0.81			
Lean mass percentage									
Model 1	-0.02	0.09	0.80	0.11	0.13	0.43			
Model 2‡	-0.06	0.09	0.53	0.04	0.13	0.78			
Model 3‡	-0.10	0.09	0.28	0.03	0.15	0.85			

All muscle characteristics were standardized in sex-specific Z-scores. * Not applicable, number of elderly outpatients able to maintain the balance condition is less than 5. Model 1: adjusted for age, model 2: as model 1 and body mass and height, model 3: as model 2 and MMSE and multimorbidity. † not adjusted for height. ‡ not adjusted for body mass. Abbreviations: MMSE, Mini Mental State Examination; ALM, appendicular lean mass.

When comparing the present study to previous studies, two aspects need to be considered. First, no exclusion criteria were applied in the present study, which contrasts other studies including healthy elderly. Elderly outpatients are more likely to have multimorbidity and deterioration in more than one system involved in standing balance [11;17;18]. Second, “balance” is inconsistently defined in literature for standing (static) and dynamic balance, i.e. not as isolated standing conditions, but as the score from SPPB [23], a sum score of the three foot positions [10;20], or as different dynamic balance tests as assessed with the Timed Up and Go test, walking speed, or chair-stand test [19]. It has been shown that standing balance tests are different from dynamic balance tests [28;29]. Therefore we discuss our results with respect to studies that measured standing balance (also called quiet stance, or static balance).

To the best of our knowledge, there are no studies describing the association of muscle strength with both the ability to maintain standing balance and the CoP movement during standing balance in elderly. In line with this study, a positive association between muscle strength and the ability to maintain balance has been described in healthy elderly [10;11] as well as elderly with mobility difficulties [19;20] aged 65 years and older. In 985 elderly women with mobility difficulties, those with a higher knee extension strength had a higher ability to maintain balance in side-by-side, semi-tandem, and tandem stance with eyes open [20]. The association between muscle strength and standing balance was not present in previous studies evaluating quality of standing balance by CoP movement in healthy elderly [14-16;28;30]. This is also in line with our study, as no association was found between muscle strength and CoP movement. However, a positive association between muscle strength and CoP movement has also been reported in healthy elderly [13] and women with osteoporosis [31].

No association between measures of muscle mass and the ability to maintain standing balance was found in the present study. A limited number of studies describe the association between muscle mass and ability to maintain standing balance [12;27]. A positive association has been described between quadriceps muscle mass and one-leg standing time in healthy elderly [12]. Furthermore, Janssen et al. reported a positive association between lean mass percentage and the ability to maintain balance in tandem stance in males aged over 60 years [27]. Previous research on the association between muscle mass and CoP movement is limited, reporting a positive association for quadriceps muscle mass [12], and no association for lean mass divided by height squared [14].

The fact that in the current study muscle strength was found to be associated with the ability to maintain standing balance rather than muscle mass, is explained by the differences between the characteristics “muscle strength” and “muscle mass”. Muscle strength appears to decline more with age than muscle mass [32-35]. Other factors in addition to muscle mass are important to generate muscle strength such as neural control, cognition, cardiovascular and joint function [35]. Furthermore, due to pain muscle strength may be underestimated [36;37]. Muscle tissue is not only a force generator, but has an important function as an internal organ, i.e. involved in glucose metabolism [38;39]. Maintenance of standing balance obviously reflects the role of muscle as a strength generator [35;40]. In this respect, this article provides further evidence to include assessment of muscle strength in clinical practice [41-43].

A possible explanation for the absence of an association between muscle characteristics and CoP movement could be selection of the fittest. CoP movement could only be assessed in outpatients who completed the standing balance conditions. Another explanation is large heterogeneity among elderly outpatients: the presence of multimorbidity and the deterioration of multiple systems involved in standing balance, i.e. sensory systems and neural control may interfere with the association between muscle characteristics and CoP movement [11;17;18]. For instance, in patients with an intact sensory system and neural control, a higher muscle mass or strength may be associated with low CoP movement. In patients with deterioration of the sensory or neural system, high muscle strength could also be the result of repetitive use of muscles as compensatory strategy. For these patients, higher muscle mass or strength would therefore be associated with higher CoP movement. A decline of distinct systems and compensatory strategies can result in comparable CoP movement [44]. In fact, lower CoP movement may not be related to better quality of standing balance, despite previously described differences in CoP movement between young and old adults [25].

The question arises whether an increase in muscle strength does improve standing balance in elderly outpatients. Physical exercise and training programmes have been shown to be beneficial in elderly, as they lead to an increase of muscle mass, muscle strength and even neuromuscular activity [45;46], although not all trials show a positive effect [47]. Suppletion of hormones [48], vitamin D, or nutrients [46;49] may increase or prevent further decrease of muscle mass and strength. However, evidence is still very weak, as large scale placebo controlled intervention studies for long term effects of interventions are missing. Regarding strength training, a systematic review of randomized controlled trials including elderly showed a positive effect of resistance training to improve balance in 18 of 33 randomized controlled trials. These studies included a range of methods (static and dynamic) to measure 'balance' [50]. Two of these randomized controlled trials included elderly with mobility difficulties [51;52]: one trial found an improved balance after training in a small number of elderly in the intervention group [51], and one trial found no effect on balance [52].

Strength of this study was the combined analyses of both muscle strength and muscle mass with the ability to maintain standing balance and CoP movement. The population of elderly outpatients is unique as there were no exclusion criteria. By assessing the ability to maintain standing balance in elderly outpatients, results of this study will be highly relevant in clinical practice. The heterogeneity of the study population implies that larger numbers of outpatients need to be assessed to relate outcome measures to function of specific systems involved in standing balance, i.e. sensory systems and neural control. Another limitation is the cross-sectional design, which prevents assessments causal inference.

Conclusion

Muscle strength rather than muscle mass is associated with the ability to maintain standing balance in community-dwelling elderly referred to a geriatric outpatient clinic. This indicates the additional value of assessment of muscle strength in clinical practice. Improvement of muscle strength is a target for potential intervention for impaired standing balance in this population of elderly outpatients with multimorbidity.

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Supplementary material

Supplementary Table 1. Center of Pressure (CoP) movement, represented by CoP parameters, within elderly outpatients able to maintain different standing positions with eyes open and eyes closed in anterior-posterior and medio-lateral direction.

	Side-by-side		Semi-tandem		Tandem	
	AP	ML	AP	ML	AP	ML
Eyes open (available)	*(n=136)*		*(n=120)*		*(n=56)*	
Mean amplitude (cm)	0.56 (0.02)	0.60 (0.02)	0.61 (0.04)	0.72 (0.03)	0.74 (0.04)	0.72 (0.03)
Range (cm)	3.38 (0.11)	3.51 (0.13)	3.88 (0.19)	4.25 (0.18)	4.94 (0.28)	3.92 (0.17)
Mean velocity (cm/s)	5.51 (0.10)	4.09 (0.10)	5.89 (0.13)	4.78 (0.13)	6.85 (0.22)	5.41 (0.21)
Amplitude variability (cm)	0.71 (0.02)	0.75 (0.03)	0.77 (0.04)	0.91 (0.04)	0.95 (0.05)	0.88 (0.04)
Velocity variability (cm/s)	7.87 (0.14)	5.70 (0.14)	8.41 (0.22)	6.76 (0.23)	9.88 (0.38)	7.55 (0.28)
Eyes closed (available)	*(n=119)*		*(n=75)*			
Mean amplitude (cm)	0.74 (0.03)	0.85 (0.03)	0.78 (0.04)	1.03 (0.04)		
Range (cm)	4.38 (0.15)	4.86 (0.17)	4.91 (0.25)	5.64 (0.23)	n.a.*	
Mean velocity (cm/s)	6.59 (0.15)	5.67 (0.14)	7.24 (0.24)	6.76 (0.26)		
Ampltiude variability (cm)	0.93 (0.03)	1.06 (0.04)	0.99 (0.05)	1.27 (0.05)		
Velocity variability (cm/s)	9.09 (0.20)	7.88 (0.20)	10.02 (0.34)	9.33 (0.37)		

Data are given in mean and standard error. *Not applicable, number of outpatients able to maintain the task is less than 5. Abbreviations: AP, anterior-posterior direction; ML, medio-lateral direction.

Supplementary Table 2. Association between muscle characteristics and Center of Pressure movement in anterior-posterior direction in different standing positions with eyes open and eyes closed.

	Side-by-side			Semi-tandem			Tandem		
	Beta	SE	p	Beta	SE	p	Beta	SE	p
Eyes open (available)		*(n=136)*			*(n=120)*			*(n=56)*	
Handgrip strength									
Model 1	0.04	0.08	0.62	0.05	0.08	0.58	0.03	0.12	0.81
Model 2	0.07	0.08	0.37	0.002	0.09	0.98	−0.01	0.13	0.96
Model 3	0.07	0.08	0.37	−0.01	0.09	0.93	−0.05	0.14	0.70
Knee extension strength									
Model 1	0.05	0.08	0.48	−0.01	0.07	0.91	−0.06	0.14	0.69
Model 2	0.11	0.08	0.18	0.02	0.07	0.76	−0.08	0.15	0.63
Model 3	0.13	0.08	0.11	0.02	0.07	0.75	-0.06	0.16	0.73
ALM/height²									
Model 1	-0.18	0.09	0.04	0.03	0.11	0.80	-0.19	0.12	0.11
Model 2†	-0.18	0.11	0.11	-0.12	0.16	0.45	-0.23	0.17	0.18
Model 3†	-0.15	0.11	0.19	-0.11	0.16	0.50	-0.22	0.18	0.22
Lean mass percentage									
Model 1	0.10	0.08	0.24	0.00	0.09	0.96	-0.03	0.11	0.82
Model 2‡	0.09	0.09	0.28	-0.02	0.10	0.80	-0.04	0.11	0.75
Model 3‡	0.14	0.09	0.14	-0.02	0.10	0.85	-0.04	0.12	0.75
Eyes closed (available)		*(n=119)*			*(n=75)*				
Handgrip strength									
Model 1	0.06	0.08	0.45	−0.11	0.10	0.28			
Model 2	0.05	0.08	0.54	−0.14	0.10	0.17	n.a.*		
Model 3	0.05	0.08	0.57	-0.18	0.11	0.11			
Knee extension strength									
Model 1	0.11	0.09	0.21	0.04	0.12	0.74			
Model 2	0.17	0.09	0.06	0.07	0.13	0.57	n.a.*		
Model 3	0.15	0.09	0.12	0.01	0.14	0.93			
ALM/height²									
Model 1	-0.05	0.11	0.68	0.22	0.15	0.16			
Model 2†	-0.14	0.14	0.32	-0.42	0.23	0.08	n.a.*		
Model 3†	-0.08	0.15	0.61	-0.31	0.25	0.23			
Lean mass percentage									
Model 1	0.02	0.09	0.87	0.02	0.13	0.89			
Model 2‡	-0.01	0.09	0.93	-0.04	0.13	0.76	n.a.*		
Model 3‡	0.00	0.09	1.00	-0.02	0.14	0.91			

All muscle characteristics were standardized in sex-specific Z-scores. * Not applicable, number of elderly outpatients able to maintain the balance condition is less than 5. Model 1: adjusted for age, model 2: as model 1 and body mass and height, model 3: as model 2 and MMSE and multimorbidity. † not adjusted for height. ‡ not adjusted for body mass. Abbreviations: MMSE, Mini Mental State Examination; ALM, appendicular lean mass.

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Chapter 4

Low cognitive status is associated with a lower ability to maintain standing balance in elderly outpatients

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Abstract

Evidence is emerging that cognitive performance is involved in maintaining balance and thereby involved in falls in the elderly. The aim of this study is to investigate the association of cognitive status with measures of standing balance in elderly outpatients.

In a cross-sectional study, 197 community-dwelling elderly (mean age (SD) 81.9 (7.1) years) referred to a geriatric outpatient clinic were included and subsequently dichotomized into a group with low and normal cognitive status based on cut-off values of the Mini Mental State Examination, Montreal Cognitive Assessment and Visual Association Test. The ability to maintain standing balance as well as the Center of Pressure (CoP) movement were assessed during ten seconds of side-by-side, semi-tandem and tandem stance with eyes open and eyes closed. Logistic and linear regression were used to examine the association between cognitive status and measures of standing balance adjusted for age, gender and highest completed education.

Low cognitive status in elderly outpatients was associated with a lower ability to maintain ten seconds of balance in side-by-side stance with eyes closed (Odds Ratio (OR) (95% CI): 3.57 (1.60;7.97)) and in semi-tandem stance with eyes open and eyes closed (OR (95% CI): 3.93 (1.71;9.00) and OR (95% CI): 2.32 (1.11;4.82), respectively). Cognitive status was not associated with CoP movement.

Low cognitive status associates with a lower ability to maintain standing balance in more demanding standing conditions in elderly outpatients. This may have implications for routine geriatric screening strategies and interpretation of results of either standing balance or cognitive tests.

Introduction

Impaired standing balance is one of the major complaints reported by elderly to physicians and is strongly related with falls [1;2]. Standing balance is required for most daily living activities. Impaired standing balance may easily result in serious medical, physical, emotional, and social consequences, including loss of independence and social isolation [1;3]. Understanding underlying determinants of impaired standing balance enables early detection and the development of tailored intervention.

Standing balance depends on the functioning of multiple organ systems, like the sensory (vestibular, proprioceptive and visual), musculoskeletal, nervous and cardiovascular system [4-6]. Moreover, it becomes more and more evident that standing balance relies on high-order cognitive performance controlled by the cerebral cortex instead of being a fully automatic process [7-9]. The involvement of the cerebral cortex on standing balance may be mediated by corticospinal loops and communication with the cerebellum and basal ganglia [10]. Involvement may grow with advanced age as neuroimaging studies showed that elderly exhibit more elaborate brain activation compared to young controls during the performance of fine motor tasks [11-14]. Deterioration of the multiple organ systems with advanced age and diseases for which must be compensated may result in increased involvement of the cerebral cortex [15]. Changes in the white matter of the cortex, like leukoaraisis and periventricular white matter change, are frequently found in dementia. Those changes may result in less ability to compensate and therefore could result in impaired balance and mobility decline [16-18].

Previous cross-sectional studies investigated the association between cognitive status with standing balance in relatively homogeneous and pre-specified study populations of middle aged to older adults. These studies showed that a lower cognitive status is associated with a lower ability to maintain standing balance [19-22] and with increased Center of Pressure (CoP) movement [15;23;24]. CoP movement is a measure for the steadiness of the body while maintaining balance and is assessed using a force plate, which measures the ground reaction forces. In general, an increased CoP movement is assumed to reflect impaired standing balance. However, the association of cognitive status with standing balance remains to be established in a clinically relevant population.

In this study, we assessed the association of cognitive status with the ability to maintain standing balance and Center of Pressure movement in a population of community-dwelling elderly referred to a geriatric outpatient clinic, with its typical variety of comorbidities, use of medication and mobility impairments. Elderly outpatients with low cognitive status were expected to exhibit worse standing balance, as reflected by less ability to maintain standing balance and increased CoP movement, compared with patients with normal cognitive status.

Methods

Study setting

The study population consisted of community-dwelling elderly (n=207) referred to a geriatric outpatient clinic in a middle-sized teaching hospital (Bronovo Hospital, The Hague, The Netherlands) between March 2011 and January 2012 for a comprehensive geriatric assessment (CGA) [25]. CGA was performed by trained nurses and medical staff during a two hour visit. All measurements were performed in the same conditions, in a quiet room and in a fixed order; first cognitive status tests, second standing balance tests. Therefore, the trained nurses and medical staff were aware of the cognitive status of the patient. Measurements took place between 9 am and 4 pm and during the day. The study was reviewed and approved by the institutional review board of the Leiden University Medical Center (Leiden, the Netherlands). Because this research is based on regular patient care, the need for individual informed consent was waived. Ten patients (4.8 %) were excluded from the analyses due to missing data, leaving 197 patients.

Elderly outpatient characteristics

Extensive characterization of the population for validity purposes was performed as described below. Patients were asked to complete questionnaires on marital status, living arrangements, highest completed education, current smoking and alcohol use. Body mass index (BMI) was assessed by measuring weight and height. Information on diseases and use of medication was extracted from medical records. Multimorbidity was defined as the presence of two or more diseases, including chronic obstructive pulmonary disease, heart failure, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson's disease, (osteo)arthritis, transient ischemic attack and stroke. Depressive symptoms were assessed by the Hospital Anxiety and Depression Scale (HADS) [26]; a depression subscore higher than 8 out of 21 points indicated depressive symptoms. Physical functioning was assessed by handgrip strength, preferred gait speed during a steady state ten meter walk and the Short Physical Performance Battery (SPPB) [27]. Furthermore, patients were asked to complete questionnaires on maximal daily physical activity, experienced falls during the previous twelve months and use of walking aids.

Cognitive status

Global cognitive status was assessed by Mini Mental State Examination (MMSE) [28] and Montreal Cognitive Assessment (MoCA) [29], assessing executive function, arithmic, memory and orientation in time and space. MMSE and MoCA scores both range from 0 to 30 points. One point was added to the total MoCA score if the highest completed education was at low or middle level (comparable with less than twelve years of education). Version A of the Visual Association Test [30], in which a maximum number of six objects can be recalled, was used to assess recollecting memory. VAT scores range from 0 to 6 points. For all cognitive tests, lower scores indicate lower cognitive status. The tests scores of the three cognitive tests were combined to form two groups of patients, i.e. a group with low and a group with normal cognitive status. Low cognitive status was defined as scoring below clinically used cut-off values (MMSE < 24 points, MoCA < 23 points and VAT < 3 points [30-32]) in minimal two out of three cognitive tests. If only two cognitive tests were available (n=40), low cognitive status was defined as scoring below clinically used cut-off values in minimal one cognitive test. The group including all other cases, i.e. scoring equal to or above the clinically used cut-off points, was defined as the normal cognitive status group. Patients with only one (n=1) or no cognitive tests (n=1) were excluded.

Standing balance

Ability to maintain standing balance

The ability to maintain balance was measured in six standing conditions, i.e. three different standing positions characterized by a progressive narrowing of the base support both with the eyes open and eyes closed. Patients wore non slip socks and were asked to maintain standing balance for ten seconds without moving their feet, first with their feet as closely together as possible (side-by-side stance), second with the medial side of the heel of one foot touching the big toe of the other foot (semi-tandem stance) and third with both feet in line while the heel of one foot touched the toes of the other foot (tandem stance). A maximum of three trials for each condition was allowed in case standing balance was lost prematurely. When the patients were not able to maintain standing balance in a specific position within the three trials allowed, the consecutive more demanding condition was not performed. All standing conditions were performed in a fixed order, starting with the measurements with eyes open, as part of the SPPB, and subsequently with eyes closed. Six of the 197 patients (3.0 %) did not attempt the standing positions with eyes closed due to lack of time or lack of motivation, leaving 191 patients for analyses of standing balance positions with eyes closed.

Center of Pressure movement

All standing conditions were performed on a triangular six degrees of freedom force plate (Forcelink B.V., Culemborg, The Netherlands) to measure CoP movement during ten seconds. Only successful trials (i.e. completion of ten seconds of maintaining standing balance) were considered for further analysis. Due to technical problems (n=18) and unknown reasons (n=29), CoP movement was available for n=136 patients.

As age-related differences have been shown to be most pronounced in medio-lateral (ML) direction [33] and impaired ability to control balance in this direction is well associated with falls [34], only CoP movement in ML direction was included in the analysis. Time series of CoP movement in ML direction were used to calculate five CoP parameters, i.e. the mean amplitude, the amplitude variability, the range, the mean velocity and the velocity variability. CoP parameters were transformed into z-scores, resulting in standardized CoP parameters with a mean of 0 and standard deviation of 1. Averaging those z-scores resulted in a composite score of the CoP movement in ML direction [33].

Statistical analysis

Continuous variables with Gaussian distribution are presented as mean and standard deviation (SD), otherwise as median and interquartile range (IQR) or number and percentage. Independent T-tests, Chi Square tests and Mann-Whitney tests were used to assess whether characteristics of both groups were significantly different. Logistic regression analysis was used to assess the association of cognitive status with the ability to maintain standing balance with adjustments for age, gender and highest completed education. The association of cognitive status with CoP movement was assessed using linear regression analysis with the same adjustments. Furthermore, a subgroup analysis was performed in all patients with available data of the HADS depression score (n=121), in which we additionally adjusted for depressive symptoms. The statistical package SPSS for Windows version 20.0 (SPSS Inc, Chicago, USA) was used for analyzing the data. P-values below 0.05 were considered statistically significant. Graphs were made with GraphPad Prism 5 (GraphPad Software, Inc., La Jolla, USA).

Results

The characteristics of the elderly outpatients are presented in Table 1 together with the characteristics stratified for low and normal cognitive status. Mean age (SD) of the patients was 81.9 (7.1) years. Measures of physical functioning, i.e. handgrip strength, gait speed and SPPB score, were lower in the low compared to the normal cognitive status group. The number of self-reported fall incidents in the previous twelve months was higher in the low cognitive status group.

Figure 1 shows the percentage of elderly outpatients able to maintain balance in different standing conditions stratified for low and normal cognitive status. Ability to maintain balance decreased in both groups with increasing difficulty of standing condition. Less than two percent of the patients were able to maintain tandem stance with eyes closed.

The CoP movement in ML direction is shown in Supplementary Table 1. The CoP parameters, used to calculate the CoP composite scores, were higher in more difficult standing conditions.

Figure 1. Ability to maintain standing balance. Percentage of elderly outpatients able to maintain balance in different standing conditions, i.e. side-by-side, semi-tandem and tandem stance with eyes open and eyes closed. Results are stratified for low and normal cognitive status.

Table 1. Elderly outpatient characteristics.

		Cognitive status		p
	All (n=197)	Low (n=56)	Normal (n=139)	
Socio-demographics				
Age, years	81.9 (7.1)	83.0 (7.5)	81.5 (6.9)	0.19
Men, n (%)	78 (39.6)	19 (33.9)	58 (41.7)	0.31
Widowed, n (%)	80 (41.5)	23 (41.8)	56 (41.2)	0.94
Independent living, n (%)	154 (79.4)	40 (72.7)	113 (82.5)	0.13
Highest completed education, n (%)				0.44
Low	48 (24.7)	17 (31.5)	31 (22.5)	
Middle	62 (32.0)	18 (33.3)	42 (30.4)	
High	55 (28.4)	12 (22.2)	43 (31.2)	
University	29 (14.9)	7 (13.0)	22 (15.9)	
Current smoking, n (%) [a]	22 (16.2)	4 (10.5)	18 (18.8)	0.25
Excessive alcohol use, n (%) [*]	8 (4.1)	1 (1.9)	7 (5.1)	0.32
Health characteristics				
BMI, kg/m^2 [b]	25.8 (4.5)	25.8 (4.0)	25.7 (4.7)	0.90
Multimorbidity, n (%) [b,†]	95 (50.3)	22 (40.0)	72 (54.5)	0.07
Number of medication, median (IQR) [b]	5 (3-7)	5 (3 - 7)	5 (3 - 7)	0.45
HADSd > 8 points, n (%) [c,‡]	28 (23.1)	9 (25.7)	19 (22.6)	0.72
Physical functioning				
Handgrip strength, kg	26.1 (8.2)	24.1 (8.4)	27.0 (8.0)	0.028
Gait speed, m/s [b,§]	0.87 (0.29)	0.73 (0.32)	0.93 (0.26)	<0.001
SPPB, points; median (IQR)	7 (5-10)	6 (4 - 8)	8 (6 - 10)	<0.001
Indoor daily physical activity, n (%)	31 (16.0)	6 (10.7)	25 (18.1)	0.20
Fall incident previous 12 months	127 (64.5)	45 (80.4)	80 (57.6)	0.003
Use of walking aid	108 (55.1)	36 (64.3)	71 (51.4)	0.10
Cognitive status, median (IQR)				
MMSE, points	27 (24 - 29)	22 (19 - 24)	28 (27 - 29)	<0.001
MoCA, points [d]	24 (20 - 26)	18 (15 - 20)	25 (23 - 27)	<0.001
VAT, points	5 (3 - 6)	2 (1 - 4)	6 (5 - 6)	<0.001

All parameters are presented as mean with standard deviation unless indicated otherwise. Data available in [a] n=136, [b] n=190, [c] n=121 and [d] n=158. * Defined as > 14 units per week for females or > 21 units per week for males. [†] Present in case of two or more diseases, including chronic obstructive pulmonary disease, heart failure, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson's disease, (osteo)arthritis, transient ischemic attack and stroke. [‡] Present with a depression subscore higher than eight on the Hospital Anxiety and Depression Scale. [§] Preferred gait speed during a steady state ten meter walk. Abbreviations: BMI, body mass index; HADSd, depression subscore of the Hospital Anxiety and Depression Scale; IQR, inter quartile range; SPPB, Short Physical Performance Battery; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; VAT, Visual Association Test.

Cognitive status and standing balance

Ability to maintain standing balance

The association between cognitive status and the ability to maintain standing balance is given in Figure 2. Patients in the low cognitive status group were less likely to be able to maintain standing balance in the semi-tandem stance with eyes open (Odds Ratio (OR) (95% CI): 3.93 (1.71; 9.00)) and in the side-by-side and semi-tandem stance with eyes closed (OR (95% CI): 3.57 (1.60; 7.97) and OR (95% CI): 2.32 (1.11; 4.82)) compared with patients in the normal cognitive status group. The odds ratio was higher for side-by-side stance with eyes closed compared with semi-tandem stance with eyes closed. Additional adjustment for depressive symptoms did not change the results (data not shown).

Center of Pressure movement

Table 2 shows the results of the association of cognitive status with CoP movement in ML direction. The association was not statistically significant for each standing position, both with eyes open and eyes closed. The association between cognitive status and CoP movement in ML direction during tandem stance with eyes closed was not applicable due to low number of patients who could perform this standing condition.

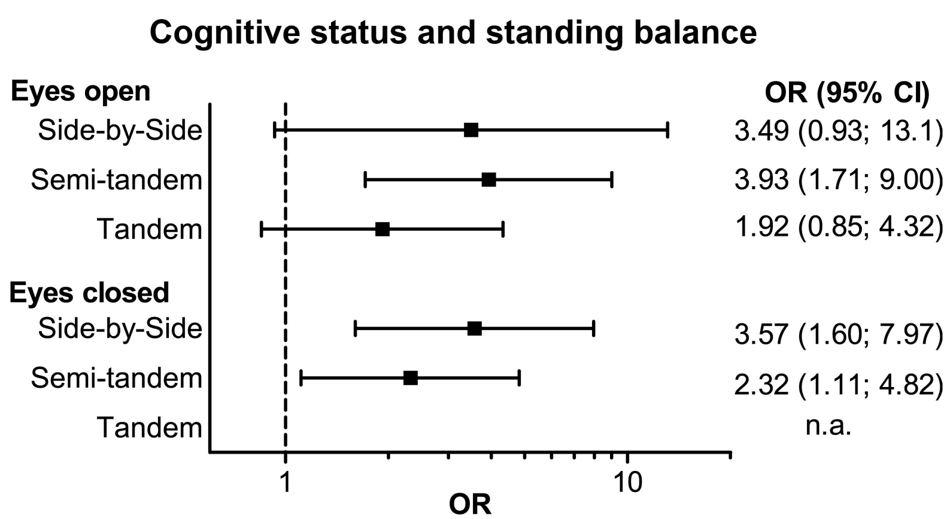

Figure 2. Association of cognitive status with the ability to maintain standing balance. Forest plot of the association between cognitive status and the ability to maintain balance in different standing condition, i.e. side-by-side, semi-tandem and tandem stance with eyes open and eyes closed. The low and normal cognitive status groups are represented by 0 and 1, respectively. The ability to maintain standing balance is defined as 0 not being able to maintain standing balance and 1 being able to maintain standing balance. Results are presented in odds ratios and 95% confidence intervals adjusted for age, gender and highest completed education. Abbreviations: OR, odds ratio; CI, confidence interval; n.a., not applicable, number of elderly outpatients able to maintain balance in the standing condition is less than five.

Table 2. Association between cognitive status and Center of Pressure movement in medio-lateral direction in different standing conditions.

	Side-by-side†			Semi-tandem‡			Tandem§		
	β	SE	p	β	SE	p	β	SE	p
Cognitive status*									
Eyes open	-0.02	0.18	0.91	0.17	0.21	0.43	0.29	0.35	0.41
Eyes closed	0.35	0.19	0.07	0.29	0.29	0.32		n.a.	

*Cognitive status with 0 representing the group of elderly outpatients with low cognitive status and 1 the group with normal cognitive status based on clinically used cut-off values. Dependent variable: Center of Pressure composite score in medio-lateral direction. Results are adjusted for age, gender and highest completed education. Abbreviations: β, estimate; SE, standard error; p, p-value; n.a., not applicable, number of elderly outpatients able to maintain balance in the standing condition is less than five. †Data available in n=135 and n=116 for eyes open and closed, respectively. ‡Data available in n=119 and n=72 for eyes open and closed, respectively. §Data available in n=56 and n=2 for eyes open and closed, respectively.

Discussion

The aim of this study was to establish the association of cognitive status with standing balance in a clinically relevant population of elderly outpatients. We found that low cognitive status was associated with a lower ability to maintain standing balance. Cognitive status was not associated with CoP movement in ML direction.

Our findings are in concordance with previous studies showing a cross-sectional association between low cognitive status and a lower ability to maintain standing balance in middle-aged to older adults in which the study population is further specified on e.g. cognitive or mobility impairments and the presence of comorbidities [19-22]. In this study, we showed that this relation is also present in community-dwelling elderly visiting the geriatric outpatient clinic with common comorbidities and mobility impairments. In this population, deterioration of the different organ systems involved in standing balance, i.e. the sensory, musculoskeletal, nervous and cardiovascular system, is very likely. The presence of the association between cognitive status and the ability to maintain standing balance supports the important role of the brain in controlling standing balance instead of being a fully automatic process [7-9]. Furthermore, it emphasizes the clinical relevance of measuring standing balance in patients with low cognitive status. Especially because of the large impact of impaired standing balance on most of daily living activities and the strong relation of impaired standing balance with falls [1;2]. The latter is also supported by this study showing a higher reported fall incidence over the previous twelve months in the low compared to the normal cognitive status group.

No differences in maximal daily physical activity were found between groups. Although, in this case it is difficult to distinguish cause and effect, as less daily activity could be caused by impaired standing balance, but less daily activity could also cause impaired standing balance.

The association between cognitive status and the ability to maintain standing balance was found in 3 of the 6 standing conditions, namely side-by-side stance with eyes closed and semi-tandem stance with eyes open and eyes closed. This could be explained by the increasing difficulty of the standing conditions, i.e. reducing the base of support and eliminating visual information. More difficult standing conditions put higher demands on balance control. Aforementioned standing conditions will therefore be more difficult for patients with a low cognitive status compared with patients with a normal cognitive status. No association between cognitive status and the ability to maintain balance in tandem stance with eyes closed could be found, as only four patients were able to maintain balance during this condition.

No association was found between cognitive status and CoP movement. The inconsistency in the association of cognitive status with the ability to maintain standing balance and CoP movement emphasizes that both outcome parameters of standing balance assess different properties. The ability to maintain standing balance is a measure of standing balance referring to whether someone is able to stay upright or not, whereas CoP movement is a more indirect measure of standing balance referring to the steadiness of the body while standing on a force plate [35]. A possible explanation for the absence of an association of cognitive status with CoP movement, is that data on CoP movement is only available from patients who were able to maintain ten seconds of standing balance, which may have led to an underestimation of the association between cognitive status and CoP movement. Another possible explanation is the heterogeneity of the study population, especially the presence of more than two diseases in more than 50% of the patients and the deterioration of multiple systems involved in standing balance [4]. As each underlying system could have a different effect on CoP movement, this may interfere with the association between cognition and CoP movement on population level [36]. Further research into the assessment of CoP movement is still needed to get insight into the causal underlying mechanisms of impaired standing balance, which are yet unknown.

One of the strengths of this study is the study population consisting of community-dwelling elderly referred to a geriatric outpatient clinic. Because no exclusion criteria were used, the study population represents an average population encountered in common geriatric practice.

This makes the results of this study highly relevant in clinical practice. Measuring standing balance in patients with low cognitive status and, the other way around, measuring cognitive status in patients with impaired standing balance will have an added value in clinical care. Furthermore, the combined assessment of the ability to maintain standing balance, as part of the SPPB, and CoP movement enables to get insight into the clinical utility of both measures. A limitation of the study is that CoP movement was measured during a relatively short time interval of ten seconds and data of only one successful trial was available, while previous studies recommend to measure CoP movement more than once and during a longer time period [35;37]. However, in clinical practice and in a population of elderly outpatients it is likely that this it is not feasible due to time limit and fatigue. The cross-sectional design of the present analysis prevents to study causality.

Conclusion

In conclusion, low cognitive status is associated with a lower ability to maintain balance for ten seconds in more demanding standing conditions in elderly outpatients. This indicates the clinical relevance of measuring standing balance in patients encompassing those with low cognitive status in routine geriatric screening. Regarding interpretation, in patients with impaired standing balance the possibility of low cognitive status must be considered and, the other way around, in case of poor performance on cognitive tests the possibility of impaired standing balance must be considered. We could not establish an additional value of assessment of CoP movement in routine geriatric assessment as we found low cognitive status not to be associated with CoP movement. A next step would be to focus on clustering of phenotypes and defining risk populations, which will be of clinical added value and will allow to investigating causality. This obviously requires large study sample sizes.

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Supplementary material

Supplementary Table 1. Center of Pressure (CoP) movement, represented by CoP parameters, within elderly outpatients able to maintain different standing positions with eyes open and eyes closed in medio-lateral direction.

	Side-by-side*	Semi-tandem†	Tandem‡
Eyes open			
Mean amplitude (cm)	0.60 (0.02)	0.72 (0.03)	0.72 (0.03)
Range (cm)	3.51 (0.13)	4.25 (0.18)	3.92 (0.17)
Mean velocity (cm/s)	4.09 (0.10)	4.78 (0.13)	5.41 (0.21)
Amplitude variability (cm)	0.75 (0.03)	0.91 (0.04)	0.88 (0.04)
Velocity variability (cm/s)	5.70 (0.14)	6.76 (0.23)	7.55 (0.28)
Eyes closed			
Mean amplitude (cm)	0.85 (0.03)	1.03 (0.04)	
Range (cm)	4.86 (0.18)	5.64 (0.23)	
Mean velocity (cm/s)	5.67 (0.15)	6.76 (0.26)	n.a.
Amplitude variability (cm)	1.06 (0.04)	1.27 (0.05)	
Velocity variability (cm/s)	7.88 (0.20)	9.33 (0.37)	

Data are given in mean with standard error. Abbreviations: n.a., not applicable, number of elderly outpatients able to maintain balance in the standing condition is less than five. * Data available in n=136 and n=119 for eyes open and closed, respectively. † Data available in n=120 and n=75 for eyes open and closed, respectively. ‡ Data available in n=56 for eyes open.

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Chapter 5

Blood pressure associates with standing balance in elderly outpatients

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Abstract

Assessment of the association of blood pressure measurements in supine and standing position after a postural change, as a proxy for blood pressure regulation, with standing balance in a clinically relevant cohort of elderly, is of special interest as blood pressure may be important to identify patients at risk of having impaired standing balance in routine geriatric assessment.

In a cross-sectional cohort study, 197 community-dwelling elderly referred to a geriatric outpatient clinic of a middle-sized teaching hospital were included. Blood pressure was measured intermittently (n = 197) and continuously (subsample, n = 58) before and after a controlled postural change from supine to standing position. The ability to maintain standing balance was assessed during ten seconds of side-by-side, semi-tandem and tandem stance, with both eyes open and eyes closed. Self-reported impaired standing balance and history of falls were recorded by questionnaires. Logistic regression analyses were used to examine the association between blood pressure and 1) the ability to maintain standing balance; 2) self-reported impaired standing balance; and 3) history of falls, adjusted for age and sex.

Blood pressure decrease after postural change, measured continuously, was associated with reduced ability to maintain standing balance in semi-tandem stance with eyes closed and with increased self-reported impaired standing balance and falls. Presence of orthostatic hypotension was associated with reduced ability to maintain standing balance in semi-tandem stance with eyes closed for both intermittent and continuous measurements and with increased self-reported impaired standing balance for continuous measurements.

Continuous blood pressure measurements are of additional value to identify patients at risk of having impaired standing balance and may therefore be useful in routine geriatric care.

Introduction

Five to 30 percent and 53 to 78 percent of elderly aged above 65 years suffer from orthostatic hypotension (OH) [1] and hypertension [2], respectively. Both OH and hypertension are signs of impaired blood pressure regulation [3;4], which is associated with increased risk of cardiovascular events [5-7], falls [8-14], and mortality [15-18]. Another important risk factor of falls is impaired standing balance [13;19;20] resulting from the deterioration of underlying systems, i.e. the sensory systems (proprioception, vision and vestibular), muscles and neural control [21].

Few studies investigated the relation between blood pressure regulation and standing balance [22-25]. In healthy elderly aged above 65 years, hypertension was found to be unrelated to quality of standing balance measured by Center of Pressure (CoP) movement [24], but was related to the score on a dynamic pull test investigating postural stability [25]. Furthermore, in healthy elderly and patients with Parkinson's disease, OH was found to be associated with higher Center of Mass (CoM) movement during standing [22;23].

In clinical practice, comparison of blood pressure measurements before and after a postural change from supine to standing position is used as a proxy for blood pressure regulation. In this study, we assessed the association of both intermittent and continuous blood pressure measurements before and after a postural change with three measures of standing balance: 1) the ability to maintain standing balance, 2) self-reported impaired standing balance and 3) history of falls, in community-dwelling elderly referred to a geriatric outpatient clinic. Results are relevant for design of routine geriatric assessment and therapeutic strategies.

Materials and Methods

Setting and study population

This cross-sectional study included 207 community-dwelling elderly who were referred to a geriatric outpatient clinic in a middle-sized teaching hospital (Bronovo Hospital, The Hague, Netherlands) for a comprehensive geriatric assessment (CGA) between March 2011 and January 2012. CGA was performed during a two hour visit including questionnaires and physical and cognitive measurements. All tests were performed by trained nurses or medical staff. The study was reviewed and approved by the institutional review board of the Leiden University Medical Center (Committee Medical Ethics (CME), Leiden, the Netherlands). The need for individual informed consent was waived, as this research was based on patient care.

Ten elderly patients (4.8%) were excluded due to missing data on standing balance, leaving 197 patients for analyses. Continuous blood pressure measurements were added to the CGA in June 2012 and were subsequently available in 62 patients. Data of four patients were excluded because of technical problems, leaving 58 patients for analysis. Of two patients who visited the outpatient clinic twice, data were used from the second visit that included the continuous blood pressure measurements.

Blood pressure measurements

Blood pressure was measured in supine position and during 3 minutes in standing position after postural change. Patients were in supine position for at least 5 minutes. An automatic lift chair (Vario 570, Fitform B.V., Best, The Netherlands) was used to provide automated support from a supine to a raised position. Subsequently patients were asked to stand up and stand unsupported for 3 minutes.

Intermittent blood pressure measurements

Systolic and diastolic blood pressure measurements were determined intermittently using an automated sphygmomanometer on the left arm (Welch Allyn, Skaneateles, USA). Blood pressure was measured after at least 5 minutes in supine position before postural change and after 1 and 3 minutes in standing position. Three blood pressure measures were determined: 1) supine blood pressure was defined as the blood pressure measured in supine position before postural change; 2) blood pressure decrease was calculated for two time points by subtracting the blood pressure taken at 1 or 3 minutes in standing position from the supine blood pressure; 3) $OH_{intermittent}$ was defined as a decrease of at least 20 mmHg systolic blood pressure or 10 mmHg diastolic blood pressure at 1 or 3 minutes in standing position compared to supine blood pressure [26].

Continuous blood pressure measurements

At the same time, systolic and diastolic blood pressure measurements were determined continuously and non-invasively using a digital photoplethysmograph with a cuff placed on the right middle finger (Finometer PRO, Finapres Medical Systems BV, Amsterdam, The Netherlands) [27]. Data were analyzed using BeatScope 1.1 software (Finapres Medical systems BV, Amsterdam, The Netherlands) resulting in beat-to-beat blood pressure data. Beat-to-beat blood pressure data were exported to Matlab (The Mathworks, Natick, MA) and averaged over 5 seconds intervals [28]. Three blood pressure measures were determined: 1) supine blood pressure was defined as the mean blood pressure in supine position during the last 60 seconds before postural change; 2) blood pressure decrease was calculated for three consecutive time periods, i.e. 0 to 15 seconds, 15 to 60 seconds and 60 to 180 seconds after postural change by subtracting the lowest averaged blood pressure measured during the time period from the supine blood pressure; 3) $OH_{continuous}$ was defined as a decrease of at least 20 mmHg systolic blood pressure or 10 mmHg diastolic blood pressure after 15 to 180 seconds in standing position compared to supine blood pressure. In addition, initial OH (iOH) was included in the definition of $OH_{continuous}$ defined as a decrease of at least 40 mmHg systolic blood pressure or 20 mmHg diastolic blood pressure during the first 15 seconds compared to supine blood pressure [29;30].

Standing balance

The ability to maintain standing balance was assessed in three standing positions characterized by a progressive narrowing of the base of support performed both with eyes open and eyes closed. Patients, wearing non-slip socks, were instructed to maintain balance for 10 seconds in each standing condition. During side-by-side stance, patients were instructed to stand with the medial malleoli as close together as possible; during semi-tandem stance, with the medial side of the heel of one foot touching the big toe of the other foot; and during tandem stance, with both feet in line while the heel of one foot touched the toes of the other. Standing positions with eyes open were first assessed as part of the Short Physical Performance Battery (SPPB) [31]. Subsequently, all standing positions were repeated with eyes closed. Patients were allowed three trials if standing balance was lost prematurely. When the patients could not complete a standing position, consecutive positions were omitted. Six patients did not attempt the standing positions with eyes closed due to lack of time or lack of motivation, leaving 191 patients for analyses of standing balance positions with eyes closed. Impaired standing balance was self-reported by answering the question whether and how often the patient experienced problems with standing balance. A positive answer was registered when the answer option 'regularly' or 'always' was given. History of falls was self-reported by answering the question whether falls in the past 12 months were experienced.

Characteristics of patients

Aforementioned items were part of a larger questionnaire obtaining information on marital status, living arrangements, smoking, alcohol use and use of walking aid. Body mass index was calculated by measuring body weight and height. Information on diseases and use of medication was extracted from medical charts. Multimorbidity was rated as the presence of two or more diseases including chronic obstructive pulmonary disease, heart failure, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson's disease, (osteo)arthritis, transient ischemic attack and stroke. The Hospital Anxiety Depression Scale (HADS) was used to detect depressive symptoms [32]; a score higher than 8 out of 21 points indicated depressive symptoms. Global cognitive functioning was assessed using the Mini Mental State Examination (MMSE) [33]. Handgrip strength was measured in standing position using a hand dynamometer (Jamar, Sammons Preston, Inc., Bolingbrook, IL, USA). The best performance of three trials alternately for each hand was used for analyses. Physical functioning was measured with a 10 meter walking test at usual pace in steady state, and with the SPPB. The SPPB comprises the ability to maintain balance in three standing positions with eyes open, a timed four meter walk and a timed sit-to-stand test.

Statistical analyses

Continuous variables with Gaussian distribution are presented as mean and standard deviation; otherwise as number and percentage or median and interquartile range. The association between blood pressure measures and 1) the ability to maintain standing balance; 2) impaired standing balance; and 3) history of falls were analyzed using logistic regression models including adjustment for demographics, i.e. age and sex. P values less than 0.05 were considered statistically significant. Statistical analyses were performed using SPSS for Windows (SPSS Inc, Chicago, USA), version 20. For visualization purposes, tertiles of blood pressure decrease were calculated. Graphs were made with GraphPad Prism 5 (GraphPad Software, Inc., La Jolla, USA).

