

Assessment of postural balance in community-dwelling older adults

- Methodological aspects and effects of biofeedback-based Nintendo Wii training

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THE 3 ORIGINAL PUBLICATIONS ARE

1. Jørgensen MG, Rathleff MS, Laessoe U, Caserotti P, Nielsen OB, Aagaard P. Time-of-day influences postural balance in older adults. *Gait Posture* 35(4): 653-657, 2012
2. Jørgensen MG, Laessoe U, Hendriksen C, Nielsen OBF, Aagaard P. Intra-rater reproducibility and concurrent validity of Nintendo Wii fit balance testing in older adults. In press at *Journal of Aging and Physical Activity*.
3. Jørgensen MG, Laessoe U, Hendriksen C, Nielsen OBF, Aagaard P. Efficacy of Nintendo Wii training on mechanical leg muscle function and postural balance in community-dwelling older adults: a randomized controlled trial. *J Gerontol A Biol Sci Med Sci*. 68(7): 845-52, 2013

INTRODUCTION

Age-related changes in postural control systems

The process of aging in humans have been studied extensively, however no clear and complete answers can be given to the question of why we age [1-4]. Nonetheless, there are numerous known ways in which the aging process can be accelerated (e.g. illness, pollution, unhealthy food and physical inactivity) and result in a shortened lifespan [5]. Sufficient signals from the sensory systems, an effective cognitive processing and a well-functioning musculoskeletal system are key factors for a good postural control [5,6]. With advancing age, however, many of these systems become damaged and/or weakened, which means that a person's physical capacity with time gradually approaches the threshold of various daily activities, consequently leading to dependency, poor quality of life and increased risk of falling [6-9]. The specific physiological age-related changes in systems of postural control will briefly be described in the following.

Somatosensory-, visual- and vestibular systems

The somatosensory system consists of a large number of proprioceptive and mechano-receptive organs located in the skin, skeletal muscles and bones. Several aspects of proprioception such as position sense and movement detection threshold have been found to deteriorate with aging e.g. significant reduction in numbers of intrafusal fibers and nuclear chain fibers per muscle in m. biceps brachii [10,11]. Similar deteriorations with aging are observed in the mechano-receptive organs causing the vibratory sensation threshold at the big toe to increase 3-fold by the age of 90 [6]. These changes in proprioceptive receptors and mechano-receptive organs result in a diminished information flow to CNS (e.g. about the position of the limbs and the pressure of the skin under the foot) [6] and has been linked to poorer balance control [12,13].

Similar age-related structural changes are seen for the human vision. Structural age-related changes within the lens of the eye result in less light being transmitted to the retina; Thus, the visual threshold defined as the minimum light needed to see an object increases with age [14]. Specific structural changes include: a loss in the visual field, a decline in visual acuity, and visual contrast sensitivity, which lead to impaired contour and depth perception [15,16]. Overall these primarily structural changes have been found to affect a broad range of functional skills, including postural control [15].

Similarly, alterations in the vestibular organs and central pathways occur with ageing (i.e. reduction of hair cells in both the canals and the otolith organs and a reduction in the number of nerve fibers), leading to impaired vestibular function [17-19]. Specifically between 40 and 70 years of age a reduction of approximately 40% in hair and nerve cells has been reported [19]. A major role of the vestibular system is to stabilize the head, and to provide an orientation reference to which the other postural systems (visual and somatosensory) may be compared and internally calibrated [20,21]. A decline in vestibular function with age may cause this reference function to become less reliable, and as a consequence the CNS shows increasing difficulties in dealing with potential conflicting afferent sensory feedback from the other sensory systems [5,22]. In result, older adults with vestibular deficits often become dizzy and oscillate significant when confronted with conflicting visual and somatosensory information [23].

Central nervous system

Afferent sensory information from the above systems trigger postural responses in the CNS, which selects, coordinates and compares the information, and if needed initiates corrective motor responses [24]. Some of the supra-spinal areas that are

heavily involved in these processes are the motor cortex, the cerebellum, the basal ganglia and the brainstem. Magnetic resonance imaging studies have explored age-related structural changes and found regional decreases in cerebral volume of 1% per year [25,26]. In addition, brain neurotransmitters and their receptors exhibit marked alterations as part of the aging process [27-29]. Several studies have investigated the effect of cognitive capacities on postural balance control [30-33]. In most of these reports older individuals show greater difficulty than younger individuals in dealing with tasks of increased cognitive complexity while concurrently performing postural balancing tasks [30,34]. The same trend between age groups is seen when reaction time [30] and skeletal muscle EMG amplitude [34] are measured while performing various complex functional tasks [31-33].

Musculoskeletal system

It is well documented that significant deteriorations occur in the musculoskeletal system with aging, comprising loss of spinal α -motor neurons, a reduction in skeletal muscle fiber number and size causing in a decreased cross-sectional area and volume, which again leads to a reduced functional capacity and ability during daily activities [35]. The decline in maximal muscle strength can amount to as much as 40% in isometric and concentric strength tests from the early 30s to the late 70s [36]. Interestingly, the corresponding rate of decline in maximal muscle power exceeds that of maximal strength by 50-100% [37-39]. In addition, the age-related decline in muscle strength appears to occur at a faster rate in the lower extremities compared to the upper extremities [40]. This is unfortunate; since maximal muscle strength of the lower limbs appears to be particular important for maintaining an optimal postural balance control [41] and poor strength levels have been identified as one of the key risk factor associated to falling [7]. Moreover, a number of experiments have shown that the capacity for explosive muscle strength (Rate of force development: RFD) plays an important role in ensuring postural stability in older adults, particularly in response to sudden perturbations in the walking gait cycle [42-44]. Additionally, researchers have found that RFD is inversely related to the magnitude of COP excursion and area [45]. Also, studies examining the effects of muscle fatigue on PB in young women have shown that fatigue of the Calf muscle increased COP amplitude and decreased velocity [46]. Finally, age-related decreases in joint range of motion and flexibility have been observed for the spine [47,48] and the ankle joint [49].

In summary, age-related changes occur within the afferent and efferent subsystems involved in postural control, and collectively these alterations appear to contribute to the deterioration in PB abilities observed in older adults. However, for some of the subsystems these deteriorations can be prevented or even partially reversed with regular exercise (strength-, cardiovascular- and/or balance training), which may result in a reduced fall risk, improved physiological and functional performance and an improved quality of life [50-58]. The following section defines and briefly discusses the definitions and terminology used in association with human postural stability in the upright standing position.

Mechanical balance, stability and postural control

Postural Balance (PB) is a generic term often used by clinicians and researchers working in a wide variety of specialties. Yet no universal accepted definition of postural balance (or equilibrium) seems to exist. Thus, the term postural balance is commonly used in association with other terms such as postural stability and

postural control [59,60]. This diversity in terminology will be explored in the following.

From a mechanical perspective an object is balanced when the resultant load actions (forces and moments) acting upon it sums to zero (Newton's first law). In other words, the ability of an object to remain in balance is related to the position of the center of mass (COM) and the area of the base of support (BOS) of that object [61]. If the vertical projection of COM (known as COG) of an object falls within BOS the object will remain in balance [62]. However, the object will become unbalanced and fall, if the vertical projection of COM is displaced outside of the BOS [59]. Mechanical stability as opposed to mechanical balance can be defined or expressed by a scale of degrees. The degree of stability depends on the amount of external force(s), which is required to move the objects' COM towards and beyond its BOS. In addition, stability depends on the placement of COM (vertically and horizontally) relative to the periphery of the BOS, the mass itself and the geometric proportion of the BOS [59].