Results

Characteristics of patients

Characteristics of patients, including intermittent blood pressure measures, are presented in Table 1. Continuous blood pressure measures for the subgroup of patients are shown in Supplementary Table 1. The mean age of all patients was 81.9 years. OHintermittent was present in 29 out of 197 patients (15%). OHcontinuous was present in 33 out of 58 patients (57%); in 19 patients (58%) also initial OH was present and in 5 patients (15%) only iOH was present. In 26 of 33 patients (79%) in which OH was present using continuous measurements, no OH was present using intermittent measurements.

Table 1. Characteristics of all elderly patients and of subgroup of elderly patients who underwent additional continuous blood pressure measurements.

	All (n = 197)	Subgroup (n = 58)
Socio-demographics		
Age, years	81.9 (7.1)	80.6 (7.0)
Men, n (%)	78 (39.6)	25 (43.1)
Widowed, n (%)	80 (41.5)	17 (29.8)
Independent living, n (%)	154 (79.4)	46 (79.3)
Current smoking, n (%) [a]	22 (16.2)	9 (15.5)
Excessive alcohol use, n (%) [e]	8 (4.1)	6 (10.3)
Health characteristics		
BMI, kg/m^2 [b]	25.8 (4.5)	26.4 (4.9)
Multimorbidity, n (%) [b, f]	95 (50.3)	26 (46.4)
Number of medication, median (IQR) [b]	5 (3-7)	5 (3-7)
HADS, depression > 8; n (%) [c]	28 (23.1)	10 (20.4)
MMSE, points; median (IQR)	27 (24-29)	28 (25-29)
Physical functioning		
Handgrip strength, kg	26.1 (8.2)	27.2 (7.9)
Gait speed, m/s	0.87 (0.29)	0.87 (0.29)
SPPB, points; median (IQR)	7 (5-10)	8 (6-10)
Self-reported, n (%)		
Fall incident previous 12 months	127 (64.5)	34 (58.6)
Impaired standing balance [g]	88 (45.1)	20 (35.1)
Use of walking aid	108 (55.1)	29 (50.0)
Supine blood pressure [h, b]		
Systolic blood pressure, mmHg	142 (24)	141 (25)
Diastolic blood pressure, mmHg	74.6 (10.1)	74.4 (11.0)
Blood pressure decrease after postural change		
Orthostatic hypotension, n (%) [i]	29 (15.4)	7 (12.5)
Systolic blood pressure decrease, mmHg [j, d]		
1 minute	3.15 (15.94)	-0.62 (18.24)
3 minutes	-0.80 (15.55)	-4.37 (16.03)
Diastolic blood pressure decrease, mmHg [j, d]		
1 minute	-2.90 (7.18)	-4.53 (7.10)
3 minutes	-4.17 (8.27)	-5.76 (9.54)

All parameters are presented as mean with standard deviation unless indicated otherwise. Data available in [a] n = 136, [b] n = 190, [c] n = 121, [d] n = 181. [e] Defined as > 14 units per week for females and > 21 units per week for males. [f] Present in case of two or more diseases, including chronic obstructive pulmonary diseases, heart failure, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson's disease, (osteo)arthritis, transient ischemic attack and stroke. [g] Defined as regularly or always self-reported impaired standing balance. [h] Measured after at least 5 minutes in supine position. [i] Orthostatic hypotension defined as decrease in systolic blood pressure of ≥ 20 mmHg or decrease in diastolic blood pressure of ≥ 10 mmHg at 1 or at 3 minutes after postural change, intermittently measured. [j] Supine blood pressure minus blood pressure at 1 or 3 minutes after postural change. Abbreviations: IQR, inter quartile range; BMI, body mass index; HADS, Hospital Anxiety and Depression Scale; MMSE, Mini Mental State Examination; SPPB, Short Physical Performance Battery.

Standing balance

Ability to maintain standing balance is shown in Figure 1. The number of patients able to maintain standing balance was lower with increasing difficulty of the standing positions, both for eyes open and eyes closed conditions. In tandem stance with eyes closed 4 (2%) patients were able to maintain balance. Comparable percentages were found for the subgroup who underwent additional continuous blood pressure measurements as shown in Figure 1B. Table 1 shows that 45% of the patients reported impaired standing balance and 65% of the patients reported at least one fall incident in the 12 months prior to the visit to the outpatient clinic.

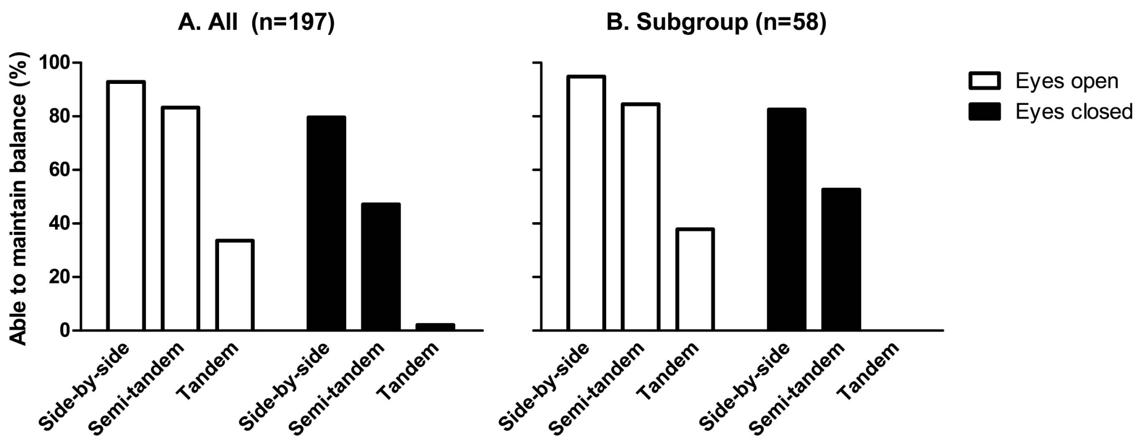


Figure 1. Ability to maintain balance in several standing positions with eyes open and eyes closed. A) all elderly patients (n = 197) and for B) subgroup who underwent additional continuous blood pressure measurements (n = 58).

Blood pressure measures and standing balance

Intermittent blood pressure measurements

The associations between intermittent blood pressure measures and the ability to maintain standing balance adjusted for age and sex are presented in Table 2. In standing positions with eyes open, intermittent blood pressure measures were not associated with the ability to maintain balance. In standing positions with eyes closed, intermittent blood pressure measures, except $OH_{intermittent}$, were not associated with the ability to maintain standing balance. Patients with $OH_{intermittent}$ were significantly less likely to be able to maintain balance in semi-tandem stance with eyes closed. All intermittent blood pressure measures were not associated with self-reported impaired standing balance and history of falls as presented in Supplementary Table 2. Additional adjustments for BMI, gait speed, MMSE score and handgrip strength did not influence the results.

Table 2. Association between intermittent blood pressure measures and the ability to maintain standing balance in all elderly patients (n = 197).

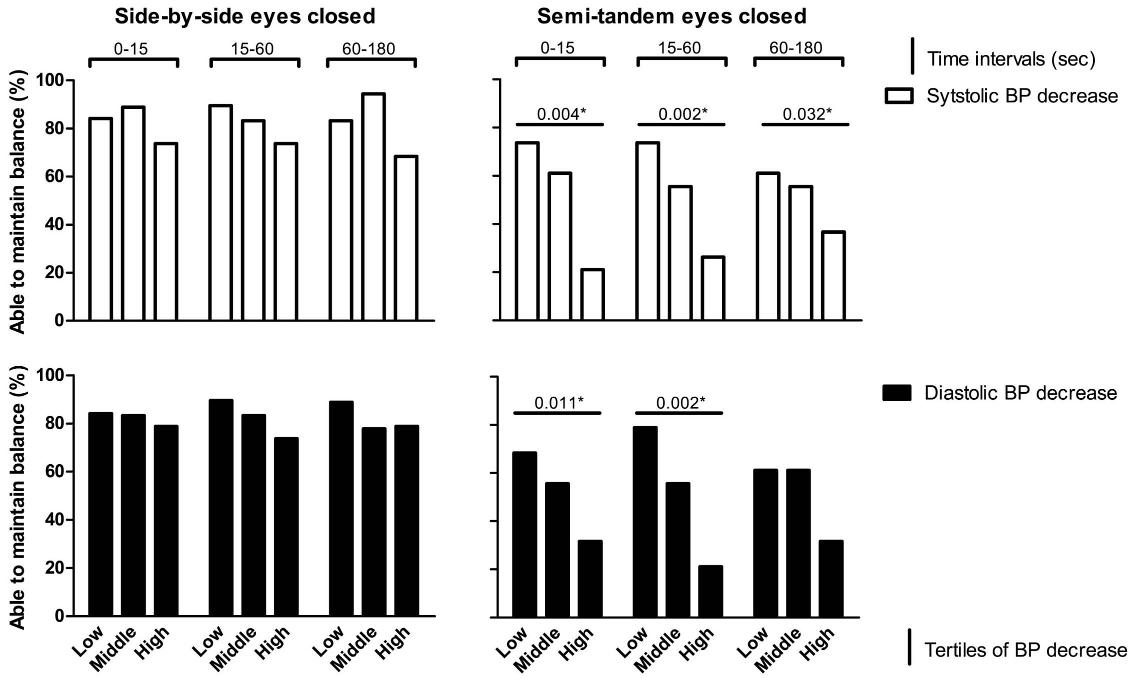
	Eyes open conditions						Eyes closed conditions					
	Side-by-side		Semi-tandem		Tandem		Side-by-side		Semi-tandem		Tandem	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Supine blood pressure [a]												
Systolic BP	0.99 (0.94-1.04)	.69	0.99 (0.97-1.02)	.67	0.99 (0.96-1.01)	.24	0.97 (0.95-1.00)	.07	0.99 (0.97-1.01)	.28		
Diastolic BP	1.07 (0.95-1.21)	.28	1.05 (0.98-1.11)	.15	1.00 (0.96-1.05)	.94	0.97 (0.95-1.00)	.07	0.99 (0.97-1.01)	.28		
Blood pressure decrease after postural change												
Orthostatic hypotension [b]	6.30 (0.29-135)	.24	1.40 (0.30-6.62)	.67	0.46 (0.13-1.57)	.22	0.52 (0.11-2.41)	.40	0.18 (0.05-0.62)	**.007**		
Systolic BP decrease [c]											n.a.	
0 to 15 sec	1.03 (0.96-1.11)	.36	1.00 (0.97-1.03)	.80	0.99 (0.96-1.01)	.22	0.98 (0.95-1.00)	.10	0.96 (0.94-0.99)	**.004**		
15 to 60 sec	1.02 (0.95-1.08)	.65	0.99 (0.96-1.02)	.38	0.98 (0.95-1.01)	.13	0.97 (0.95-1.00)	.08	0.96 (0.93-0.98)	**.002**		
60 to 180 sec	0.99 (0.93-1.06)	.83	1.02 (0.98-1.06)	.45	0.98 (0.94-1.01)	.16	0.97 (0.95-1.00)	.09	0.97 (0.94-1.00)	**.03**		
Diastolic BP decrease [c]												
0 to 15 sec	1.12 (0.99-1.27)	.08	1.03 (0.98-1.09)	.30	1.00 (0.96-1.04)	.83	0.97 (0.93-1.02)	.25	0.95 (0.91-0.99)	**.01**		
15 to 60 sec	1.13 (0.98-1.31)	.10	1.02 (0.96-1.08)	.49	0.97 (0.93-1.02)	.24	0.96 (0.91-1.01)	.08	0.91 (0.86-0.97)	**.002**		
60 to 180 sec	1.02 (0.89-1.17)	.77	1.09 (0.99-1.19)	.07	0.97 (0.92-1.03)	.34	0.96 (0.91-1.02)	.23	0.96 (0.90-1.01)	.09		

All data are from logistic regression analysis with adjustments for age and sex. Ability to maintain standing balance: 0 = unable, 1 = able. [a] Measured after at least 5 minutes in supine position. [b] Orthostatic hypotension: 0 = absent, 1 = present; defined as decrease in systolic blood pressure of $\geq$ 20 mmHg or decrease in diastolic blood pressure of $\geq$ 10 mmHg during 3 minutes after postural change. [c] Supine blood pressure minus blood pressure at 1 or 3 minutes after postural change. n.a. = not applicable, number of elderly patients able to maintain this balance condition is less than 5.

Continuous blood pressure measurements

The associations between continuous blood pressure measures and the ability to maintain standing balance adjusted for age and sex are displayed in SupplementaryTable 3. The main findings are visualized in Figure 2. In standing positions with eyes open, blood pressure measures were not associated with the ability to maintain balance. In standing positions with eyes closed, patients with a higher decrease in systolic blood pressure in each time period after postural change and patients with a higher decrease in diastolic blood pressure during the first 15 seconds or during 15 to 60 seconds after postural change were significantly less likely to be able to maintain balance in semi-tandem stance with eyes closed. Patients with $OH_{continuous}$ were significantly less likely to be able to maintain balance in semi-tandem stance with eyes closed. Additional adjustments for BMI, gait speed, MMSE score and handgrip strength did not influence the results.

The associations between continuous blood pressure measures and self-reported impaired standing balance and history of falls adjusted for age and sex are displayed in Figure 3 using a forest plot. This plot shows the odds ratio and 95% confidence interval per association, in which no overlap with 1.0 indicates a significant difference. Patients with a higher decrease in systolic or diastolic blood pressure during the first 15 seconds or during 15 to 60 seconds after postural change were significantly more likely to report impaired standing balance. Patients with a higher decrease in systolic or diastolic blood pressure during 15 to 60 seconds after postural change were significantly more likely to experience falls in the last 12 months. In addition, patients with a higher decrease in diastolic blood pressure in the first 15 seconds after postural change were significantly more likely to have a history of falls. Patients with OHcontinuous were significantly more likely to report impaired standing balance, but not to experience falls in the last 12 months. Additional adjustments for BMI, gait speed, MMSE score and handgrip strength did not influence the results.



Tertiles of BP decrease:

	Systolic BP decrease (mmHg)						Diastolic BP decrease (mmHg)					
	0-15 sec		15-60 sec		60-180 sec		0-15 sec		15-60 sec		60-180 sec	
	max	min	max	Min	max	min	max	min	max	min	max	min
Low	14	-11	2	-24	-6	-26	8	-20	-1	-20	-2	-16
Middle	39	14	29	2	12	-6	20	8	11	1	8	-2
High	103	39	71	29	87	12	66	20	49	11	38	8

Figure 2. Percentage of elderly patients able to maintain balance during side-by-side and semi-tandem stance with eyes closed. Data is given for tertiles of systolic and diastolic blood pressure (BP) decrease, continuously measured, during the time period in seconds after postural change. *P values derived from logistic regression analyses with adjustments for age and sex.

Discussion

Significant associations between continuously measured blood pressure decrease after postural change and the ability to maintain standing balance in conditions with eyes closed, self-reported impaired standing balance and history of falls were found in community-dwelling elderly referred to a geriatric outpatient clinic. Furthermore, OH determined with continuous measurements was associated with reduced ability to maintain standing balance and with increased self-reported impaired standing balance, but not with falls.

This is the first study that investigated the association of blood pressure measures with ability to maintain standing balance and self-reported impaired standing balance in elderly outpatients. In previous studies, no association was found between hypertension and quality of standing balance, measured by CoP movement, in healthy elderly [24]. However, hypertension has been associated with standing balance during a dynamic test, in which the patient was pulled backward and the response was quantified [25]. In this study, no association was found between blood pressure in supine position and measures of standing balance. Previous studies in healthy elderly and Parkinson patients found an association between OH, determined using blood pressure measurements at rest, after standing up and after one, two and three minutes of standing, and quality of standing balance, measured by CoM movement; elderly with OH were found to have an increased CoM movement during

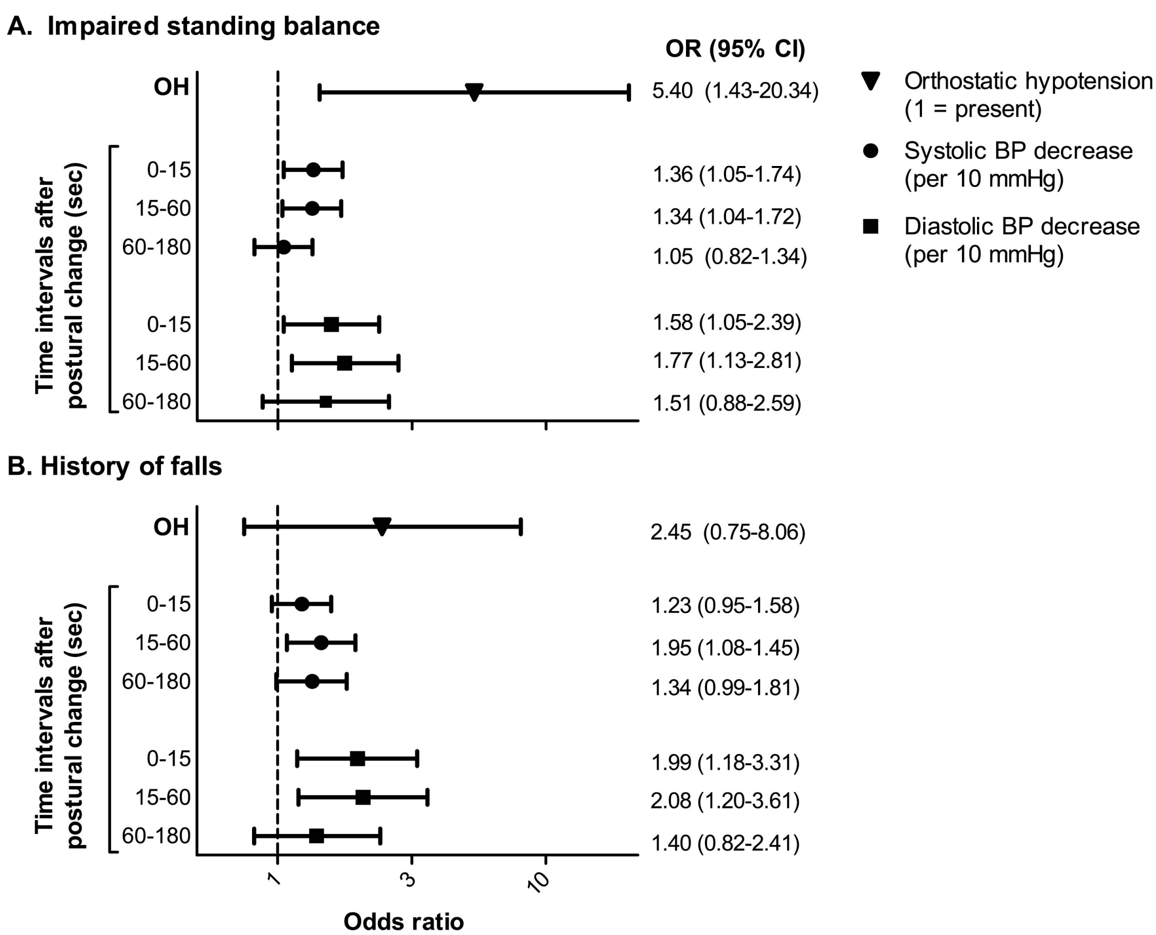


Figure 3. Forest plots of the association between blood pressure and A) reported impaired standing balance and B) history of falls. Blood pressure measures were determined with continuous measurements in subgroup who underwent additional continuous blood pressure measurements (n = 58). Orthostatic hypotension: 0 = absent, 1 = present; defined as a decrease in systolic blood pressure of ≥ 40 mmHg or in diastolic blood pressure of ≥ 20 mmHg during 15 seconds after postural change or a decrease in systolic blood pressure of ≥ 20 mmHg or diastolic blood pressure of ≥ 10 mmHg between 15 and 180 seconds after postural change. Reported impaired balance: 0 = never or sometimes, 1 = regularly or always. History of falls: 0 = no falls, 1 = falls. Results are presented in odds ratios per 10 mmHg blood pressure decrease and 95% confidence intervals with adjustments for age and sex. No overlap with 1.0 indicates a significant difference.

stance compared to elderly without OH [22;23]. In accordance with those studies, we found an association of presence of OH and blood pressure decrease with subjective (i.e. self-reported impaired standing balance) and objective (i.e. ability to maintain standing balance) measures of standing balance.

Previous studies investigated the association between blood pressure measures and falls. In this study continuous blood pressure measures did associate with falls, which is conflicting with other studies [9;12;28]. In accordance with other studies, no association was found between intermittent blood pressure measures and falls [8;11;28]. Conflicting results could be due to variance in assessment and the lack of an uniform definition of OH. Furthermore, falls were assessed in different ways, i.e. retrospective, self-reported versus prospective assessment during a follow up period or use of self-administrated fall risk profiles.

The association between blood pressure decrease and reduced ability to maintain standing balance may be explained by cerebral hypoperfusion. Cerebral autoregulation modulates cerebral blood flow and cerebral perfusion in order to maintain sufficient oxygenation of the brain regions with fluctuations in blood pressure [34] and is affected by impaired blood pressure regulation [35;36]. As a result, rapid or large decreases in blood pressure may lead to a decrease in cerebral blood flow [37-39], which increases the risk of repetitive transient hypoperfusion of the brain resulting in ischemic brain damage and impaired neural control [40-43]. As neural control is involved in standing balance, this can result in impaired standing balance. This hypothesis is supported by previous findings of a negative association between ischemic brain damage quantified by white matter hyperintensities on magnetic resonance imaging (MRI) and the ability to maintain balance during specific conditions [42;44-46]. Furthermore, white matter hyperintensities were associated with higher CoP movement which is assumed to reflect poor quality of standing balance [47]. An alternative explanation may be a common-cause, i.e. impaired blood pressure regulation and impaired standing balance both are the result of the same factor, e.g. comorbidities, neurodegeneration or cerebrovascular lesions without a direct causal relation. Further research is needed to get better insight in the causal underlying mechanisms between blood pressure and standing balance.

The association between blood pressure decrease and the ability to maintain standing balance became apparent in standing positions with eyes closed. During this specific standing condition, the nervous system has to compensate for the elimination of visual information by use of sensory reweighting [48]. The sensory systems deteriorates with increasing age [49] and elderly have to rely on less accurate and reliable sensory information in case of elimination of the visual information, which makes standing with eyes closed more difficult. Besides the sensory systems involved in standing balance, sensory systems involved in blood pressure regulation, e.g. baroreceptors, deteriorate with age and age related diseases [50;51]. This is a possible explanation for the fact that the association between blood pressure decrease and the ability to maintain standing balance was only present in standing positions with eyes closed.

The association between blood pressure decrease and standing balance was detected using objective (i.e. the ability to maintain standing balance) as well as subjective measures of standing balance (i.e. self-reported impaired standing balance and history of falls). Comparable results for the ability to maintain balance and falls were found, as impaired standing balance is a risk factor for falls[13;19;20]. Comparable results between the ability to maintain balance and self-reported impaired balance confirm the relation between the subjective and objective measures of standing balance and strengthen the clinical value of the outcome.

No association was observed between supine blood pressure and the ability to maintain standing balance, self-reported impaired standing balance or history of falls. However, previous research showed that hypertension, measured in sitting position, was associated with an increase in brain damage and concurrent impairments in mobility, cognition and mood in elderly with a mean age of 75 years [40;42]. These conflicting results might be explained by age differences. In the very old (aged above 85 years) high blood pressure is associated with better survival, mediated by poor health status and frailty in the subject with lower blood pressure. In contrast, high blood pressure in a younger population (mean age 74 years) is associated with poor survival[18]. It is unknown if there is a certain age or state of cardiovascular disease in which a high blood pressure becomes of benefit due to better perfusion. A next step would be to focus on different age groups, which will be of clinical added value. This requires large study sample sizes.

In this study, the largest decrease in blood pressure was found during the first 60 seconds after postural change by use of continuous blood pressure measurements, which is in accordance with previous research [12]. Using intermittent blood pressure measurements only one time point is recorded, which has as consequence that peak blood pressure decreases may be missed. In this study, OH determined with intermittent measurements was present in 15 percent of the patients compared to 57 percent of the patients when OH was established with continuous measurements, which is in accordance with previous findings [52]. Seventy-nine percent of these elderly were established as OH patients only with continuous measurements. The use of intermittent measurements may therefore underestimate the number of OH patients.

Strength of this study was the unique study population of elderly patients. No exclusion criteria were applied. The population is representative for the community-dwelling elderly visiting the geriatric outpatient clinic. Furthermore, the use of continuous blood pressure measurements provided additional information about the blood pressure during the first 60 seconds after postural change and made it possible to include iOH in the analyses. As blood pressure was measured during 3 minutes after postural change, delayed OH, which occurs ten minutes or more after postural change [53], could not be measured. Limitation of this study is the cross-sectional design, which makes it impossible to draw conclusions about a causal relation between blood pressure regulation and standing balance. Furthermore, history of falls was measured using questionnaires which could result in recall bias. Despite the lower number of patients with continuous blood pressure measurements, we were able to find valuable associations of blood pressure decrease with standing balance.

Conclusion

In conclusion, only by using continuous blood pressure measurements as a proxy for blood pressure regulation, associations with the ability to maintain standing balance, self-reported impaired standing balance and history of falls were found. The fact that previous associations could not be detected with intermittent blood pressure measurements, demonstrates the additional value of continuous over intermittent blood pressure measurements in routine geriatric assessment.

Supplementary material

Supplementary Table 1. Blood pressure measures determined with continuous measurements in subgroup of elderly patients who underwent additional continuous blood pressure measurements (n = 58).

	Subgroup (n = 58)
Supine blood pressure [a]	
Systolic blood pressure, mmHg	152 (27)
Diastolic blood pressure, mmHg	75.9 (14.5)
Blood pressure decrease after postural change	
Orthostatic hypotension, continuously measured; n (%) [b]	33 (56.9)
Systolic blood pressure decrease, mmHg [c]	
0 to 15 seconds	29.0 (25.0)
15 to 60 seconds	17.4 (24.1)
60 to 180 seconds	8.4 (23.2)
Diastolic blood pressure decrease, mmHg [c]	
0 to 15 seconds	15.0 (15.5)
15 to 60 seconds	7.48 (14.35)
60 to 180 seconds	4.40 (11.82)

All variables are presented as mean with standard deviation unless indicated otherwise. [a] Mean blood pressure in supine position of the last 60 seconds before postural change. [b] Orthostatic hypotension defined as decrease in systolic blood pressure of ≥ 40 mmHg or diastolic blood pressure of ≥ 20 mmHg during 15 seconds after postural change or decrease in systolic blood pressure of ≥ 20 mmHg or diastolic blood pressure of ≥ 10 mmHg between 15 and 180 seconds after postural change. [c] Supine blood pressure minus lowest blood pressure measured in the time period after postural change.

Supplementary Table 2. Association between blood pressure measures determined with intermittent measurements and reported impaired standing balance and history of falls in all elderly patients (n = 197).

	Reported impaired balance		History of falls	
	OR (95% CI)	p	OR (95% CI)	p
Supine blood pressure [a]				
Systolic BP	1.01 (1.00-1.03)	.05	1.01 (1.00-1.03)	.04
Diastolic BP	1.01 (0.98-1.04)	.51	1.00 (0.97-1.03)	.82
Blood pressure decrease after postural change				
Orthostatic hypotension [b]	2.17 (0.95-4.95)	.06	1.70 (0.70-4.16)	.24
Systolic BP decrease [c]				
1 minute	1.02 (1.00-1.03)	.13	1.01 (0.99-1.03)	.20
3 minutes	1.01 (0.99-1.04)	.16	1.01 (0.99-1.03)	.29
Diastolic BP decrease [c]				
1 minute	1.02 (0.98-1.07)	.31	1.02 (0.97-1.06)	.47
3 minutes	1.01 (0.97-1.05)	.63	1.01 (0.97-1.05)	.71

All data are from binary logistic regression analysis with adjustments for age and sex. Reported impaired standing balance: 0 = never or sometimes, 1 = regularly or always. History of falls: 0 = no falls, 1 = falls. [a] Measured after at least 5 minutes in supine position. [b] Orthostatic hypotension 0 = absent, 1 = present defined as a decrease in systolic blood pressure of ≥ 20 mmHg or diastolic blood pressure of ≥ 10 mmHg during 3 minutes after postural change. [c] Supine blood pressure minus blood pressure at 1 or 3 minutes after postural change.

Supplementary Table 3. Association between blood pressure measures determined with continuous measurements and the ability to maintain standing balance in subgroup of elderly patients who underwent additionally continuous blood pressure measurements (n = 58).

	Eyes open conditions						Eyes closed conditions					
	Side-by-side		Semi-tandem		Tandem		Side-by-side		Semi-tandem		Tandem	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Supine blood pressure [a]												
Systolic BP	1.01 (0.99-1.04)	.33	1.00 (0.98-1.01)	.65	1.00 (0.99-1.02)	.79	1.00 (0.98-1.01)	.91	1.00 (0.98-1.01)	.42		
Diastolic BP	1.04 (0.99-1.10)	.15	1.01 (0.97-1.04)	.76	1.00 (0.90-1.03)	.93	1.03 (0.99-1.07)	.13	1.01 (0.98-1.04)	.59		
Blood pressure decrease after postural change												
Orthostatic hypotension[b]	1.32 (0.25-7.01)	.75	1.10 (0.37-3.29)	.87	0.82 (0.31-2.17)	.69	0.66 (0.25-1.72)	.39	0.33 (0.12-0.89)	**.03**	n.a.	
Systolic BP decrease [c]												
1 minute	1.04 (1.00-1.08)	.07	1.01 (0.98-1.03)	.51	1.01 (0.98-1.03)	.60	1.01 (0.99-1.03)	.48	1.00 (0.98-1.02)	.73		
3 minutes	1.02 (0.98-1.07)	.34	1.00 (0.98-1.03)	.86	1.01 (0.98-1.03)	.64	1.00 (0.98-1.03)	.84	0.99 (0.97-1.02)	.60		
Diastolic BP decrease [c]												
1 minute	1.05 (0.96-1.14)	.32	1.05 (0.99-1.11)	.09	1.00 (0.96-1.05)	.88	1.03 (0.98-1.08)	.32	0.99 (0.95-1.04)	.75		
3 minutes	1.02 (0.93-1.12)	.63	1.01 (0.96-1.07)	.63	1.01 (0.96-1.05)	.82	0.99 (0.94-1.04)	.57	0.99 (0.95-1.03)	.63		

All data are from logistic regression analysis with adjustments for age and sex. Ability to maintain balance: 0 = unable, 1 = able. [a] Mean blood pressure in supine position of the last 60 seconds before postural change. [b] Orthostatic hypotension: 0 = absent, 1 = present; defined as a decrease in systolic blood pressure of ≥ 40 mmHg or in diastolic blood pressure of ≥ 20 mmHg during 15 seconds after postural change or a decrease in systolic blood pressure of ≥ 20 mmHg or diastolic blood pressure of ≥ 10 mmHg between 15 and 180 seconds after postural change. [c] Supine blood pressure minus lowest blood pressure measured in the time period after postural change. n.a. = not applicable, number of elderly patients able to maintain this balance condition is less than 5.

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Part II

Assessment of standing balance


balance
disturbances
deterioration
compensation
control
training
steps
sensory
used
impaired
strategies
systems
elderly
cognitive
underlying
assessment
movement
information
interventions
clinical
joint
motor
reduced
increase
activities
measure
combined
different
task
needed
loop
effect
specific
nervous
identification
proprioception
possible
power
efferent
tests
time
maintain
muscle
conditions
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pushes
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elimination
comprises
population
individual
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external
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alternative
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optimization
fail
angles
impact

Chapter 6

Age-related differences in quality of standing balance using a composite score

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Abstract

Age related differences in standing balance are not detected by testing the ability to maintain balance. Quality of standing balance might be more sensitive to detect age related differences. To study age related differences in quality of standing balance, Center of Pressure (CoP) movement was evaluated using a wide range of CoP parameters in several standing conditions in healthy young and old participants.

In 35 healthy young (18 to 30 years) and 75 healthy old (70 to 80 years) participants, CoP movement was assessed in eight standing conditions on a force plate, including side-by-side, one-leg, semi-tandem, and tandem stance, both with eyes open and eyes closed. Direction specific CoP composite scores were calculated from standardized single CoP parameters (mean amplitude, amplitude variability, mean velocity, velocity variability and range), in anterior-posterior (AP) and medial-lateral (ML) direction. Linear regression analysis was used to detect age related differences in single CoP parameters and composite scores, adjusted for gender, height and weight.

Overall, single CoP parameters were higher in old participants compared to young, but no single CoP parameter consistently demonstrated the largest effect size for all standing conditions. Age related differences were demonstrated for CoP composite scores in AP direction (tandem eyes open; semi-tandem eyes closed) ($p<0.001$). CoP composite scores in ML direction were consistently higher for all standing conditions in old compared to young participants ($p<0.001$).

CoP composite scores in ML direction were the most consistent parameters to detect age related differences in quality of standing balance in healthy participants and might be of clinical value to detect subtle changes in quality of standing balance.

Introduction

Diminished ability to maintain standing balance at old age results in an increased risk of falls and fractures [1]. The ability to maintain standing balance depends on the quality of balance, which is predominantly determined by integrated functioning of sensory systems (vestibular system, proprioception and vision), muscle properties and neural control [2]. Changes in quality of standing balance may be the result of degeneration of these underlying systems, by cumulative tissue damage as occurs with aging, specific diseases and medication use [3-6]. In clinical practice, the ability to maintain balance is tested using several standing conditions [7]. Difficulty of standing conditions can be varied by standing in several positions on firm or compliant ground, or standing with eyes open or eyes closed and are used as functional tests for sensory pathways by eliminating sensory information [8;9]. Assessment of the ability to maintain balance in several standing conditions is part of clinical observational tests such as the Berg Balance Scale [10], Tinetti balance test [11] and the Short Physical Performance Battery [12], which are predictive of falls and mortality in elderly [13;14]. In contrast to the dichotomous assessment of the ability to maintain standing balance, assessment of the quality of standing balance during maintenance of standing balance results in a continuous parameter and is potentially a sensitive method to detect early stage changes of the underlying systems involved in standing balance due to for example aging [15]. The quality of standing balance may thus contribute to the assessment and understanding of the role of degeneration of the underlying systems in impaired standing balance and eventually falling.

Loss of standing balance occurs when the body's center of mass (CoM) moves out of the base of support [16]. The CoM is controlled by corrective forces as response to disturbances. The changes in corrective forces can be measured by assessing Center of Pressure (CoP) movement, representing the location of the vertical ground reaction forces. CoP movement therefore represents the quality of standing balance [17]. CoP movement can be represented by parameters in anterior-posterior (AP) or medial-lateral (ML) direction [18]. With CoP parameters, subtle changes in quality of balance can be detected in individuals who still have the ability to maintain standing balance [19]. Quality of standing balance in ML direction might be more important than AP direction as balance in ML direction is needed for stepping out in case of falling (i.e. compensatory stepping) [20;21]. Previous research focusing on age related differences in CoP movement is limited by methodological issues, such as consistency in the use of CoP parameters, differences in used standing conditions and sample size of well characterized participants, resulting in conflicting results [18;19;22-26]. Knowledge on the most sensitive CoP parameter in combination with the most sensitive standing condition is required to evaluate the potential of quality of standing balance as an outcome parameter in clinical practice.

In this study we evaluated age related differences in quality of standing balance in a group of healthy young and old participants, by comparing a comprehensive set of CoP parameters assessed during a range of standing positions with both eyes open and eyes closed, to detect the most sensitive combination with respect to age and the most consistent one over conditions.

Methods

Study design

This study comprises 35 young (aged 18 to 30 years) and 75 relatively healthy and cognitively active old participants (aged 70 to 80 years), recruited between July 2010 and March 2011 in Leiden, the Netherlands, as part of the European cohort study MYOAGE. Exclusion criteria were applied to select healthy and (cognitively) active participants, i.e. dependent living situation, low cognitive function, unable to walk a distance of 250 m, presence of morbidity (neurologic disorders; metabolic diseases; rheumatic diseases; recent malignancy; heart failure; severe chronic obstructive pulmonary disease ; haemocoagulative syndromes), use of specified medication (immunosuppressive drugs, insulin, anticoagulation), immobilization for one week during the last three months, and orthopedic surgery during the last two years or still causing pain or functional limitation. This study was approved by an independent ethics committee of the Leiden University Medical Center, Leiden, The Netherlands (P10.060). All participants gave their written informed consent.

Participant characteristics

A questionnaire was used to assess living situation, level of education, alcohol use, smoking, and experienced mobility difficulties. Living situation was defined as living without or with partner. Education level was grouped into low, moderate and high defined by basic school, high school and university, respectively. Excessive alcohol use was defined as an intake of more than 21 units per week for males or more than 14 units per week for females. Smoking was defined as current smoking. Experienced mobility difficulties were registered for specific activities (i.e. walking 1000 m, walking 250 m, walking stairs, walking across a room, bending to pick up an object) when the answer option 'always difficult' was marked on the question about how much difficulty was experienced during that specific activity.

Anthropometric data included height and body composition measured by dual-energy X-ray absorptiometry (DXA) (Hologic QDR 4500, Hologic Inc., Bedford, USA). Morbidities were registered including mild chronic obstructive pulmonary disease, hypertension, neoplasm in the past, and osteoarthritis. The use of medication was documented. The cognitive function was estimated with the Mini Mental State Examination (MMSE) and depressive symptoms were assessed by use of the Geriatric Depression Scale (GDS). Handgrip strength was measured using the Jamar dynamometer handle (Sammons Preston Inc, Bolingbrook, IL). Isometric knee extension torque was measured with a knee extension dynamometer chair (Forcelink B.V., Culemborg, the Netherlands). Walking speed was determined by a 6 minute walking test at normal pace.

Standing balance

Standing balance was assessed in several standing conditions, performed on a 6 DoF triangular force plate (Forcelink B.V., Culemborg, the Netherlands) consisting of six load cells (Revere Transducers Europe B.V., Breda, The Netherlands). Participants were instructed to stand as still as possible for 30 seconds or until loss of balance, i.e. stepping out, with the hands clasped in front of the body to avoid any arm sway. Four standing positions were performed both with eyes open and eyes closed, i.e. in total eight standing conditions, in a standardized order, namely side-by-side, one-leg, semi-tandem and tandem stance. For each condition, participants were allowed three attempts if standing balance was lost before the 30 seconds were completed. Rest periods of minimally 30 seconds were inserted between attempts. During side-by-side stance, participants were instructed to stand with the medial malleoli of both feet as closely together as possible; during one-leg stance participants were instructed to stand on the preferred leg, i.e. the leg the participant preferred when asked to stand on one leg; during semi-tandem stance, participants were standing with the medial side of the heel of the self-chosen foot touching the big toe of the other foot; during tandem stance, participants were standing with both feet in line while the heel of the self-chosen foot touched the toes of the other. All standing conditions were performed once, except side-by-side stance and one-leg stance both with eyes open and eyes closed, which were performed twice following the European protocol of the cohort study MYOAGE. During the conditions participants wore non-slip socks.

Quality of standing balance

Center of Pressure parameters

The quality of standing balance was assessed by measuring CoP movement. For all analyses, only successful trials (with 30 seconds completed) were used. Side-by-side stance data of two participants were missing due to technical errors. Force plate data were recorded with a sample frequency of 1 kHz. Data were digitally low pass filtered with a cut off frequency of 10 Hz. Data processing was performed using Matlab (The MathWorks, Natick, MA).

Reconstructions of CoP movement in AP and ML direction were calculated for 30 second periods out of the forces and moments measured with the force plate. From these coordinates time series were determined in AP and ML direction. The AP and ML time series were defined relative to the mean CoP by subtracting the mean CoP of the AP and ML time series [18]. Figure 1 shows an example of a time series in both AP and ML direction of one old and one young participant.

Out of each time series the following parameters were calculated. The mean amplitude represents the average distance from the mean CoP. The amplitude variability is the overall standard deviation. The range is determined by the maximal distance between any two points on the CoP path. The sum of the distances between consecutive points on the CoP path represents the path length. The path length normalized to the analysis time was used to calculate mean velocity and velocity variability. The mean frequency in AP and ML direction is the frequency of a sinusoidal oscillation with an average value of the mean amplitude and a total path length of total excursions [18].

In addition to the time series, the area of CoP movement was evaluated. The 95% confidence ellipse represents the area of the ellipse which covers the 95% confidence interval of CoP movement. The 95% sway area represents the size of CoP movement and was determined by calculating the area of a constructed circle with a radius of 95% of the largest amplitude (see Figure 1). The eccentricity is a parameter for the strength of the angle of the area of CoP movement. In case of a circle, the eccentricity equals zero and in case of a line it equals one.

Of the standing positions which were performed twice, i.e. side-by-side stance and one-leg stance, the parameters of the first and second trial were averaged for further analysis to reduce random noise and to obtain optimal parameter estimates.

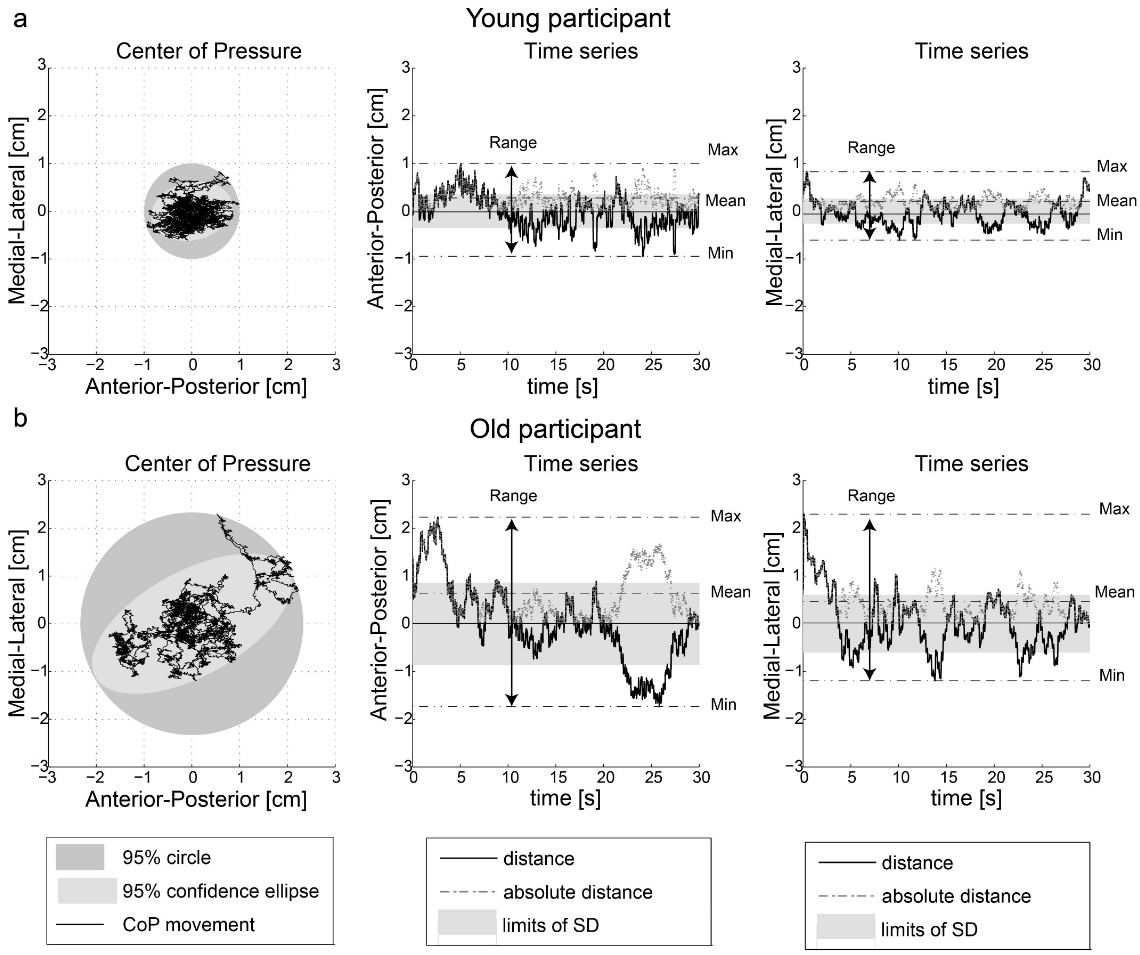

Figure 1. Representative example of Center of Pressure (CoP) movement and time series in anterior-posterior and medial-lateral direction with the calculated parameters of one young (a) and one old (b) participant in side-by-side stance with eyes open. In black the measured CoP movement is shown. In gray the absolute value of CoP movement is shown. Abbreviations: Max, maximum; Min, minimum; SD, standard deviation.