Compared to inanimate objects, the human body has the ability to control stability and modulate body posture (i.e. when the vertical projection of COM approaches BOS an adequate response of muscular activity typically is generated) [63]. This ability to control COM in relation to BOS emerges from a complex interaction of musculoskeletal and afferent/efferent neural systems, often collectively termed as "postural control". The specific demand of the postural control system in a given situation is dependent upon the task at hand, the individual's abilities and the environment [64]. Postural control has been defined as: "the act of maintaining, achieving or restoring a state of balance during any posture or activity" [59]. To accomplish i.e. an upright standing position the neuromuscular subsystems generate forces to control the motion of the COM, and these forces are traceable in the form of Center of Pressure (COP) excursions, which can be recorded using instrumented force plate analysis.

Falling in the aging population

Fall accidents are associated with elevated morbidity, mortality, poorer overall functioning and early admission to long-term care facilities in the older population [65-67]. The prevention of falls among older people is therefore an urgent public health challenge, not only in Denmark but worldwide. Among approximately +400 risk factors known to be associated with fall accidents, decreased lower extremity muscle strength and impaired PB have been identified as key risk factors (Table 1)[68,69]. For prophylactic reasons, it thus becomes of great interest to target and reduce these key risk factors.

TABLE 1:

Risk Factor	Mean OR or RR*	Range
LE Weakness	4.4	1.5-10.3
History of falls	3	1.7-7.0
Gait Deficit	2.9	1.3-5.6
Balance Deficit	2.9	1.6-5.4
Use of Assistive Device	2.6	1.2-4.6
Visual Deficit	2.5	1.6-3.5
Arthritis	2.4	1.9-2.9
Impaired ADLs	2.3	1.5-3.1
Depression	2.2	1.7-2.5
Impaired Cognition	1.8	1.0-2.3
Age > 80 years	1.7	1.1-2.5

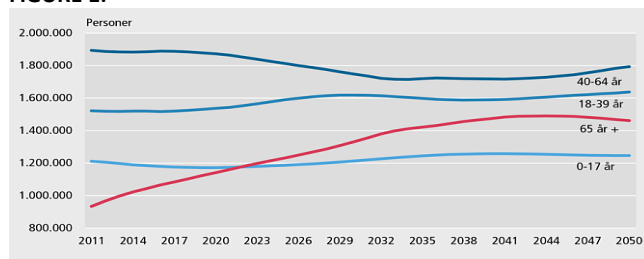
Displays primary risk factors associated to falling (Adapted from Rubenstein & Josephson, 2006)

In 2006 emergency room units in the United States treated 2.2 million non-fatal fall injuries among older adults, of which

+582,000 patients were hospitalized [70]. In 2000, the total medical costs related to fall injuries in older American adults +65 years of age exceeded \$19 billion [71]. A similar trend was seen in Denmark in 2006 where emergency room units were contacted by ~40.000 older fallers, of which approximately 30% (~12.000 patients) were hospitalized [72]. In older Danish fallers (2007-2009) predominant injury sites were located around the hip area, as approximately 19% of the 75-84 year old and 29% of the +85 year suffered from injuries in this region [73]. Severe hip fractures have been estimated to amount on average to ~67.000 \$ (or 365.000 Danish kroner) per year per patient [74] leading to a ~20% mortality rate within 6 months [72]. Thus, the outcome of falling in the older population not only has serious consequences for the individual per se but is also associated with severe socio-economic consequences for the society.

Adding to the severity of this scenario, the amount of U.S. residents aged 65 years or above is estimated to increase from 38.7 million in 2008 to 88.5 million in 2050 [75]. Likewise, the proportion of older adults in Denmark aged 65 years and above is predicted to increase dramatically from 934.000 in 2011 to 1.491.000 in 2044 (Figure 1) [76], in turn prompting the complications mentioned above increasingly important to solve.