Center of Pressure composite scores

To combine several CoP parameters to one sensitive parameter representing quality of standing balance consistently over conditions, each CoP parameter was transformed into z-scores resulting in standardized CoP parameters with a mean of 0 and standard deviation of 1. A CoP composite score for the AP and ML direction was calculated by averaging the z-scores of the mean amplitude, amplitude variability, mean velocity, velocity variability and range. Path length was not taken into account as it represents the same as the mean velocity (i.e. path length divided by a constant analysis time). Mean frequency was also not taken into account as it was calculated from the included parameters mean amplitude and mean velocity.

Statistics

Participant characteristics with a Gaussian distribution are presented as mean and standard deviation. Otherwise, median and interquartile range or count and percentage are presented. To compare several CoP parameters, each CoP parameter was standardized into z-scores resulting in standardized CoP parameters with a mean of 0 and standard deviation of 1. Linear regression analysis was performed to test significant differences in CoP parameters and CoP composite scores between young (coded with 0) and old participants (coded with 1), with adjustments for gender, height and weight. Because of the number of dependent variables tested, a Bonferroni correction was applied to avoid type I errors. P values below 0.002 were considered statistically significant. The statistical package SPSS version 17 (SPSS Inc., Chicago, USA) was used for analyzing the data. Graphs were made with GraphPad Prism 5 (GraphPad Software, Inc., La Jolla, USA).

Results

Participant characteristics

Characteristics of the group of healthy young and healthy old participants are presented in Table 1.

Ability to maintain standing balance

The ability to maintain balance in several standing conditions is shown in Figure 2. All young and old participants were able to maintain balance 30 seconds in side-by-side stance both with eyes open and eyes closed and semi-tandem stance with eyes open. For the other standing conditions, the percentage of old participants able to maintain standing balance was lower than the percentage of young participants. With eyes open, 100% (n=35) young participants and 69% (n=52) old participants successfully maintained balance in one-leg stance and 100% (n=35) young participants and 93% (n=70) of old participants in tandem stance. With eyes closed, these numbers were 43% (n=15) for young participants and 0% (n=0) for old participants in one- leg stance, 100% (n=35) for young and 92% (n=69) for old participants in semi-tandem and 77% (n=27) for young and 7% (n=5) for old participants in tandem stance.

Table 1. Participant characteristics stratified by age group.

	Young (n=35)	Old (n=75)
Age, years	21.4 (2.7)	74.2 (3.1)
Females, n (%)	20 (57.1)	36 (48.0)
Living with partner, n (%)	4 (11.4)	54 (72.0)
Highly educated, n (%)	32 (91.4)	52 (69.3)
Excessive alcohol use *, n (%)	5 (14.3)	6 (8.0)
Current smoking, n (%)	4 (11.4)	9 (12.0)
Anthropometry		
Height, m	1.77 (0.09)	1.72 (0.08)
Weight, kg	73.7 (11.8)	74.6 (11.1)
BMI, kg/m^2	23.5 (3.1)	25.2 (3.3)
Body composition		
Lean mass, kg	55.9 (10.6)	54.2 (8.8)
Fat, %	23.7 (8.7)	27.4 (7.4)
Health characteristics		
Sum score of diseases †, median (IQR)	0 (0-0)	0 (0-1)
Number of medications ‡, median (IQR)	1 (0-1)	1 (0-2)
MMSE, median (IQR)	29 (29-30)	29 (29-30)
GDS, median (IQR)	0 (0-0)	0 (0-1)
Physical function		
Handgrip strength, kg	41.7 (10.5)	33.9 (8.0)
Knee extension torque, Nm	238 (78)	147 (46)
Walking speed, m/s	1.4 (0.1)	1.3 (0.1)
Self-assessed mobility §		
Walking 1000 m, n (% always difficult)	0 (0)	0 (0)
Walking 250 m , n (% always difficult)	0 (0)	0 (0)
Walking stairs, n (% always difficult)	0 (0)	2 (2.7)
Walking across room , n (% always difficult)	0 (0)	2 (2.7)
Bending to pick up an object , n (% always difficult)	0 (0)	3 (4.0)

Data are presented in mean and standard deviation, unless otherwise indicated. * For males >21 units and for females >14 units per week. † Sum score of thyroid disease, non insulin dependent diabetes mellitus, osteoarthritis, hypertension and other diseases. ‡ Number of oral and inhaled medication. § Answer from questionnaire to how much difficulties were experienced during these activities, with answer options: no problems, a bit difficult, or always difficult. Abbreviations: MMSE, Mini Mental State Examination; GDS, Geriatric Depression Scale; IQR, inter quartile range.

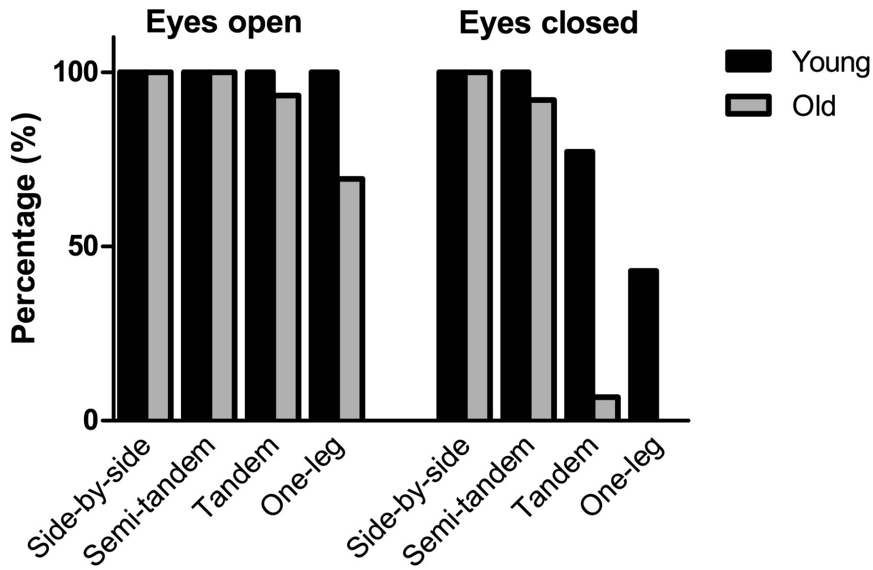

Figure 2. Ability to maintain balance in several standing positions with eyes open and eyes closed in young and old participants.

Age related differences in quality of standing balance

Center of Pressure parameters

Figure 3a shows the standardized differences between age groups of all standardized CoP parameters for all standing positions with eyes open. In side-by-side stance no age related differences were observed in AP direction. Old participants had higher values in ML direction for the mean amplitude ($p<0.001$) amplitude variability ($p<0.001$) and range ($p<0.001$). In one-leg stance, old participants had higher values for mean velocity ($p=0.001$) in AP direction, and for all CoP parameters ($p<0.001$) in ML direction. In semi-tandem stance, no age related differences were detected in AP direction. Old participants had higher values in ML direction for the mean velocity ($p<0.001$), velocity variability ($p<0.001$) and range ($p<0.001$). Age related differences in tandem stance were present for amplitude variability ($p=0.001$) and range ($p<0.001$) in AP direction and for all CoP parameters in ML direction ($p<0.001$). Supplementary Table 1 represents the mean and standard error stratified by age group of all CoP parameters for all standing positions with eyes open.

Figure 3b shows the standardized differences between age groups of all standardized CoP parameters for all standing positions with eyes closed. In side-by-side stance, only the range in AP direction ($p<0.001$) was higher in old participants compared to young participants. The majority of CoP parameters in ML direction were higher in old participants ($p<0.001$) compared to young participants; mean frequency ($p=0.02$) was an exception. In semi-tandem stance, old participants had higher values for the majority of CoP parameters ($p<0.002$) in both directions except for the mean amplitude (p=0.005) in AP direction and the mean frequency in both directions (p=0.16 and p=0.79, respectively). In tandem stance, higher values compared to young participants were observed in ML direction for most CoP parameters (p<0.001), except mean frequency (p=0.34). Supplementary Table 2 represents the mean and standard error stratified by age group of all CoP parameters for all standing positions with eyes closed.

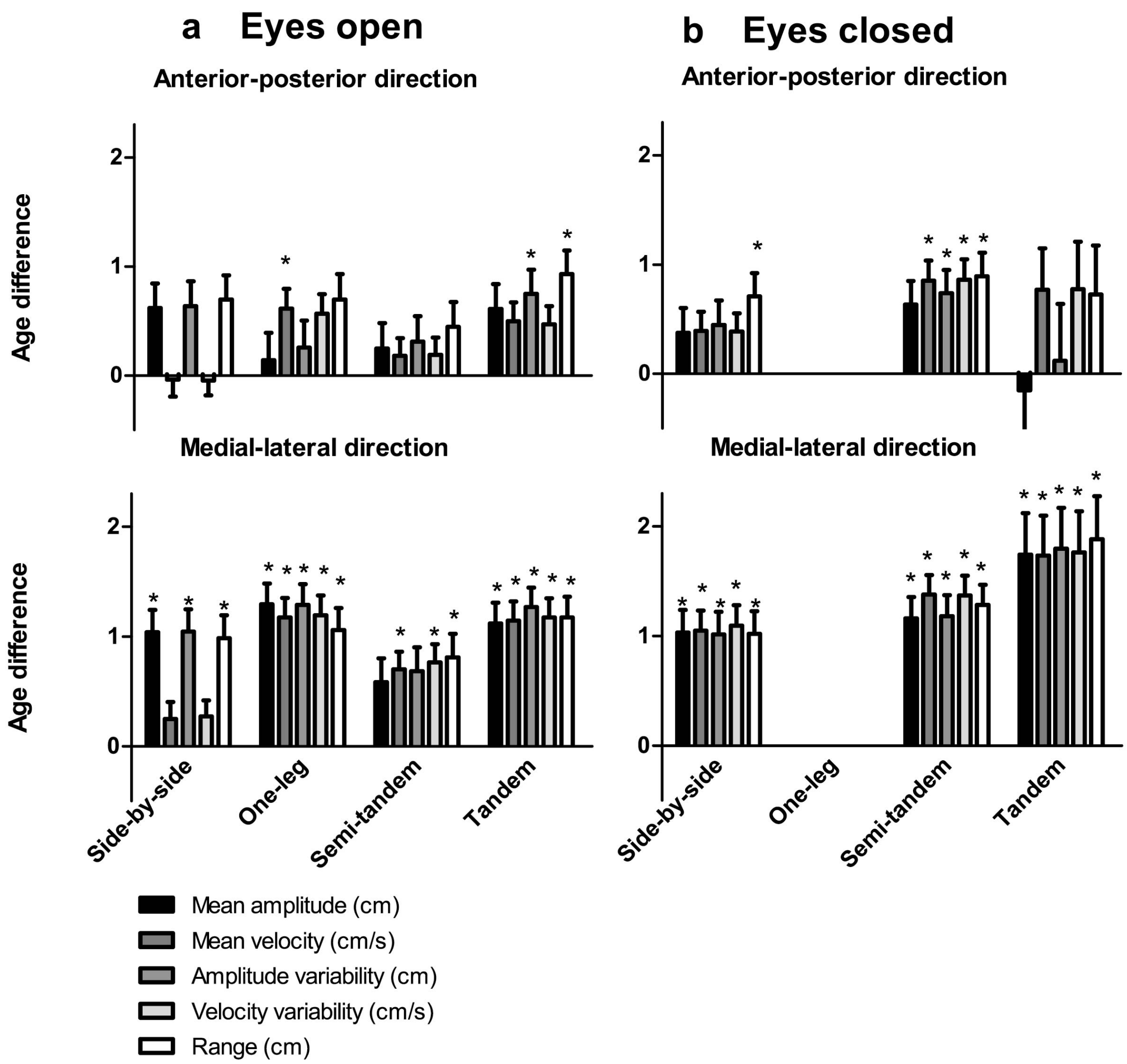

Figure 3. Standardized differences between young and old participants of quality of standing balance, represented by several Center of Pressure parameters, in all standing positions with eyes open (a) and with eyes closed (b) presented in betas and standard errors, computed with linear regression analyses with adjustments for gender, height and weight. Independent variable was age group (young=0, old=1). *=P value <0.002.

Comparing the effect sizes of the single CoP parameters, the order of single CoP parameters with the largest effect size was not consistently over all standing conditions. Overall, the effect sizes of CoP parameters, and therewith the age related differences, were larger in eyes closed conditions compared with eyes open conditions. Effect sizes in ML direction were largest.

Center of Pressure composite scores

In Table 2 the age related differences in CoP composite scores are shown for all standing conditions. In AP direction old participants had higher CoP composite score compared to young in tandem stance with eyes open ($p<0.001$) and in semi-tandem stance with eyes closed ($p<0.001$). In ML direction this difference in CoP composite score was observed in all standing conditions ($p<0.001$). Comparing the CoP composite score in different directions, the effect sizes were largest in ML direction in all standing conditions.

Table 2. Differences in quality of standing balance, represented by Center of Pressure composite scores, between young and old participants in several standing positions with eyes open and eyes closed.

	Side-by-side		One-leg		Semi-tandem		Tandem	
	Beta (SE)	p	Beta (SE)	p	Beta (SE)	p	Beta (SE)	p
Eyes open								
AP	0.37 (0.15)	.013	0.45 (0.19)	.02	0.28 (0.16)	.08	0.65 (0.16)	**<.001**
ML	0.72 (0.14)	**<.001**	1.20 (0.17)	**<.001**	0.71 (0.16)	**<.001**	1.18 (0.16)	**<.001**
Eyes closed								
AP	0.46 (0.17)	.007	n.a.	n.a.	0.79 (0.18)	**<.001**	0.45 (0.38)	.25
ML	1.04 (0.18)	**<.001**	n.a.	n.a.	1.28 (0.17)	**<.001**	1.78 (0.32)	**<.001**

Differences are given in betas with standard errors, computed with linear regression analyses with adjustments for gender, height and weight. Dependent variable was age group (young=0, old=1). Center of Pressure composite scores are the mean of z scores of mean amplitude, amplitude variability, range, mean velocity, velocity variability. Abbreviations: AP, anterior-posterior direction; ML, medial-lateral direction. Bold indicates significant p-values (< 0.002).

Discussion

Higher values of CoP parameters were observed in healthy old compared to young participants, indicating age related differences in quality of standing balance. Overall, largest age related differences between young and old participants were observed in ML direction for all standing conditions. Comparing single CoP parameters in the assessment of age differences, no single CoP parameter showed consistently the largest effect size for all standing conditions, due to differences in standing conditions in which different strategies are needed to maintain balance. Introducing a CoP composite score combines the single CoP parameters and gives the advantage that the CoP composite score in ML direction is consistently associated with age in all standing conditions, and shows the largest effect size. In more difficult standing conditions, age related differences were demonstrated in both (AP and ML) directions. Measuring CoP movement as parameter for quality of standing balance instead of the ability to maintain standing balance overcomes the plateau effect in this study. Therefore, assessment of CoP composite scores might be of additive value to detect subtle changes in quality of standing balance in clinical care.

Previous studies have described age related differences in CoP parameters in several standing conditions in healthy and community-dwelling elderly as compared to young participants [18;23;24;26-29]. In line with the present study, CoP parameters in ML direction were suggested to detect age related differences in quality of standing balance [22;30], however not in all studies [18]. Others found that mean amplitude [23] or mean velocity [18;23;27;29] in AP direction, instead of ML direction, was the most consistent CoP parameter to detect age related differences. Conflicting results might be due to the use of less difficult standing conditions in aforementioned studies. In accordance with our study, previous research showed that the effect size for age related differences in CoP parameters is larger in more difficult standing conditions [28]. Furthermore, our study indicated that no single CoP parameter consistently showed the largest effect size in all standing conditions.

In this study, age related differences in ML direction were largest and became larger in more difficult standing positions. ML direction is thought to be more important than AP direction for stepping out in case of falling (i.e. compensatory stepping) [20;21] and as a predictor for falling [31;32]. Increasing the base of support by standing more widely is a compensatory mechanism for changes in quality of standing balance in ML direction. This increases stability margins and reduces lateral rotation around the ankle joints, which requires less active postural responses [33;34]. In this study, several standing positions were tested with narrowing the base of support in side-by-side, semi-tandem and tandem stance compared to normal stance. This requires increased corrective forces by the ankle muscles in ML direction [35]. In elderly, these corrective forces could be compromised due to lower muscle strength, poorer proprioception, visual and vestibular function, or a higher reaction time [36]. Additional hip strategy, i.e. movement of the trunk around the hip joint, is needed to prevent falling [37]. Since the force production around the hip joint to regulate lateral trunk movement could also be impaired in elderly [38], this will result in increased CoP movement in ML direction [9;39]. This may explain why age related differences are most prominent in ML direction in standing positions with a narrowed base of support.

Age related differences were more prominent in standing positions with eyes closed as compared to eyes open. With eyes closed, the nervous system has to integrate information from the vestibular system and proprioception to generate proper corrective forces to maintain standing balance. With increasing age the functioning of the vestibular and proprioceptive systems is known to decline resulting in conflicting or inaccurate sensory information [2;30]. Adaptation of the nervous system to cope with these changes is called sensory reweighting. Inaccurate sensory information will be used less and accurate sensory information will be used more by the nervous system to generate corrective forces to maintain standing balance [40]. Additionally, slowing or a defect of the central information processing could reduce the ability to compensate for less sensory information by closing the eyes [41;42]. This will result in a change in quality of standing balance and may explain the larger differences between young and old participants in standing positions with eyes closed.

Strength of this study is the comprehensive way in which CoP parameters in relation to standing conditions were compared resulting in a composite score to detect age related differences. Selection of a healthy and cognitively active, well phenotyped group of young and old participants ensured that detected differences in CoP movement could be mainly attributed to chronological age. As consequence, the results of this study could not be generalized to the whole population. A risk of type II errors is acknowledged, as the number of included participants was not based on power calculation specific for the outcome variables of this particular study. The cross-sectional design of the study is a limitation, which makes causal inference impossible. Not all standing conditions were performed twice. Previous studies recommended to average results over trials to increase reliability [43;44]. Although reliability in our study generally showed to be acceptable, we averaged data over trials when available to obtain optimal parameter estimates. However, in clinical care it may be preferable to perform the balance conditions only once, due to lack of time and fatigue of a patient. Absence of systematic difference between trials support this practice acknowledging acceptance of random noise.

Conclusion

In conclusion, CoP composite score in ML direction consistently detect differences in quality of standing balance in healthy elderly compared to young. Further investigations should focus on other populations such as elderly making use of clinical care in which a composite score could be used as risk predictor. Furthermore, the additional value of the quality of standing balance on clinical outcome parameters such as physical performance should be examined.

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Supplementary material

Supplementary Table 1. Quality of standing balance, represented by Center of Pressure parameters, in young and old participants in several standing positions with eyes open.

	Side-by-side			One leg			Semi-tandem			Tandem		
	Young	Old	p	Young	Old	p	Young	Old	p	Young	Old	p
Anterior-Posterior direction												
Mean amplitude (cm)	0.39 (0.02)	0.45 (0.02)	.007	0.64 (0.03)	0.67 (0.02)	.59	0.40 (0.03)	0.45 (0.03)	.29	0.48 (0.03)	0.63 (0.03)	.008
Mean velocity (cm/s)	6.34 (0.19)	6.35 (0.14)	.79	6.79 (0.19)	7.82 (0.17)	**.001**	6.32 (0.18)	6.52 (0.14)	.25	6.91 (0.19)	7.57 (0.14)	.005
Amplitude variability (cm)	0.48 (0.03)	0.56 (0.02)	.005	0.79 (0.04)	0.85 (0.02)	.31	0.50 (0.03)	0.56 (0.03)	.18	0.58 (0.03)	0.80 (0.04)	**.001**
Velocity variability (cm/s)	8.76 (0.24)	8.75 (0.19)	.74	9.31 (0.25)	10.55 (0.22)	.002	8.73 (0.23)	8.98 (0.19)	.24	9.39 (0.24)	10.20 (0.19)	.006
Range (cm)	2.49 (0.11)	2.84 (0.09)	.002	4.15 (0.19)	4.92 (0.14)	.004	2.61 (0.15)	3.14 (0.20)	.06	3.18 (0.15)	4.84 (0.23)	**<.001**
Mean frequency (Hz)	3.11 (0.13)	2.80 (0.12)	.02	2.04 (0.10)	2.14 (0.06)	.81	3.10 (0.16)	3.03 (0.16)	.54	2.83 (0.16)	2.43 (0.10)	.03
Medial-Lateral direction												
Mean amplitude (cm)	0.31 (0.01)	0.38 (0.01)	**<.001**	0.41 (0.01)	0.59 (0.02)	**<.001**	0.41 (0.02)	0.47 (0.02)	.008	0.40 (0.02)	0.60 (0.02)	**<.001**
Mean velocity (cm/s)	4.22 (0.12)	4.43 (0.08)	.11	4.89 (0.13)	6.42 (0.14)	**<.001**	4.28 (0.12)	4.80 (0.08)	**<.001**	4.58 (0.11)	6.00 (0.13)	**<.001**
Amplitude variability (cm)	0.38 (0.02)	0.47 (0.01)	**<.001**	0.51 (0.02)	0.73 (0.02)	**<.001**	0.51 (0.02)	0.60 (0.02)	.002	0.48 (0.01)	0.74 (0.02)	**<.001**
Velocity variability (cm/s)	5.56 (0.15)	5.83 (0.10)	.06	6.50 (0.17)	8.58 (0.18)	**<.001**	5.62 (0.15)	6.38 (0.11)	**<.001**	6.17 (0.15)	8.07 (0.17)	**<.001**
Range (cm)	2.06 (0.07)	2.52 (0.07)	**<.001**	2.80 (0.08)	3.74 (0.12)	**<.001**	2.63 (0.10)	3.43 (0.14)	**<.001**	2.72 (0.10)	3.89 (0.11)	**<.001**
Mean frequency (Hz)	2.64 (0.12)	2.24 (0.08)	**<.001**	2.19 (0.07)	1.98 (0.05)	**.001**	1.93 (0.09)	1.92 (0.06)	.55	2.15 (0.09)	1.85 (0.05)	**<.001**
CoP path												
Sway area (ellipse) (cm/s)	0.11 (0.01)	0.16 (0.01)	**<.001**	0.25 (0.02)	0.39 (0.02)	**<.001**	0.15 (0.01)	0.22 (0.02)	.02	0.17 (0.01)	0.38 (0.02)	**<.001**
Sway area (circle) (cm/s)	0.24 (0.02)	0.35 (0.02)	**<.001**	0.64 (0.07)	0.94 (0.07)	.05	0.32 (0.03)	0.63 (0.14)	.09	0.44 (0.04)	1.00 (0.10)	**.001**
Eccentricity	0.74 (0.02)	0.71 (0.01)	.01	0.76 (0.02)	0.64 (0.02)	**<.001**	0.80 (0.02)	0.71 (0.01)	**.001**	0.68 (0.02)	0.69 (0.02)	>.99

Data are given in mean and standard error for all successful completed trials. p = p-value adjusted for gender, height and weight. Bold indicates significant p-values (< 0.002).

Supplementary Table 2. Quality of standing balance, represented by Center of Pressure parameters, in young and old participants in several standing positions with eyes closed.

	Side-by-side			One leg			Semi-tandem			Tandem		
	Young	Old	p	Young	Old	p	Young	Old	p	Young	Old	p
Anterior-Posterior direction												
Mean amplitude (cm)	0.56 (0.03)	0.61 (0.02)	.10	0.95 (0.05)	n.a.	n.a.	0.62 (0.04)	0.76 (0.03)	.005	0.93 (0.09)	0.83 (0.08)	.78
Mean velocity (cm/s)	6.60 (0.19)	7.09 (0.15)	.03	8.30 (0.19)	n.a.	n.a.	6.80 (0.19)	8.21 (0.20)	**<.001**	8.05 (0.22)	9.01 (1.05)	.05
Amplitude variability (cm)	0.69 (0.04)	0.77 (0.03)	.05	1.21 (0.06)	n.a.	n.a.	0.77 (0.04)	0.97 (0.04)	**.001**	1.16 (0.10)	1.12 (0.10)	.82
Velocity variability (cm/s)	9.02 (0.26)	9.63 (0.20)	.02	11.67 (0.29)	n.a.	n.a.	9.25 (0.25)	11.15 (0.28)	**<.001**	11.13 (0.50)	12.47 (1.45)	.09
Range (cm)	3.54 (0.17)	4.36 (0.15)	**.001**	7.28 (0.47)	n.a.	n.a.	4.18 (0.20)	6.00 (0.31)	**<.001**	6.91 (0.83)	8.14 (1.21)	.12
Mean frequency (Hz)	2.36 (0.13)	2.25 (0.09)	.22	1.59 (0.07)	n.a.	n.a.	2.14 (0.12)	2.04 (0.07)	.16	1.82 (0.14)	1.97 (0.23)	.90
Medial-Lateral direction												
Mean amplitude (cm)	0.53 (0.03)	0.67 (0.02)	**<.001**	0.89 (0.03)	n.a.	n.a.	0.75 (0.03)	1.08 (0.04)	**<.001**	0.93 (0.03)	1.22 (0.02)	**<.001**
Mean velocity (cm/s)	4.56 (0.14)	5.53 (0.11)	**<.001**	7.17 (0.26)	n.a.	n.a.	5.13 (0.13)	7.93 (0.24)	**<.001**	6.64 (0.17)	8.68 (0.59)	**<.001**
Amplitude variability (cm)	0.66 (0.03)	0.85 (0.02)	**<.001**	1.08 (0.03)	n.a.	n.a.	0.94 (0.04)	1.34 (0.05)	**<.001**	1.14 (0.04)	1.49 (0.03)	**<.001**
Velocity variability (cm/s)	6.06 (0.18)	7.43 (0.15)	**<.001**	9.71 (0.33)	n.a.	n.a.	6.85 (0.18)	10.83 (0.35)	**<.001**	9.18 (0.24)	11.95 (0.74)	**<.001**
Range (cm)	3.60 (0.18)	4.70 (0.15)	**<.001**	5.16 (0.17)	n.a.	n.a.	5.02 (0.19)	7.01 (0.22)	**<.001**	5.49 (0.16)	7.24 (0.46)	**<.001**
Mean frequency (Hz)	1.65 (0.07)	1.54 (0.04)	.02	1.45 (0.05)	n.a.	n.a.	1.27 (0.06)	1.33 (0.03)	.79	1.30 (0.05)	1.26 (0.09)	.34
CoP path												
Sway area (ellipse) (cm/s)	0.29 (0.03)	0.42 (0.03)	**.001**	0.83 (0.06)	n.a.	n.a.	0.44 (0.04)	0.84 (0.06)	**<.001**	0.85 (0.10)	1.03 (0.08)	.21
Sway area (circle) (cm/s)	0.61 (0.06)	0.97 (0.06)	**.001**	1.95 (0.28)	n.a.	n.a.	1.01 (0.08)	2.07 (0.20)	**<.001**	2.33 (0.74)	3.54 (1.24)	.12
Eccentricity	0.68 (0.02)	0.62 (0.01)	.01	0.59 (0.03)	n.a.	n.a.	0.76 (0.02)	0.75 (0.01)	.77	0.68 (0.02)	0.67 (0.07)	.96

Data are given in mean and standard error for all successful completed trials. p = p-value adjusted for gender, height and weight. Bold indicates significant p-values (< 0.002).

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Chapter 7

Ability to maintain standing balance a measure for impaired standing balance in routine geriatric clinical assessment

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Abstract

Balance is one of the most important factors for successful live trajectories. Evaluation of the value of the ability to maintain standing balance as a measure for impaired standing balance in routine geriatric clinical assessment.

In a cross-sectional cohort study, 197 community-dwelling elderly referred to a geriatric outpatient clinic of a middle-sized teaching hospital were included. Ability to maintain balance was assessed during six standing conditions, i.e. ten seconds of side-by-side, semi-tandem and tandem stance, with both eyes open and eyes closed and compared to experienced impaired balance in daily life and falls in the previous 12 months assessed by questionnaires as well as quality of standing balance by Center of Pressure (CoP) movement in medio-lateral (ML) direction during side-by-side stance. Logistic regression analyses were used to test the associations between the measures.

Ability to maintain balance in side-by-side and semi-tandem stance with eyes closed was associated with experienced impaired balance. Ability to maintain balance in semi-tandem stance with eyes open and side-by-side stance with eyes closed was associated with falls. Ability to maintain balance in tandem stance with eyes open and in side-by-side stance with eyes closed was associated with CoP movement in ML direction.

Ability to maintain standing balance associates with experienced impaired standing balance, falls and CoP movement. As all associations were found with the ability to maintain balance in side-by-side stance with eyes closed, this test condition can be recommended as a simple measure for impaired standing balance in routine geriatric assessment.

Introduction

Impaired standing balance is a common complaint of elderly and is frequently reported to physicians [1;2]. Elderly with impaired standing balance have an increased risk of falling [3-5], which results in fractures, a decrease in functional status [6] and mortality [3]. This has a major socio-economic impact [7]. In routine geriatric care, various measures are used to assess standing balance. An easy but subjective way is asking the patient whether and how often he or she experiences problems with balance. Ability to maintain standing balance is an objective and relatively simple test which is part of physical performance tests, such as the Short Physical Performance Battery (SPPB) [8] and the Berg Balance Scale (BBS) [9]. Ability to maintain balance may be tested during various standing conditions, which differ e.g. in availability of sensory information (e.g. eyes open or eyes closed) or in size of the base of support (e.g. side-by-side, semi-tandem and tandem stance). Posturography is a measure of quality of standing balance [10;11]. Using inertial sensors or a force plate, human body movement (Center of Mass (CoM) movement) or forces and moments acting below the feet on the ground (Center of Pressure (CoP) movement) are measured.

In previous studies in specific populations (i.e. community-dwelling elderly, elderly with a history of falls or healthy elderly) abnormal scores on performance-based clinical balance tests, such as the SPPB, BBS and Tinetti's Performance-Oriented Mobility Assessment (POMA), were found to be associated with self-reported limitations in activities of daily living [8;12-14] and with increased CoP movement [15;16]. Furthermore, abnormal scores on clinical balance tests were found to be associated with falls, an outcome measure of impaired standing balance [17-19].

It remains unknown whether in routine geriatric care the ability to maintain standing balance is sufficient to use as measure for impaired standing balance. We therefore assessed the association between the ability to maintain balance measured during several standing conditions and alternative measures of standing balance, i.e. experienced impaired balance, falls and CoP movement in a population of community-dwelling elderly referred to a geriatric outpatient clinic.

Methods

Setting

This cross-sectional study included 207 community-dwelling elderly who were referred to a geriatric outpatient clinic in a middle-sized teaching hospital (Bronovo Hospital, The Hague, Netherlands) for a comprehensive geriatric assessment (CGA) between March 2011 and January 2012. CGA was performed during a two-hour visit comprising questionnaires, physical and cognitive measurements. All tests were performed by trained nurses or medical staff. Medical charts were retrospectively evaluated. Because research data were obtained within regular patient care, the need for individual informed consent was waived by the institutional review board of the Leiden University Medical Center (Leiden, the Netherlands). In the present analyses, ten outpatients (4.8%) were excluded due to missing data on standing balance, leaving 197 outpatients for further analyses.

Characteristics of outpatients

Questionnaires included information on marital status, living arrangements, current smoking and alcohol use. Body mass index was calculated using measured weight and height. Information on diseases and use of medication were extracted from medical charts. Multimorbidity was rated as the presence of two or more diseases, including chronic obstructive pulmonary disease, heart failure, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson's disease, (osteo) arthritis, transient ischemic attack and stroke. The Hospital Anxiety and Depression Scale (HADS) was used to detect depressive symptoms [20], which was indicated by a score higher than 8 out of 21 points. Global cognitive function was assessed using the Mini Mental State Examination (MMSE) [21]. Physical functioning was assessed by handgrip strength, walking speed on a ten meter walk at usual pace in steady state, and SPPB score, composed of the ability to maintain balance in three different standing positions with eyes open, a timed four meter walk and a timed sit-to-stand test.

Standing balance

Ability to maintain standing balance

The ability to maintain standing balance was tested in six standing conditions. Outpatients, wearing non-slip socks, were instructed to maintain balance for ten seconds in each standing condition. Three different standing positions, characterized by a progressive narrowing of the base of support, were performed both with eyes open and eyes closed. During side-by-side stance, outpatients were instructed to stand with the medial malleoli as close together as possible; during semi-tandem stance with the medial side of the heel of one foot touching the big toe of the other foot and during tandem stance with both feet in line while the heel of one foot touching the toes of the other. Standing positions were primarily assessed with eyes open as part of the SPPB. Subsequently, all standing positions were repeated with eyes closed. Three trials were allowed in case standing balance was lost prematurely. When a certain standing position could not be completed even after three trials, consecutive positions were not performed. Six outpatients (3%) did not attempt the standing positions with eyes closed due to lack of time or lack of motivation, leaving 191 outpatients for analyses of standing balance conditions with eyes closed.

Experienced impaired standing balance

Experienced impaired standing balance was registered when ‘regularly’ or ‘always’ was answered to the question how often problems with standing balance were experienced (other options were ‘never’ and ‘ sometimes’).

Falls

History of falls was self-reported by answering the question whether falls were experienced in the 12 months prior to the visit to the geriatric outpatient clinic.

Center of Pressure movement

To measure CoP movement, standing conditions were performed on a triangular six degrees of freedom force plate (Forcelink B.V., Culemborg, The Netherlands). Only successful trials, i.e. completion of ten seconds of maintaining balance without stepping out in case of loss of balance, were considered for further analyses. As the number of successful trials decreased with increasing difficulty of standing condition, only trials of side-by-side stance with eyes open were analysed. Because of missing data due to technical problems (n=18) and unknown reasons (n=29), CoP movement was available in 136 outpatients in side-by-side stance with eyes open. As age-related differences have been shown to be most pronounced in medio-lateral (ML) direction [22], only time series of CoP movement in ML direction were used to calculate single CoP parameters. A CoP composite score was calculated from five standardized single CoP parameters, i.e. mean amplitude, amplitude variability, mean velocity, velocity variability and range [23]. CoP movement was dichotomized in a group with high

CoP movement (CoP composite score≥0) and a group with low CoP movement (CoP composite score<0).

Statistical analyses

Continuous variables with Gaussian distribution are presented as mean and standard deviation (SD), otherwise as median and interquartile range (IQR) or number (n) and percentage (%). Logistic regression analysis was used to assess the association between the ability to maintain standing balance and 1) experienced impaired standing balance, 2) falls and 3) CoP movement. The statistical package SPSS for Windows version 20.0 (SPSS Inc, Chicago, USA) was used for analysing the data. P-values below 0.05 were considered statistically significant. Graphs were made with GraphPad Prism 5 (GraphPad Software, Inc., La Jolla, USA).

Results

Characteristics of outpatients

Characteristics of outpatients are presented in Table 1. The mean age of all outpatients was 81.9 years. Of them, 88 (45.1%) experienced impaired standing balance and 127 (64.5%) reported at least one fall incident in the 12 months prior to the visit to the geriatric outpatient clinic. The ability to maintain standing balance is shown in Figure 1. The number of outpatients able to maintain balance was lower with progressive narrowing of the base of support and with closing the eyes.

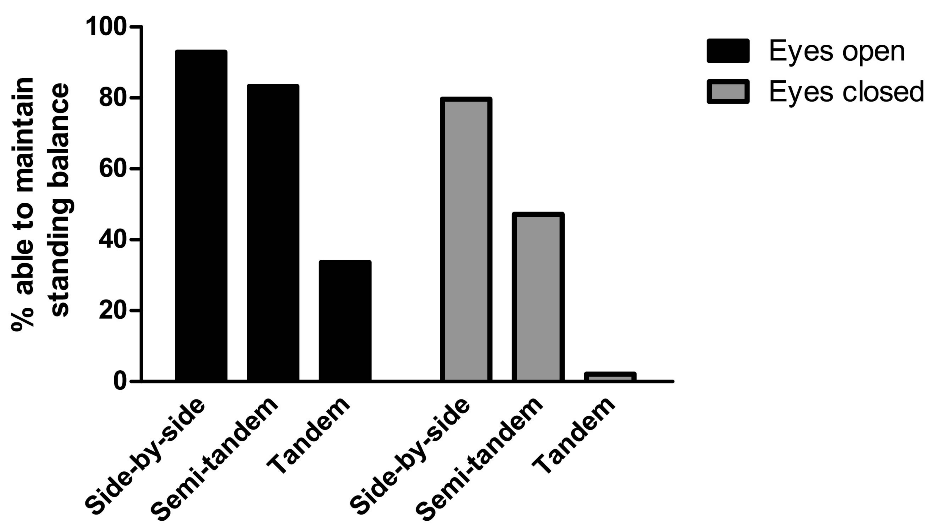

Figure 1. Percentage of the elderly outpatients able to maintain balance in various standing conditions, i.e. side-by-side, semi-tandem and tandem stance with eyes open and eyes closed.

Table 1. Elderly outpatient characteristics.

	All (n=197)
Socio-demographics	
Age, years	81.9 (7.1)
Men, n (%)	78 (39.6)
Widowed, n (%)	80 (41.5)
Independent living, n (%)	154 (79.4)
Current smoking, n (%) [a]	22 (16.2)
Excessive alcohol use, n (%) [*]	8 (4.1)
Health characteristics	
BMI, kg/m^2 [b]	25.8 (4.5)
Multimorbidity, n (%) [b, †]	95 (50.3)
Number of medication, median (IQR) [b]	5 (3-7)
HADS, depression > 8; n (%) [c]	28 (23.1)
MMSE, points; median (IQR)	27 (24-29)
Physical functioning	
Handgrip strength, kg	26.1 (8.2)
Gait speed, m/s [b]	0.87 (0.29)
SPPB, points; median (IQR)	7 (5-10)
Self-reported, n (%)	
Fall incident previous 12 months	127 (64.5)
Impaired standing balance [‡]	88 (45.1)

All parameters are presented as mean with standard deviation unless indicated otherwise. Data available in a n=136, b n=190, c n=121. * Defined as >14 units per week for females and >21 units per week for males. † Present in case of two or more diseases, including chronic obstructive pulmonary diseases, heart failure, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson's disease, (osteo) arthritis, transient ischemic attack and stroke. ‡ Defined as regularly or always self-reported impaired standing balance. Abbreviations: IQR, inter quartile range; BMI, body mass index; HADS', Hospital Anxiety and Depression Scale; MMSE, Mini Mental State Examination; SPPB, Short Physical Performance Battery.

Association of the ability to maintain standing balance with experienced impaired balance

The associations between the ability to maintain balance in various standing conditions with experienced impaired standing balance are shown in Figure 2a. Outpatients who were able to maintain balance in side-by-side stance and semi-tandem stance with eyes closed were significantly less likely to have experienced impaired standing balance (OR (95% CI): 0.43 (0.21; 0.88), p = 0.02 and OR (95% CI): 0.43 (0.24; 0.78), p = 0.005, respectively).

Association of ability to maintain standing balance with falls

The associations between ability to maintain balance in various standing conditions and falls are represented in Figure 2b. Outpatients who were able to maintain balance in semi-tandem stance with eyes open and side-by-side stance with eyes closed were significantly less likely to have experienced falls in the previous 12 months (OR (95% CI): 0.35 (0.14; 0.89) , p = 0.03 and OR(95% CI): 0.39 (0.17; 0.89), p = 0.03, respectively).

Association of ability to maintain standing balance with CoP movement

The associations between the ability to maintain balance in various standing conditions and CoP movement in ML direction in side-by-side stance with eyes open are presented in Figure 2c. Outpatients who were able to maintain balance during tandem stance with eyes open and during side-by-side stance with eyes closed were significantly less likely to have a high CoP movement in ML direction during side-by-side stance with eyes open (OR (95% CI): 0.36 (0.17; 0.73), p = 0.005 and OR (95% CI): 0.18 (0.06; 0.57), p = 0.004, respectively).

Discussion

In community-dwelling elderly referred to a geriatric outpatient clinic, the ability to maintain standing balance was associated with experienced impaired standing balance, falls and CoP movement in ML direction in side-by-side stance with eyes open. All associations were significant in side-by-side stance with eyes closed.

This is the first study that investigated the association between various measures of standing balance in a clinical relevant population of elderly outpatients. Previous studies investigated the relation between measures of standing balance in other study populations, such as elderly with and without a history of falls [16;24;25], healthy elderly [14] and community-dwelling elderly [13;15]. Aforementioned studies found an association of extensive clinical balance tests, such as the SPPB and BBS, with self-reported measures, which is in accordance with our study; elderly with a lower score on clinical balance tests showed more impaired function [8;12-14] and a lower score on the BBS was found in falling elderly [17-19]. Furthermore, studies showed an association of the SPPB, BBS and POMA, with CoP movement [15], which is also in accordance with our results.

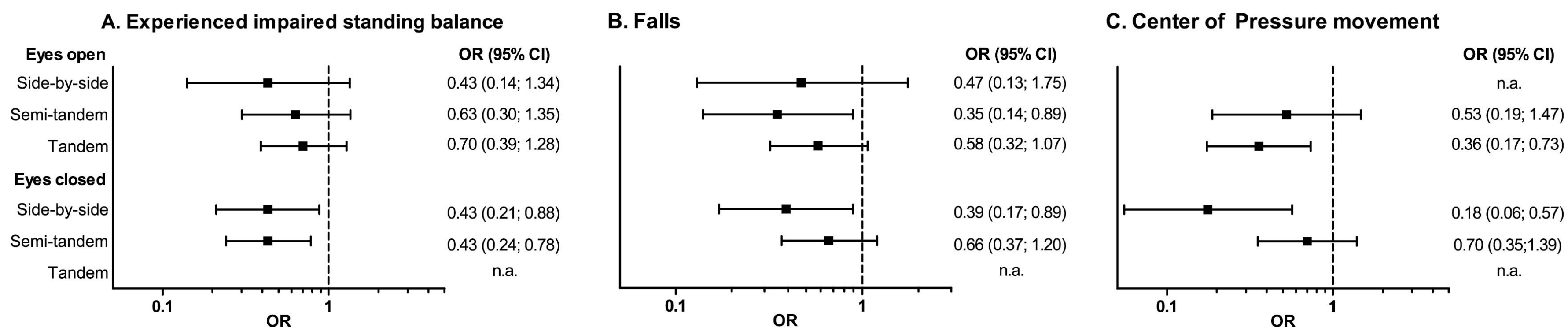

Figure 2. Forest plots of the associations between the ability to maintain standing balance in various standing conditions and A) experienced impaired standing balance, B) falls, and C) Center of Pressure (CoP) movement in medio-lateral direction in side-by-side stance with eyes open. The ability to maintain standing balance is defined as 0 not being able to maintain standing balance and 1 being able to maintain standing balance. Experienced impaired standing balance is defined as 0 reporting never or ometimes impaired standing balance and 1 reporting regularly or always impaired standing balance. Falls is defined as 0 not fallen and 1 fallen. The CoP movement is defined as 0 low CoP movement and 1 high CoP movement. Results are presented in odds ratios and 95% confidence intervals. Abbreviations: OR, odds ratio; CI, confidence interval; n.a., not applicable, number of elderly outpatients able to or not able to maintain balance in this standing condition is less than five.

Previous studies described that self-reported measures were representative of social, health and psychological factors, such as cognition, depression, health status and self-efficacy, which is in contrast with performance-based measures that are more representative of physical attributes [13;26]. This indicates that self-reported measures do not provide equivalent information about someone's standing balance as performance-based measures. Therefore, previous studies recommended to use both measures complementary in the assessment of standing balance [13;27].

A significant association was found between the ability to maintain standing balance and falls, an outcome measure of impaired balance. This indicates that ability to maintain standing balance could be used as a clinically relevant measure for impaired standing balance.

Furthermore, we found an association between the ability to maintain balance in more difficult standing conditions and CoP movement in ML direction during side-by-side stance with eyes open. This confirms the general assumption that impaired balance is accompanied with an increased CoP movement. During more difficult standing positions, the size of the base of support became smaller or visual information was eliminated by closing the eyes. By reducing the size of the base of support, balance in ML direction needs more control, resulting in increased CoP movement. By eliminating visual information, elderly has to rely only on sensory information of proprioception and the vestibular system to generate a corrective movement, which also result in increased CoP movement. Therefore, outpatients who already exhibit increased CoP movement in ML direction during side-by-side stance are not able to withstand those changes in size of the base of support and changes in availability of sensory information. This explains why outpatients who are not able to maintain balance during more difficult standing conditions will have an increased CoP movement in ML direction during side-by-side stance.

In literature, the interpretation of CoP movement is under debate. In general, increased CoP movement is considered to reflect impaired standing balance. However, to control balance, several strategies can be applied, e.g. co-contraction, a hip strategy or ankle strategy [28], which have different influences on CoP movement. CoP movement may increase with increased movement around the ankle joint, but may decrease with decreased movement around the hip joint. Furthermore, CoP movement could also decrease by stiffening the body using co-contraction. The downside of this strategy is that the resistance to unexpected disturbances decreases [29]. This means that impaired balance is not always accompanied with increased CoP movement. Furthermore, as several underlying organ systems are involved in maintaining balance, deficits on those systems could also affect CoP movement differently [10;11]. This may seriously increase interpretation difficulties of the CoP movement in populations which are encountered in geriatric clinical care.

Strength of this study is the unique study population of elderly outpatients. In our study, we included a heterogeneous population of elderly irrespective of diseases and impairments. No exclusion criteria were applied and therefore this population is representative for the community-dwelling elderly visiting the geriatric outpatient clinic. Limitation of this study is the cross-sectional design, which makes it impossible to draw conclusions about a causal relation between the various measures of standing balance. Assessing history of falls retrospectively could be influenced by recall bias. Furthermore, CoP movement of one successful trial of ten seconds was analysed, while previous studies recommended to measure CoP movement more than once and during a longer time period [30]. However, in clinical practice and in a population of elderly outpatients, this is not feasible due to time limits and fatigue. CoP movement was only available in 136 outpatients, who were able to maintain balance in side-by-side stance with eyes open, which reduces the power of the statistical analyses.

Conclusion

In conclusion, in elderly outpatients the ability to maintain balance in side-by-side stance with eyes closed was found to be associated with experienced impaired standing balance, falls and CoP movement, indicating the value of the ability to maintain balance in side-by-side stance with eyes closed as a measure for clinically relevant impaired standing balance. This emphasizes the importance of measuring the ability to maintain balance in side-by-side stance with eyes closed in routine geriatric clinical assessment.

Acknowledgements

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Part III

System identification to assess standing balance

balance
disturbances
deterioration
training
steps
sensory
strategies
compensation
control
impaired
used
interventions
clinical
assessment
movement
information
systems
tests
maintain
elderly
cognitive
underlying
change
prevention
identify
applied
nervous
identification
proprioception
increase
motor
reduced
measure
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possible
proper
power
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amplitudes
difficulty
fibers
rely
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decrease
simultaneous
muscle
body
contraction

Chapter 8

Sensory reweighting of proprioceptive information of the left and right leg during human balance control

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Herman van der Kooij
*authors contributed equally
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Abstract

To keep balance, information from different sensory systems is integrated to generate corrective torques. Current literature suggests that this information is combined according to the sensory reweighting hypothesis, i.e. more reliable information is weighted stronger than less reliable information. In this approach no distinction has been made between the contributions of both legs. Here, we investigated how proprioceptive information from both legs is combined to maintain upright stance.

Healthy subjects maintained balance with closed eyes while proprioceptive information of each leg was perturbed independently by continuous rotations of the support surfaces (SS) and the human body by platform translation. Two conditions were tested: perturbation amplitude of one SS was increased over trials, while the other SS 1) did not move or 2) was perturbed with constant amplitude. Using system identification techniques, the response of the ankle torques to the perturbation amplitudes (i.e. the torque sensitivity functions) was determined and how much each leg contributes to stabilize stance (i.e. stabilizing mechanisms) was estimated.

Increased amplitude of one SS resulted in a decreased torque sensitivity. The torque sensitivity to the constant perturbed SS showed no significant differences. The properties of the stabilizing mechanisms remained constant during perturbations of each SS.

This study demonstrates that proprioceptive information from each leg is weighted independently and the weight decreases with perturbation amplitude. Weighting of proprioceptive information of one leg has no influence on the weight of the proprioceptive information of the other leg. According to the sensory reweighting hypothesis vestibular information must be up weighted, as closing the eyes eliminated visual information.

Introduction

Balance is described as the ability to maintain upright posture in a gravitational field [1] and is involved in many daily life activities, like bipedal stance, walking and cycling. For small deviations the gravitational pull effectively is a negative stiffness; a deviation from a perfect upright position results in a torque that accelerates the body further away from this position. External mechanical disturbances, like a misstep or a slip, and conflicting information of the sensory systems can disturb the equilibrium of the balance system. The central nervous system (CNS) has to cope with these disturbances to maintain the body in upright position. The CNS receives feedback about the body orientation from three main sensory systems: the visual, proprioceptive and vestibular system. The CNS integrates this sensory feedback and subsequently generates a corrective, stabilizing torque by selectively activating muscles [2].

Nowadays, it is still not fully understood how sensory feedback of the different sensory systems is integrated by the CNS to generate corrective torques [2]. The integration of the signals from the different sensory systems seems to be dynamically regulated to adapt to changes in the environment and the available sensory information, i.e. sensory reweighting [2-9]. The hypothesis of Peterka (2002) states that the CNS adapts to different circumstances by adjusting the relative weight of the different sensory sources that control stance. When one sensory modality becomes less reliable, for example the proprioception by rotation of the support surface, the CNS reduces the relative weight of this sensory system and has to rely more on the other sensory systems [2;10].

The sensory reweighting hypothesis has been confirmed by experiments in which a sensory system was perturbed with increasing perturbation amplitude. With increasing perturbation amplitude the body sway saturated; i.e. a nonlinear relationship between the perturbation amplitude and the response amplitude was found. The relative response to larger amplitude perturbations decreased in accordance with the sensory reweighting hypothesis [2;7]. Peterka (2002) showed with model fits that the decrease in response of the body sway to the perturbation by increasing perturbation amplitude was due to a decrease in the weight of the perturbed sensory system [2]. Vestibular loss patients with closed eyes did not show sensory reweighting, i.e. they present a linear relationship between the perturbation amplitude and the response amplitude. Due to the loss of vestibular information and elimination of visual information by closing the eyes, only proprioceptive information was available to keep balance and reweighting between sensory channels was not possible.

To date, no distinction is made between the proprioceptive contribution of each leg, as the support surfaces of both feet were perturbed simultaneously [2]. Consequently, it is unknown whether the CNS uses the proprioceptive information of both legs independently to maintain balance, if so, how this information is integrated and if this influences how the legs contribute to stabilize stance (i.e. the stabilizing mechanisms).

By perturbing proprioceptive information of both legs independently, multiple ways of integrating sensory information are plausible. In a situation where visual information is eliminated by closing the eyes and the proprioceptive information of one leg is perturbed, there are the following theoretical possibilities: The first possibility is, a down weighting of proprioceptive information of both legs accompanied by an up weighting of vestibular information. The second possibility could be that proprioceptive information of only the perturbed leg is down weighted and the vestibular information is up weighted for this leg only. The third possibility is a down weighting of the proprioceptive information of the perturbed leg with an up weighting of the proprioceptive information of the opposite (unperturbed) leg, which would implicate asymmetry between the stabilizing mechanisms of the legs.

Here, we investigated the sensory reweighting of proprioceptive information of both legs independently in healthy subjects. In our approach, we consider two sensory sources (i.e., proprioception of the right and left leg) and two actuators (i.e., the musculature of both ankles). We identified whether separate perturbations of the proprioceptive information of the left and right leg, caused by rotation of the support surfaces, will result in sensory reweighting of the proprioceptive information of each leg independently. Concurrently, we investigated the influence of the separate sensory perturbations on the stabilizing mechanisms using constant platform accelerations in posterior-anterior direction.

We hypothesized that when applying different proprioceptive perturbations to each leg, sensory reweighting mechanisms would account for the sensory integration of the separate proprioceptive information from both legs. The CNS will down weight the less reliable information of one leg and up weight the more reliable information from other sensory systems. In other words, we hypothesized that in bipeds proprioceptive information of both legs is weighted separately and combined in balance control [11;12].

Materials and methods

Subjects

Ten healthy subjects (six women, age 25.8 ± S.D. 2.4 years, weight 75.8 ± S.D. 10.9 kg) with no history of balance disorders, no injuries of the legs and no use of medication, which affects balance, participated. This study was performed according to the principles of the Declaration of Helsinki and all subjects gave written informed consent to participate in this study.

Apparatus

In this study a bilateral ankle perturbator (BAP) was used to perturb the proprioceptive information of both legs independently by applying support surfaces rotations of both feet separately around the ankle axis, see Figure 1 [13]. Each support surface consists of a custom-made 6 DoF force plate (Forcelink B.V., Culemborg, The Netherlands) connected to a servomotor via a lever arm. The actual angles of rotation (i.e. motor angles) and the applied torques to both support surfaces (i.e. motor torques) are available for measurement.

The BAP was placed on a 6 DoF motion platform (Motek Medical B.V., Amsterdam, The Netherlands) to apply support surface translations in the anterior-posterior direction to the BAP with the subject on top. The platform translation (s_{ext}) accelerates the base of support which is equivalent to a virtual torque applied at the ankles. The magnitude of the perturbation depends on the mass of the subjects and the center of mass location (equation 1) [14].

$$d_{ext} = \frac{d^2 s_{ext}}{dt^2} \cdot m \cdot l_{com} \qquad (1)$$

Procedure

Before the trials, data was recorded for ten seconds while the subjects stood still on the BAP. This trial was used to calculate the height of the centre of mass (l_{CoM}) [15]. Furthermore the maximum amplitude of the platform perturbations a subject could withstand without falling or stepping during rotation of the support surfaces, was determined by the experimenter (on average 3.1 cm).

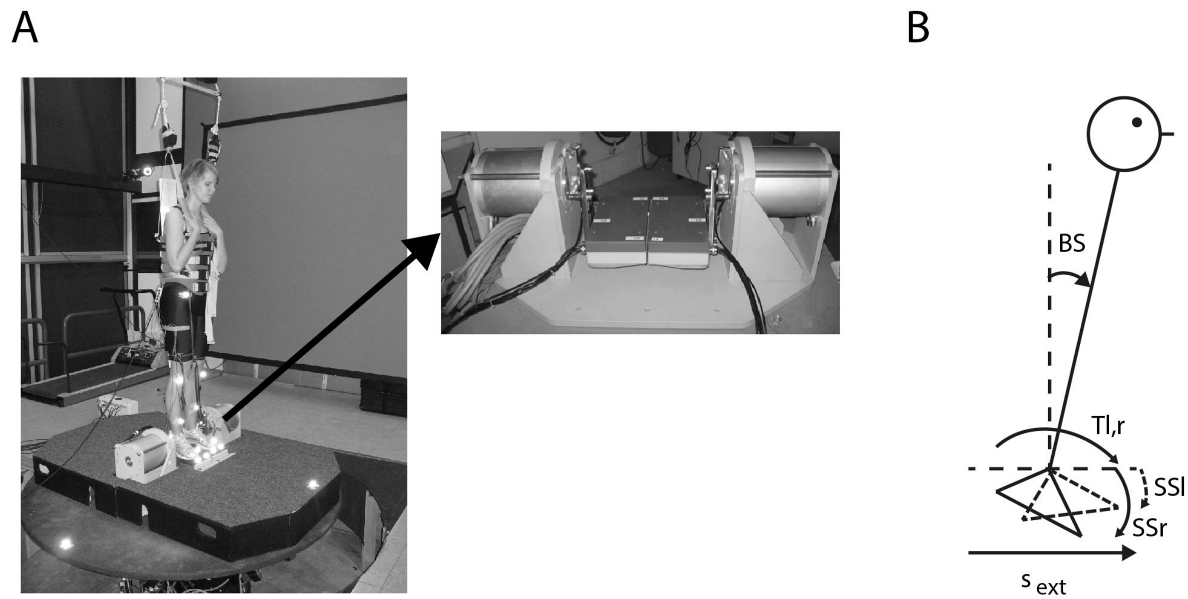

Figure 1. A) Experimental set-up with a subject standing on the bilateral ankle perturbator (BAP) on top of the motion platform. The hip was fixed using a backboard and the subject wore a safety harness to prevent a fall. The inset on the right displays the BAP with the support surfaces (i.e. 6 DoF force plates) and the servomotors. B) Schematic figure of the experimental set-up with sext the platform movement in anterior-posterior direction and $SS_{l,r}$ the platform rotations around the ankle axis applied separately to each leg. The ankle torques ($T_{l,r}$) and the body sway (BS) are the outcome measures.

In the main experiment the subjects were instructed to close their eyes and the subjects wore a backboard (mass 1.2 kg, moment of inertia 0.134 kgm^2 around the axis through the center located at the subjects' center of mass (l_{CoM})) minimize the use of the hip joint [16] and stood with their arms crossed over their chest. The subjects were repeatedly instructed to distribute their body weight equally over both legs during the trials to eliminate the influence of weight bearing asymmetry [17].

The experiments consisted of two conditions: 1) the left support surface rotated with different amplitudes, while the right support surface did not rotate; 2) the right support surface rotated with different amplitudes, while the left support surface rotated with constant amplitude. In addition, the motion platform with the BAP was translated in anterior-posterior direction (see Table 1).

The amplitude of the rotations of the support surfaces is given in radians. The platform perturbation amplitude (on average 3.1 cm) was set by the experimenter for each subject individually to the maximal value a subject could withstand without falling or stepping.

Table 1. Overview of the different conditions.

Condition	Platform (d_{ext})	Left support surface (SS_l) [rad]	Right support surface (SS_r) [rad]
One-leg perturbation			
L1R0	√	0.01	-
L3R0	√	0.03	-
L8R0	√	0.08	-
Two-leg perturbation			
L3R1	√	0.03	0.01
L3R3	√	0.03	0.03
L3R8	√	0.03	0.08

Each condition was presented twice in random order and each trial lasted 180 seconds. Before each trial the subjects were given about 30 seconds to get accustomed to the perturbations, to close their eyes and to reach a steady state. Between trials subjects were given sufficient time to rest.

Perturbation signals

Three different pseudo-random unpredictable perturbation signals were used in this study, namely for the left and right support surface rotation (SS rotation) and for the anterior-posterior platform translation [18]. To be able to disentangle the effects of the different perturbations, the signals were designed to have separate frequency contents, see Figure 2.

Pseudorandom ternary sequences (PRTS) of numbers were designed [19] as support surface angular velocity. Integration of these velocity signals provided the reference SS rotations. The method described in Peterka (2002) was used [2] to generate two different perturbation signals for the left and right support surface with a time increment of Δt=0.16 s and Δt=0.08 s, respectively. In this case the period of each signal was 29.04 s and 14.52 s, respectively.

The platform perturbation was a multisine signal consisting of 30 frequencies between 0.0517 and 4.0461 Hz having a flat velocity spectrum resulting in a declining position spectrum [18] (see Figure 2). All excited frequencies were multiples of 0.0172 Hz, resulting into a period of 58.08 s. Crest optimization was applied to minimize the root mean square of both the position and the acceleration of the multisine to guarantee a good signal to noise ratio [18].

The perturbation signals of the left and right support surface each fit exactly 2 and 4 times in the platform perturbation signal, respectively. This resulted into a total length of the perturbation signals of 58.08 s per cycle. Each trial consisted of three whole cycles of the perturbation signals.

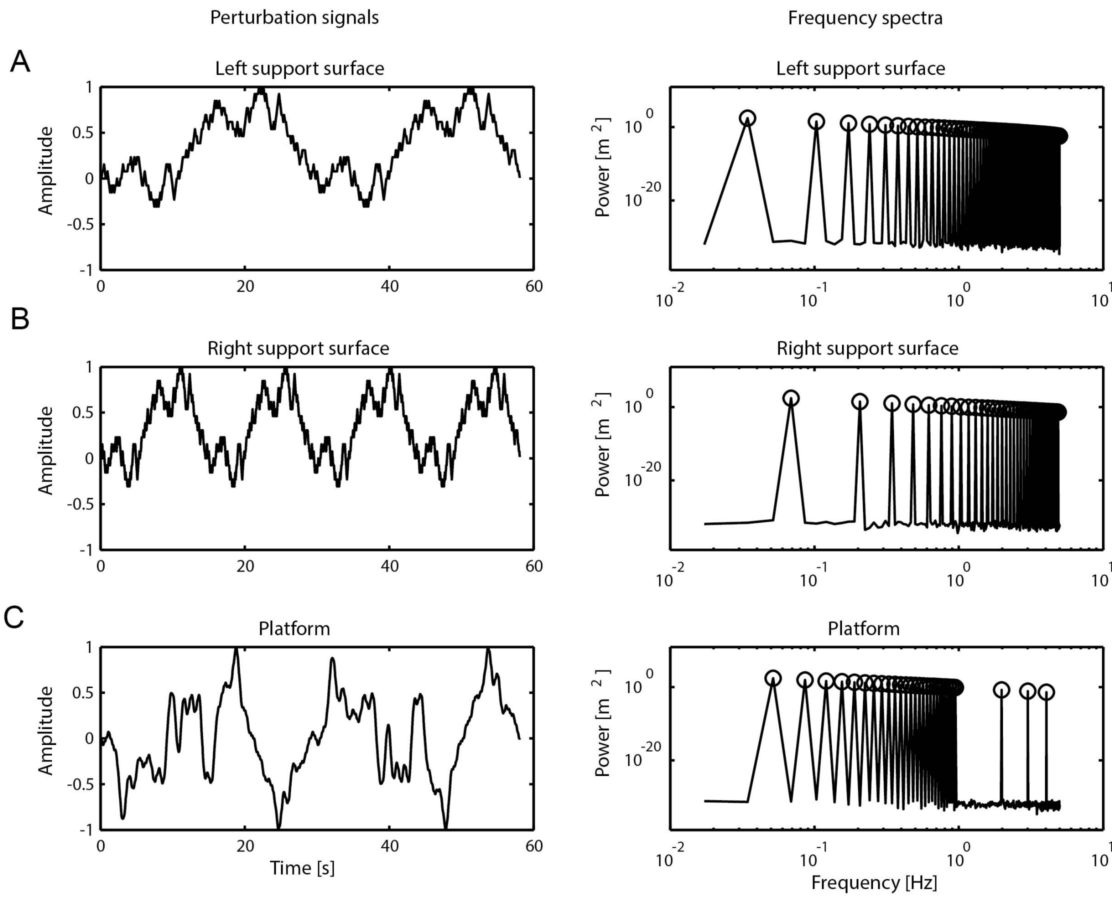

Figure 2. Time signals (left column), presented with normalized amplitude, and the corresponding power spectra (right column) of the perturbation of the left (A) and right support surface (B) of the bilateral ankle perturbator (BAP) and the perturbation of the motion platform (C).

Data recording and processing

Kinematic data were collected using a 6 camera motion capture system (Vicon Motion Systems Ltd., Oxford, UK), at a sample frequency of 120 Hz. Reflective spherical markers were attached bilaterally to the subject on the toe, lateral malleolus, heel, tibialis, knee, anterior superior iliac spine and shoulder to measure the movement of the body segments. Furthermore, three markers were attached to the platform. The motor angles, motor torques, and the signals of the force plates were recorded using the Vicon Workstation with a sample frequency of 2520 Hz. Data analysis was performed with Matlab (The MathWorks, Natick, MA).

The anterior-posterior platform movement (s_{ext}) was determined by averaging the three markers on the platform. From the markers on the body the location of the Centre of Mass (CoM) was determined according to Winter et al. (1990) [15]. The body sway angle (BS) was calculated from the anterior-posterior movement of the CoM and the distance between the lateral malleolus and the CoM, i.e. the length of the pendulum (l_{CoM}). The data of the force plates, motor angles (SS) and motor torques were resampled from 2520 Hz to 120 Hz. The data were filtered with a second order low pass digital Butterworth filter with cut-off frequency of 10 Hz. The ankle torques (T_l, T_r) were obtained by subtracting the contribution of the mass and inertia of the support surfaces from the recorded motor torques. The data of the 6 DoF force plates were corrected for the influence of the inertia and mass of the top layer according to the procedure of Preuss and Fung (2004) [20]. Weight bearing of the subject was calculated by dividing the mean vertical force below the left foot by the mean of the summed vertical forces below both feet.

The time series were split into three data blocks of 58.08 seconds (i.e. the length of the perturbation signal). Data blocks with missing markers were excluded from further analysis. The two trials of each condition resulted in six data blocks (2 trials of 3 data blocks).

Data analysis

Movement of one support surface influences the movement of the whole body and as such influences both ankle torques. Due to this biomechanical coupling between the legs it is difficult to indicate the effects of the right and left support surface perturbations on both ankle torques in time domain. Therefore, Frequency Response Functions (FRFs) were estimated based on a two-leg approach of postural control. In this approach the human body is assumed to move as an inverted pendulum, which is stabilized by the sum of the two corrective ankle torques generated by two stabilizing mechanisms, see Figure 3 [17]. The stabilizing mechanisms comprise of passive and active components of the CNS. However, the passive stabilizing mechanisms alone are not sufficient enough to keep balance [21]. The active stabilizing mechanisms are formed by the parts of the CNS that processes sensory signals, send efferent signals to the muscles and the muscles themselves. Stabilizing mechanisms of both legs incorporate vestibular and left and right proprioceptive information.

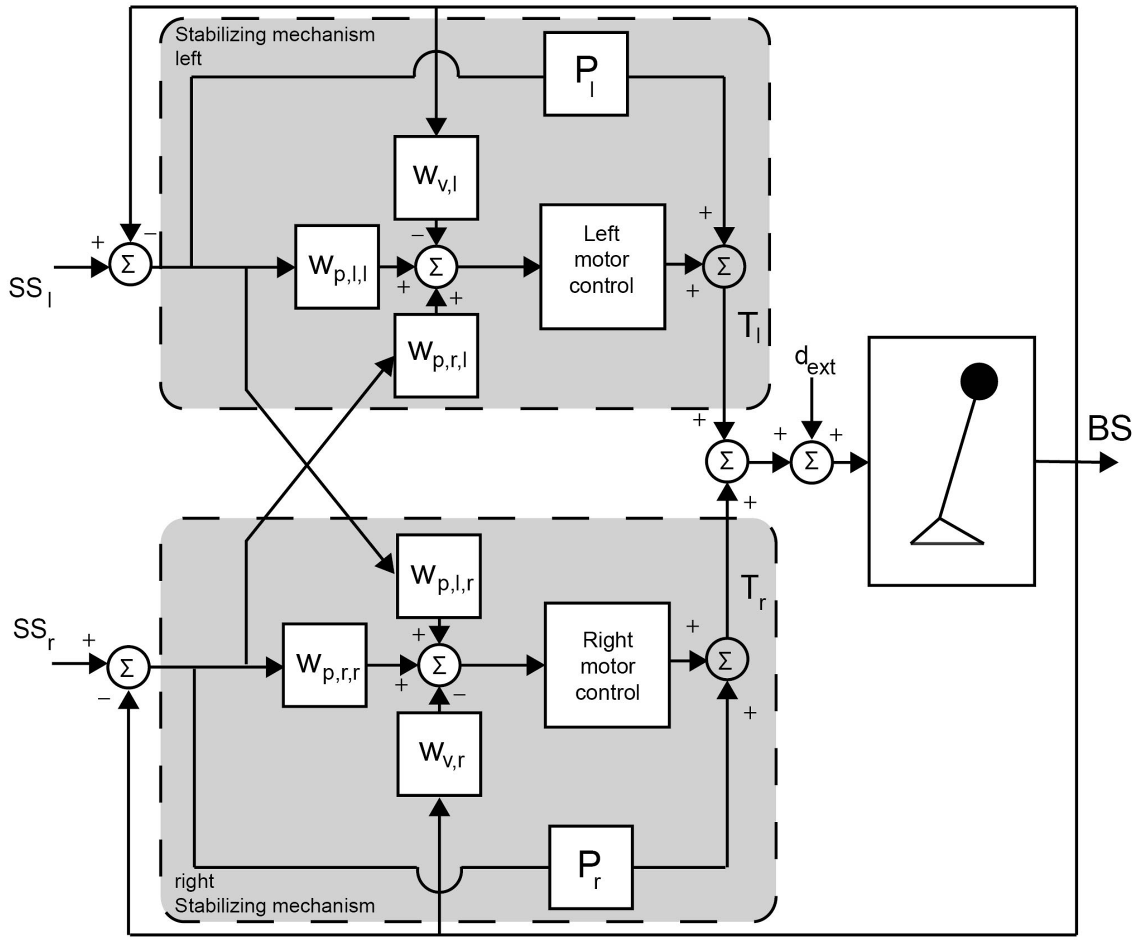

Figure 3. The two-leg approach of the balance control system. The body is represented as an inverted pendulum. Each leg has a stabilizing mechanism consisting of the passive feedback mechanism (Pl,r),weighting factors of the vestibular system (W_v), left ($W_{p,l}$) and right ($W_{p,r}$) proprioception and a (motor) controller. The torques (T_l, T_r) generated by each stabilizing mechanism affect the body sway (BS) angle. The control loop can be disturbed by sensory perturbations of the proprioceptive information of both legs (SS_l, SS_r) and by external perturbations (dext).

According to the sensory reweighting hypothesis each sensory system is presented by a sensory channel consisting of a weighting factor, which represents the relative weight of the sensory information [22]. The sum of all weighting factors equals one [22]. Therefore, a decrease in the weighting factor of one sensory channel must always be accompanied by an increase in the weighting factor of another sensory channel. This approach allows for asymmetry between the stabilizing mechanisms, i.e. the sum of weights used by the left stabilizing mechanism can be different from the sum of weights used by the right stabilizing mechanism ($\sum W_l \neq \sum W_r$).

To be able to detect sensory reweighting of the separate legs, the stabilizing mechanisms should only be influenced by the sensory weights. Two other factors could also contribute to asymmetry between the stabilizing mechanisms: 1) asymmetry in weight bearing [17] and 2) asymmetry of left and right muscle properties and neural feedback loops. Therefore, subjects were instructed to distribute their weight equally over both legs, so it was reasonable to assume that the muscle and neural (passive) feedback properties were similar for both legs.

Sensory perturbations of proprioceptive information by rotation of the left and right support surfaces affect the output of the stabilizing mechanisms, which are represented by the ankle torques of the left and right leg. To assess sensory reweighting and the properties of the stabilizing mechanisms, the closed loop balance control system will be disturbed by sensory perturbations (i.e. support surface rotations) and external perturbations (i.e. platform translation in anterior-posterior direction) [2].

Frequency Response Functions

The data was transformed to the frequency domain. The periodic part of the frequency coefficients was determined by averaging over the data blocks [23]. The Power Spectral Densities (PSD) and Cross Spectral Densities (CSD) were computed to calculate the FRFs according to Pintelon and Schoukens [14;18]. Only the excited frequencies were analyzed (see 'Perturbation Signals').

The stabilizing mechanisms were estimated using the joint input-output approach (equation 2) [14].

$$\begin{bmatrix} C_{AP,r}(f) \\ C_{AP,l}(f) \end{bmatrix} = \begin{bmatrix} \Phi_{dext,Tr}(f) \\ \Phi_{dext,Tl}(f) \end{bmatrix} \cdot \left[\Phi_{dext,BS}(f)\right]^{-1} \qquad (2)$$

In which $\Phi_{dext,T}$ is the CSD of the platform perturbation (d_{ext}) and the left and right ankle torque (T_l and T_r) and Φdext,BS the CSD of dext and the body sway (BS).

Sensory reweighting is illustrated by the sensitivity functions. First, the body sway sensitivity function describes the relationship between the sensory perturbations and the body sway per frequency [2]. Secondly, the total torque sensitivity function describes the relationship between the sensory perturbations and the torque exerted by both ankles. To identify the influence of the perturbations on each leg separately, the torque sensitivity functions of each leg were estimated. Hence, a total of six different sensitivity functions were estimated. The sensitivity functions are estimated by calculating the Frequency Response Functions (FRFs) from support surface rotation to ankle torque. The effect of increased support surface rotation amplitude could be indicated [2] on the perturbed and on the contralateral leg. Therefore, four sensitivity functions were estimated; from the left and right ankle torque to the left support surface rotation (${}^{SSl}S_{Tl}$ and ${}^{SSl}S_{Tr}$) and from the left and right ankle torque to the right support surface rotation (${}^{SSr}S_{Tr}$ and ${}^{SSr}S_{Tl}$). The sensitivity functions were estimated using the indirect approach (equation 3) [14].

$$ {}^{SS}S_T(f) = \Phi_{SS,T}(f) \cdot \left[\Phi_{SS,SS}(f)\right]^{-1} \qquad (3) $$

In which $\Phi_{SS,T}$ is the CSD of the left and right support surface rotation (SS_l and SS_r) and the left and right ankle torque (T_l and T_r) and $\Phi_{SS,SS}$ the PSD of the left and right support surface rotation (SS_l and SS_r). As the corrective torque which has to be delivered by the subject is dependent on gravity, the FRFs were normalized for the subject's mass and length, i.e. the gravitational stiffness (mglCoM).

Coherence

The (magnitude-squared) coherence was calculated between the perturbations and ankle torques or body sway using equation 4.

$$ \gamma^2_{x,y}(f) = \left|\Phi_{x,y}(f)\right|^2 \cdot \left[\Phi_{x,x}(f) \cdot \Phi_{y,y}(f)\right]^{-1} \qquad (4) $$

In which x represents a perturbation signal (SS_l, SS_r or d_{ext}) and y an output signal (T_l, T_r or BS). By definition coherence varies between 0 and 1, where coherence close to one indicates a good signal to noise ratio and linear behavior.

Statistical analysis

For statistical analysis the PSDs and CSDs were averaged within seven frequency bands (0.03-0.1 Hz, 0.1-0.3 Hz, 0.3-0.7 Hz, 0.7-1.4 Hz, 1.4-2.2 Hz, 2.2-3.1 Hz and 3.1-4.1 Hz) before calculating the FRFs according to the method of Peterka (2002) in which the number of points over which is averaged increases with frequency [2]. Subsequently, the gain of each FRF was log transformed to make the data normally distributed.

The one-leg and two-leg conditions were analyzed separately. First it was tested whether the weight bearing differed across conditions with a one-way repeated measures (RM) analysis of variance (ANOVA). In addition, to test for changes in strategy, a two-way RM ANOVA was performed to evaluate the effect of the perturbation amplitude (condition) across the different frequency bands and their interaction (condition x frequency band) on the averaged gain of the left and right stabilizing mechanisms. Within conditions, it was tested whether there were balance control asymmetries by comparing the left and right stabilizing mechanisms (covariate body side). Finally, to test for sensory reweighting a two-way RM ANOVA was performed to evaluate the effect of the perturbation amplitude (condition) across the frequency bands and their interaction (condition x frequency bands) on the gains of the sensitivity functions. The gains of the sensitivity functions ${}^{SSl}S_{Tl}$ and ${}^{SSl}S_{Tr}$ of the two-leg conditions were also compared with condition L3R0. During those conditions the perturbation of the left leg was constant.

For all tests significance (α) was set at 0.05. Sphericity was tested with the Mauchly's test. In case of lack of sphericity a Huynh-Feldt correction was applied. When a significant difference was found, a post-hoc test was performed using pair wise comparison with Bonferroni correction. All analyses were performed with SPSS version 16.0 (SPSS, Chicago, IL).

Results

Table 2 gives an overview of the average weight bearing (percentage of weight on left leg) during all conditions. It was tested whether weight bearing differed between conditions, as this can cause an asymmetry in the stabilizing mechanisms [17]. Weight bearing was not significantly different for the one-leg perturbation conditions ($p=0.87$). However, there was a significant difference between the two-leg perturbation conditions ($p=0.024$). This was due to a difference between the L3R8 condition and the L3R1 condition ($p=0.06$), showing that subjects tended to distribute their weight asymmetrically in L3R8 condition. Note that due to the Bonferroni correction the significant difference reduced to a trend towards asymmetrical weight bearing.

Time series

Figure 4 shows the time series of the support surface rotations, the platform disturbance, the ankle torques and the body sway of a typical subject for the two-leg perturbation conditions (i.e. L3R1, L3R3 and L3R8). A nonlinear relationship between the perturbation amplitude and the ankle torques is indicated by the saturation of the torque of the most perturbed leg during the L3R8 condition. Note that the body sway also saturated across conditions. The same phenomenon was found for the one-leg perturbation condition (not shown).

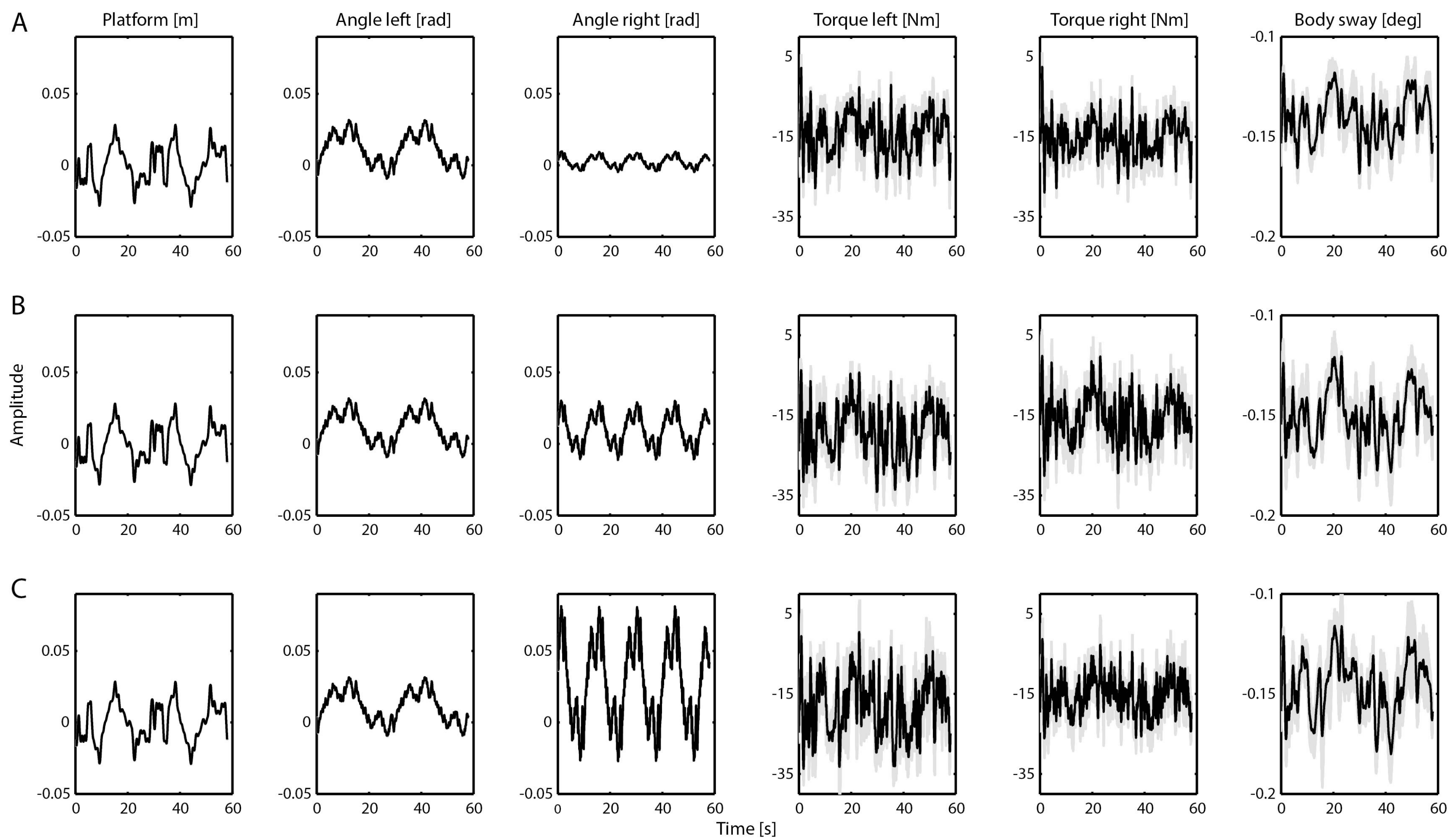

Figure 4. Time series of the condition with translation of the platform and rotations of both support surfaces, with constant amplitude of the left support surface and increasing amplitude of the right support surface (condition L3R1 (A), L3R3 (B) and L3R8 (C)). Data are for a typical subject per condition with the mean (solid line) and standard deviation over the six cycles (grey area).

Table 2. Weight bearing during each condition.

Condition	Weight [%]¶
One-leg perturbation	
L1R0	49.7 ± 5.5
L3R0	49.5 ± 5.3
L8R0	49.4 ± 6.1
Two-leg perturbation	
L3R1	50.1 ± 5.9
L3R3	50.8 ± 7.4
L3R8	52.1 ± 6.9*

¶ The mean ± SD over all subjects is shown for the weight bearing on the left leg. * indicates p value < 0.05.

Frequency Response Functions

Stabilizing mechanisms

Figure 5 shows an example of the mean stabilizing mechanisms from one test condition to illustrate the variability between subjects. Figure 6 shows the left and right stabilizing mechanisms for all conditions. The perturbation amplitude of the support surface rotations had no significant influence on the stabilizing mechanisms during the one-leg perturbation conditions (p=0.39) and during the two-leg perturbation conditions (p=0.59).

There was no significant main difference between the left and right stabilizing mechanisms during the one-leg (p=0.77) and two-leg (p=0.17) perturbation conditions, However, during the two-leg perturbation conditions an interaction effect was found between body side (i.e. left and right stabilizing mechanism) and perturbation amplitude (p=0.002). Post-hoc analysis showed that the gain of the left stabilizing mechanism was significantly higher than the gain of the right stabilizing mechanism in condition L3R8 (p=0.017) between frequency 0.03 and 1.4 Hz (p=0.001, p<0.001, p=0.007 and p=0.004 respectively) (see Figure 5). This means that there was an asymmetry between the left and right stabilizing mechanisms in the L3R8 condition, i.e. the left leg contributed more to total body stability. Note that subjects also tended to put more weight on the left leg during this condition.

Sensitivity functions

One-leg perturbation

Figure 7 shows an example of the mean torque sensitivity functions of one condition to illustrate the variability across the subjects. Figure 8 presents the body sway and total torque sensitivity functions to the perturbations. These sensitivity functions both decrease with increasing perturbation amplitude.

In Figure 9 the torque sensitivity functions are displayed for the conditions with rotation of one support surface (condition L1R0, L3R0 and L8R0). The gains of $^{SSl}S_{Tl}$ and $^{SSl}S_{Tr}$ decreased both for higher amplitudes (both $p<0.001$), indicating a saturation of the ankle torques with increasing support surface rotation amplitude. Hence, the perturbation of the left leg was suppressed more when the perturbation stimulus amplitude increased.

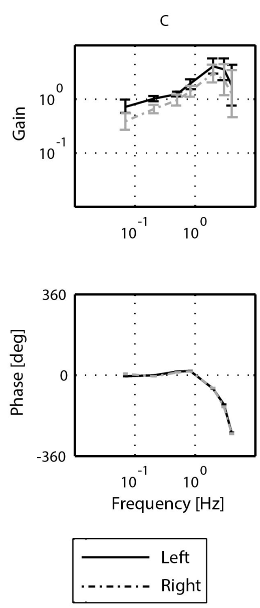

Figure 5. Example of the estimated left (black) and right (gray) stabilizing mechanisms averaged over all subjects for condition L3R8. The gain and phase are shown as average over the frequency bands with standard deviation.

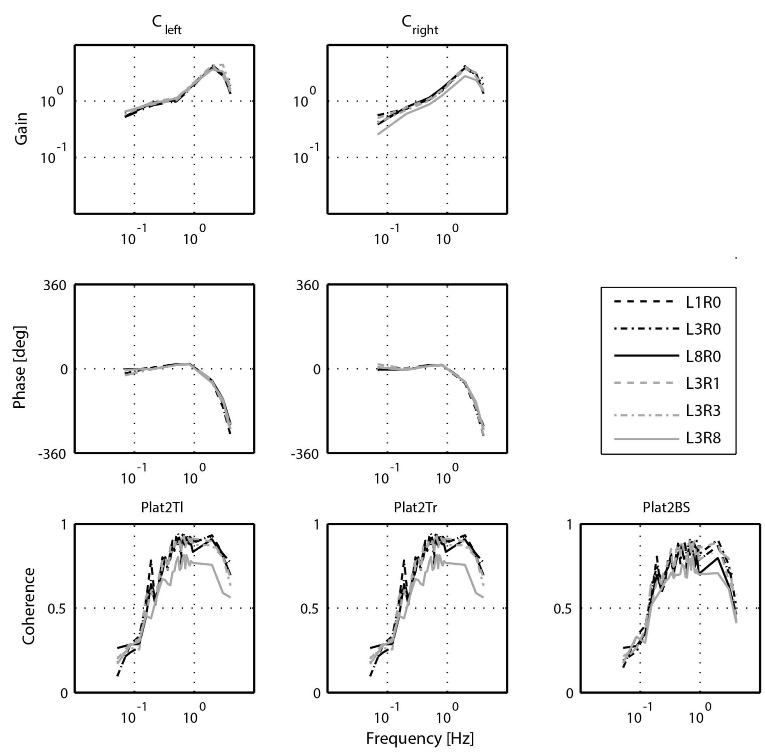

Figure 6. Estimated left and right stabilizing mechanisms (C_{left} and C_{right}) averaged over all subjects for all conditions. The gain and phase are shown for the excited frequencies. The coherence is shown between the platform perturbation and the left and right ankle torque (Plat2Tl and Plat2Tr) and between the platform perturbation and the body sway (Plat2BS).

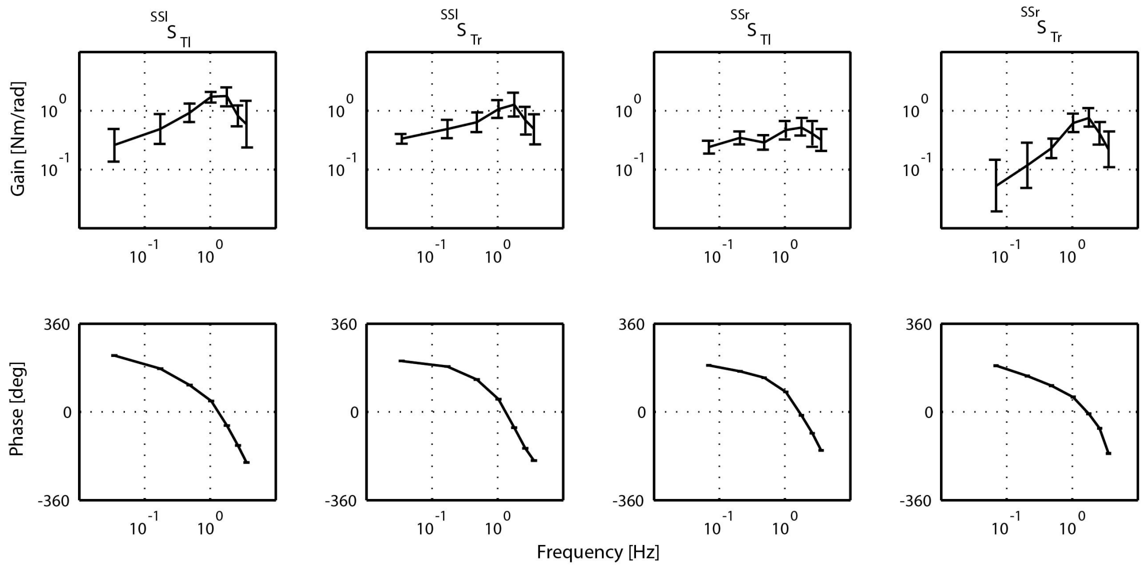

Figure 7. Example of the mean sensitivity functions over the subjects for the condition L3R8. The sensitivity functions of the left torque and of the right torque to the rotation of the left support surface (${}^{SSl}S_{Tl}$ and ${}^{SSl}S_{Tr}$) and the sensitivity functions of the left torque and of the right torque to the rotation of the right support surface (${}^{SSr}S_{Tl}$ and ${}^{SSr}S_{Tr}$) are shown as average over the frequency bands with standard deviation.