FIGURE 1:



Prediction of the age group demography in Denmark 2011-2050 (The National Danish Institute of Statistics 2011)

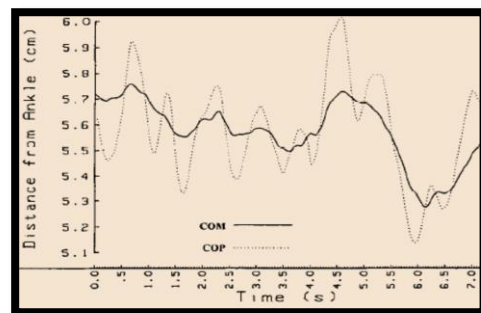
Despite the growing number of older adults in Denmark the amount of hip or thigh fractures, nonetheless have declined from around 9000 fractures in 1994 to around 7000 fractures in 2009 [73]. The causes for this decline most likely are multifactorial and linked to medicine reorganization, increasing prescription of physical exercise to the elderly, implementation of fall prevention strategies at Danish hospitals and a more effective treatment of osteoporosis with D-vitamin, calcium and bisphosphonate etc. Regardless, an increased emphasis on pre-injury diagnostics, prophylactic intervention and effective regimes of post-injury rehabilitation still seems needed. As a result of such increasing efforts individuals with signs of impaired physiological and/or functional capacity may be identified at an early stage, and appropriate interventions may be initiated to prevent future fall accidents and associated muscular-skeletal injuries from happening. However, for this to be accomplished improved assessment methods, tools and screening protocols, which more precisely can identify and characterize patients with impaired PB, need to be developed, reproducibility tested and externally validated. One of the most promising methods in achieving some of these goals is provided by force plate analysis (so called posturography). This technique is a cornerstone in the present thesis and will be described and discussed with detail in the following section.

Assessment of static postural balance

As described previously static balance control is achieved and maintained when the vertical projection of COM is kept safely

within the border of the BOS. However, this is not a trivial task during upright standing. Humans compared to four-legged animals have a very small BOS combined with a relatively high COM (during static standing located approximately 0.55 times the body-height above the supporting surface). Gravitational forces constantly pull the body towards the ground. These gravitational forces are counteracted by muscular adjustments of joint momentum, making the upright stance possible [77,78]. These biomechanical and external properties cause the body to perform small oscillations about the vertical axis of the ankle joints. If BOS is reduced in size (i.e. by a narrow stance or in unilateral single leg stance) the magnitude of this body sway will be amplified. The specific oscillatory movements (or sway paths) are obtainable and/or quantifiable by recording and analyzing the horizontal COP using a force plate [79-81]. COP is defined as the point location of the vertical ground reaction force vector. As such, the COP represents a weighted average of all the forces exerted on the surface of the force plate at any given point in time [82]. With the geometrical location of the COP a number of variables of displacement, area, speed or combinations can be calculated and analyzed. Seen in the sagittal plane, the human body can be represented as an inverted pendulum with pivots around the ankle joints as modeled by David Winter and coworkers [82]. On the basis of the inverted pendulum model, the COM is constantly guided and kept in place by the COP (Fig.2).

FIGURE 2:



Concurrent recordings of the horizontal COM trajectory path and the COP excursion path (the latter recorded by the force plate) during quite bilateral standing. COP excursions oscillate to either side of the COM and display a higher frequency and greater horizontal amplitude than COM (Adapted from Winter et al. 1990).

Force plate derived COP variables (sway velocity, area, etc.) can be regarded as an overall outcome variable from ongoing actions in the postural control system and may be interpreted to represent a measure of postural balance or postural stability. A full evaluation of all sensory-motor processes and/or interactions involved within the postural control system would require simultaneous measurements of muscle EMG, brain EEG, H-wave reflexes, TMS responses etc. However, more simple and integrative measures are needed in large scale clinical patient settings. Thus, COP variables may serve as an objective and pragmatic outcome measure derived from the postural control system.