In addition, an interaction effect between perturbation amplitude and frequency band was found for ${}^{SSl}S_{Tl}$ ($p<0.001$) indicating that sensory reweighting is frequency dependent. No interaction effect was found for ${}^{SSl}S_{Tr}$ ($p=0.36$). Both torque sensitivity functions, ${}^{SSl}S_{Tl}$ and ${}^{SSl}S_{Tr}$, showed a significant difference between the three conditions in all frequency bands, except between 2.2 and 3.1 Hz for the ${}^{SSl}S_{Tl}$ and between 0.3 and 0.7 and between 3.1 and 4.1 Hz for ${}^{SSl}S_{Tr}$.

Two-leg perturbation

The estimated torque sensitivity functions of the conditions with rotation of two support surfaces (condition L3R1, L3R3 and L3R8) are presented in Figure 10. The gains of ${}^{SSr}S_{Tr}$ and ${}^{SSr}S_{Tl}$ significantly decreased with increasing perturbation amplitude (both $p<0.001$), which indicates a saturation of the ankle torques. An interaction effect between perturbation amplitude and frequency band was found for ${}^{SSr}S_{Tr}$ ($p<0.001$), indicating a frequency dependent effect of perturbation amplitude. No interaction effect was found for ${}^{SSr}S_{Tl}$ ($p=0.08$). Post-hoc analysis showed that both torque sensitivity functions were significantly different in all frequency bands across all three conditions.

The gains of the torque sensitivity functions to the constantly rotating left support surface ($^{SSl}S_{Tl}$ and $^{SSl}S_{Tr}$) did not change over conditions (p=0.26 and p=0.32, respectively). This indicates that increasing the amplitude of the right support surface does not affect the sensitivity on the left support surface perturbation.

Condition L3R8 differed from the L3R1 and L3R3 conditions with respect to weight bearing and the stabilizing mechanisms. Changes between the stabilizing mechanisms across conditions could result in changes of the sensitivity functions. In this case it would be impossible to draw conclusions about sensory reweighting. Therefore, the statistical analysis was also performed without the L3R8 condition.

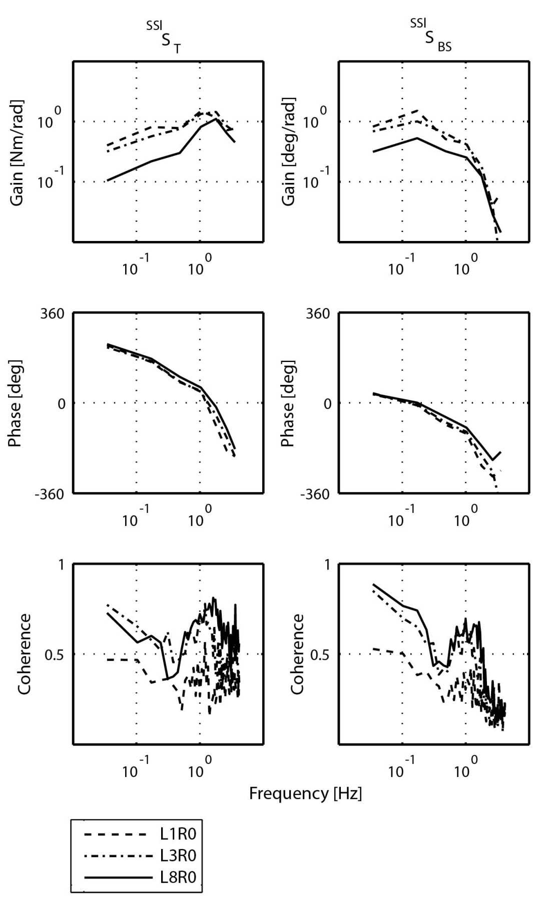

Figure 8. Sensitivity functions (mean over subjects) of the three conditions with perturbation of only the left support surface (condition L1R0, L3R0 and L8R0). The gain and phase of the sensitivities of the total torque to the rotation of the left support surface ($^{SSl}S_T$) and of the body sway to the left support surface ($^{SSl}S_{BS}$) are shown. The coherence is shown between the perturbation and the torque and the body sway.

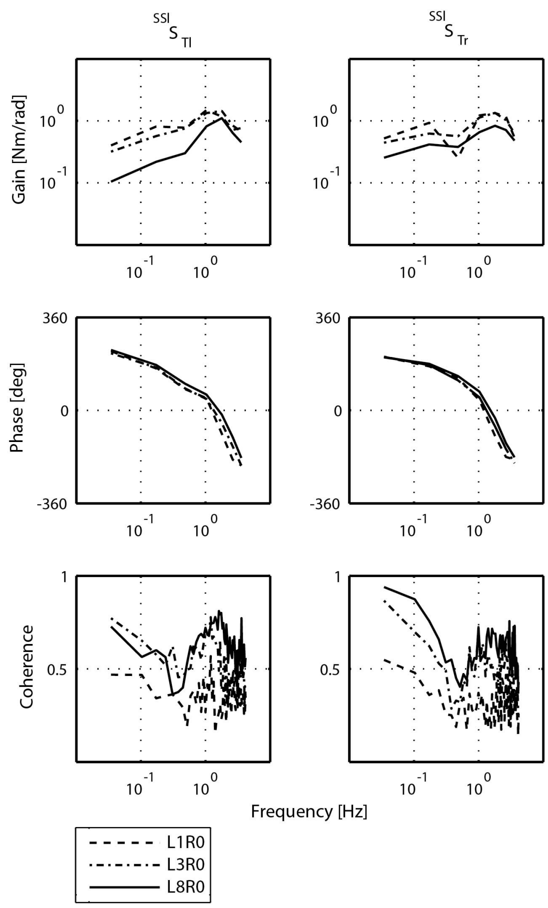

Figure 9. Mean sensitivity functions over the subjects of the three conditions with only perturbation of the left support surface (condition L1R0, L3R0 and L8R0). The gain and phase of the sensitivities of the left torque to the rotation of the left support surface ($^{SSl}S_{Tl}$) and of the right torque to the rotation of the left support surface ($^{SSl}S_{Tr}$) are shown. The coherence is shown between the perturbation and the left and right ankle torque.

These comparisons still showed a significant decrease of the gains of the SSrSTr and SSrSTl sensitivity functions (p<0.001 and p=0.001, respectively) and no significant difference in the gains of SSlSTl and SSlSTr (p=0.15 and p=0.49, respectively).

Coherence

The coherence between the platform translation and the torques or body sway increased with higher frequencies (Figure 6). Coherence between the support surface rotations and the torques was high for low frequencies and frequencies higher than 0.5 Hz (Figure 9 and Figure 10). With higher amplitudes the coherence increased, likely due to the increased signal to noise ratio with higher perturbation amplitudes, i.e. more signal power.

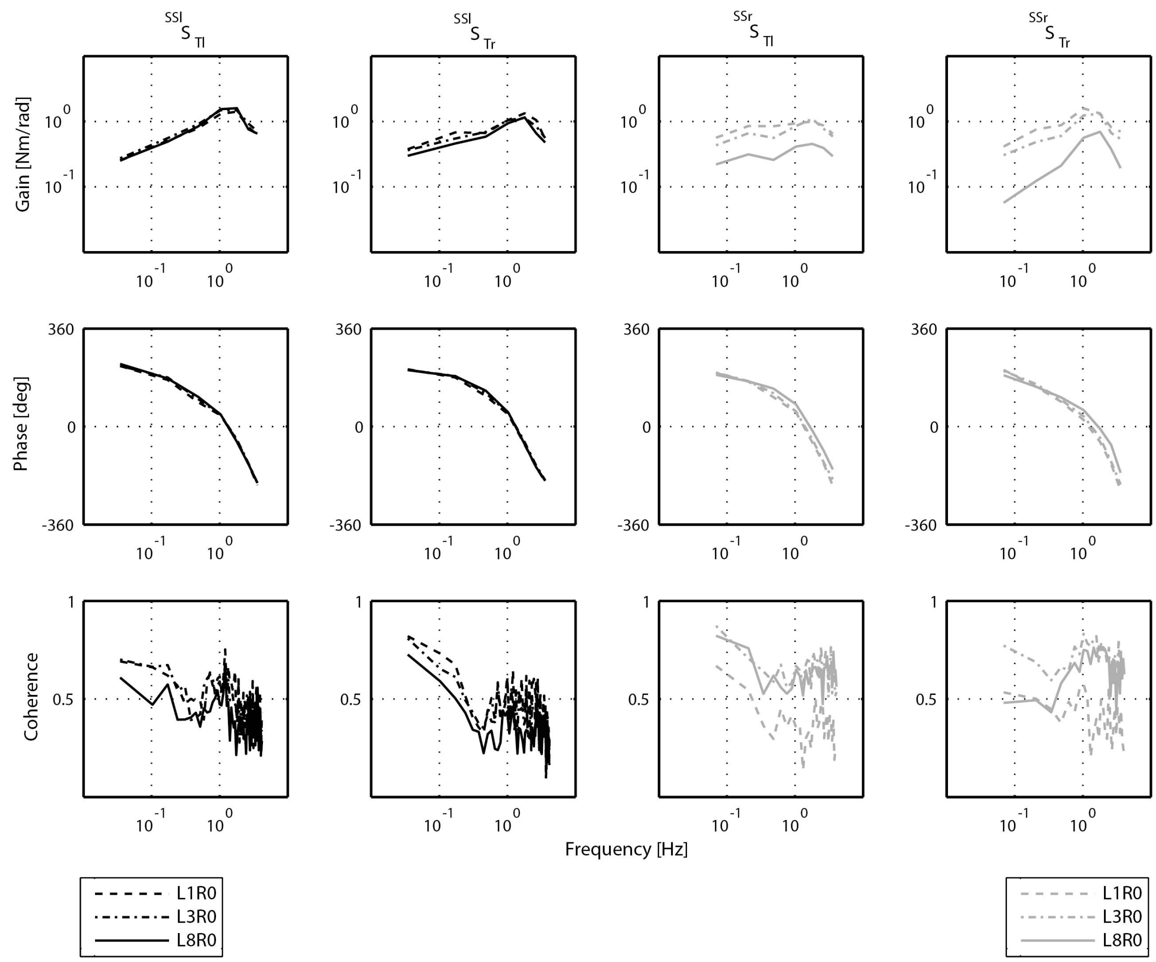

Figure 10. Mean sensitivity functions of the conditions with perturbation of both support surfaces (condition L3R1, L3R3 and L3R8). The sensitivity functions of the left torque and of the right torque to the rotation of the left support surface ($^{SSl}S_{Tl}$ and $^{SSl}S_{Tr}$) and the sensitivity functions of the left torque and of the right torque to the rotation of the right support surface ($^{SSr}S_{Tl}$ and $^{SSr}S_{Tr}$) are shown for the three conditions. Both phase and gain are displayed. The coherence is shown between each perturbation and the left and right ankle torque.

Discussion

Balance control involves the stabilization of the body in response to perturbations, i.e. ankle torques are generated to control body sway. Body sway is sensed by different sensory systems (vision, proprioception, vestibular system) and used by the (motor) controller. The (motor) controller, muscles and sensory systems together form a stabilizing mechanism. Here, we applied platform perturbations to investigate this stabilizing mechanism in combination with support surface rotations to investigate the relative weights of the different sensory systems, i.e. sensory reweighting. The support surface rotations affect both the active and passive feedback mechanisms.

Methodological issues

When considering small deviations around an operating point, a nonlinear system, like balance control, can be linearized. In this experiment linear models were used to identify nonlinear characteristics over the different operating points (i.e. the different conditions). By applying support surface rotations, the variables that cause the nonlinearity (i.e. sensory weights) are controlled experimentally. The coherence indicates that the system can be considered linear in the operation points. By changing the stimulus amplitude the nonlinearities become apparent demonstrated by the variation between the conditions (as expressed by the sensitivity functions).

Stabilizing mechanisms

Theoretically, asymmetry between the stabilizing mechanisms can be due to a) asymmetry between the sums of weights of each stabilizing mechanism, b) asymmetry in weight bearing [17] or c) asymmetry in controller properties (i.e. muscle properties and neural pathways). Previous studies [2] showed differences in controller properties (stiffness, damping and time delay) between conditions, indicating that the CNS used also other adaptive strategies besides sensory reweighting. As our goal was to investigate whether sensory reweighting between legs is possible, it was important that the stabilizing mechanisms of each leg were only influenced by the sensory weights. To check whether this was the case, both the weight bearing and the stabilizing mechanisms of each leg were calculated.

The stabilizing mechanisms of both legs were constant and symmetrical during all conditions, except for the L3R8 condition. Although significant, the resulted differences between the left and right stabilizing mechanism during this condition were very small. Note that the asymmetry in the L3R8 condition was accompanied by a trend towards asymmetrical weight bearing. This indicates that the found balance control asymmetry is most likely due to a weight bearing asymmetry.

Using model simulations [24] it was shown that the dynamics of the stabilizing mechanism do not need to change during increasing amplitude sensory perturbations. Here, we confirmed these findings in human subjects using non-parametric system identification techniques. Also, similar to previous findings, the stabilizing mechanisms and weight bearing were coupled in this study [17]. These results showed that the sums of weights of each stabilizing mechanism remained constant and symmetrical between stabilizing mechanisms throughout the experiment.

Sensory reweighting between legs

Sensory reweighting is the ability of the human body to suppress erroneous sensory information, while becoming more sensitive to the other available sensory information. To date, studies investigating balance control have considered the proprioceptive information of both legs as one sensory source [2-5], which is a simplification as humans have two legs. These studies found that the proprioceptive weight decreased with support surface rotation amplitude.

In this study we applied support surface rotations to each leg individually; either only the left support surface rotated with different amplitudes or the right support surface rotated with different amplitudes while the left support surface rotated with constant amplitude.

One-leg perturbations

During one-leg perturbation the gain of the torque sensitivity functions to support surface perturbation (${}^{SSl}S_{Tl}$ and ${}^{SSl}S_{Tr}$) decreased significantly with increasing support surface rotation amplitude. These results are comparable with the results found in previous studies where both legs were perturbed simultaneously [3;5;22]. The decrease in gain implies a relative reduction in responsiveness to the proprioceptive perturbations (the input), i.e. a decrease in the proprioceptive weighting factor. The CNS used a different combination of sensory channel weights, such that the proprioceptive weight decreased and the other weights increased.

The sensory reweighting differs on specific frequency ranges. At low frequencies, the sensory reweighting was most pronounced. This was expected as the proprioceptive sensory system is especially sensitive to slow movements [2]. At higher frequencies, the body sway response became increasingly dominated by inertial torques and sensory reweighting had no effect [2].

Two-leg perturbations

During two-leg perturbation the gain of the torque sensitivity functions to the right support surface perturbation (${}^{SSr}S_{Tl}$ and ${}^{SSr}S_{Tr}$) decreased significantly with increasing amplitude of the right support surface. These results are similar to the condition with one-leg perturbation and to previous studies where both legs were perturbed simultaneously.

In the two-leg perturbation conditions, the torque sensitivity functions to the left (constant) support surface perturbation (${}^{SSl}S_{Tl}$ and ${}^{SSl}S_{Tr}$) could also be estimated. Results showed that they were not influenced by increasing the amplitude of the right support surface, indicating that the sensory weights of the left proprioceptive information did not change. Hence, when perturbing two legs, the weight of the proprioceptive information of the least perturbed leg was not influenced by the decreased weight of the proprioceptive information of the most perturbed leg.

Sensory reweighting within legs

Down weighting of the proprioceptive information of one leg has to be accompanied by up weighting of another sensory system [2]. In this case, the vestibular information should be up weighted, as the visual system is eliminated and the weight of proprioceptive information of the other leg remained constant. More specifically, the weight of the ipsilateral vestibular information was increased, because the stabilizing mechanisms remained constant and symmetrical across conditions. This is in accordance with a study of Day et al. (2010) who showed that vestibular information of both labyrinths (i.e., also coming from two sensors), provided independent estimates of head motion [11]. Our results also confirm the findings by Van der Kooij et al. (2001) in another experimental setting. Because both legs are perturbed, proprioceptive information from both legs is less reliable and a conflict appears between the proprioceptive information of both legs and the other sensory systems. Van der Kooij et al. (2001; 2011) showed that vestibular information is necessary to solve sensory conflicts [3;24]. In conclusion, our results indicate that sensory reweighting of both legs is independent.

Conclusions

In sum, this study demonstrates that proprioceptive information of the left and right leg is weighted independently during balance control. Sensory information of a perturbed leg (by support surface rotations) is down weighted with perturbation amplitude, irrespective whether the contralateral leg is perturbed or not. The down weighting of proprioceptive information of one leg is compensated by up weighting of the vestibular information and not by up weighting of the proprioceptive information of the contralateral leg.

Implications

To our knowledge this is the first study which demonstrates that proprioceptive information of both legs is weighted independently during balance control. Surprisingly, down weighting the proprioceptive information of one leg was accompanied by up weighting of the vestibular information and not by up weighting of the proprioceptive information of the contralateral leg. The question arises why people do not up weigh the proprioceptive information of the contralateral leg. Whether people are able to up weigh proprioceptive information of the contralateral leg, could be tested in vestibular loss patients, who have no vestibular contribution at all.

Distinguishing between the balance contribution of both legs and sensory reweighting of individual limbs may also have clinical applications for certain neurological disorders, such as Parkinson's disease (PD) [25;26] and stroke [27], possibly aiding in the development and evaluation of treatments. In both disorders it has been shown that asymmetry in balance control is an issue. This asymmetry cannot be attributed solely to weight bearing asymmetries [17;25;28]. Therefore, it has been hypothesized that the lower limb proprioception and regulation of sensory weights has been affected [27;29-31]. With our new approach we are able to test this, creating new unique insights into the pathophysiology of Parkinson’s disease and stroke.

Acknowledgements

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Chapter 9

Changes in sensory reweighting of proprioceptive information during standing balance with age and disease

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Abstract

Sensory reweighting is the strategy of selecting reliable over unreliable sensory information during balance by dynamically combining proprioceptive, vestibular and visual information. We used system identification techniques to show the weight and the adaptive process of weight change of proprioceptive information during standing balance with age and specific diseases.

Ten healthy young, aged between 20 and 30 years, and 44 elderly, aged above 65 years, encompassing ten healthy elderly, ten with cataract, ten with polyneuropathy and fourteen with impaired balance, participated in the study. During stance, proprioceptive information of the ankles was disturbed by rotation of the support surface with specific frequency content where disturbance amplitude increased over trials. Body sway and reactive ankle torque were measured to determine sensitivity functions of these responses to the disturbance amplitude. Model fits resulted in a proprioceptive weight (changing over trials), time delay, force feedback, active stiffness and active damping.

The proprioceptive weight was higher in healthy elderly compared to young and higher in elderly with cataract and elderly with impaired balance compared with healthy elderly. Proprioceptive weight decreased with increasing disturbance amplitude; decrease was similar in all groups. In all groups, the time delay was higher and the active stiffness was lower compared to young or to healthy elderly.

In conclusion, proprioceptive information is weighted more with age, in patients with cataract and impaired balance. With age and in specific diseases the time delay was higher and active stiffness was lower. These results illustrate the opportunity to detect the underlying cause of impaired balance in elderly using system identification as a focus for targeted interventions.

Introduction

Impaired standing balance is a common problem in elderly [1;2] and one of the main causes of falls [3]. Underlying organ systems, such as the motor, nervous and sensory systems (i.e. vestibular system, vision and proprioception) interact with each other to maintain balance in a closed loop, in which cause and effect are interrelated. For example, changes in muscle force have an impact on body sway and the other way around, detection of body sway changes by the sensory system have an impact on muscle force. Each underlying system is prone to deterioration with advanced age and is influenced by age-related diseases and medication use [4-6]. Systems can compensate for each other's deterioration. Failing compensation strategies may eventually result in impaired standing balance, which finally may result in falling.

One possible compensation strategy is sensory reweighting [7;8]. According to this strategy, the nervous system prefers reliable sensory information over less reliable information within a continuous dynamically weighting process. Information of each sensory system is weighted by a weighting factor relative to the contribution of the other sensory information. Deterioration of a sensory system will affect its own weight and the weights of other systems. For example, deficient vestibular information will result in a lower vestibular weight (i.e. downweighting) and will be subsequently compensated by more use of the other sensory information (i.e. a higher weight, upweighting) to maintain standing balance [8]. Reweighting of sensory information also depends on environmental conditions, like standing on uneven ground or in a dark room.

Previous research investigated sensory reweighting using posturography by eliminating or disturbing sensory information using external disturbances, such as by closing the eyes or movement of the visual scene or support surface. The ratio of the Center of Pressure (CoP) or Center of Mass (CoM) movement with and without external disturbances is used to indicate the diminished reliability of sensory information. These studies showed that healthy old individuals rely more on their visual information during standing balance compared with healthy young individuals [9;10]. Furthermore, it was shown that with age the nervous system loses ability to adapt to altered sensory conditions [4;9;11-17]. Elderly with deteriorated vision (i.e. elderly with cataract or glaucoma) relied more on vestibular and proprioceptive information during standing balance and showed therefore poor performance in altered sensory conditions in which vestibular or proprioceptive information was disturbed [18-22]. Elderly with deteriorated proprioception (i.e. elderly with polyneuropathy) showed increased reliance on the visual system during balance control and showed therefore poor performance in altered sensory conditions in which visual information was disturbed [23-27].

It is difficult to interpret the results of posturography, as changes in CoP and CoM movement are affected by all systems involved in standing balance, i.e. the motor system, the sensory systems and nervous system, and also by the use of other compensation strategies to withstand the disturbances. System identification techniques potentially allow for disentangling the interrelation between the underlying systems and the contribution of each individual system [8;14;28-32]. Underlying system dynamics can be quantified by fitting a model of the balance control system on the response of the human body to well-known disturbances. This allows for investigating the weight of sensory information regardless of changes in the other underlying systems involved in standing balance and used compensation strategies. Furthermore, by applying sensory disturbances with increasing disturbance amplitude over trials, it is possible to investigate sensory reweighting [8;33].

In this study, we applied system identification techniques to assess sensory reweighting of proprioceptive information during standing balance in elderly using disturbances of proprioceptive information of the ankle; proprioception is defined as sensory information about leg orientation relative to the support surface. We investigated sensory reweighting as function of age and specific diseases interfering with sensory systems to study how these diseases affect the reliance on proprioceptive information and the adaptation to proprioceptive disturbances. This is the first study investigating sensory reweighting using system identification techniques in a large group of elderly with specific diseases in a clinical setting. Healthy old individuals were compared with healthy young individuals to investigate the age effect on proprioceptive reweighting. To investigate the effect of specific sensory deficits, elderly with polyneuropathy and with cataract were compared with healthy old individuals. To show the possibility to detect underlying changes in a heterogeneous population with various causes of impaired balance, elderly with impaired balance were compared with healthy old individuals.

Our hypotheses were based on the sensory reweighting theory and Bayesian decision theory [8;34]. It was hypothesized that with age the use of proprioceptive information increased, as the vestibular and visual system deteriorate more with age compared with the proprioceptive system resulting in a more sensory noise in the vestibular and visual information [4;30]. In case of cataract an increased reliance on proprioceptive information was hypothesized due to more sensory noise in visual information and therefore a higher proprioceptive weight. In case of polyneuropathy we hypothesized less reliance on proprioceptive information compared to healthy old individuals due to more sensory noise in proprioceptive information resulting in a lower proprioceptive weight. In elderly with impaired balance, a mix of previous scenarios and a higher interindividual variability in proprioceptive weight was expected as impaired balance could be the result of deterioration of multiple sensory systems. Changes in adaptation to increasing proprioceptive disturbances was only expected in case of proprioceptive deficits, i.e. with polyneuropathy and impaired standing balance, in which the sensory noise in the proprioceptive information was increased resulting in less decrease in proprioceptive weight with increasing proprioceptive disturbance.

Materials and methods

Participants

Ten healthy young participants, aged between 20 and 30 years, and 44 elderly, aged above 65 years, were included. The group of elderly composed of ten healthy old participants, ten elderly with cataract, ten elderly with polyneuropathy and fourteen elderly with impaired standing balance. Inclusion criteria for the group of young and healthy elderly were applied following the EU-FP7 MYOAGE study [35] to reduce possible confounding by (co)morbidities. Exclusion criteria were being in a dependent living situation, inability to walk a distance of 250 m, presence of co-morbidity (neurologic disorders; metabolic diseases; rheumatic diseases; recent malignancy; heart failure; severe chronic obstructive pulmonary disease; dementia), use of certain medication (immunosuppressive drugs, insulin, anticoagulation), immobilization for one week during the last three months, and orthopedic surgery during the last two years still causing pain or functional limitation. Inclusion criteria of the other three groups consisted of being scheduled for cataract surgery (cataract group), being diagnosed with polyneuropathy (polyneuropathy group) and unable to perform a ten seconds stance with both feet in one line (i.e. tandem stance) with eyes open (impaired standing balance group) regardless of the underlying cause. This study was performed according to the principles of the Declaration of Helsinki and was approved by the Medical Ethics Committee of the Leiden University Medical Center, Leiden, the Netherlands. All participants gave written informed consent to participate in this study.

Participant characteristics

Participants completed questionnaires, which provided information on age, gender, experienced impaired balance, fall incidents and walking difficulties. Weight and height were measured. Medication use and presence of diseases were obtained by standardized interviewing before inclusion and checked by reviewing available medical records. Cognition was assessed using the Mini-Mental State Examination (MMSE) [36]. Depressive symptoms were assessed using the Hospital Anxiety and Depression Scale (HADS) [37]. Depression was indicated by a score of 8 or more on the HADS depression scale. Physical functioning was assessed by handgrip strength and the Short Physical Performance Battery (SPPB) [38]. Walking speed was measured over 10 meter during a 15 meter walk at preferred walking speed.

Apparatus

A Bilateral Ankle Perturbator (BAP) (Forcelink B.V., Culemborg, The Netherlands) was used to disturb the proprioceptive information of both ankles by applying support surface (SS) rotations around the ankle axis [39] (Figure 1). The actual angles of rotation (i.e. motor angles) and the applied torques to both SS of the BAP (i.e. motor torques) were measured.

Figure 1. Experimental set-up with the Bilateral Ankle Perturbator (BAP). The participant wore a safety harness to prevent a fall and looked at a poster on the wall.

Procedure

During all experiments participants wore anti-slip socks (Basset home socks). Prior to the experiment, data was recorded for 30 seconds while the participant kept his balance on the BAP without SS rotation (i.e. static condition). During the main experiment, the participant was instructed to stand with the arms crossed over the chest and to keep both feet on the SSs. Both SSs rotated simultaneously following a continuous disturbance signal with increasing zero-to-peak amplitude over trials. Each participant performed 3 trials with increasing disturbance amplitude, in the range of 0.01, 0.02, 0.04 and 0.08 radians. The applied disturbance amplitudes were dependent on the amplitude each participant could maximally withstand. If a participant was not able to perform a trial with amplitude of 0.08 radians, a trial with amplitude of 0.01 radians was performed. Thus, all participants performed 3 trials, including 2 conditions with disturbance amplitude 0.02 and 0.04 radians and 1 condition based on the ability of the participant, either 0.01 or 0.08 radians. The trials were presented in random order and each trial lasted 116.16 seconds. Before each trial the participant was given about 30 seconds to get accustomed to the disturbances. Visual information was standardized by instructing the subject to look at a landscape poster on the wall. Between trials, the participant was offered sufficient resting time depending on individual needs. The participant wore a safety harness to prevent falling, which did not constrain movement and did not provide support or orientation information.

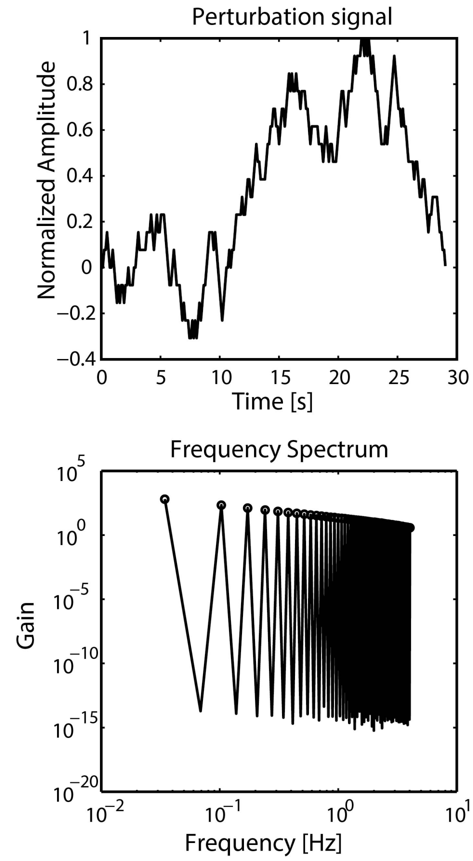

Figure 2. Time signal (upper), presented with normalized amplitude, and the corresponding power spectrum (lower) of the disturbance signal.

Disturbance signal

A pseudorandom ternary sequence (PRTS) of numbers was designed [40] and used as SS angular velocity. Integration of this velocity signal provided an unpredictable disturbance signal of the SS rotation with a wide spectral bandwidth (Figure 2). A PRTS signal with a time increment of Δt=0.12 s was generated, resulting in a signal with a period of 29.04 s. The starting value of the PRTS signal was selected so that about 80% of the rotation occurred in toe down direction [8] to prevent initial balance disturbance as humans tolerate larger angles of ankle rotation in toe down direction. Each trial consisted of four complete cycles of the disturbance signal (i.e. a total time of 116.16 s).

Data recording and processing

Lower and upper body segmental movements were measured in both anterior-posterior and medio-lateral direction using four draw-wire potentiometers (Sentech SP2, Celesco, Chatsworth, CA, United States) at a sample frequency of 1000 Hz. The potentiometers were connected to the participant's trunk and right upper leg. The motor angles and motor torques were recorded using a Matlab interface with a sample frequency of 1000 Hz. Data analysis was performed with Matlab (The MathWorks, Natick, MA, United States).

Leg and hip angles were calculated from potentiometer data. Both were calculated relative to the average body position during the static condition. The leg angle represents the segment angle of the lower leg relative to the vertical and the hip angle represents the joint angle of the hip, i.e. the angle of the trunk relative to the lower leg. The body sway was represented by the CoM movement, which was calculated using the leg and hip angles and body geometry of individual segments [41]. The data of the motor angles (i.e. SS rotation) and motor torques were filtered with a second order low pass digital Butterworth filter with cut-off frequency of 20 Hz (Matlab function: filtfilt). The ankle torques (Tl, Tr) were obtained from the recorded motor torques (i.e. the applied torque to the SSs of the BAP) by subtracting the contributions of the mass and inertia of the SSs of the BAP from the measured motor torque. The ankle torques were corrected for the distance between the rotation point of the SS and the real rotation point of the ankle by dividing the ankle torques by the distance between the SS and the rotation point and multiplying it by the distance between the SS and the ankle joint. The time series were segmented into four data blocks of 29.04 seconds (i.e. the length of the disturbance signal).

Data analysis

Body sway descriptors

A description of the response of the leg and hip angle was given by the absolute mean and the Root Mean Square (RMS) of the mean time series of the leg and hip angle representing the mean angle and variance, respectively.

Sensitivity functions

To indicate the effect of the disturbances on the ankle torque and body sway, Frequency Response Functions (FRFs) were estimated. The support surface disturbances, ankle torque, leg and hip angle, and body sway were transformed to the frequency domain. The periodic part of the frequency coefficients was determined by averaging over the data blocks [42]. The Power Spectral Densities (PSD) and Cross Spectral Densities (CSD) were computed to calculate the FRFs [32]. Only the excited frequencies were analyzed (see ‘Disturbance Signal’). The FRFs were estimated using the indirect approach [32]:

$$^{SS}S_x(f) = \Phi_{SS,x}(f)\cdot\left[\Phi_{SS,SS}(f)\right]^{-1} \tag{1}$$

In which $\Phi_{SS,x}$ represents the CSD of the SS rotation and x, which represents the total ankle torque ($T_l + T_r$), leg angle (LA), hip angle (HA) or body sway (BS), and $\Phi_{SS,SS}$ the PSD of the SS rotation. The FRF magnitude and the FRF phase represent the amplitude ratio and the relative delay, respectively, between the SS rotation and the ankle torque, leg angle, hip angle or body sway. Four sensitivity functions were estimated: 1) the ankle torque sensitivity function describes the relationship between the SS rotation and the torque exerted by both ankles ($^{SS}S_T$); 2) the leg angle sensitivity function describes the relationship between the SS rotation and the leg angle per frequency ($^{SS}S_{LA}$); 3) the hip angle sensitivity function describes the relationship between the SS rotation and the hip angle per frequency ($^{SS}S_{HA}$); and 4) the body sway sensitivity function describes the relationship between the SS rotation and the body sway in anterior-posterior direction per frequency ($^{SS}S_{BS}$). As the corrective torque has to compensate for the gravitational torque, the FRFs of the ankle torque were normalized for the gravitational stiffness, i.e. participant’s mass and the distance from the ankles to the CoM times the gravitational acceleration (mgl_{CoM}).

Model description and validation

To give physiological meaning to the sensitivity functions, a model of the balance control system was used to describe the sensitivity functions. This model consists of several parameters describing the behavior of the system (Table 1). The present model is based on previous models [8;32;43;44] (Figure 3, Appendix A). The balance control system is approached by a one-segmental inverted pendulum model rotating around the ankle joint (Figure 3), which is stabilized by a corrective ankle torque. This corrective torque is generated by a stabilizing mechanism. The stabilizing mechanism is formed by the neural controller that processes sensory signals and sends efferent signals to the muscle as well as the muscles itself, which both contribute to the corrective torque. The stabilizing mechanism incorporates visual, vestibular and proprioceptive information. Each sensory system is presented by a sensory channel consisting of a weighting factor (W_{prop}, $W_{ves+vis}$) representing the relative contribution of each sensory system to maintain balance. The sum of the weighting factors always equals one. The information of the sensory channels is sent to a controller representing the nervous system and the muscles. The controller consists of a PD controller (K_p and K_d) with a time delay (τ) representing the neural delay due to transport and processing time of all sensory information and the reaction time of the motor system, and activation dynamics representing the muscles consisting of a relative damping and natural frequency (β and ω). Within the controller there is a force feedback to represent the function of the Golgi tendon organ and other force sensors, which gives feedback to the input of the neural control represented by a gain divided by a time constant (K_f/τ_f).

Balance control modelling

The parameters describing the sensitivity functions were estimated using the mathematical FRFs of the balance control model (see Appendix A). The mathematical FRFs of the SS rotation to the ankle torque and to the body sway of the different trials were used to fit the model on the experimental FRFs. To limit the number of unconstrained fit parameters, we used fixed values of relative damping (β = 0.7) and natural frequency (ω= 5π rad/s) [44] and direct measurements of mass, pendulum length and estimated the inertia by multiplying mass with squared pendulum length (ml_{CoM}^2).

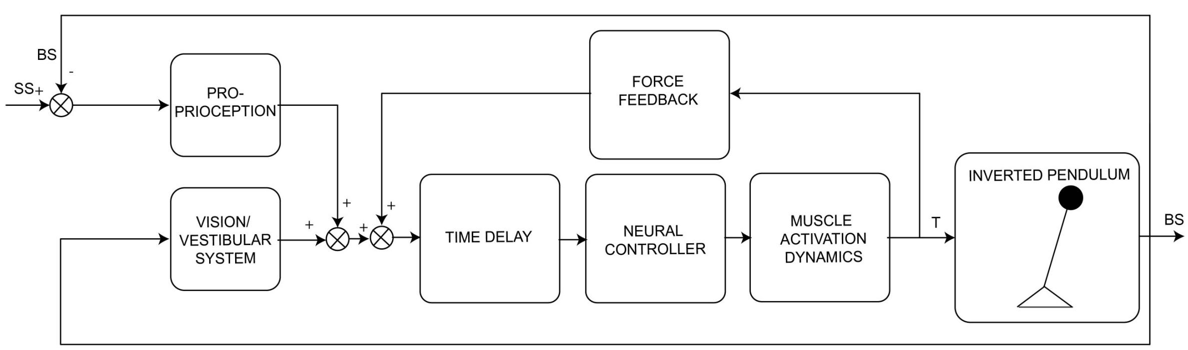

Figure 3. The model of the balance control system in which the body is represented by an inverted pendulum. This inverted pendulum is controlled by the stabilizing mechanism consisting of the weighting factors of the visual, vestibular and proprioceptive information and a motor controller, which consists of a neural controller, force feedback, time delay and muscle activation dynamics. The torque (T) generated by the stabilizing mechanism affect the body sway (BS) angle. The control loop can be disturbed by support surface rotation (SS) resulting in a sensory disturbance of the proprioceptive information.

Table 1. Overview of estimated model parameters.

Parameter	Abbreviation	Unit	Used in model fit	Value
Length	l_{CoM}	m	Fixed value	Measured
Mass	m	kg	Fixed value	Measured
Inertia	I	kgm^2/s^2	Fixed value	ml_{CoM}^2
Vestibular and visual weight	$W_{ves+vis}$	-	Calculated	$1\text{-}W_{prop}$
Proprioceptive weight	W_{prop}	-	Variable over conditions	
Active stiffness	K_p	Nm/rad	Variable over conditions	
Active damping	K_d	Nms/rad	Variable over conditions	
Time delay	τ	s	Constant over conditions	
Relative damping	β	-	Fixed value	0.7
Natural frequency	ω	rad/s	Fixed value	5π
Force feedback	K_f/τ_f	rad/Nm/s	Constant over conditions	

The time delay and force feedback were kept constant over trials. Of the weighting factors only the proprioceptive weight was estimated, in which the sum of the visual and vestibular weight equals one minus the proprioceptive weight. The proprioceptive weight, active stiffness and active damping were variable between trials. This resulted in an estimation of 11 parameters per participant (Table 1). The model was fitted on all individual experimental FRFs using a nonlinear least-square fit (Matlab function: lsqnonlin) by minimizing the vector-valued function:

$$\varepsilon(x) = \sqrt{\frac{\gamma_{SS,x}(x)}{1+f(x)}} \cdot \left| \log\left(\frac{H_{\exp}(x)}{H_{est}(x)} \right) \right| \tag{2}$$

In which $\gamma_{SS,x}$ represents the coherence between SS rotation and ankle torque or body sway, H_{exp} the experimental sensitivity function and H_{est} the estimated sensitivity function based on the estimated model parameters. The coherence varies between 0 and 1, in which a coherence close to one reflects a good signal to noise ratio. To evaluate the goodness of the model fit, the Goodness of Fit (GOF) in the frequency domain was calculated using equation 3.

$$GOF = \left[1 - \frac{\sum_{k=1}^{N} \left| S_{est}(\omega_k) - S_{\exp}(\omega_k, p) \right|^2}{\sum_{k=1}^{N} \left| S_{est}(\omega_k) \right|^2} \right] \times 100\% \tag{3}$$

In which $S_{est}(\omega)$ represents the estimated sensitivity function per frequency and $S_{exp}(\omega,p)$ the experimental sensitivity function per frequency and parameter set. To compare parameters between participants, the parameters K_p and K_d were normalized for the participant's gravitational stiffness (mgl_{CoM}).

Statistical analysis

The characteristics of the participants were represented by mean and standard deviation in case of a Gaussian distribution. Else, median and inter quartile range or number and percentage were presented. For statistical analysis, the PSDs and CSDs were averaged within seven frequency bands before the FRFs were calculated, according to the method of Peterka in which the number of points averaged increases with frequency [8], resulting in the frequency bands 0-0.1 Hz, 0.1-0.3 Hz, 0.3-0.7 Hz, 0.7-1.4 Hz, 1.4-2.2 Hz, 2.2-3.1 Hz and 3.1-4.1 Hz. Subsequently, the magnitude of each FRF was log transformed to make the data normally distributed.

Linear mixed models were used to test significant differences in FRFs between groups and disturbance amplitudes. Frequency band was included as covariate to adjust for differences due to frequencies. Groups, disturbance amplitude and frequency band were fixed effects. Participant intercept was included as random effect to take the measurement repetitions and differences in conditions into account, as not all participants performed conditions with the same disturbance amplitude.

The proprioceptive reweighting was based on the conditions performed by all participants (i.e. conditions with disturbance amplitude 0.02 and 0.04 radians) and was assessed by fitting individual slopes between disturbance amplitude and proprioceptive weight using linear regression analysis, representing the proprioceptive weight change in response to a 1 radian increase of the disturbance amplitude. A negative value indicated downweighting of proprioceptive information. To test significant differences in estimated parameters (i.e. proprioceptive weight, proprioceptive reweighting, active stiffness and damping, time delay and force feedback) between groups and disturbance amplitudes, linear mixed models were used, with group and disturbance amplitude as fixed effects and participant intercept as random effect. All analyses were adjusted for age and gender by including those factors in the mixed models. The analyses of the comparison between healthy young and healthy old participants were only adjusted for gender. For all tests, significance (α) was set at 0.05. All analyses were performed with SPSS version 20.0 (SPSS, Chicago, IL).

Results

Below the results of this study are presented. Differences between groups in the response to the proprioceptive disturbances are summarized in Table 2.

Table 2. Summary of results.

	Old vs. Young	Cataract vs. Old	PNP vs. Old	Impaired balance vs. Old	Cataract vs. PNP
Body sway descriptors					
Mean ankle angle	=	↑	=	=	↑
Variance ankle angle	=	↑	=	↑	↑
Mean hip angle	↑	↑	=	↑	=
Variance hip angle	↑	↑	=	↑	=
Sensitivity functions					
Ankle torque	↑	↑	=	↑	↑
Ankle angle	=	↑	=	↑	=
Hip angle	↑	↑	=	↑	=
Body sway	↑	↑	=	↑	=
Estimated parameters					
W_p	↑	↑	=	↑	=
ΔW_p	=	=	=	=	=
τ	↑	↑	↑	↑	=
K_p	↓	↓	↓	↓	=
K_d	↑	=	=	=	↓
K_f/τ_f	=	=	=	=	=

Results are summarized by three symbols; ↓ representing a significant lower value, ↑ representing a significant higher value, and = representing no significant differences between groups.

Participant characteristics

Table 3 represents the participant characteristics per group. Healthy old participants showed no significant differences in characteristics compared with young participants, except for age. Between the elderly groups, no differences were found in age. Elderly with polyneuropathy experienced more impaired standing balance and showed lower walking speed and lower SPPB score compared with healthy old participants. Elderly diagnosed with impaired balance showed more medication use, more multimorbidity, lower physical functioning and more self-reported walking difficulties compared with healthy old participants. Twenty-nine participants (53.7%) were not able to perform the trial with the highest disturbance amplitude of 0.08 radians and therefore performed the trial with disturbance amplitude of 0.01 radians. This group comprised 1 (10%) healthy old, 5 (50%) elderly with cataract, 9 (90%) elderly with polyneuropathy and 14 (100%) elderly with impaired balance.

Table 3. Participants characteristics stratified by group.