Traditionally in the literature large COP measures excursions (i.e. sway length, velocity, area, ellipse area) have been interpreted as impaired postural balance control, while conversely small values have been taken to represent a good postural balance control [83,84]. This general assumption is driven by a simple logic that the larger the sway, the less effective postural control and the greater the risk of crossing the boundaries of BOS resulting in loss of balance or falling. Although occasionally challenged [83] this notion has been supported by numerous studies, which

have demonstrated that the magnitude of COP movement increases with age as young, middle-age and older adults differ significantly from each other [85,86,86-89]. This impression is further supported by case-control studies where patients and healthy controls can be readily separated by means of force plate analysis [90-92]. In addition, reports have shown that static posturography recordings are capable of predicting survival [93], fall risk [94] and ADL levels [95] to some extent in older adults. However, it is also important to point out that short-comings certainly exists with posturography, as some studies have shown difficulty in discriminating Parkinson's patients, known to have poor postural balance control, from healthy controls [83,96] although not seen in all studies [97]. Nonetheless, posturography is a widely used, reproducible and valid method of quantifying postural balance control in various populations [86,98-101].

Despite a widespread use of the force plate technique in a great number of scientific and clinical settings, a lack of consensus seems to exist on a number of methodological aspects related to this technology. For instance, control of the time-of-day during the recording of postural sway is rarely explicitly mentioned, despite that COP excursion is known to vary significantly throughout the day in younger subjects with [102-105] or without sleep deprivation [106,107], suggesting that the circadian rhythm might affect postural balance control. The present thesis examined this aspect for the first time in older adults (Study I).

The force plate technique is sensitive, objective and quantitative (on a continuous scale) however unfortunately also expensive, highly immobile and often technically difficult to carry out and subsequently process. Thus, a need exists to identify and/or develop low-cost objective quantitative tools for the clinical evaluation of PB in older adults. One such evaluation tool might be the NWBB (Nintendo, Minami-ku Kyoto, Japan). The NWBB is an easy-to-use, portable and low-cost force platform instrumented with sensitive force sensors positioned in each corner. Good-to-excellent test-retest reproducibility has been demonstrated during a static bilateral stance in thirty young individuals by extracting raw vertical force data from the NWBB using custom-build software [108]. In addition, good-to-excellent concurrent validity was observed when COP recordings based on the NWBB were compared to similar data obtained using a 'Gold standard' laboratory force plate (AMTI model) [108]. This type of approach requires custom made analysis software to be developed, which is typically not feasible for the working clinician. However, the possibility exist that standard built-in Nintendo Wii software (Wii Fit Plus) can be used for assessing PB capacity in older adults. Two Wii Fit Plus software based tests seem particularly relevant for evaluating PB: the Stillness and Agility test. Presently the reproducibility and concurrent validity of these PB tests have not been examined in community-dwelling older adults. Assuming that the tests were reproducible and demonstrated a verified biomechanical validity, the NWBB and Wii Fit Plus software might provide an objective low-cost assessment tool for clinical evaluation of static PB in community-dwelling older adults (Study II).

The Nintendo Wii system (software and Wii-board) was primarily intended as an entertainment device by the Nintendo Corporation and not as a potential training tool. Nonetheless, the NWBB combined with the Wii-console and build-in game software is capable of on-line detection of COP excursions, which in turn controls a virtual character (Avatar), displayed on a television screen (e.g. steering a downhill skier through successive gates). The Nintendo Wii system enables the user to perform complex balance and muscular tasks involving extensive neuromuscular

coordination and exertion of substantial muscle force accompanied by on-line biofeedback (instantaneous physiological feedback). Biofeedback training appears to be a psychological motivating element for participants undertaking this type of training [109,110], likely due to the instantaneous feedback on the individuals' performance. Thus, a randomized controlled trial (RCT) with the Nintendo Wii system was planned and executed, and the effects of this type of training was evaluated in the last study of the thesis (study III).

AIMS OF THE THESIS

General aim

The general aim of the present thesis was to investigate selected methodological aspects and novel approaches related to the measurement of static PB in older adults, and to examine the effects of biofeedback-based Nintendo Wii training on physiological, psychological and functional parameters in community-dwelling older adults.

Specific aims

1. Examine the influence of time-of-day on PB in older adults (Study I).
2. Evaluate reproducibility of the Nintendo Wii Stillness and Agility tests (Study II).
3. Examine the relationship between the Nintendo Wii Stillness and Agility Tests outcomes and selected force plate variables to evaluate concurrent validity (Study II).
4. Determine if biofeedback-based Nintendo Wii training induce improvements in static PB, mechanical lower limb muscle function, and functional performance in community-dwelling older adults (Study III).
5. Investigate the motivation of biofeedback-based Nintendo Wii training in community-dwelling older adults (Study III).

MATERIALS & METHODS

Characteristics of study participants

STUDY I

Study participants were recruited from senior citizens' clubs and a senior society organization in Aalborg, Denmark. Community-dwelling adults aged 65 years or older and capable of understanding the verbal instructions were included for the study. Participants were excluded if they had sustained a fracture in the lower extremities or underwent orthopedic surgery within the last 6 months, had a neurological disease or were affected by previous neurological disease, had diabetes type I and II (or showed side effects such as: arteriosclerosis, neuritis, diabetic eye, kidney disease), took medicine effecting balance (psychotropic, hypnotics, anti-depressive). Prior to assessment of postural balance participants were screened and questioned about their medical history, number and type of prescribed intake of medication per day, and number of fall accidents within the last 6 months. Two of the participants in the study were lost to drop-out as they did not return for the afternoon measures (16:00). Selected characteristics of participants in study I are displayed in Table 2.

STUDY II

Participants for Study II were recruited from senior citizens' clubs and a senior society organization in Aalborg, Denmark. Inclusion and exclusion criteria were identical to study I, with the exception that individuals, who had sustained a fall, were excluded from this

TABLE 2:

Participants	Study	N (no.)	Sex, % women	Age (yrs.)	BMI (kg/m ²)	Medical preparations (no.)	Physical activity (hours per week)
Subjects	I	34	71	73.2±5.0	26.1±4.1	2.0±1.0	3.2±2.1
Subjects	II	30	73	71.8±5.1	24.4±3.1	1.7±1.8	9.7±4.1
Active	III	28	68	75.9±5.7	26.4±4.1	3.2±3.1	4.1±2.5
Controls	III	30	70	73.7±6.1	25.9±4.2	4.1±3.5	4.0±2.1

Baseline characteristics of experimental subjects included in studies I, II and III. Subjects = Community-dwelling older adults, Active = participants in the Nintendo Wii training group, Controls = EVA insoles group, BMI = body mass index (body weight/height²), Medical preparations = the number of prescription drugs, Physical activity = the number of hours of physical activity within the last week. Values are presented as Mean ± SD, percent or number.

study. This difference in criteria's was chosen in an attempt to recruit a more well-functioning study group, which also seems to have worked. The selected anthropometric characteristics are shown in Table 2.

STUDY III

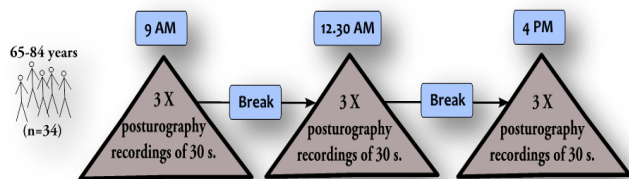
Participants were recruited through advertisements in local newspapers, senior citizens' clubs and senior society organizations in Aalborg, Denmark for this study. At inclusion participants had to be 65 years or older with a self-reported balance of poor-to-average (scored on a discrete scale: good, average, poor) and capable of understanding the verbal instructions. Participants were excluded if they had undergone orthopedic surgery within the previous 6 months, had been acute ill within the previous three weeks, had received physiotherapy within the previous month or had poor visual acuity (not capable of identifying visual features on a TV screen). Selected characteristics of participants included in study III is displayed in Table 2.

Study Design

STUDY I

A repeated intra-day within-subject design was applied in this study. Posturography was performed at three different time-points throughout the day (09:00, 12:30 and 16:00) with a total of three recordings of 30 seconds in each test session. The rest intervals between successive recordings were set to 30 seconds (Figure 3). For each of the selected COP variables the mean value from the three recordings at each session was calculated and used for further statistical analysis [98]. On the day of testing participants were asked not to exercise, perform heavy work and consume food or intake beverages other than water 1½ hours prior to each testing time-point.