	Young	Old			
		Healthy	Cataract	PNP	Imp. balance
	n = 10	n = 10	n = 10	n = 10	n = 14
Age, years	25.4 (2.2)	76.8 (1.8)	76.7 (6.8)	73.7 (8.0)	83.5 (6.3)
Women (n, %)	6 (60)	4 (40)	5 (50)	3 (30)	3 (21.4)
Health status					
Multimorbidity (n, %) *	0 (0)	0 (0)	2 (20)	2 (20)	4 (28.6)
# of medication (median, IQR)	0.5 (0-1)	1 (0-2)	1 (0-6.25)	2 (1-4.5)	5 (3.75-8)
MMSE, points (median, IQR)	30 (30-30)	29.5 (28-30)	28.5 (28-30)	29 (27-30)	29 (28.7-29.3)
Depressive symptoms (n, %) ‡	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)
Anthropometry					
Height, cm	178 (11)	171 (9)	172 (11)	175 (10)	174 (9)
Weight, kg	71.1 (6.7)	73.3 (7.9)	73.8 (17.0)	86.4 (10.4)	79.5 (17.3)
Physical functioning					
Handgrip strength, kg	44.6 (9.4)	35.7 (5.9)	33.8 (10.9)	37.5 (9.3)	32.1 (8.9)
SPPB score, points (median, IQR)	12 (12-12)	12 (11-12)	12 (10-12)	10 (9.5-11.3)	7.5 (6-10)
Walking speed, m/s §	1.48 (0.21)	1.34 (0.12)	1.23 (0.22)	1.07 (0.30)	1.00 (0.26)
Fall incident (n, %)	0 (0)	2 (20)	2 (20)	3 (30)	8 (57.1)
Impaired standing balance (n, %)	0 (0)	0 (0)	0 (0)	5 (50)	8 (57.1)
Walking difficulties (n, %)	0 (0)	0 (0)	1 (10)	8 (80)	10 (71.4)
BAP performance (n, %)					
Amplitude 0.01 rad	0 (0)	1 (10)	5 (50)	8 (80)	14 (100)
Amplitude 0.02 rad	10 (100)	10 (100)	10 (100)	10 (100)	14 (100)
Amplitude 0.04 rad	10 (100)	10 (100)	10 (100)	10 (100)	12 (85.7)
Amplitude 0.08 rad	10 (100)	9 (90)	5 (50)	1 (10)	-

All parameters are presented as mean with standard deviation unless indicated otherwise. *Present in case of two or more diseases, including chronic obstructive pulmonary disease, heart failure, rheumatic disorder, dementia, diabetes mellitus, malignancy, Parkinson's disease, (osteo)arthritis, transient ischemic attack and stroke. ‡Present with a depression subscore higher than eight on the Hospital Anxiety and Depression Scale. §Preferred gait speed during a steady state ten meter walk. Abbreviations: PNP, polyneuropathy; IQR, interquartile range; MMSE, Mini-Mental State Examination; SPPB, Short Physical Performance Battery.

Body sway descriptors

Figure 4 shows the RMS of the leg and hip angle for each group and each disturbance amplitude. Healthy old participants showed a higher mean and variance of the hip angle (p=0.003 and p=0.002). Comparing elderly with cataract and healthy old participants, elderly with cataract showed higher mean and variance in both leg and hip angle (leg: p=0.020, p=0.013, hip: p=0.021, p=0.012). Between healthy old participants and elderly with polyneuropathy no significant differences were in mean and variance of the leg and hip angle. Elderly with impaired balance had higher leg and hip angle variance (p=0.058 and p=0.013)

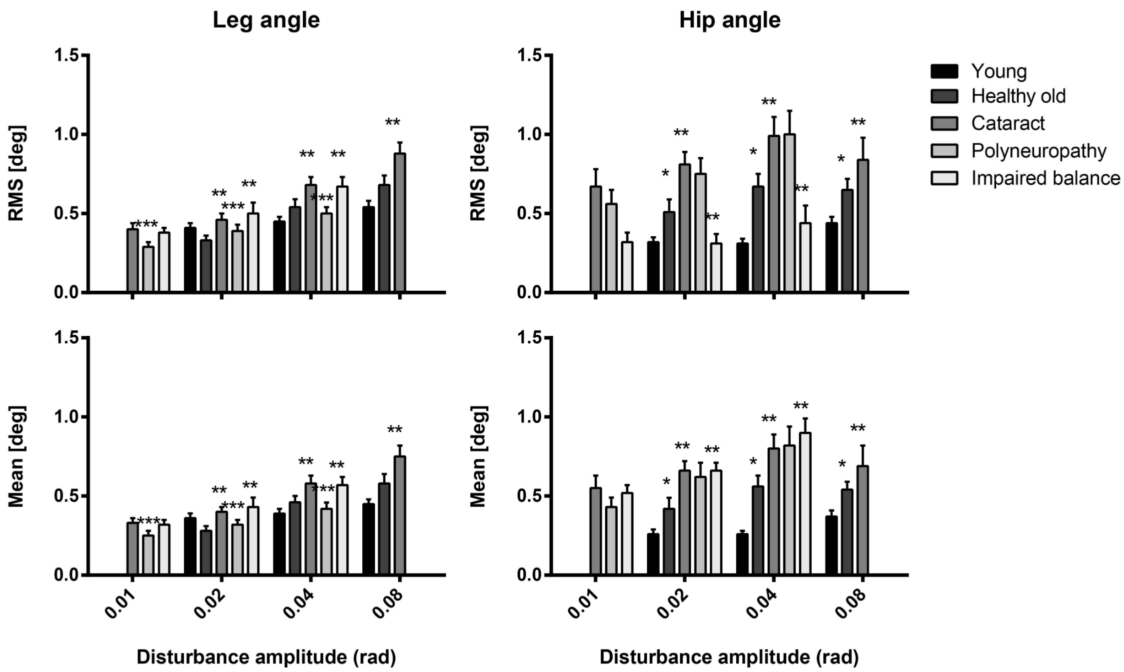

Figure 4. Absolute mean and root mean square (RMS) of leg and hip angle of each group and each trial. * significantly different (p<0.05) compared with young, ** significantly different (p<0.05) compared with healthy old, *** significantly different (p<0.05) compared with elderly with cataract.

and higher mean hip angle (p=0.014) compared with healthy old participants. Elderly with cataract had only differences in mean and variance of leg angle compared with elderly with polyneuropathy (p=0.017 and p=0.017).

Sensitivity functions

Figure 5 shows the mean sensitivity functions of the ankle torque, leg angle, hip angle and body sway to the disturbance with amplitude of 0.02 radians averaged over participants for each group. In all groups, the magnitude of all sensitivity functions significantly decreased

with increasing disturbance amplitude, indicating a saturation of the ankle torque, leg angle, hip angle and body sway with increasing disturbance amplitude. The magnitude of all sensitivity functions of the ankle torque, hip angle and body sway were higher in healthy old compared with healthy young participants (p<0.001, p<0.001 and p<0.001, respectively), indicating a higher response to the disturbance. No significant difference in the sensitivity of the leg angle was found between young and healthy old participants (p=0.33). All sensitivity function magnitudes were higher in the elderly with cataract (p=0.038, p=0.019, p=0.004 and p=0.005, respectively) and in the elderly with impaired balance (p=0.012, p=0.042, p=0.017

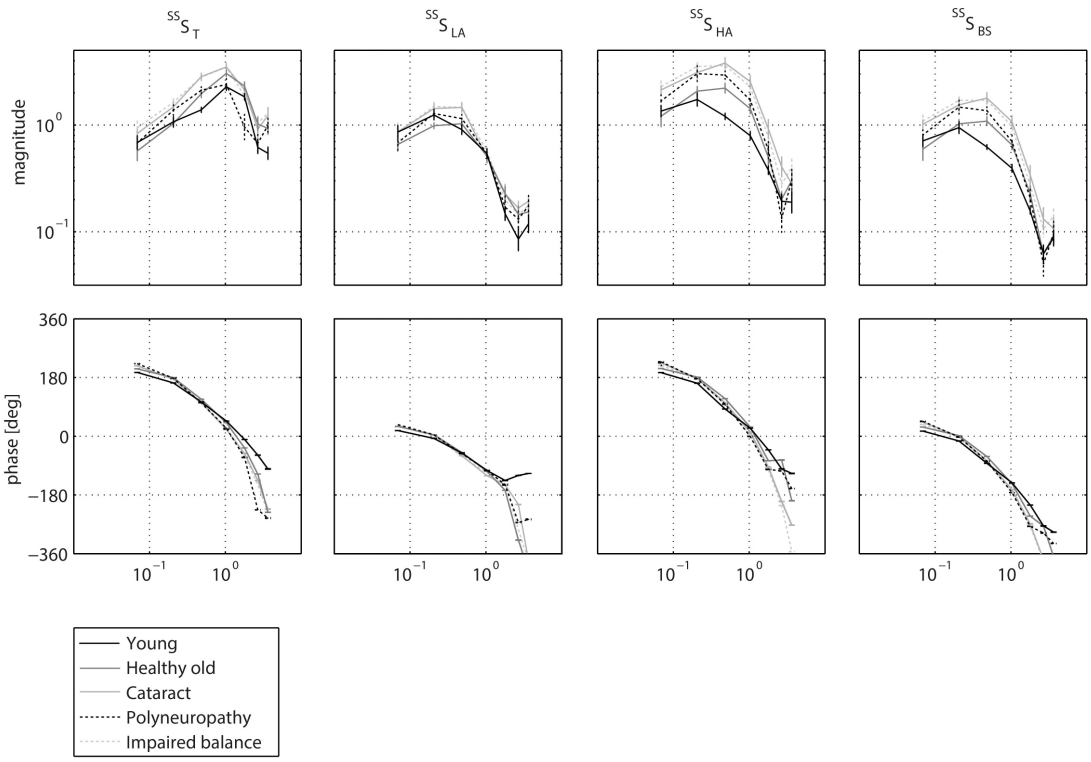

Figure 5. Mean sensitivity function of each group of the trial with disturbance amplitude of 0.02 radians. The magnitude and phase of the sensitivities of the ankle torque (${}^{SS}S_T$), the leg angle (${}^{SS}S_{LA}$), the hip angle (${}^{SS}S_{HA}$) and the body sway (${}^{SS}S_{BS}$) to the rotation of the support surface are shown.

and p=0.017, respectively) compared with healthy old participants. There were no significant differences in the magnitude of the sensitivity functions of the ankle torque, leg angle, hip angle and body sway between the healthy old participants and the elderly with polyneuropathy (p=0.82, p=0.54, p=0.30 and p=0.43, respectively). Comparing elderly with cataract with elderly with polyneuropathy showed a higher magnitude of the sensitivity function of the ankle torque in the elderly with cataract (p=0.042). No significant differences were found in the other sensitivity functions (leg angle: p=0.074, hip angle: p=0.18 and body sway: p=0.10).

Estimated model parameters

Table 4 shows the GOF per trial per group representing the goodness of the model fits. The GOF was higher in trials with higher disturbance amplitude. The GOF of the fitted model in the elderly with cataract, elderly with polyneuropathy and elderly with impaired balance was lower compared with the young and healthy old participants. Figure 6 shows the estimated proprioceptive weight and proprioceptive reweighting for each group and each disturbance amplitude. In all groups, the proprioceptive weight significantly decreased with increasing

Table 4. Goodness of Fit of the Frequency Response Function $^{SS}S_T$ model fits per trial per group.

	Young	Old			
		Healthy	Cataract	PNP	Imp. balance
0.01 rad, %	-	-	58.7 (8.2)	53.0 (4.7)	55.1 (5.4)
0.02 rad, %	78.5 (2.4)	76.2 (6.0)	78.4 (1.7)	68.6 (3.7)	69.2 (4.3)
0.04 rad, %	86.0 (1.4)	84.7 (2.8)	79.7 (3.8)	68.4 (9.7)	79.9 (3.0)
0.08 rad, %	90.1 (0.4)	85.4 (2.2)	87.5 (3.1)	-	-

All parameters are given in mean with standard error. Abbreviations: PNP, polyneuropathy.

disturbance amplitude ($p<0.001$), as also shown by the sensory reweighting parameter. Healthy old participants showed higher proprioceptive weight ($p<0.001$) and no differences in proprioceptive reweighting ($p>0.99$) compared with young participants. Compared with healthy old participants, elderly with cataract showed a higher proprioceptive weight ($p=0.018$) and no significant difference in proprioceptive reweighting ($p=0.64$). Elderly with polyneuropathy showed no significant differences in proprioceptive weight ($p=0.42$) and proprioceptive reweighting ($p=0.90$) compared with healthy old participants. Elderly with impaired balance showed a higher proprioceptive weight ($p=0.005$) and no differences in proprioceptive reweighting ($p=0.77$) compared with healthy old participants. There were no significant differences between elderly with cataract and elderly with polyneuropathy in proprioceptive weight ($p=0.13$) and proprioceptive reweighting ($p=0.87$).

Figure 7 represents the other estimated parameters for each group and each disturbance amplitude. Healthy old participants showed lower active stiffness ($p=0.004$), higher active damping ($p=0.003$) and higher time delay ($p<0.001$) compared with young participants. No significant differences in force feedback ($p=0.80$) were found.

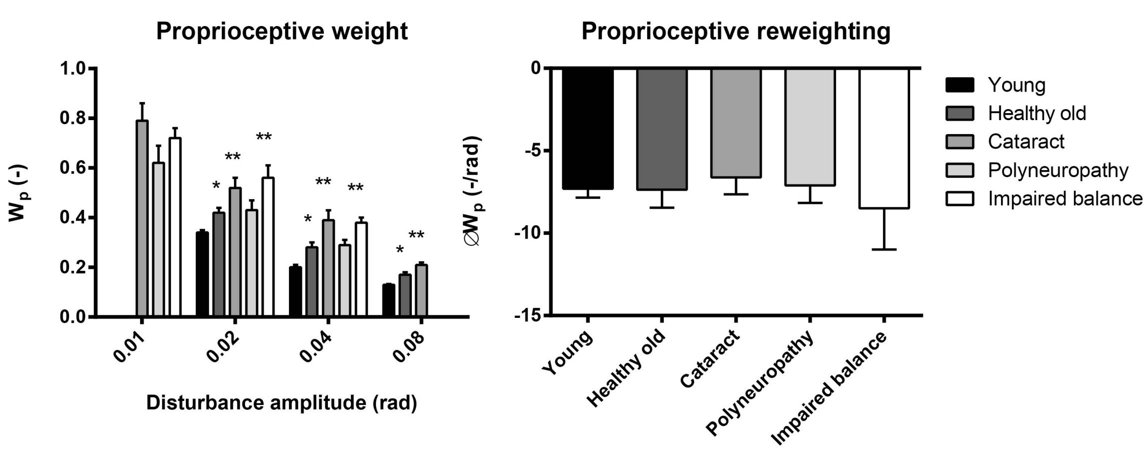

Figure 6. Proprioceptive weight and reweighting per radian increase of disturbance amplitude, of each group and each trial. * significantly different ($p<0.05$) compared with young, ** significantly different ($p<0.05$) compared with healthy old, *** significantly different ($p<0.05$) compared with elderly with cataract.

Compared with healthy old participants, elderly with cataract showed a lower active stiffness (p=0.013) and a higher time delay (p=0.009). No differences in active damping (p=0.12) and force feedback (p=0.81) were found. Elderly with polyneuropathy with had a lower active stiffness (p=0.003) and higher time delay (p=0.007) compared with healthy old participants.

There were no significant differences found in active damping (p=0.51) and force feedback (p=0.42). Elderly with impaired balance showed a lower active stiffness (p=0.027) and a higher time delay (p=0.002) compared with healthy old participants and no difference in active damping (p=0.67) and force feedback (p=0.36). Compared with elderly with cataract, elderly with polyneuropathy showed a higher active damping (p=0.029). There were no significant differences between elderly with cataract and elderly with polyneuropathy in active stiffness (p=0.25), time delay (p=0.46) and force feedback (p=0.39).

Discussion

The results of this study showed that the proprioceptive weight was higher with age and higher with cataract and impaired balance and showed no differences in proprioceptive reweighting with age and specific diseases.

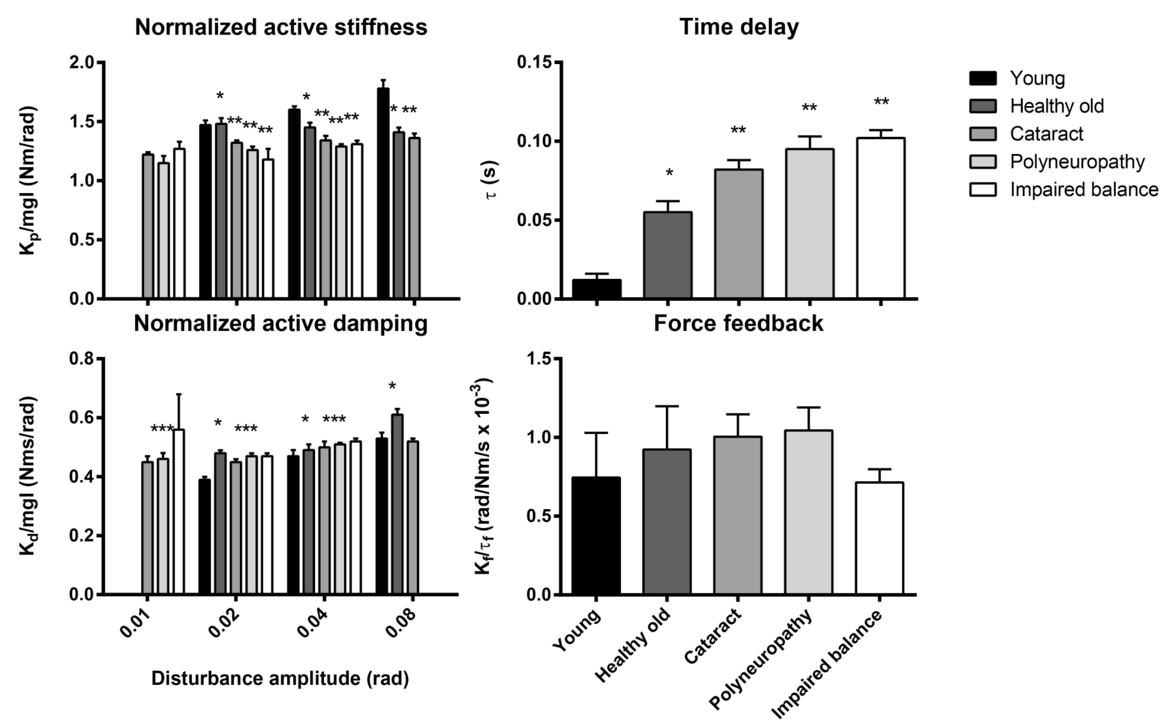

Figure 7. Normalized active stiffness and damping, time delay and force feedback, of each group and each trial. * significantly different (p<0.05) compared with young, ** significantly different (p<0.05) compared with healthy old, *** significantly different (p<0.05) compared with elderly with cataract.

Results are consistent with the hypothesis that sensory reweighting is an adaptive process to prevent loss of balance in case of deficits in the underlying sensory systems; increasing the disturbance amplitude of the proprioceptive information resulted in a decrease in proprioceptive weight, i.e. downweighting. The way the process of proprioceptive information changes depends on the deteriorated sensory system. Deficits of the visual system were compensated by an increase in proprioceptive weight and changes in the nervous system, while deficits of the proprioceptive system only showed changes in nervous system.

Proprioceptive weight changes with age

We demonstrated that healthy old participants rely more on their proprioceptive information during standing balance compared with healthy young participants, represented by a higher proprioceptive weight. Previous studies showed contradictory results according to the use sensory information in elderly, in which studies using posturography showed more use of visual information [9;10] and studies using system identification techniques showed more use of proprioceptive information [44]. The proprioceptive downweighting is comparable between age groups; healthy old participants have the same ability to compensate for unreliable sensory information as young participants. This is in accordance with previous studies in which sensory reweighting of visual information was investigated in healthy young and elderly [14], but in contrast with others [4;9;11-17]. Compared to previous studies, we included elderly with a higher age, i.e. 75 years or older instead of 65 years or older.

The increased use of proprioceptive information compared with young participants is following expectations, as explained by the deterioration of the other sensory systems with age [4;30]. Previous studies argued that the vestibular system deteriorates the most with age [4;10;46;47], which will result in less reliable vestibular information. This may be compensated for by upweighting of the other sensory information resulting in a higher visual and/or proprioceptive weight. Our results showed that the nervous system is still able to compensate for disturbances of the proprioceptive information, represented by similar proprioceptive downweighting in young and healthy old participants. However, when the higher proprioceptive weight of the healthy old participants is taken into account, the old participants downweight their proprioceptive information relatively less compared with young participants.

Proprioceptive weight changes with cataract

In patients with cataract we found a higher proprioceptive weight compared with healthy old, which means that elderly with cataract rely more on their proprioceptive information. This is in accordance with previous studies, which showed that elderly with visual problems rely more on vestibular and proprioceptive information [18-22]. Furthermore, these studies showed that elderly have more problems with maintaining balance during trials in which proprioceptive information is more disturbed, which is in accordance with our results. However, we found no differences in proprioceptive downweighting compared with healthy old participants in case of proprioceptive disturbances.

The higher proprioceptive weight could be explained by the compensation for less reliable visual information in cataract patients; less reliable visual information is downweighted, which is accompanied by upweighting of the sensory information of the other sensory systems, i.e. the proprioception and/or vestibular system [18;20-22]. An explanation for the comparable downweighting in healthy old participants could be that the nervous system still can compensate for the unreliable proprioceptive information by more use of the vestibular information instead of the visual information. This will result in the same amount of downweighting of the proprioceptive information despite deterioration of the visual system. When we take the already higher proprioceptive weight into account, elderly with cataract downweight their proprioceptive information relatively less compared with healthy old participants. This could also explain why elderly with cataract are not able to perform conditions with high disturbance of the proprioceptive information.

No changes in the use of proprioceptive information with polyneuropathy

It was expected that participants with polyneuropathy would rely less on proprioception due to the expected deficits in this particular sensory channel. However, we did not detect differences in the weight of proprioceptive information between healthy old and elderly with polyneuropathy. This is in contradiction with previous studies, which showed more reliance on vestibular and visual information during standing balance in this population group [24;25;27;48]. However, participants included in these studies were younger compared with the participants included in our study. Furthermore, no differences in downweighting of proprioceptive information in elderly with polyneuropathy compared with healthy old participants were found.

That we did not find differences between elderly with polyneuropathy and healthy old participants could be explained by the variation in degree of polyneuropathy resulting in a high group variability. It might be that the small tactile nerves are earlier damaged compared with larger afferent nerves of the muscle spindles and the Golgi tendon organs, resulting in a small difference between healthy elderly and elderly with polyneuropathy. Furthermore, this could also mean that the neural controller still works sufficient and therefore is still able to recognize unreliable information and to downweight proprioceptive information. However, it is remarkable that elderly with polyneuropathy show less ability to maintain standing balance in more demanding test conditions. This implies deterioration of other underlying systems involved in standing balance, such as the nervous system.

In contrast with our expectations, we did not find a difference between elderly with cataract and elderly with polyneuropathy in the use of proprioceptive information. This could be explained by the high variability in the group of elderly with polyneuropathy, as mentioned before.

Proprioceptive weight changes with impaired balance

In elderly with impaired balance the results showed a higher proprioceptive weight compared with healthy old participants and no differences in proprioceptive downweighting. The included elderly with impaired balance are comparable to elderly with a history of falls included in previous studies investigating sensory integration [14;28;49]. Previous studies found a comparable sensory downweighting of visual information between fall-prone elderly with a history of unexplained falls and healthy old participants [14], which is in accordance with our study. Taking the higher proprioceptive weight at the lowest disturbance amplitude into account, the results show that elderly with impaired balance downweight their proprioceptive information relatively less compared with healthy old participants. A higher proprioceptive weight with a higher disturbance amplitude means a higher sensitivity to the proprioceptive disturbance. This increases the possibility of a too large body sway with proprioceptive disturbance, which may result in falls. This could also explain why elderly with impaired balance are less able to perform the condition with the highest perturbation amplitude.

Nervous system changes with age and sensory deficits

Besides changes in sensory reweighting using system identification changes in the nervous system could be detected, i.e. active stiffness, active damping and neural time delay, with age and sensory deficits. We found that healthy old participants had a higher neural time delay, consisting of transport and processing time of all sensory information and the reaction time of the motor system, compared with healthy young participants, which is consistent with previous studies [12;50]. This could be explained by slow nerve conduction speed in afferent or efferent pathways, a slow muscle activation or slow central processing time due to a decrease in the number of neurons and loss of myelination, which both occur with age [4;46;47]. In healthy old participants, we found a lower active stiffness and higher active damping compared with healthy young. This means that healthy old participants had a lower reflexive response to maintain balance compared with young participants. This is in contrast with Cenciarini et al. (2010) who found an increase of both active parameters [44]. Davidson et al. (2011) only found a higher active damping in old participants compared with young participants [50].

In elderly with cataract, polyneuropathy and impaired balance we found a lower active stiffness compared with healthy old indicating a lower response of ankle torque as a result from changes in body sway to maintain balance compared with healthy old participants. In addition, we found a higher neural time delay in those groups compared with healthy old participants, probably due to the sensory deficits. The neural time delay represented the transport and processing time of all sensory information, i.e. the individual time delays are lumped. Deficits in sensory systems could result in longer conduction [51] and processing time [15;52] and therefore a higher neural time delay. A higher active damping found in elderly with polyneuropathy compared with healthy old participants could be a strategy to overcome the higher neural time delay as a higher active damping could result in less effective time delay. The found changes in the nervous system might explain the lower ability to maintain standing balance during more demanding test conditions (i.e. higher disturbance amplitude of the proprioceptive information).

Methodological considerations

In this study system identification techniques were used to disentangle cause and effect relations, allowing to detect the underlying changes in proprioceptive weight and reweighting during standing balance, despite changes in compensation strategy and deterioration of other underlying systems [30]. Previous studies used system identification techniques in healthy young participants, healthy old participants and patients with dysfunction of the vestibular organ to assess sensory reweighting [8;43;44;53]. Compared to these studies, we found a lower proprioceptive weight in young and healthy old participants. This could be explained by differences in used conditions in which visual information was eliminated by closing the eyes or disturbed by visual stimulations, both resulting in a higher proprioceptive weight. In the presented study participants stood with their eyes open as conditions with eyes closed were too difficult for our study population. This had no consequences for our conclusion, as we were only interested in the weight and reweighting of proprioceptive information.

The models used in previous studies [8;44] formed the basis for the model used in the present study. Passive properties were not included in the present model, as inclusion did not result in better fits and gave unrealistic values for the passive parameters. The effect of excluding the passive dynamics from the model on the other estimated parameters and the goodness of fits was small and therefore did not affect the conclusions drawn in this study. It only resulted in somewhat higher active stiffness; previous studies showed that active dynamics were dominant over passive dynamics [8;53]. Estimated active stiffness and active damping of the current study are within the ranges previously found in the literature [8;43;44;50;53] varying from 898 Nm/rad till approximately 1500 Nm/rad for the active stiffness and from 288 till approximately 480 Nms/rad for the active damping.

In extension to previous models, muscle activation dynamics were added in the present model, which resulted in better model fits. However, inclusion of muscle activation dynamics interferes with the neural time delay as the reaction time of the motor system (i.e. electromechanical delay) is included. Therefore, the estimated neural time delay is not comparable with the neural time delay found in previous studies [8;43;44;50;53].Probably the used activation dynamics were too slow resulting in low values of the neural time delay. As we assumed that the activation dynamics were the same in all groups, possible differences in activation dynamics between the groups also showed up in the neural time delay.

We fitted the model on three conditions at the same time with restrictions to the variability over conditions, i.e. neural time delay and force feedback were assumed constant over the conditions with increasing disturbance amplitude, which is supported by literature [8]. Furthermore, it was previously shown that the active stiffness and time delay were related [8]; when the active stiffness increases, the time delay decreases. This could also explain why we did not find a variation of active stiffness with increasing disturbance amplitude in all groups; the time delay was kept constant over conditions restricting changes in active stiffness over conditions.

In this study we modelled the human body by a one-segmental inverted pendulum. However, the results showed that during the disturbances both ankle and hip strategies were used to maintain an upright position, which differed between groups and over conditions. Previous studies tried to eliminate movement around the hip joint by using a rigid backboard [8;33]. However, this was less feasible in this population of elderly. Peterka (2002) compared sensory reweighting results with and without the use of a backboard and found no differences in sensory reweighting between the conditions. To identify the control of the ankle and the hip independently using system identification techniques, two independent mechanical disturbances are required [54]. This allows for detection of the underlying changes in the use of the ankle and hip joint [31]. This is a subject for further study.

In this study we were interested in the contribution of proprioceptive information to standing balance. To determine which information is upweighted in case of downweighting of proprioceptive information further research has to be done, in which disturbances of proprioceptive information has to be combined with disturbances of visual or vestibular information to unravel the contribution of all sensory systems in standing balance.

Conclusion

This study showed that using system identification techniques it is possible to detect differences in proprioceptive weight during standing balance with age and specific diseases regardless of changes in the nervous system. With aging, with visual deficits and with impaired balance proprioceptive information becomes more reliable relative to the other sensory information. No changes in proprioceptive downweighting were found with age and disease. Furthermore, with age and disease the nervous system changed, representedby a higher neural time delay and a lower active stiffness. The results of this study indicate the opportunities provided by system identification techniques in detecting the underlying cause of impaired standing balance and therefore in applying targeted interventions to improve standing balance.

Acknowledgements

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Appendix A

A model of the balance control system was used to estimate parameters describing the behavior of the system. The human body is approached by a one-segmental inverted pendulum rotating around the ankle joint. The linearized transfer function from ankle torque to body sway of the inverted pendulum is given by equation A.1.

$$H_{IP}(s) = \frac{1}{Is^2 - mgl_{CoM}} \tag{A.1}$$

In which I represents the inertia, m the mass and l_{CoM} the pendulum length.

The human body is controlled by a neural controller. The neural control is represented by a PD controller with a neural time delay and the muscle activation, as described in equation A.2.

$$H_C(s) = (K_p + K_d s)e^{-\tau s} \cdot \frac{\omega^2}{s^2 + 2\beta\omega s + \omega^2} \tag{A.2}$$

In which K_p represents the active stiffness, K_d the active damping, τ the time delay, β the relative damping and ω the natural frequency of the muscle activation.

The neural control consists of force feedback of the force sensors in the tendon and muscles. The force feedback is represented by the transfer function as described in equation A.3.

$$H_{FF}(s) = \frac{K_f}{\tau_f s + 1} \tag{A.3}$$

In which K_f represents the gain of the force feedback and τ_f the time constant. As τ_f is much larger than K_f, this equation could be simplified to equation A.4.

$$H_{FF}(s) = \frac{K_f}{\tau_f}\frac{1}{s} \tag{A.4}$$

The sensory systems send information about the body position to the neural control. How much the information of each sensory system is used, is described by a weighting factor. As we are interested in the use of the proprioceptive weight (W_p) we made use of proprioceptive disturbances. The sum of all weighting factors always equals one. The vestibular and visual weight together ($W_{ves+vis}$) therefore equals 1- W_p. The transfer function of the proprioceptive disturbance, i.e. the SS rotation, to the ankle torque and of the SS rotation to the body sway can now be described as in equation A.5.

$$^{SS}H_T = \frac{W_{prop}H_C}{1 - H_{FF}W_{prop}H_C + H_{IP}W_{prop}H_C}, \; ^{SS}H_{BS} = H_{IP}H_{SS2T} \tag{A.5}$$

Chapter 10

Reliability of system identification techniques to assess standing balance in healthy elderly

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Abstract

System identification techniques have the potential to assess standing balance. By applying well-known disturbances, the contribution of the underlying systems in standing balance can be identified. In this study, we investigated the reliability of standing balance parameters obtained with multivariate closed loop system identification techniques.

Twelve healthy elderly participated in this study. Balance tests were performed twice a day during three days. First, body sway was tested using posturography during 2 minutes of standing with eyes closed. The Balance test Room (BalRoom) was used to apply four disturbances simultaneously: two sensory disturbances, to the proprioceptive and the visual system, and two mechanical disturbances applied at the leg and trunk segment. Using system identification techniques, sensitivity functions to the sensory disturbances and the neuromuscular controller were estimated. Systematic errors were assessed using linear mixed models, including trial and day and their interaction as fixed effects and participant intercept as random effect. Reliability was assessed using the generalizability theory, which allows for computing indexes of dependability (ID), standard error of the measurement (SEM) and minimal detectable change (MDC). To test validity, the BalRoom test was performed with increasing disturbance amplitude of the proprioceptive disturbance.

Results showed a systematic error between the first and second trial in the parameters describing the sensitivity functions. No systematic error was found in the neuromuscular controller and body sway. The reliability of the BalRoom parameters and body sway were moderate to excellent when the results of two trials on three days were averaged. To reach an excellent reliability of the BalRoom on one day, at least ten trials must be averaged. When the disturbance amplitude was increased, sensitivity functions to the proprioceptive disturbance decreased, whereas the sensitivity functions to the visual disturbances increased, which supports the validity of the method.

This study shows the possibility to use of system identification techniques to assess standing balance in elderly. As a systematic error was shown between the first and second trial on one day, it is concluded that assessment of steady state balance needs a training session and at least ten trials on one day to reach an excellent reliability.

Introduction

Impaired standing balance is a significant problem in elderly [1;2] and is one of the main risk factors and causes of falling [3;4]. Falls often result in serious injuries, and also in death [5]. In standing balance, several underlying systems (i.e. muscles, neural system and sensory systems) interact, which results in a closed loop system in which cause and effect are interrelated [6]. The underlying systems deteriorate with age and are influenced by diseases and medication use [7-10]. Due to redundancy, these systems can compensate for each other's deterioration. Therefore, the underlying cause of impaired standing balance is difficult to detect and hence, to intervene with targeted therapies [11].

Current clinical balance tests do not take aforementioned cause and effect relations and redundancy of standing balance into account and therefore cannot detect the underlying cause of impaired standing balance [11]. Previous research showed that system identification techniques are useful to assess the underlying systems of standing balance, in which the response to well-known disturbances are assessed [12-16]. A clear advantage is that this method takes into account the cause and effect relation and separates the contribution of the underlying systems. This gives the opportunity to improve diagnosis of impaired balance and, eventually, to prevent falling by targeted interventions [6]. Before introducing the method into clinical practice for diagnosing or monitoring treatment of impaired balance, it is important to assess the reliability of this technique and compare it with posturography, which is yet unknown.

In this study we investigated the reliability of standing balance parameters obtained with four disturbances applied simultaneously and system identification techniques to assess standing balance in healthy elderly and compared this with a parameter obtained with posturography, namely body sway. We used the generalizability theory (G theory) [17], which takes into account both systematic and random measurement errors. Furthermore, recommendations will be given for study designs to reduce the measurement errors and therefore improve the reliability.

Materials and methods

Participants

Twelve healthy elderly aged 70 years or older participated in this study. Participants were recruited from the database of the Center of Human Drug Research, Leiden, the Netherlands, and the MyoAge study database of the Leiden University Medical Center, Leiden, the Netherlands. Participants were screened before entry to the study. Participants were excluded in case of low cognitive function (Mini Mental State Examination (MMSE) score ≤ 26 [18]), presence of clinical significant morbidity (haematological, renal, endocrine, pulmonary, gastrointestinal, cardiovascular, hepatic, psychiatric, neurological, musculoskeletal or allergic disorders), presence of orthostatic hypotension and use of medication. This study was approved by the Medical Ethics Committee of the Leiden University Medical Center, Leiden, the Netherlands, and was performed according to the principles of the Declaration of Helsinki and the International Conference on Harmonization/Good Clinical Practice (ICH/GCP). All participants gave written informed consent before entry to the study.

Participant characteristics

Prior to participation, a screening procedure was performed. Medical history was recorded including general questions about smoking, alcohol use, medication use and information on diseases. Anthropometric data included height and body composition measured with a bioelectrical impedance analysis (BIA, InBody 720, Biospace Co., Ltd, Seoul, Korea). Cognitive function was assessed with the MMSE [18]. Orthostatic hypotension was assessed by measuring blood pressure after at least 5 minutes in supine position and 3 minutes after postural change to standing position. Handgrip strength was measured using the Jamar dynamometer handle (Jamar, Sammons Preston Inc, Bolingbrook, IL, USA). Physical functioning was measured with the Short Physical Performance Battery (SPPB) [19]. Walking speed was determined by a 4 meter walking test at normal pace, as part of the SPPB.

Apparatus

Standing balance was assessed using the Balance test Room (BalRoom), a custom-made device applying specifically designed disturbances during stance (Motekforce Link, Culemborg, the Netherlands, and University of Twente, Enschede, the Netherlands) (Figure 1). The BalRoom consists of three separated modules. The first module consists of two support surfaces (SS), which are independently actuated and rotate around the ankles [20]. By rotation of the SS around the ankle axis the proprioceptive information of the ankle is disturbed. The second module is a visual scene (VS) in front of the participant, which rotates around the ankle axes. Rotating the VS around the ankle axis results in a disturbance of the visual information. The third module consists of two rods applying forces at hip and shoulder level (FH and FS, respectively) resulting in movements around the ankle and hip joint. These disturbances are used to investigate the contribution of the ankles and hips and their coupling to standing balance [14]. All disturbances can be applied simultaneously.

The body sway was measured in a single plane using a string potentiometer (Celesco SP2-50, Celesco, Chatsworth, CA, United States), which integrates the amplitude of unidirectional body movement transferred through a string attached to the waist of the participant.

Disturbance signals

All disturbances were multisine signals with a unique combination of frequencies (Figure 2). All excited frequencies were multiples of the frequency 0.0625 Hz resulting in a disturbance period of 16 s. The SS rotated following a continuous position disturbance signal with increasing zero-to-peak amplitude over trials, i.e. 0.02, 0.03 and 0.04 radians, and a flat velocity spectrum with frequencies between 0.125 and 6.9375 Hz. The VS rotated following a continuous position disturbance signal with constant zero-to-peak amplitude of 0.03 radians over trials and a flat velocity spectrum with frequencies between 0.0625 and 1 Hz. The FH and FS disturbances are independent continuous force disturbance signals with constant zero-to-peak amplitude of 30 Newton over trials consisting of frequency contents between 0.75 and 7 Hz. All disturbances were repeated eight times resulting in a total duration of 128 seconds.

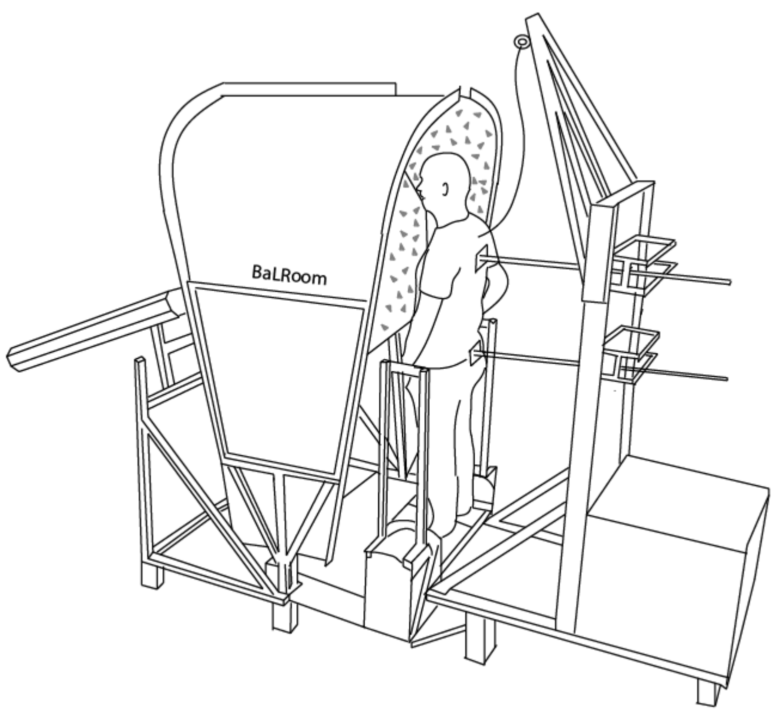

Figure 1. Set up of the Balance test Room consisting of three modules; 1) a visual scene to apply disturbances to the visual system (VS rotation), 2) support surfaces to apply disturbances to the proprioceptive system (SS rotation), and 3) two rods to apply mechanical disturbances by giving pushes and pulls at hip and shoulder level (FH and FS).

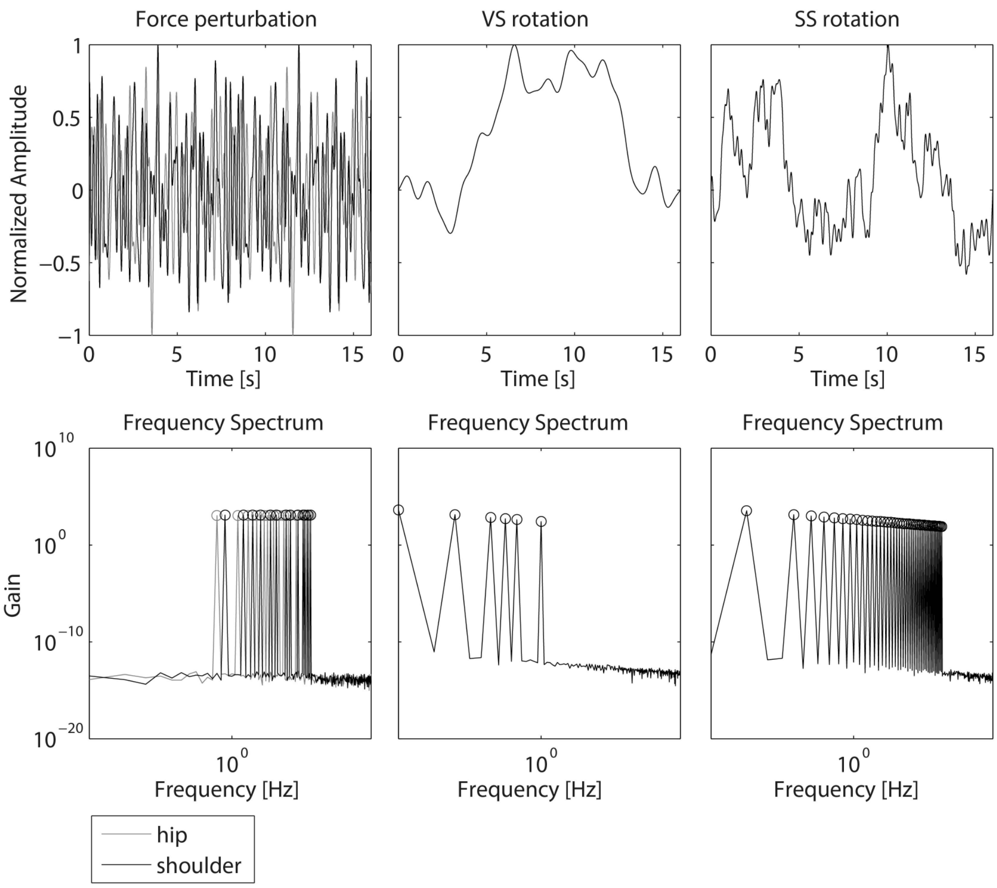

Figure 2. Normalized time signals and frequency spectra of the disturbances of the support surface (SS) rotation, the visual scene (VS) rotation and the rods applying forces at hip and shoulder level (FH and FS, respectively).

Procedure

During the screening visit for inclusion up to 21 days before the start of the study, each participant had a training session to familiarize with the BalRoom test and disturbances and with the body sway test. No data were recorded. During the study, the tests were performed during three sessions separated by one week, allowing assessment of intersession variability. Per session the tests were performed twice separated by one hour, allowing assessment of intrasession variability. During all tests the participant wore comfortable flat shoes. During the BalRoom test, the participant was instructed to stand with the arms resting along the body, with both feet in place on the support surfaces. The two sensory (SS and VS) and mechanical (FH and FS) disturbances were applied simultaneously. Each test consisted of three conditions with increasing disturbance amplitude of the SS rotation (i.e. 0.02, 0.03 and 0.04 radians), while the amplitudes of the VS, FH and FS disturbances remained constant. The three conditions were presented in random order. Before recording each condition the participant was allowed about 10 seconds to get accustomed to the disturbances. Between conditions, the participant was offered ample resting time depending on individual needs. The participant wore a safety harness to prevent falling, which did not constrained movement nor provided support or orientation information.