FIGURE 3:



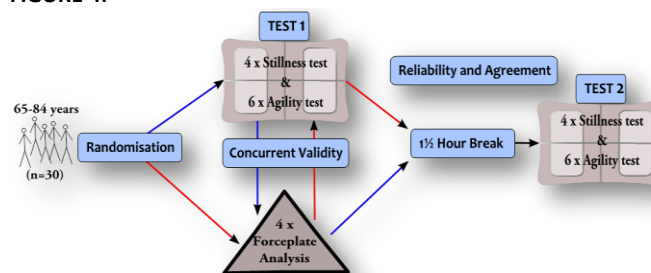
Experimental design used in study I

STUDY II

This study followed an intra-rater intra-day test-retest design and was performed and analyzed according to established guidelines for reliability and agreement studies (GRRAS) [111]. An experienced tester (Principal Author) used a standardized assessment

protocol for all participants. Prior to the initial test session (Test 1) subjects were randomized to either start measurements on the force plate (red track) followed by Nintendo Wii tests, or vice versa (blue track) (Figure 4). Resting periods of 30 seconds were administered between successive recordings, while a pause of 2-3 minutes was given between force plate tests and Nintendo Wii tests. Initial tests (Test 1) and re-tests (Test 2) were separated by a time period of 90±10 min.

FIGURE 4:

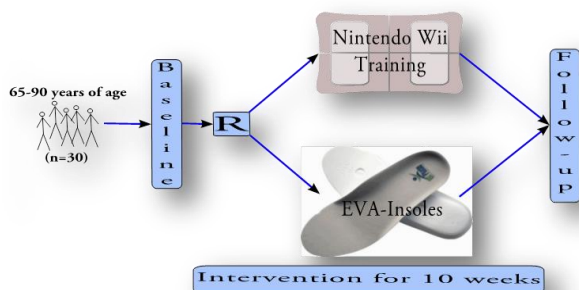


Experimental design used in study II

STUDY III

This study was carried out as a randomized, observer-blinded, controlled parallel-group design with an intervention period of 10 weeks. Participants were stratified by sex and randomly assigned by computer-generated random numbers in permuted blocks to participation in either a Nintendo Wii exercise program (active group: WII) or daily use of Ethylene Vinyl Acetate polymer (EVA) shoe insoles (control group: CON) for 10 weeks (Figure 5). All participant allocation procedures were handled by the Laboratory's chief nurse, who was not involved in any other parts of the study. The participants in CON served as a sham-treated control group, since several studies have shown that EVA insoles do not affect postural balance [112,113]. The use of EVA insoles was intended to blind CON participants, as to whether they received an active form of treatment or not. Thus, CON participants were explicitly informed (orally, and via written material) that the use of insoles was expected to increase the tactile stimuli from the feet to CNS, leading to an improved postural balance. This approach was chosen in an attempt to minimize the placebo effect known to exist for certain subjective outcome measures [114]. All participants were tested at the Geriatric Research Clinic at Aalborg University Hospital, Denmark, prior to randomization (PRE) and after 10 weeks of intervention (POST).

FIGURE 5:



Experimental design used in study III

Descriptive variables

PHYSICAL ACTIVITY LEVEL

Physical activity level of participants was reported at inclusion in all three studies. The physical activity level was operationally defined as regular house-work and/or walking, running, cycling etc. and reported as the amount of activity (in hours) during the previous seven days.