During the body sway test, the participant was asked to stand still and comfortable for a period of 2 minutes, with the feet approximately 10 cm apart and the hands in a relaxed position along the body and eyes closed.

Data recording and processing

The actual angles of SS rotation (i.e. motor angles), applied forces at hip and shoulder level (FH and FS forces) and the applied torques to the SS (i.e. motor torques) were available for measurement. Lower and upper body segmental movements were measured in anterior-posterior direction using two draw wire potentiometers (Celesco SP2-50, Celesco, Chatsworth, CA, United States) at a sample frequency of 1000 Hz. The potentiometers were connected to the hip and the shoulders by magnets and straps. The motor angles, segment angles,motor torques and applied FH and FS forces were recorded using a Matlab interface with a sample frequency of 1000 Hz. Data analysis was performed with Matlab (The MathWorks, Natick, MA, United States). The leg and hip angle were calculated using goniometry and using the segment movement of the lower and upper body [21]. The ankle torque was obtained by subtracting the contribution of the mass and inertia of the support surfaces from the recorded motor torques. The hip torque was obtained using the applied FH and FS forces and leg and hip angles using inverse dynamics [21]. The time series were segmented into eight data blocks of 16 seconds (i.e. the period of the disturbance signal).

Data analysis

To indicate the effect of the disturbances on the ankle torque, hip torque and joint angles, Frequency Response Functions (FRFs) were estimated. The time series of the disturbances, ankle torque, hip torque, leg and hip angle were transformed to the frequency domain. The periodic part of the frequency coefficients was determined by averaging over the data blocks. The Power Spectral Densities (PSD) and Cross Spectral Densities (CSD) were computed to calculate the FRFs [22]. For each disturbance, only the excited frequencies were analyzed.

Sensitivity functions

The sensitivity functions of the ankle torque, hip torque, leg angle and hip angle to the SS rotation and the VS rotation were estimated using the indirect approach using equation 1 [12;22].

$$^{d}S_{x}(f) = \Phi_{d,x}(f) \cdot \left[\Phi_{d,d}(f)\right]^{-1} \quad (1)$$

In which $\Phi_{d,x}$ represents the CSD of the disturbance (d) (i.e. SS rotation or VS rotation) and x, which represents the ankle torque (T_a), hip torque (T_h), leg angle (θ_l), or hip angle (θ_h), and $\Phi_{d,d}$ the PSD of the disturbance. This results in 8 FRFs; 1) SS rotation to ankle torque ($^{SS}S_{Ta}$), 2) SS rotation to hip torque ($^{SS}S_{Th}$), 3) SS rotation to leg angle ($^{SS}S_{\theta l}$), and 4) SS rotation to hip angle ($^{SS}S_{\theta h}$), and 5) to 8) the VS rotation to each torque and angle ($^{VS}S_{Ta}$, $^{VS}S_{Th}$, $^{VS}S_{\theta l}$, $^{VS}S_{\theta h}$). Each FRF is represented by a magnitude and phase representing the ratio between the input and output and the relative timing both as function of frequency. The magnitude of the sensitivity function of the ankle and hip torque is normalized to the gravitational stiffness (mgl_{CoM}). The average magnitude on the low frequencies (<0.375 Hz and <0.1875 Hz, for SS and VS respectively) and the phase on higher frequencies (0.68 Hz and 0.375 Hz, for SS and VS respectively) are the parameters of interest. Different values of frequencies were used for SS and VS due to differences in frequency content. They represent the sensitivity to the disturbances and the time lag between the disturbance and the reaction of the body, respectively, resulting in 16 parameters.

Neuromuscular controller

The neuromuscular controller is the link between the sensory systems and the muscles, where the sensory information is combined and muscle commands are generated to keep the body in upright position. The multi-input-multi-output (MIMO) approach was used to estimate the ankle and hip controller according to the method described by Engelhart et al. (2014) and equation 2 [14].

$$H_{c}(f) = -\Phi_{d,T}(f) \cdot \left[\Phi_{d,\theta}(f)\right]^{-1} \quad (2)$$

In which $\Phi_{d,T}$ and $\Phi_{d,\theta}$ are the CSD matrices between the external disturbance (d) (i.e. FH and FS)) and the corrective ankle and hip torques (T) and the leg and hip angles (θ) resulting in a two-by-two FRF matrix (Hc). This results in 4 FRFs; 1) ankle torque to ankle angle ($H_{Ta2\theta l}$), 2) ankle torque to hip angle ($H_{Ta2\theta h}$), 3) hip torque to hip angle ($H_{Th2\theta h}$), and 4) hip torque to ankle angle ($H_{Th2\theta l}$). The magnitude is normalized to the gravitational stiffness (mgl_{CoM}).The average magnitude on the low frequencies (<1 Hz) and the phase on higher frequencies (2.3

Hz) are the parameters of interest and represent the normalized effective stiffness and the time lag between the torques and angles, resulting in 8 parameters [14].

Body sway

The body sway (x_{BS}) was measured over 2 minutes. The movement of the body was expressed as millimeters of sway.

Statistical analysis

The characteristics of the participants were represented by mean and standard deviation in case of a Gaussian distribution. Else, median and inter quartile range or number and percentage were presented. The parameters obtained with system identification techniques (i.e. sensitivity and time lag of the sensitivity functions, and normalized effective stiffness and time lag of the neuromuscular controller) are given as mean and standard deviation.

Reliability was assessed using the G theory in three steps [17]. First, systematic errors were identified using linear mixed models with trial (intrasession), day (intersession) and their interaction as fixed effects and participant intercept as random effect. The various sources of measurement errors were assessed using a random effects repeated measures analysis of variance (ANOVA) including participant, trial, day and their interactions. This resulted in the variance of the participants (σ_p^2), the variance of the trials (σ_t^2), the variance of the day (σ_d^2), the variance of their interactions (σ_{pt}^2, σ_{pd}^2 and σ_{td}^2) and the variance of the residual ($\sigma_{ptd,e}^2$). All were presented as percentages of the total variance. Negative variance components were set to zero. The sources of variance were used to calculate the index of dependability (ID), the standard error of the measurement (SEM) and the minimal detectable change (MDC) using equation 3 [17;23].

$$\begin{aligned}
&\sigma_\Delta^2 = \frac{\sigma_t^2}{n_t} + \frac{\sigma_d^2}{n_d} + \frac{\sigma_{pt}^2}{n_t} + \frac{\sigma_{pd}^2}{n_d} + \frac{\sigma_{td}^2}{n_t n_d} + \frac{\sigma_{ptd,e}^2}{n_t n_d} \\
&ID = \frac{\sigma_p^2}{\sigma_p^2 + \sigma_\Delta^2} \\
&SEM = \sqrt{\sigma_\Delta^2} \\
&MDC = 1.96 * \sqrt{2} * SEM
\end{aligned} \tag{3}$$

In which, nt is the number of trials and nd the number of days.

Comparable with an intraclass correlation coefficient (ICC), the ID ranges between 0 and 1 and can be interpreted as; ID < 0.40 represents poor reliability, 0.40 < ID < 0.75 represents moderate reliability, and ID > 0.75 represents excellent reliability [24]. The SEM indicates the absolute reliability and is represented by an absolute value and a percentage of the overall mean. The MDC shows which effect (e.g. treatment effect) can be detected with the parameters of interest and therefore indicates the clinical relevance. A low SEM and MDC are indicative of a reliable and clinical relevant parameter.

Second, a decision study was performed in which the effect of different measurement protocols on the reliability was investigated. Aforementioned equations show that increasing the number of trials or number of days results in an increase of ID and a decrease of SEM and MDC, i.e. an improvement of reliability. In the decision study, the number of trials was varied between 1and 40 trials and the number of days between 1 and 3. Per number of days, the number of trials needed to reach an excellent reliability was determined in this group of healthy elderly (ID > 0.75).

Third, a validity study was performed to assess whether differences in the sensitivity functions represented by the sensitivity and time lag due to increasing disturbance amplitude of the SS rotation could be detected. A linear mixed model was constructed with disturbance amplitude as fixed effect and participant intercept as random effect. Statistical analysis was performed with SPSS version 20 (SPSS Inc., Chicago, USA). Graphs were made with Matlab (The MathWorks, Natick, MA, United States).

Results

Participant characteristics

Table 1 presents the characteristics of the healthy old participants. Figure 3, 4 and 5 displays the FRFs of the sensitivity functions to the SS rotations and the VS rotations, and of the neuromuscular controller.

Systematic errors

Table 2 reports the systematic errors. No systematic errors were found for the body sway (x_{BS}). The sensitivity functions show both a main effect of trial and day. Overall, the sensitivity to the SS rotation was lower during the first trial compared with the second trial in the sensitivity functions (i.e. ${}^{SS}S_{\theta h}$, ${}^{SS}S_{\theta l}$ and ${}^{SS}S_{Ta}$) and it was lower during the first day compared to the second and third day (for ${}^{SS}S_{Th}$ and ${}^{SS}S_{Ta}$).

The sensitivity function to the VS rotation shows the opposite result; the sensitivity of the first trial was higher compared with the second trial for all sensitivity functions (${}^{VS}S_{\theta h}$, ${}^{VS}S_{\theta l}$, ${}^{VS}S_{Th}$ and ${}^{VS}S_{Ta}$). Furthermore, the time lags of some sensitivity functions (i.e. ${}^{SS}S_{Ta}$ and ${}^{VS}S_{\theta l}$) were higher in the first trial compared with the second trial. The time lags of ${}^{VS}S_{Ta}$ and ${}^{VS}S_{Th}$ were also lower during the first day compared with the third day.

The normalized effective stiffness estimated using the FS and FH disturbances showed an effect of the trial; one component of the neuromuscular controller ($H_{\theta l2Th}$) was lower during the first trial compared with the second trial. No effect of trial and day was found for the time lags of all components of the neuromuscular controller.

Variance components

Table 3 shows the magnitude of the variance components as percentage of the total variance. Variance of the participant (σ_p^2) was on average 20.8% and varied between 0.0% and 87.3%. The contribution of the trial variance (σ_t^2) was on average 6.6% and varied between 0.0% and 28.8%. The contribution of the day variance (σ_d^2) was on average 2.5% and varied between 0.0% and 12.5%.

Table 1. Participant characteristics.

	All (n=12)
Age, years	73.3 (3.4)
Men, n (%)	6 (50)
Anthropometry	
Weight, kg	72.2 (9.1)
Height, m	1.70 (0.08)
BMI, kg/m^2	24.9 (2.4)
Health characteristics	
Number of medication, median (IQR)	0 (0-0)
MMSE, points; median (IQR)	29 (28-30)
Physical function	
Handgrip strength, kg	34.7 (8.6)
Gait speed, m/s	1.28 (0.16)
SPPB, points; median (IQR)	11 (10-12)

All parameters are presented as mean with standard deviation unless indicated otherwise. BMI: body mass index, MMSE: Mini Mental State Examination, SPPB: Short Physical Performance Battery, IQR: inter quartile range.

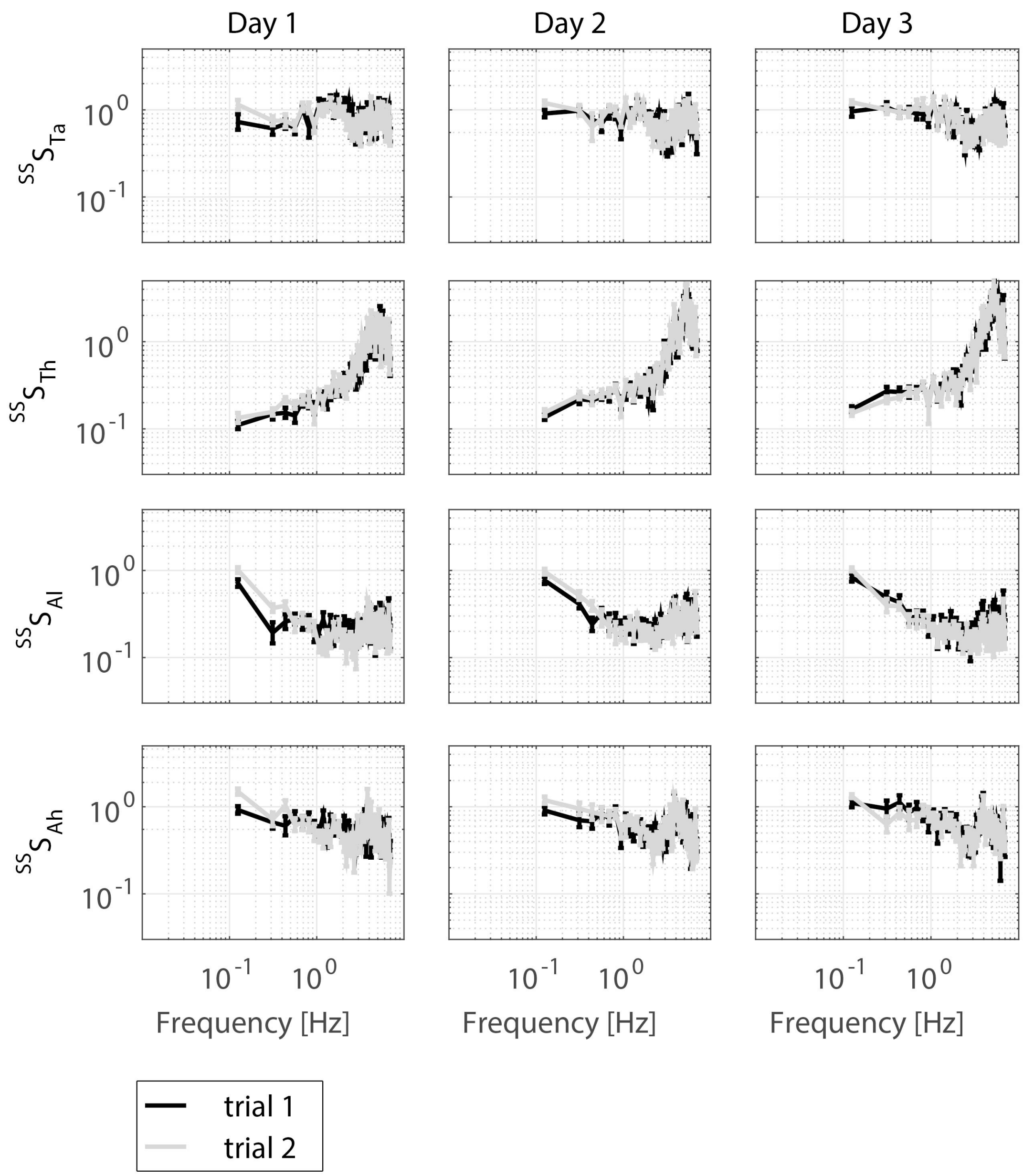

Figure 3. Average sensitivity functions of the ankle torque ($^{SS}S_{Ta}$), hip torque ($^{SS}S_{Th}$), leg angle ($^{SS}S_{\theta l}$) and hip angle ($^{SS}S_{\theta h}$) to the rotation of the support surfaces per day per trial are presented by mean and standard error, only magnitude is shown.

The error variance related to the interactions between the participant and trial (σ_{pt}^2), between participant and day (σ_{pd}^2) and between trial and day (σ_{td}^2) were low; on average they were 4.3%, 13.4% and 4.4%, respectively.

The largest proportion of measurement variability was due to the participant variability (σ_p^2) and the other interactions combined with the residual error ($\sigma_{ptd,e}^2$) contributing on average 48.0% ranging from 7.2% to 80.8%.

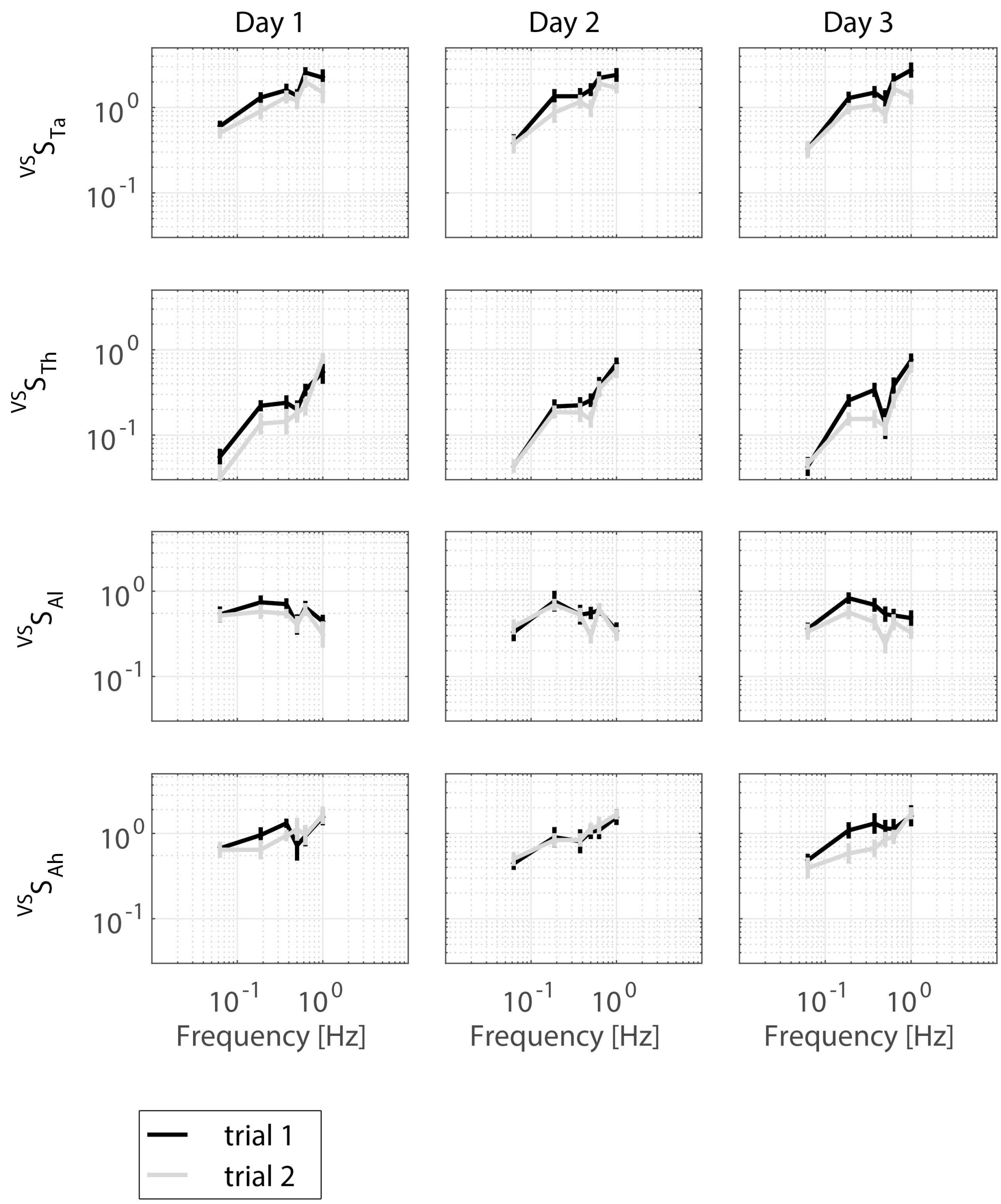

Figure 4. Average sensitivity functions of the ankle torque ($^{VS}S_{Ta}$), hip torque ($^{VS}S_{Th}$), leg angle ($^{VS}S_{\theta l}$) and hip angle ($^{VS}S_{\theta h}$) to the rotation of the visual scene per day per trial are presented by mean and standard error, only magnitude is shown.

Reliability

Table 4 presents the results of the reliability measures. In this study design, the ID of 4 out of 25 parameters was higher than 0.75 and in 12 out of 25 parameters ID was between 0.40 and 0.75. The SEM and SEM % were inverse related with the ID. Furthermore, the MDC was lower with increased ID. To reach an ID of 0.75, for 32% (8/25) of the parameters at least ten trials are needed to average over one day. Increasing the number of days resulted in less trials needed per day to reach an ID higher than 0.75.

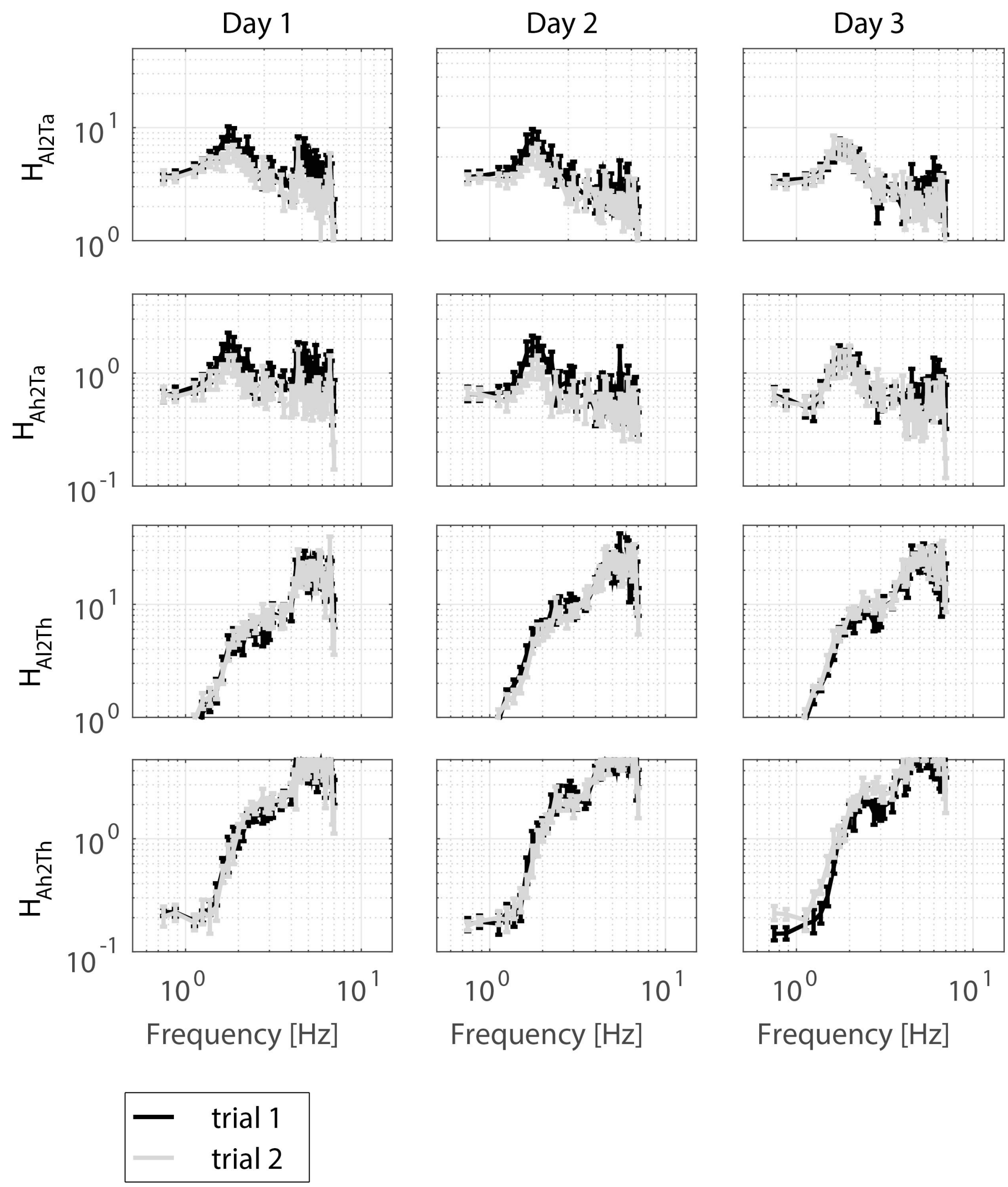

Figure 5. Average Frequency Response Functions of the neuromuscular controller (i.e. $H_{Ta2\theta l}$, $H_{Ta2\theta h}$, $H_{Th2\theta l}$, $H_{Th2\theta h}$) per day per trial are presented by mean and standard error, only magnitude is shown.

Validity

Table 5 presents the results of the validity study. The mean and standard deviation of the parameters of the second trial at the first day are given for each condition. All sensitivities to the SS rotation decreased with increasing disturbance amplitude and all sensitivities to the VS rotation increased with increasing disturbance amplitude. No significant differences were found for the time lag of the sensitivities to the SS rotation and VS rotation. No significant differences were found between the conditions for the parameters describing the neuromuscular controller.

Discussion

In this study, we assessed the reliability of a comprehensive set of parameters obtained with four disturbances applied simultaneously and (MIMO closed loop) system identification techniques describing standing balance in a group of healthy elderly. Results were obtained by measuring standing balance twice during three days. A distinction was made between systematic and random errors. The results showed a systematic error between the first and second trial with the BalRoom on one day, which was not found using body sway measurements. The reliability ranged from moderate to excellent when averaging two trials on three days. This is the first study that investigated the reliability of system identification techniques to assess standing balance in healthy elderly.

Systematic errors

In general, the sensitivity to the SS rotation was lower in the first trial compared with the second trial, while the sensitivity to the VS rotation was higher in the first trial compared to the second trial. These results are confirmed by the variance component of the trial (σ_t^2) and day (σ_d^2); a high variance component of trial and day indicates a systematic error. Previous studies using system identification techniques also showed a systematic error between the first and second trial or between days. These differences were explained by motor learning, changes in posture or stretching of the joints [25-27]. In contrast, in a previous study no learning effects were found. These results might be due to the practice session all participants performed prior to participation in this study [28].

In this study, the differences between the first trial compared with the second trial (i.e. a lower sensitivity to proprioception and a higher sensitivity to vision during the first trial) could be explained by a difference in strategy used to maintain standing balance or familiarization during the test.

According to the sensory reweighting hypothesis, sensory information is weighted based on reliability; the weight of the proprioception increased at the cost of a decrease of the weight of the other sensory information [12]. As the sensitivity to the disturbances represents the contribution of the proprioceptive and visual information, the sensitivity to the SS rotation increases, while the sensitivity to the VS rotation decreases.

Table 2. Systematic errors of all parameters using linear mixed model with day, trial and their interaction as fixed effect and subject intercept as random effect.

			p-value			Post hoc analyse	
	Mean	SD	trial (t)	day (d)	t x d	trial	day
Body sway							
x_{BS}, mm	330.53	139.12	0.18	0.47	0.29	-	-
Sensitivity functions							
Sensitivity							
$^{SS}S_{\theta h}$	1.05	0.38	**0.005**	0.19	**0.008**	Day 1 and 2: Trial 1 < Trial 2	-
$^{SS}S_{\theta l}$	0.65	0.17	**<0.001**	0.05	0.076	Trial 1 < Trial 2	-
$^{SS}S_{Ta}$	0.99	0.27	**0.001**	**0.007**	0.38	Trial 1 < Trial 2	Day 1 < Day 3
$^{SS}S_{Th}$	0.18	0.05	0.66	**0.001**	**0.011**	Day 3: Trial 1 > Trial 2	Day 1 < Day 2 and 3
$^{VS}S_{\theta h}$	0.78	0.29	**0.012**	0.55	0.39	Trial 1 > Trial 2	-
$^{VS}S_{\theta l}$	0.61	0.20	**0.026**	0.43	0.89	Trial 1 > Trial 2	-
$^{VS}S_{Ta}$	0.84	0.28	**0.001**	0.35	0.85	Trial 1 > Trial 2	-
$^{VS}S_{Th}$	0.13	0.06	**0.001**	0.66	0.26	Trial 1 > Trial 2	-
Time lag							
$^{SS}S_{\theta h}$, deg	118.42	22.60	0.16	0.68	0.30	-	-
$^{SS}S_{\theta l}$, deg	-92.34	27.47	0.069	0.83	0.11	-	-
$^{SS}S_{Ta}$, deg	17.76	16.71	0.37	0.075	**0.020**	Day 1: Trial 1 > Trial 2	-
$^{SS}S_{Th}$, deg	-42.72	24.36	0.91	0.21	0.20	-	-
$^{VS}S_{\theta h}$, deg	64.75	102.49	0.22	0.53	0.56	-	-
$^{VS}S_{\theta l}$, deg	-97.26	34.96	**0.003**	0.17	0.24	Trial 1 > Trial 2	-
$^{VS}S_{Ta}$, deg	39.19	23.81	0.15	**0.031**	0.070	-	Day 1 < Day 3
$^{VS}S_{Th}$, deg	-14.07	46.08	0.84	**0.025**	0.54	-	Day 1 < Day 3
Neuromuscular controller							
Normalized effective stiffness							
$H_{\theta h2Ta}$	0.70	0.33	0.93	0.83	0.96	-	-
$H_{\theta h2Th}$	0.21	0.10	0.085	**0.022**	0.12	-	Day 1 > Day 2
$H_{\theta l2Ta}$	3.70	1.30	0.83	0.21	0.86	-	-
$H_{\theta l2Th}$	0.36	0.21	**0.015**	0.75	0.85	Trial 1 < Trial 2	-
Time lag							
$H_{\theta h2Ta}$, deg	-109.72	61.91	0.72	0.21	0.25	-	-
$H_{\theta h2Th}$, deg	96.07	31.93	0.42	0.10	0.73	-	-
$H_{\theta l2Ta}$, deg	-112.58	38.74	0.83	0.47	0.80	-	-
$H_{\theta l2Th}$, deg	117.88	28.01	0.48	0.34	0.86	-	-

Significant differences identified in bold. n.s. : not significant.

Table 3. Relative magnitude of the variance components obtained with the G-study for all parameters obtained with system identification techniques.

	participant (p), %	trial (t) , %	day (d) , %	p x t, %	p x d, %	t x d, %	p x t x d, e, %
Body sway							
x_{BS}	87.3	0.2	0.0	0.0	4.7	0.5	7.2
Sensitivity functions							
Sensitivity							
$^{SS}S_{\theta h}$	24.9	5.5	0.0	3.1	8.7	20.7	37.1
$^{SS}S_{\theta l}$	11.0	28.8	0.0	4.7	9.4	9.8	36.5
$^{SS}S_{Ta}$	19.6	15.5	6.7	0.0	11.0	2.2	44.9
$^{SS}S_{Th}$	11.2	0.0	12.5	4.0	23.2	16.9	32.1
$^{VS}S_{\theta h}$	26.0	10.1	0.3	0.0	0.0	0.0	63.6
$^{VS}S_{\theta l}$	0.0	16.2	0.0	22.2	6.7	0.0	54.9
$^{VS}S_{Ta}$	0.0	23.7	3.5	19.3	17.2	0.0	36.2
$^{VS}S_{Th}$	39.1	16.7	0.0	0.0	5.9	3.6	34.8
Time lag							
$^{SS}S_{\theta h}$	27.7	1.6	0.0	1.4	0.0	6.3	63.0
$^{SS}S_{\theta l}$	6.9	6.4	0.0	0.0	0.0	5.9	80.8
$^{SS}S_{Ta}$	18.9	0.0	0.0	6.0	12.8	17.2	45.1
$^{SS}S_{Th}$	29.6	0.0	0.0	0.0	9.4	6.0	55.0
$^{VS}S_{\theta h}$	7.5	5.4	6.0	13.5	14.3	0.0	53.3
$^{VS}S_{\theta l}$	3.9	16.0	0.0	12.7	21.3	4.2	41.9
$^{VS}S_{Ta}$	41.8	0.0	2.3	0.0	0.0	5.1	50.9
$^{VS}S_{Th}$	20.3	0.0	10.0	0.2	11.9	0.8	56.8
Neuromuscular controller							
Normalized effective stiffness							
$H_{\theta h2Ta}$	48.1	1.2	1.8	0.0	0.0	0.0	48.9
$H_{\theta h2Th}$	34.6	1.7	2.5	0.0	4.7	5.0	51.5
$H_{\theta l2Ta}$	48.9	1.0	3.4	0.0	0.0	0.0	46.8
$H_{\theta l2Th}$	21.7	9.0	2.4	0.0	0.0	0.0	66.9
Time lag							
$H_{\theta h2Ta}$	18.4	0.0	0.0	0.0	33.5	0.3	47.8
$H_{\theta h2Th}$	7.8	0.0	6.0	7.9	55.3	1.2	21.7
$H_{\theta l2Ta}$	19.0	0.0	0.0	4.9	25.2	0.0	50.9
$H_{\theta l2Th}$	13.4	0.0	1.4	4.2	50.1	0.5	30.3
Mean	**20.8**	**6.6**	**2.5**	**4.3**	**13.4**	**4.4**	**48.0**

The combination of mechanical disturbances with sensory disturbances of the visual and proprioceptive information could have resulted in a longer adaptation time or a redundancy of applied strategies to withstand the disturbances. However, comparable systematic errors within a day were found in healthy elderly (unpublished data) in a previous study using only SS rotation to disturb proprioceptive information (Pasma et al. submitted), which suggest that the longer adaptation time is not due to the combination of multiple disturbances. In contrast, no systematic errors were found in healthy young adults (unpublished data). This is an indication of increased adaptation time in elderly compared with young adults.

When a steady state of standing balance is to be assessed, a familiarization trial is needed on the same day to overcome the systematic error between trials. Excluding the first trial of each day resulted in less systematic errors between days.

Reliability

The variance component of the participant (σ_p^2) corresponds to the ICC when both nt and nd are equal to one. The reliability of the parameters ranged from poor to moderate. To increase reliability of steady state balance assessment, multiple trials on more than one day have to be performed. The ID values indicate that performing two trials on three days results in a reliability ranging from moderate to excellent needed to discriminate between healthy old individuals. A high residual variance ($\sigma_{ptd,e}^2$) component indicates that a majority of the measurement error is random or can be attributed to error sources not identified in the study.

In this study, relative low SEM% were found (<20%), which is comparable with other studies using system identification techniques [25]. A low SEM% indicates that the parameter could detect changes over time within the same participant (e.g. effects of intervention or changes in conditions). However, the SEM values depend on the number of trials performed on the number of days. The MDC values are in the same order as in a previous study using only SS rotation in healthy elderly (unpublished data) and indicates which change in the parameters can be minimally detected, when comparing groups or within the same participant. It is difficult to interpret the MDC results of new parameters. To get more feeling for this measure and to get more insight in the clinical relevance, it is recommended to assess standing balance using system identification techniques in several groups of elderly with a large variance in impaired balance severity and clinical phenotypes [23].

Table 4. Reliability statistics.

	ID	SEM	SEM %	MDC	# trials / 1 day >0.75	# trials / 2 days >0.75	# trials / 3 days >0.75
Body sway							
x_{BS}	**0.97**	25.01	7.57	69.32	1	1	1
Sensitivity functions							
Sensitivity							
$^{SS}S_{\theta h}$	0.60	0.17	16.23	0.47	>40	6	3
$^{SS}S_{\theta l}$	0.28	0.10	15.25	0.27	>40	>40	32
$^{SS}S_{Ta}$	0.48	0.13	13.45	0.37	>40	22	6
$^{SS}S_{Th}$	0.34	0.03	14.86	0.07	>40	>40	>40
$^{VS}S_{\theta h}$	0.62	0.13	17.14	0.37	8	4	3
$^{VS}S_{\theta l}$	0.00	0.12	19.97	0.34	>40	>40	>40
$^{VS}S_{Ta}$	0.00	0.19	22.41	0.52	>40	>40	>40
$^{VS}S_{Th}$	0.70	0.03	19.85	0.07	5	2	2
Time lag							
$^{SS}S_{\theta h}$, deg	0.68	8.94	7.55	24.78	7	4	3
$^{SS}S_{\theta l}$, deg	0.28	14.78	16.01	40.97	36	18	12
$^{SS}S_{Ta}$, deg	0.52	7.42	41.79	20.57	>40	>40	11
$^{SS}S_{Th}$, deg	0.69	9.58	22.42	26.55	>40	6	3
$^{VS}S_{\theta h}$, deg	0.23	59.54	91.95	165.03	>40	>40	>40
$^{VS}S_{\theta l}$, deg	0.12	19.85	20.41	55.03	>40	>40	>40
$^{VS}S_{Ta}$, deg	**0.81**	8.39	21.41	23.26	4	2	2
$^{VS}S_{Th}$, deg	0.54	19.82	140.83	54.92	>40	37	7
Neuromuscular controller							
Normalized effective stiffness							
$H_{\theta h2Ta}$	**0.84**	0.13	18.01	0.35	4	2	2
$H_{\theta h2Th}$	0.73	0.04	18.07	0.11	8	3	2
$H_{\theta l2Ta}$	**0.84**	0.48	12.89	1.32	3	2	1
$H_{\theta l2Th}$	0.57	0.12	32.21	0.32	10	5	4
Time lag							
$H_{\theta h2Ta}$, deg	0.49	29.55	26.93	81.90	>40	>40	>40
$H_{\theta h2Th}$, deg	0.22	16.64	17.33	46.14	>40	>40	>40
$H_{\theta l2Ta}$, deg	0.50	17.55	15.59	48.64	>40	>40	>40
$H_{\theta l2Th}$, deg	0.35	13.97	11.85	38.72	>40	>40	>40

ID = Index of Dependability (>0.75 identified in bold), SEM = Standard Error of Measurement, MDC = Minimal Detectable Change

The results showed that at least 10 trials on one day are needed to reach an excellent reliability for steady state balance assessment in one third of the parameters. In this study, averaging trials across days seems to be more effective than averaging more trials per day. These results are consistent with the variance component of interaction; the variance component of participant x day (σ_{pd}^2) is much higher than the variance component of participant x trial (σ_{pt}^2). This means that the parameters for each participant were more affected by between day than within day sources of error, relative to the other participants. These results are in accordance with previous studies; Lariviere et al. (2015) also showed that one till ten trials were needed to assess an excellent reliability for parameters obtained with system identification techniques [25]. A lower reliability seems to be a general feature of position stabilization task in contrast to tracking tasks [26].

Validity

The validity study showed that differences could be detected within participants by changing the experimental condition. It was possible to detect changes over conditions using one trial. Increasing the disturbance amplitude of the SS rotation resulted in a decreased sensitivity to the SS rotation and an increased sensitivity to the VS rotation. This result was expected according to the sensory reweighting hypothesis, as mentioned before. Our findings are therefore also in line with previous studies investigating sensory reweighting during standing balance using system identification techniques [12;15].

No changes were found in the neuromuscular controller by increasing the disturbance amplitude of the SS rotation. This is following our expectations, as changes in sensory information does not influence the stiffness and damping of the neuromuscular controller. These results are also in accordance with a previous study, in which we showed that the neuromuscular controller did not change with increasing disturbance amplitude of the SS rotation [15].

System identification techniques compared to posturography

System identification techniques are a new engineering approach to assess standing balance. In contrast with posturography, a general used technique to assess standing balance, it is possible to detect underlying systems and used strategies in standing balance [6;11]. In this study, we assessed standing balance with both system identification techniques and posturography (i.e. body sway). Compared to system identification techniques, no systematic errors and a higher reliability were found for posturography.

Table 5. Mean and standard deviation of the parameters corresponding to three conditions with increasing disturbance amplitude, combined with statistical results.

	0.02 rad		0.03 rad		0.04 rad		p-value
	Mean	SD	Mean	SD	Mean	SD	
Sensitivity functions							
Sensitivity							
$^{SS}S_{\theta h}$	1.13	0.31	0.94	0.41	0.82	0.24	**0.003**
$^{SS}S_{\theta l}$	0.73	0.14	0.58	0.13	0.48	0.09	**<0.001**
$^{SS}S_{Ta}$	1.08	0.21	0.93	0.20	0.75	0.13	**<0.001**
$^{SS}S_{Th}$	0.19	0.05	0.18	0.05	0.15	0.03	**0.001**
$^{VS}S_{\theta h}$	0.73	0.22	0.82	0.28	0.93	0.27	0.18
$^{VS}S_{\theta l}$	0.58	0.14	0.63	0.16	0.77	0.28	0.079
$^{VS}S_{Ta}$	0.73	0.25	0.90	0.23	1.04	0.39	**0.044**
$^{VS}S_{Th}$	0.12	0.04	0.14	0.05	0.17	0.07	**0.015**
Time lag							
$^{SS}S_{\theta h}$, deg	114.74	19.76	114.47	21.32	115.66	19.37	0.98
$^{SS}S_{\theta l}$, deg	-98.15	24.46	-105.43	20.26	-92.20	30.52	0.42
$^{SS}S_{Ta}$, deg	16.34	11.98	15.39	8.90	22.39	12.54	0.094
$^{SS}S_{Th}$, deg	-37.66	32.00	-41.71	12.53	-41.50	15.35	0.81
$^{VS}S_{\theta h}$, deg	52.80	117.92	23.45	140.10	94.19	42.41	0.32
$^{VS}S_{\theta l}$, deg	-96.04	31.73	-105.29	44.74	-102.27	19.63	0.80
$^{VS}S_{Ta}$, deg	43.44	25.46	36.72	27.95	40.84	18.80	0.73
$^{VS}S_{Th}$, deg	-0.46	32.38	-9.24	31.00	-9.29	24.15	0.33
Neuromuscular controller							
Normalized effective stiffness							
$H_{\theta h2Ta}$	0.70	0.26	0.80	0.49	0.75	0.28	0.61
$H_{\theta h2Th}$	0.18	0.05	0.20	0.08	0.19	0.11	0.74
$H_{\theta l2Ta}$	3.70	1.21	3.93	1.60	3.93	1.03	0.80
$H_{\theta l2Th}$	0.42	0.25	0.39	0.22	0.29	0.15	0.29
Time lag							
$H_{\theta h2Ta}$, deg	-89.99	73.93	-76.50	66.69	-78.23	78.66	0.89
$H_{\theta h2Th}$, deg	102.46	39.66	119.09	44.69	119.24	36.63	0.42
$H_{\theta l2Ta}$, deg	-110.27	58.82	-86.77	37.46	-108.93	48.49	0.28
$H_{\theta l2Th}$, deg	123.08	36.14	136.45	31.24	138.22	29.81	0.37

In comparison with our results of system identification techniques, studies investigating the reliability of the Sensory Organization Test (SOT) showed a learning effect in healthy young due to changes in postural strategies or through reweighting of sensory information. Remarkably, this learning effect was only present in more demanding test conditions [29]. Studies investigating the reliability of Center of Pressure (CoP) parameters did not find systematic errors [30;31], which is comparable with our results of the body sway, but in contrast with the system identification techniques results. This could be explained by the influence of used strategies to maintain balance on the parameters. CoP parameters only describe objectively standing balance, while system identification techniques also describe the underlying changes. Therefore, changes in strategies between trials will not be detected by CoP parameters and do not influence the reliability of CoP parameters.

The reliability of the SOT was moderate in noninstitutionalized old adults when 2 sessions of the test were performed 1 week apart. To improve the reliability of the computer-generated scores of the SOT, a modification of the scoring system was recommended [32]. The reliability of CoP parameters depends on the test condition, study design, study population and therapeutic interventions [33]. To reach an excellent reliability of CoP parameters, the duration of the trial must be minimal 90 seconds, must by three to five times repeated and must be measured with eyes closed and on a firm surface [33]. Santos et al. (2007) showed that at least 10 repetitions must be performed to reach an excellent reliability for CoP parameters [34]. This is comparable with our study, in which measurements of approximately two minutes were used to assess standing balance and must be repeated ten times to reach an excellent reliability. The found relative low SEM% (<20%) are comparable with other studies using CoP parameters [34].

Clinical recommendations

First, the results indicated that there is a systematic error between the first trial and the second trial. This could be due to changes in used strategies to maintain standing balance and time needed to reach a steady state. Therefore, to assess steady state balance we recommend to perform one familiarization trial on each day. As in this study only two trials were performed per day, it was not possible to assess the number of trials needed to reach an excellent reliability when omitting the first trial from analysis. Second, results showed that averaging over days is more effective than averaging within days. However, in clinical practice it is not feasible to measure on more than one day. Performing multiple measurements on one day could be hampered by fatigue or boredom of the participant, which has to be taken into account.

As mentioned before, systematic errors might be due to more time needed for reaching a steady state balance or a redundancy of applied strategies . This implies that parameters obtained with system identification techniques are sensitive for detection of adaptation strategies. Besides steady state balance, adaptation strategy and adaptation time may have clinical meaning and need further exploration. System identification techniques are sensitive tools to assess the duration of adaptation of sensory reweighting [35] in contrast to e.g. CoP measurement.

Strengths and limitations

The strength of this study is the selection of healthy old participants, resulting in a well phenotyped group. However, this also affects ICC and ID. Low variability within the participants (i.e. a homogeneous population) results in lower ICC and ID values and therefore lower relative reliabilities [36;37]. SEM(%) and MDC are measures of absolute reliability and important measures when interpreting results of repeated measures effects of intervention. Another strength of this study is the set up with exactly one week between sessions. A limitation of this study is the relative low number of participants. As only two trials per day were performed, reliability within a day could not be assessed excluding the first (familiarization) trial.

Conclusion

This study investigated the reliability of a comprehensive set of parameters obtained with system identification techniques to assess standing balance in a population of healthy elderly. Systematic errors were present between trials showing sensitivity of parameters obtained with system identification techniques for detection of adaptation strategies. To assess steady state balance a training session is recommended. As only a single trial per day resulted in poor to moderate reliability, it is recommended to perform more trials on separate days. Within the present framework, acceptable reliability of steady state balance assessment could be achieved by measuring and averaging at least ten trials on the same day.

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Part IV

General discussion and summary

balance
disturbances
compensation
control
deterioration
impaired
sensory
training
steps
strategies
systems
used
assessment
movement
information
elderly
cognitive
underlying
interventions
nervous
proprioception
identification
clinical
increase
reduced
motor
different
measure
combined
activities
current
age
tests
maintain
possible
intensity
force
proper
visual
joint
hip
ankle
effect
loop
needed
task
techniques
selection
attentional
primary
types
specific
changes
improve
preventing
identify
detect
decrease
applied
fibers
rely
time
conditions
simultaneously
sense
power
case
delay
result
individual
population
comprises
decline
processing
sensitivity
amplitudes
difficulty
depending
challenging
method
virtual
allows
position
subsequently

Chapter 11

General discussion

Impaired standing balance is one of the main causes and risk factors of falls in the elderly population [1]; one third of the elderly falls at least once a year [2]. These falls often result in serious injuries, but also in death [3]. To maintain standing balance, several underlying systems, e.g. the nervous system, muscular system and sensory systems, are working together via efferent and afferent pathways resulting in a closed loop in which cause and effect are interrelated [4]. These systems deteriorate with age and are influenced by diseases and medication use [4-7]. Due to redundancy, the underlying systems can compensate for each other's deterioration. Failing of these compensation strategies may result in impaired standing balance. Together, this makes it difficult to unravel the mechanisms of standing balance in elderly. To treat impaired standing balance with targeted interventions, it is important to know and understand the underlying and primary cause of impaired standing balance, especially at an early stage.

In this thesis, we investigated the role of several underlying systems in impaired standing balance in community-dwelling elderly referred to a geriatric outpatient clinic, resulting in an overview of the multi causal problem of impaired balance. The use of several balance tests in clinical practice was investigated answering the question which balance test can be used as measure for impaired standing balance in elderly outpatients. As the current balance tests do not provide information about the underlying primary cause of impaired balance, a new engineering approach was introduced to assess standing balance, which was validated in an elderly population.

Key findings

Part I described the associations between underlying systems involved in standing balance and impaired standing balance. The muscular system was represented by muscle characteristics (i.e. muscle mass and muscle strength). The nervous system was represented by cognition and blood pressure regulation. Associations were found with the ability to maintain standing balance in elderly outpatients and:

- Muscle strength (i.e. handgrip and knee extension strength)
- Cognition
- Blood pressure regulation (i.e. orthostatic hypotension)

No associations were found between Center of Pressure (CoP) movement and aforementioned systems. The results indicated the multi causality of impaired standing balance in a population of elderly outpatients.

Part II described the value of currently used tests to assess standing balance in clinical practice. Using CoP movement, age-related differences were detected in the quality of standing balance. These differences were most prominent in medio-lateral direction and during more demanding standing conditions. In a population of elderly outpatients, the ability to maintain standing balance in side-by-side stance with eyes closed associated with self-reported impaired standing balance, history of falls and CoP movement. These results indicated that the ability to maintain standing balance in side-by-side stance with eyes closed is a useful clinical measure to detect impaired standing balance in elderly outpatients.

In Part III, system identification techniques were introduced to unravel the primary cause of impaired balance by ’opening’ the closed loop using well-known disturbances. We showed that the use of proprioceptive information of each leg during standing balance can be measured using rotations of the support surfaces of the left and right leg independently applied with a Bilateral Ankle Perturbator (BAP, Motekforce Link, Culemborg, the Netherlands) [8]. Previous research showed that sensory information is combined based on their reliability in an adaptive process, i.e. sensory reweighting [9], in which a decrease in the use of sensory information is always accompanied with an increase in the use of other available sensory information. In this study, we showed that a decrease in the proprioceptive weight of the left leg was not accompanied with a change in the proprioceptive weight of the right leg, indicating an independent reweighting of proprioceptive information of both legs.

The BAP was validated in an elderly population with specific diseases. Results showed a clear difference in proprioceptive (re)weighting. With respectively age, cataract and impaired balance proprioceptive weighting increased; no differences were found in reweighting of proprioceptive information with increasing disturbance amplitude. This indicated that it is possible to distinguish underlying changes in the use of proprioceptive information during standing balance using system identification techniques.

With the Balance test Room (BalRoom) (Motekforce Link, Culemborg, the Netherlands and University of Twente, Enschede, the Netherlands), disturbances were simultaneously applied to the proprioceptive and visual system and to the leg and trunk segment to unravel the underlying contribution of the sensory systems and inter segmental coupling between the ankle and hip joint to standing balance. The reliability of this new method was investigated in healthy elderly showing a systematic error between the first and second trial on one day. The reliability was moderate to excellent when averaging the results measured twice a day on three separate days.

Reflection

Impaired balance in elderly outpatients

In Part I, associations between representatives of the underlying systems and the ability to maintain standing balance appeared only in more demanding standing conditions, i.e. with eyes closed and in tandem stance. These manipulations of specific elements of standing balance resulted in changes in the availability of sensory information and the size of the base of support, for which must be compensated. For example, to maintain standing balance in more demanding conditions increased cognitive load [10] and higher muscle strength are needed. Therefore, deterioration of the underlying systems may become apparent in more demanding conditions.

No associations were found between representatives of the underlying systems and CoP movement due to the interaction of the underlying systems in a closed loop. CoP movement is a combined measure of the quality of standing balance, representing the quality of all systems together. Deterioration in the underlying systems, due to age, disease and medication use [4-7] may result in similar CoP movement. For example, deterioration in the muscular system will result in higher CoP movement by a decrease in muscle force. On the other hand, deterioration in the sensory systems could also result in higher CoP movement. In this case, inaccurate information about the body movement sensed by the sensory systems is transmitted to the central nervous system, which might result in generation of less muscle force causing higher CoP movement. The underlying systems may compensate for each other's deterioration, e.g. by sensory reweighting or co contraction. This hampers interpretation of CoP movement. In our study population of elderly outpatients, a variety of underlying system deterioration patterns is present, as about 50 percent has multi morbidity and 75 percent used between three and seven medications. This could explain why we did not find associations between the representatives of the underlying systems and CoP movement in elderly outpatients.

Use of current clinical balance tests

In Part II, it is shown that the ability to maintain standing balance in side-by-side stance with eyes closed is an easy applicable clinical measure, which is not time consuming, to detect impaired standing balance in elderly outpatients. Self-reported impaired standing balance could be influenced by factors, such as depression, cognition and self-efficacy, resulting in a less reliable measure [11;12]. Self-reported history of falls, a proven predictor for recurrent falls [13], could be influenced by recall bias resulting in an underestimation of the risk on impaired standing balance.

The ability to maintain standing balance associated with other balance measures, such as history of falls, CoP movement and self-reported impaired balance, only in more demanding test conditions, i.e. side-by-side stance with eyes closed. This could be explained by the difficulty of the condition. Increasing difficulty by manipulation of the test condition, i.e. changes in the size of the base of support and available sensory information, results in failing of the balance system at some point. In other words, the balance system will always fail at one point, as long as the condition is made difficult enough. The moment the balance system fails, depends on the quality of the underlying systems and the possibility to use compensation strategies to maintain standing balance. The required test condition to detect failure of standing balance depends on the severity of the deterioration; in a healthy population with less deterioration of the underlying systems a more difficult test condition is needed. In elderly outpatients, standing in side-by-side stance with eyes closed is a useful measure to detect impaired standing balance. However, using this specific standing condition it is not possible to detect deterioration of the underlying systems at an early stage in elderly.

To detect changes in the quality of standing balance before failure, CoP movement can be used, which is an objective measure of postural responses. Reliable CoP measurements require a condition in which the balance system does not fail. More demanding test conditions evoke more response and are more sensitive to detect changes in CoP movement. In Chapter 6, we showed that deteriorations due to age can be detected in several standing conditions, which became more apparent in more demanding conditions. This implies that CoP movement can be used to detect changes in standing balance at an early stage.

Measuring CoP movement is less achievable in elderly outpatients. First, not everyone is able to maintain standing balance in each standing condition, which means that it is not possible to measure CoP movement in the same condition in all elderly. Secondly, to reach an excellent reliability, previous studies recommended to measure CoP movement a time period of 90 seconds and more than once [14;15], which is less feasible in clinical practice and in elderly outpatients due to fatigue and limited time. Thirdly, CoP movement acts in a specific range, namely the size of the base of support. This range limits the CoP movement and limits the possibility to detect differences between or within participants. Most importantly, as already mentioned in part I, interrelation between the underlying systems involved in standing balance makes it difficult to interpret changes in CoP movement and to draw conclusions about the primary cause of impaired balance. Due to aforementioned drawbacks, previous studies already doubt about the clinical use and interpretation of CoP movement [16-18].

System identification techniques to assess balance in elderly

In Part III, we showed that applying well-known disturbances during standing balance made it possible to distinguish cause and effect relations in a closed loop and to measure the contribution of the underlying systems involved in standing balance. In contrast with aforementioned measures, this gives the opportunity to detect deterioration of standing balance at an early stage and to unravel the primary cause of impaired standing balance.

In Chapter 8 we showed that it is possible to identify the contribution of proprioceptive information in healthy young adults using proprioceptive disturbances and system identification techniques. Submaximal disturbances were used, which could be withstand by the participant. In Chapter 9, we adapted the protocol to take the individual ability to maintain balance in the elderly population into account; participants were allowed to use visual information by standing with eyes open and the amplitude of the applied disturbance was dependent on the ability of the participant. By this protocol only information could be obtained about the use of proprioceptive information and no distinction could be made about the use of the visual and vestibular information.

To get more insight in the use of the other sensory information, we introduced a visual disturbance by rotation of a visual scene in Chapter 10. Furthermore, mechanical disturbances of the leg and trunk segment were introduced to investigate inter segmental coupling between the ankle and hip joint. The protocol used in this study was feasible for all healthy elderly participants. To use this method in elderly with impaired balance, the protocol must also be validated in this population. The amplitude of the disturbances must be low enough to be able to maintain standing balance, but also high enough to detect a response and to apply system identification techniques; submaximal disturbance amplitudes are needed.

In healthy elderly, the reliability of the system identification techniques used to assess standing balance, in case of four disturbances applied simultaneously, was moderate to excellent when measured twice per day on three separate days (Chapter 10). A systematic error between the first and second trial on one day suggested that the elderly needed time to reach a steady state or used a variety of adaptation strategies to withstand the disturbances, i.e. a learning effect was present. To reach an excellent reliability of steady state balance assessment, several tests must be performed on one or more days; on one day at least ten trials must be performed. When measuring on more than one day, less trials per day are needed to reach an excellent reliability. As there is limited time in clinical practice, it is less feasible to divide measurements over more than one day. When measurements are repeated on one day, the fatigue and boredom of the participant may play an important role.

In this thesis, conclusions are mainly based on nonparametric analysis describing the measured responses to the disturbances. However, to give physiological meaning to the responses a proper model of the balance system is required, which describes the underlying systems involved in standing balance. In Chapter 9, we already used a model based on previous studies [9;19-21], describing the responses to the proprioceptive disturbances. The next step is to develop a model including all sensory systems and describing the human body by a two-segmented inverted pendulum including both the ankle and the hip joint, to give physiological meaning to the responses to all disturbances applied by the BalRoom. It is important to keep in mind the goal of the model to simulate the physiological behavior of standing balance, which will allow physiological interpretation. A balance must be found between the number of parameters and the goodness of the model fit; a small number of parameters results in poor fits, but also in less variance within the parameters and therefore more accurate estimated parameters. On the other hand, a large number of parameters results in better fits, but could result in interaction between parameters and more variance within the parameters resulting in less accurate estimated parameters. In this case, parameters may not provide information about the system. The reliability of the parameters estimated using the new model must be investigated.

Clinical implications

The associations of underlying systems, represented by muscle characteristics, cognition and blood pressure regulation, with impaired standing balance underpin the importance of investigating the underlying pathophysiology by measuring both physical functioning, represented by i.e. walking speed and the ability to maintain standing balance, and the quality of the underlying systems in geriatric care. Deterioration in the underlying systems and physical functioning have clinical meaning. For example, low cognitive function could be a warning for deterioration in standing balance, and, the other way around, a deterioration in standing balance could also be a warning for deterioration in cognitive function.

The ability to maintain standing balance in side-by-side stance with eyes closed is a useful measure to detect impaired balance in elderly outpatients, but only detects failure of the compensation strategies. With this measure underlying changes in standing balance cannot be detected at an early stage. CoP movement gives more insight in changes in the quality of standing balance at an early stage, e.g. with age. Both CoP movement and the ability to maintain standing balance during side-by-side stance with eyes closed do not allow for assessing the underlying primary cause of impaired balance.

With system identification techniques underlying changes in standing balance can be detected, which gives high expectations for the use of this method in clinical practice. To reach an excellent reliability, a training session must precede testing to overcome a systematic error and to assess a steady state balance. Furthermore, at least ten tests must be performed on one day. To assess steady state it is important which test condition is used. In a more demanding test condition several strategies can be used to maintain balance resulting in high inter trial variability. Both the time to reach a steady state and the used strategy, e.g. stepping strategies, may also be important parameters in diagnosis of impaired standing balance in elderly.

More evidence is needed for using the BalRoom and system identification in clinical practice by validating, next to the proprioceptive disturbances, also the other disturbances (i.e. visual disturbance and force disturbances) in an elderly population with specific diseases. Furthermore, the sensitivity of the method can be validated by comparing the effect of treatment (e.g. drugs that are known to affect standing balance) on parameters measured with both system identification techniques and current used clinical balance tests.

General conclusion and future directions

The first aim of this thesis was to investigate the role of underlying systems in impaired standing balance in a heterogeneous population of community-dwelling elderly referred to a geriatric outpatient clinic. This thesis showed that underlying systems, represented by the muscle characteristics, cognition and blood pressure regulation, are associated with the ability to maintain standing balance, which represented the multi causal problem of standing balance.

The second aim was to assess the implementation of current balance tests to measure standing balance in clinical practice. Results showed that the ability to maintain standing balance in side-by-side stance with eyes closed is a useful clinical measure to detect impaired balance in elderly outpatients, but lacks in detecting underlying deteriorations at an early stage. CoP movement measures deterioration in standing balance at an early stage, but it still lacks in acquiring information about the deterioration of the underlying systems involved in standing balance.

The third aim of this thesis was to validate a new engineering approach for diagnosing impaired standing balance in elderly. We showed that system identification techniques are useful to distinguish the contribution of the underlying systems to maintain balance at an early stage. Changes in sensory (re)weighting of proprioceptive information with age and specific diseases were detected. Applying disturbances with the BalRoom unravels the contribution of all sensory systems and the use of the ankle and hip joint in standing balance. To measure reliable parameters of steady state balance with the BalRoom, a training session and multiple trials must be performed.

Before the BalRoom and system identification techniques can be implemented in clinical care, the method must be tested in a clinical population of elderly with several unknown underlying causes of impaired balance. Combining system identification techniques with clinical measures makes it possible to cluster phenotypes. This will show whether system identification techniques can be used as diagnostic tool to unravel the primary cause of impaired balance in elderly. Detection of the primary cause will allow for development of new targeted interventions to improve standing balance at an early stage and therefore to prevent falling. The BalRoom and system identification techniques may also play an important role in evaluation of new-developed targeted interventions and monitoring treatment effects.

Together, implementation of the BalRoom and system identification techniques as diagnostic tool gives more insight in the underlying cause of impaired balance in elderly. Early detection may help to reduce the progression of impaired balance and ultimately falls in the elderly.

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Chapter 12

Summary

Introductie

Het hebben van evenwichtsproblemen is een veelvoorkomend probleem bij ouderen en is een van de hoofdoorzaken van vallen. Het risico op vallen neemt toe wanneer je last hebt van evenwichtsproblemen [1]; een derde van de ouderen valt minstens een keer per jaar [2]. Vallen kan resulteren in serieuze verwondingen, met de dood tot gevolg [3]. Bij het bewaren van het evenwicht werken verschillende onderliggende systemen samen, zoals het zenuwstelsel, de spieren en sensorische systemen, via efferente en afferente paden [4]. Dit resulteert in een gesloten lus waarin oorzaak en gevolg aan elkaar zijn gerelateerd. Met het ouder worden, maar ook door invloed van ziekten en medicatiegebruik, gaan de onderliggende systemen achteruit [4-7]. De onderliggende systemen kunnen voor elkaars achteruitgang compenseren. Dit maakt het lastig om de primaire oorzaak van evenwichtsproblemen in ouderen te ontrafelen. Echter is het belangrijk om de onderliggende en primaire oorzaak vast te stellen en dit het liefst in een vroeg stadium, zodat er een doelgerichte behandeling kan worden gegeven.

In dit proefschrift laten we zien in welke mate verschillende onderliggende systemen een rol spelen in evenwichtsproblemen bij een populatie van thuiswonende ouderen die doorgestuurd zijn naar een geriatrische polikliniek (*hoofdstuk 3-5*). Dit heeft geresulteerd in meer inzicht in de multicausale aard van evenwichtsproblemen bij ouderen. Daarnaast is het gebruik van verschillende evenwichtstesten in een klinische omgeving onderzocht, waarmee de vraag is beantwoord welke evenwichtstest het beste gebruikt kan worden voor het vaststellen van evenwichtsproblemen bij poliklinische ouderen (*hoofdstuk 6-7*). Echter geven huidige evenwichtstesten geen informatie over de onderliggende en primaire oorzaak van evenwichtsproblemen. In *hoofdstuk 8* wordt een nieuwe technische benadering om evenwicht te meten geïntroduceerd en vervolgens is deze techniek gevalideerd in ouderen (*hoofdstuk 9-10*).

Hoofdbevindingen

Deel 1 van dit proefschrift beschrijft de associaties tussen onderliggende systemen betrokken bij het evenwicht en evenwichtsproblemen. In een populatie van bijna 200 ouderen, verwezen naar het Behandeladviescentrum Ouderengeneeskunde van het Bronovo ziekenhuis in Den Haag, is een uitgebreid geriatrische onderzoek uitgevoerd. Hierbij werden onder andere de spierkracht, spiermassa, bloeddrukregulatie en cognitie gemeten, welke respectievelijk de spieren en het zenuwstelsel representeren. Daarnaast werd het fysiek functioneren gemeten door middel van de Short Physical Performance Battery, bestaande uit evenwichtstesten, een 4 meter loop test en een zit-naar-stand test, een 10 meter loop test en de Timed Up and Go test. De evenwichtstesten werden uitgevoerd op een krachtenplaat, waarmee de beweging van de grondreactiekrachten (Center of Pressure, CoP) werd gemeten. Resultaten laten zien dat de achteruitgang in spierkracht (zowel handknijpkracht als knie-extensiekracht) (*hoofdstuk 3*), in cognitie (*hoofdstuk 4*) en in bloeddrukregulatie (*hoofdstuk 5*) geassocieerd zijn met de mogelijkheid om het evenwicht te bewaren in bepaalde condities. In andere woorden, een lage spierkracht, een verminderde cognitie en een hoge bloeddrukdaling na opstaan gaan gepaard met een slechter evenwicht. De achteruitgang van deze systemen is niet geassocieerd met de CoP beweging.

Deel II beschrijft de waarde van huidige evenwichtstesten in het beoordelen van het evenwicht in de klinische praktijk. *Hoofdstuk 5* laat zien dat leeftijdgerelateerde verschillen kunnen worden vastgesteld met behulp van het meten van de CoP beweging, een maat voor de kwaliteit van het evenwicht. Deze leeftijdgerelateerde verschillen waren meer prominent aanwezig in medio-laterale richting en tijdens meer inspannende condities. *Hoofdstuk 6* beschrijft dat in een populatie van poliklinische ouderen de mogelijkheid om het evenwicht te bewaren in een stand met de voeten naast elkaar en tegen elkaar (zij-aan-zij stand) met de ogen dicht geassocieerd is met zelfgerapporteerde evenwichtsproblemen, een geschiedenis van vallen en CoP beweging. Dit impliceert dat het niet kunnen blijven staan met de voeten naast en tegen elkaar met de ogen dicht een indicatie is voor evenwichtsproblemen en een goede methode is om evenwichtsproblemen te detecteren bij poliklinische ouderen.

In deel III is een nieuwe methode, namelijk systeem identificatie techniek, geïntroduceerd om de onderliggende en primaire oorzaak van evenwichtsproblemen te ontrafelen. Met behulp van welbekende verstoringen van de onderliggende systemen, kan de gesloten lus worden geopend. In *hoofdstuk 8* is aangetoond dat met behulp van rotaties van de ondergrond aangebracht met een Bilaterale Enkel Verstoorder (BAP, Motekforce Link, Culemborg, Nederland) het gebruik van proprioceptie van het linker- en rechterbeen kan worden bepaald in jongeren [8]. Eerder onderzoek liet al zien dat sensorische informatie wordt gecombineerd op basis van de betrouwbaarheid. In dit proces, ook wel sensorische herweging genoemd, wordt minder betrouwbare informatie minder gebruikt en gewogen bij het bewaren van het evenwicht, wat altijd gepaard gaat met meer gebruik en weging van de andere sensorische informatie [9]. In deze studie hebben we laten zien dat de afname van de proprioceptieve weging van het linkerbeen niet gepaard gaat met veranderingen in de proprioceptieve weging van het rechterbeen. Dit betekent dat de proprioceptieve informatie van beide benen onafhankelijk van elkaar wordt gewogen.

Vervolgens is de BAP gevalideerd in een groep ouderen met specifieke ziekten (*hoofdstuk 9*). In deze studie waren 10 jongeren, 10 gezonde ouderen, 10 ouderen met polyneuropathie, 10 ouderen met staar en 14 ouderen met evenwichtsproblemen geïncludeerd. Resultaten laten zien dat proprioceptieve informatie meer wordt gebruikt bij het bewaren van het evenwicht in geval van een hogere leeftijd, staar en evenwichtsproblemen. Echter is er geen verschil in de mate van herweging van proprioceptieve informatie bij toenemende verstoring van de proprioceptieve informatie. Deze resultaten geven aan dat systeem identificatie techniek kan worden gebruikt bij het onderscheiden van de onderliggende veranderingen in het gebruik van proprioceptieve informatie tijdens het evenwicht.

In *hoofdstuk 10* is de Balance test Room (BalRoom) (Motekforce Link, Culemborg, Nederland en Universiteit Twente, Enschede, Nederland) geïntroduceerd, waarmee meerdere verstoringen tegelijkertijd kunnen worden aangebracht om de bijdrage van de onderliggende sensorische systemen en het gebruik van het enkel- en heupgewricht bij het houden van het evenwicht te ontrafelen. De betrouwbaarheid van deze methode was onderzocht in gezonde ouderen door het uitvoeren van twee BalRoom metingen op 3 onafhankelijke dagen. De resultaten laten een systematische fout tussen de eerste en tweede meting op een dag zien. De betrouwbaarheid is matig tot excellent wanneer de resultaten van twee metingen op 3 dagen (in totaal 6 metingen) worden gemiddeld.

Reflectie

Evenwichtsproblemen in poliklinische ouderen

De associaties tussen de onderliggende systemen en de mogelijkheid om het evenwicht te bewaren werden alleen gevonden tijdens meer inspannende condities, namelijk met ogen dicht en in een stand met de voeten achterelkaar geplaatst. Deze manipulaties van specifieke elementen van het evenwicht resulteren in veranderingen in de beschikbare sensorische informatie en de grootte van het standvlak. Hiervoor kan worden gecompenseerd door de cognitieve belasting [10] te vergroten of door meer spierkracht te leveren. Dit verklaart waarom de achteruitgang in onderliggende systemen meer naar voren komt in meer inspannende condities.

Door de interactie tussen de onderliggende systemen zijn er geen associaties gevonden tussen de onderliggende systemen en de CoP beweging. De CoP beweging beschrijft de kwaliteit van het evenwicht en representeert daardoor de kwaliteit van de onderliggende systemen samen. Achteruitgang van de onderliggende systemen, veroorzaakt door leeftijd, ziektes en medicatiegebruik [4-7], kan resulteren in dezelfde CoP beweging. Achteruitgang van de spieractivatie zal bijvoorbeeld resulteren in meer CoP beweging, doordat ook de spierkracht afneemt. Aan de andere kant, achteruitgang in de sensorische systemen resulteert in minder accurate informatie over de lichaamsbeweging. Deze informatie wordt naar het zenuwstelsel gestuurd en zal minder spierkracht veroorzaken. Dit zal vervolgens ook resulteren in meer CoP beweging. Daarnaast kunnen de onderliggende systemen ook voor elkaars achteruitgang compenseren, bijvoorbeeld door sensorische herweging of door cocontractie. Dit bemoeilijkt de interpretatie van CoP beweging. In onze populatie van poliklinische ouderen heeft bijna 50 procent meerdere ziekten (multi morbiditeit) en 75 procent gebruikt drie tot zeven medicijnen. Dit resulteert in een grote variatie in de achteruitgang van de onderliggende systemen, wat kan verklaren waarom we geen associaties vinden tussen de onderliggende systemen en CoP beweging in poliklinische ouderen.

Het gebruik van huidige klinische evenwichtstesten

In deel II tonen we aan dat de mogelijkheid om het evenwicht te bewaren in zij-aan-zij stand met de ogen dicht een makkelijk toepasbare klinische maat is om evenwichtsproblemen bij poliklinische ouderen te detecteren. Daarnaast kost het weinig tijd om op deze wijze te meten. Zelfgerapporteerde evenwichtsproblemen kunnen daarentegen worden beïnvloed door andere factoren, zoals depressie, cognitie en zelfovertuiging [11;12], waardoor dit een minder betrouwbare maat is om te gebruiken in de kliniek. Zelfgerapporteerde geschiedenis van vallen is een goede voorspeller voor meerdere vallen [13], maar kan ook worden beïnvloed door herinneringsbias. Dit zal resulteren in een onderschatting van het risico op evenwichtsproblemen.

De associatie tussen de mogelijkheid om het evenwicht te houden en andere evenwichtsmaten, zoals geschiedenis van vallen, CoP beweging en zelfgerapporteerde evenwichtsproblemen werd alleen gevonden in meer inspannende condities, namelijk in zij-aan-zij stand met de ogen dicht. Dit kan worden verklaard door de moeilijkheidsgraad van de conditie. Wanneer de moeilijkheidsgraad toeneemt door het manipuleren van de testconditie, bijvoorbeeld door het veranderen van de grootte van het standvlak of de beschikbaarheid van sensorische informatie, zal dit op een bepaald moment resulteren in falen van het evenwicht. In andere woorden, het evenwicht zal altijd op een bepaald punt falen, zolang de conditie maar moeilijk genoeg is. Het moment van falen is afhankelijk van de kwaliteit van de onderliggende systemen en de mogelijkheid om compensatiestrategieën te gebruiken. De benodigde testconditie hangt af van de ernst van de achteruitgang; in een gezonde populatie met weinig achteruitgang van de onderliggende systemen is een moeilijkere testconditie nodig dan in poliklinische ouderen. In deze laatste populatie is de zij-aan-zij stand met de ogen dicht een gevoelige testconditie voor het meten van evenwichtsproblemen. Echter met deze conditie kunnen evenwichtsproblemen niet in een vroeg stadium worden vastgesteld.

Om veranderingen in de kwaliteit van het evenwicht te meten voordat het evenwicht faalt, kan gebruik worden gemaakt van CoP beweging, een objectieve maat van lichamelijke reacties. Om CoP beweging betrouwbaar te kunnen meten moet er gebruik worden gemaakt van een conditie waarbij het evenwicht niet faalt. Daarnaast moet er ook gekozen worden voor een meer inspannende conditie. Deze zal resulteren in meer respons en is gevoeliger voor veranderingen in CoP beweging. In *hoofdstuk 6* laten we zien dat de leeftijdgerelateerde achteruitgang van het evenwicht kan worden vastgesteld in verschillende condities met behulp van CoP beweging, waarbij deze achteruitgang duidelijker werd tijdens meer inspannende condities. Dit impliceert dat CoP beweging kan worden gebruikt voor het vaststellen van veranderingen in het evenwicht in een vroeg stadium.

Het meten van CoP beweging is minder haalbaar bij poliklinische ouderen. Als eerste kan niet iedereen blijven staan tijdens elke testconditie, wat betekent dat het niet mogelijk is om bij iedereen tijdens dezelfde conditie CoP beweging te meten. Ten tweede moet CoP beweging gedurende 90 seconden en meerdere malen worden gemeten om een betrouwbare CoP beweging te verkrijgen [14;15]. Dit is minder haalbaar in poliklinische ouderen door vermoeidheid van de patiënt en beschikbare tijd in de klinische praktijk. Ten derde kan CoP beweging alleen worden gemeten in een bepaalde range, namelijk de grootte van het standvlak. Deze range zorgt ervoor dat de CoP beweging wordt gelimiteerd en maakt het lastiger om verschillen tussen en binnen proefpersonen te vinden. Als laatste is het door de interrelatie tussen de onderliggende systemen betrokken bij het evenwicht moeilijk om veranderingen in CoP beweging te interpreteren en conclusies te trekken over de primaire oorzaak van evenwichtsproblemen. Voorgenoemde nadelen zijn al eerder door onderzoeken laten zien en zij geven dan ook aan te twijfelen over de klinische toepassing en interpretatie van CoP beweging [16-18].

Systeem identificatie techniek voor het meten van het evenwicht in ouderen

In deel III laten we zien dat met het aanbrengen van welbekende verstoringen het mogelijk is om oorzaak en gevolg te onderscheiden in een gesloten lus en de bijdrage van de onderliggende systemen te meten. In tegenstelling tot voorgaande evenwichtsmaten geeft systeem identificatie techniek de mogelijkheid om achteruitgang in het evenwicht in een vroeg stadium te meten en daarbij ook de primaire oorzaak van evenwichtsproblemen te achterhalen.

In *hoofdstuk 8* hebben we laten zien dat het mogelijk is om de bijdrage van proprioceptieve informatie aan het evenwicht te identificeren met gebruik van proprioceptieve verstoringen en systeem identificatie techniek. Submaximale verstoringsamplitudes zijn gebruikt waarbij de proefpersonen konden blijven staan. In *hoofdstuk 9* was het protocol aangepast aan de nieuwe doelgroep, namelijk ouderen. De proefpersonen konden gebruik maken van hun visuele informatie en de amplitude van de verstoringen was afhankelijk van de mogelijkheden van de proefpersoon. Door gebruik te maken van dit protocol was het alleen mogelijk om informatie te verkrijgen over het gebruik van de proprioceptieve informatie. Er kon geen onderscheid worden gemaakt tussen het gebruik van visuele en vestibulaire informatie.

Om meer inzicht te krijgen in het gebruik van de andere sensorische informatie is in *hoofdstuk 10* een visuele verstoring door rotatie van een scherm gecombineerd met de proprioceptive verstoring. Verder is er gebruik gemaakt van mechanische verstoringen van het been- en rompsegment om de intersegmentale koppeling tussen het enkel- en heupgewricht te onderzoeken. Amplitudes waren zo vastgesteld dat het nog mogelijk was voor de proefpersoon om te blijven staan. Dit protocol was haalbaar voor gezonde ouderen. Of dit protocol ook haalbaar is in ouderen met evenwichtsproblemen zal moeten worden gevalideerd. Daarbij moet rekening worden gehouden dat de amplitudes van de verstoringen laag genoeg zijn zodat de proefpersoon zijn evenwicht kan houden, maar ook hoog genoeg zijn zodat een respons wordt gegenereerd en systeem identificatie techniek kan worden toegepast. In andere woorden, submaximale verstoringamplitudes moeten worden gebruikt.

De betrouwbaarheid van de parameters die het evenwicht beschrijven en verkregen zijn met systeem identificatie techniek is matig tot excellent in ouderen, wanneer er tweemaal gedurende 3 dagen wordt gemeten (*hoofdstuk 10*). Een systematische error tussen de eerste en tweede meting op een dag suggereert dat ouderen tijd nodig hebben om een stabiele toestand te bereiken of dat ze verschillende adaptatiestrategieën gebruiken om de verstoringen te weerstaan. Om een excellent betrouwbaarheid te behalen moet er daarom meerdere malen worden gemeten op een of meerdere dagen. Wanneer er op een dag wordt gemeten, moeten minstens tien metingen worden gedaan. Wanneer er op meerdere dagen wordt gemeten, zijn er minder metingen per dag nodig om een excellent betrouwbaarheid te behalen. Omdat er in de klinische praktijk maar beperkte tijd is, is het meten op meerdere dagen minder haalbaar. Echter bij het herhalen van metingen op een dag moet er rekening worden gehouden met de vermoeidheid en motivatie van de proefpersoon.

In dit proefschrift zijn de conclusies voornamelijk gebaseerd op nonparametrische analyse van de menselijke reactie op de verstoringen. Om een fysiologische betekenis te kunnen geven aan deze reacties is er een model van het evenwicht nodig die de onderliggende systemen betrokken bij het evenwicht beschrijft. In *hoofdstuk 9* maken we al gebruik van een model gebaseerd op eerdere onderzoeken [9;19-21]. Dit model beschrijft alleen de reactie op de proprioceptieve verstoringen. De volgende stap is om dit model uit te breiden naar een model dat de reactie op alle verstoringen van de BalRoom kan beschrijven. Hiervoor moet het model worden uitgebreid met een beschrijving van de andere sensorische systemen en meerdere segmenten moeten worden toegevoegd die verbonden worden door het enkel- en heupgewricht. Bij het maken van een model is het belangrijk om het doel van het model in de gaten te houden, namelijk om het fysiologische gedrag van het evenwicht in kaart te brengen. In dat geval zal het mogelijk zijn de parameters fysiologisch te interpreteren. Een balans moet worden gevonden tussen het aantal parameters en de goedheid van de modelbenadering. Een klein aantal parameters zal resulteren in een minder goede benadering, maar ook in weinig variantie binnen de parameters. Dit betekent dat de geschatte parameters nauwkeuriger zullen zijn. Een groot aantal parameters zal resulteren in een betere benadering, maar kan ook resulteren in interactie tussen de parameters en meer variantie binnen de parameters. Dit betekent dat de geschatte parameters minder nauwkeurig zullen zijn en misschien geen informatie geven over het onderliggende systeem. De betrouwbaarheid van het nieuwe model moet vervolgens worden onderzocht.

Klinische implicaties

De associatie van de onderliggende systemen betrokken bij het evenwicht met evenwichtsproblemen laat zien hoe belangrijk het is om de onderliggende pathosfysiologie te onderzoeken door het meten van het fysiek functioneren, bijvoorbeeld loopsnelheid en de mogelijkheid om het evenwicht te houden, en het meten van de kwaliteit van de onderliggende systemen in de geriatrische zorg. Achteruitgang van de onderliggende systemen en het fysiek functioneren is van klinisch belang. Wanneer bijvoorbeeld een achteruitgang in cognitie wordt vastgesteld, kan dit een waarschuwing zijn voor achteruitgang in het evenwicht. Dit geldt ook andersom: een achteruitgang in het evenwicht kan een waarschuwing zijn voor achteruitgang in cognitie.

De mogelijkheid om het evenwicht te bewaren tijdens zij-aan-zij stand met de ogen dicht is een bruikbare maat voor het detecteren van evenwichtsproblemen bij ouderen, maar deze worden alleen gedetecteerd door het falen van compensatiestrategieën. De onderliggende veranderingen in het evenwicht kunnen niet in een vroeg stadium worden gedetecteerd. Het meten van de CoP beweging geeft meer inzicht in de veranderingen van de kwaliteit van het evenwicht in een vroeg stadium, bijvoorbeeld met verandering van leeftijd. Echter is het zowel met het meten van de CoP beweging als met het meten van de mogelijkheid om te blijven staan tijdens zij-aan-zij stand met de ogen dicht niet mogelijk om de onderliggende primaire oorzaak van evenwichtsproblemen vast te stellen.

Met systeem identificatie techniek kunnen onderliggende veranderingen in het evenwicht worden gedetecteerd. Dit geeft hoge verwachtingen met betrekking tot het gebruik van deze methode in de klinische praktijk. Voor het behalen van een excellent betrouwbaarheid moet vooraf een trainingsessie met de BalRoom worden gedaan. Hierdoor zal het evenwicht in een stabiele toestand worden gemeten en worden systematische fouten voorkomen. Verder moeten er minstens tien metingen worden gedaan op een dag. Daarbij is het ook belangrijk welke testconditie wordt gebruikt. Tijdens meer inspannende testcondities is het mogelijk om verschillende strategieën te gebruiken om het evenwicht te houden wat kan resulteren in een hoge variabiliteit tussen metingen. De tijd die nodig is om een stabiele toestand te verkrijgen en de gebruikte strategie kunnen ook belangrijke parameters zijn in de diagnose van evenwichtsproblemen bij ouderen.

Meer bewijs is nodig voor het gebruik van de BalRoom en systeem identificatie techniek in de klinische praktijk. Dit kan worden verkregen door ook de andere verstoringen, naast de proprioceptieve verstoring, te valideren in een oudere populatie met specifieke ziekten. Vervolgens kan ook de gevoeligheid van de methode worden gevalideerd met behulp van behandeleffecten, bijvoorbeeld bij gebruik van medicatie waarvan we weten dat deze invloed heeft op het evenwicht. De gevoeligheid van de parameters gemeten met systeem identificatie techniek en huidige klinische testen kunnen worden vergeleken.

Conclusie en toekomstig onderzoek

Het eerste doel van dit proefschrift was het onderzoeken van de rol van de onderliggende systemen in evenwichtsproblemen in een heterogene populatie van ouderen die verwezen waren naar een geriatrische polikliniek. Dit proefschrift laat zien dat onderliggende systemen, gerepresenteerd bij spierkarakteristieken, cognitie en bloeddrukregulatie, geassocieerd zijn met de mogelijkheid om het evenwicht te bewaren. Dit resultaat laat de multicausale aard van evenwichtsproblemen zien.

Het tweede doel was het analyseren van de implementatie van huidige evenwichtstesten in de klinische praktijk. De resultaten laten zien dat de mogelijkheid om het evenwicht te bewaren in zij-aan-zij stand met de ogen dicht een bruikbare maat is om evenwichtsproblemen te detecteren bij poliklinische ouderen. Echter ontbreekt hierbij de mogelijkheid om de veranderingen in een vroeg stadium vast te stellen. Dit is wel mogelijk bij het meten van de CoP beweging, maar hierbij wordt geen informatie verkregen over de achteruitgang van de onderliggende systemen betrokken bij het evenwicht.

Het derde doel van dit proefschrift was het valideren van een nieuwe technische benadering voor de diagnose van evenwichtsproblemen bij ouderen. We hebben laten zien dat systeem identificatie techniek bruikbaar is om de bijdrage van de onderliggende systemen bij het houden van het evenwicht te onderscheiden in een vroeg stadium. Als eerste kunnen veranderingen met leeftijd en specifieke ziekten in sensorische herweging van proprioceptieve informatie worden gedetecteerd. Als tweede maakt het aanbrengen van meerdere verstoringen met de BalRoom het mogelijk om de bijdrage van de sensorische systemen en het gebruik van het enkel- en heupgewricht tijdens het evenwicht te ontrafelen. Om betrouwbare parameters tijdens een stabiele toestand te meten, moet er eerst een trainingsessie worden gedaan en moeten er meerdere metingen worden uitgevoerd.

Voordat de BalRoom en systeem identificatie techniek kunnen worden geïmplementeerd in de klinische zorg, moet de methode eerst worden getest in een klinische populatie van ouderen met verschillende onbekende onderliggende oorzaken van evenwichtsproblemen. Door systeem identificatie techniek te combineren met klinische maten kunnen er clusters met verschillende fenotypes worden gemaakt. Dit zal laten zien of systeem identificatie techniek een toegevoegde waarde heeft als een diagnostisch apparaat om de onderliggende primaire oorzaak van evenwichtsproblemen bij ouderen te ontrafelen. Het detecteren van de primaire oorzaak maakt het mogelijk om nieuwe doelgerichte interventies te ontwikkelen waarmee het evenwicht in een vroeg stadium kan worden verbeterd en daardoor vallen tegen kan worden gaan. De BalRoom en systeem identificatie techniek kunnen ook een belangrijke rol spelen in de evaluatie van nieuw ontwikkelde doelgerichte interventies en het monitoren van behandeleffecten.

Samengenomen zal het implementeren van de BalRoom en systeem identificatie techniek als een diagnostisch apparaat meer inzicht geven in de onderliggende oorzaak van evenwichtsproblemen bij ouderen. Vroege detectie zal helpen om de progressie van evenwichtsproblemen, en daarmee vallen, te reduceren bij ouderen.

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Part V

Appendices


balance
disturbances
compensation
control
deterioration
impaired
sensory
training
steps
strategies
used
clinical
interventions
nervous
identification
possible
elderly
proprioception
underlying
cognitive
changes
assessment
movement
information
systems
tests
maintain
conditions
increase
measure
joint
motor
different
reduced
activities
ankle
hip
loop
effect
specific
primary
selection
attentional
needed
quality
task
techniques
CoM
age
current
comprises
decline
proper
visual
case
result
external
force
intensity
sensitivity
time
method
virtual
applied
identify
preventing
improve
detect
decrease
fibers
relay
power
efferent
sense
best
resistance
elimination
Perturbation
distinguish
delay
pushes
processing
amplitudes
difficulty
depending
challenging
simultaneous
involve
contraction
fail
individual
significant
ability
accurate
consequence
combined
pressure
optimization
alternative
perceived
stability
physical
frequency
population
prioritized
adaptation
shows
allows
subsequently
angles
response
increased

List of publications

List of publications

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Curriculum Vitae

Curriculum Vitae

Jantsje Henrieke Pasma was born on 16th of July 1986 in Borne, the Netherlands. In 1999 she attended the secondary school at the OSG Bataafse Kamp (Hengelo, the Netherlands) and graduated from the Gymnasium in 2004. In September 2004, she started her study Biomedical Engineering at the University of Twente (Enschede, the Netherlands), where she received her bachelor degree in November 2007.

In September 2007, she started the master Biomedical Engineering with specialization Human Function Technology. During her study she organized a three weeks study tour to Brazil. Additionally, she followed three courses at the faculty of Human Movement Science at the Free University (Amsterdam, the Netherlands). She did her master internship at the department of Research, Development and Education of the Sint Maartenskliniek (Nijmegen, the Netherlands). In September 2009, she started her master assignment at the department of Biomechanical Engineering at the University of Twente investigating the asymmetry of proprioceptive reweighting between the left and right leg during standing balance. In September 2010 she received her master degree.

After her study, she worked as a researcher at the department of Biomechanical Engineering of the University of Twente during 5 months. In March 2011, she started as PhD student of the BalRoom project (NeuroSIPE, STW) at the department of Rehabilitation Medicine in collaboration with the department of Gerontology and Geriatrics of the Leiden University Medical Center (Leiden, the Netherlands). During 4 years she worked on the studies described in this thesis. Since March 2015, she works as postdoctoral researcher on the EMBalance project (FP7-610454) at the department of Biomechanical Engineering of the Delft University of Technology (Delft, the Netherlands).

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