MEDICATION

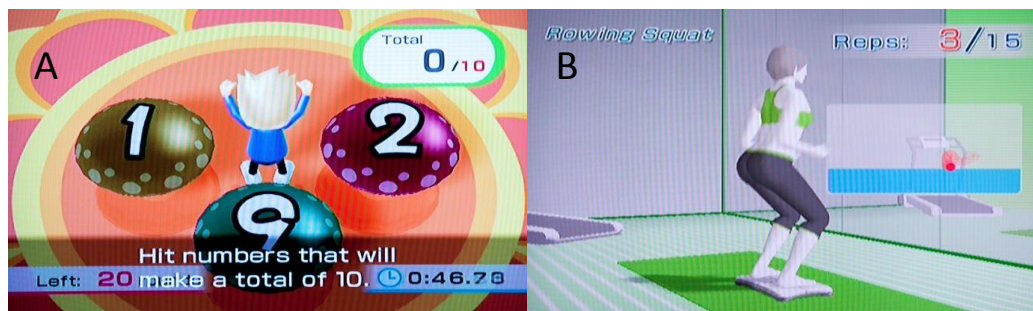
Intake of medicine was defined as the number of different prescription drugs consumed by the participant during the last week prior to inclusion of either study I, II or III. The participants were specifically asked to bring a list of their prescribed medication with them at inclusion.

Description of Interventions

NINTENDO WII TRAINING

Nintendo Wii training was performed twice a week for 10 weeks with effective training of approximately 35±5 minutes. However, participants were paired together and rotated between exercises and pauses, and thereby on average training sessions lasted for 70±10 min. All sessions were supervised by a trained physiotherapist. Each training session was designed to include an initial balance exercise sequence (2/3 of total session’s duration) followed by a muscle exercise sequence (1/3 of session’s duration) (Figure 6). Participants could freely choose between five different balance exercises (table tilt, slalom ski, perfect 10, tight rope tension, Penguin Slide) during the balance exercise sequence,

FIGURE 6:



Shows a balance task (A) and muscle strength conditioning task (B) from the Nintendo Wii training.

while a single obligatory exercise (standing rowing squat) was used in the subsequent sequence of muscle conditioning.

EVA INSOLE INTERVENTION

Participants were instructed to wear the EVA insoles in their shoes every day for the entire duration of the trial. Phone interviews were conducted on three occasions (weeks 3, 6 and 9) by a physiotherapist to ensure adherence to the intervention and to check that problems with the EVA insoles had not emerged.

Outcome measures

Table 3 provides an overview of the different outcome measures used in studies I, II and III. Participants provided their written informed consent and all study procedures were approved by the local Ethics Committee (Danish North Jutland Region). All physical tests and data recording were performed by the author of this thesis. Test conditions (light, temperature, humidity and noise, time of day) were standardized for all data collection sessions.

TABLE 3:

Outcomes	Paper I	Paper II	Paper III
Maximal muscle strength			X
Rapid force capacity			X
Posturography	X	X	X
Nintendo Wii (evaluation)		X	
TUG			X
FES-I (short form)			X
30-s. Chair Stand Test			X
Motivation evaluation			X

Outcome variables used in studies I, II and III

MUSCLE STRENGTH ASSESSMENTS

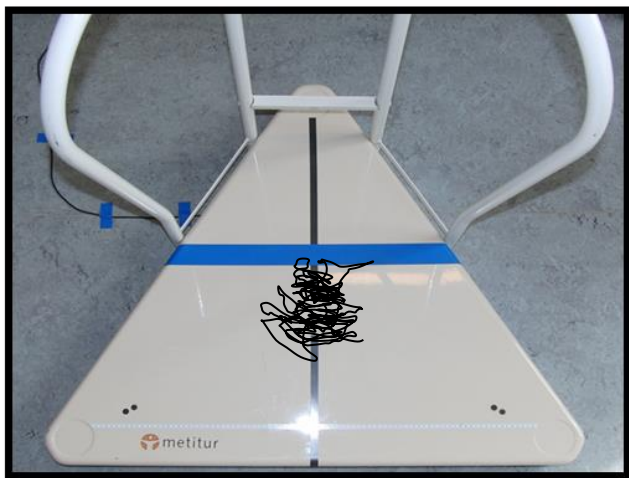
Maximal isometric contraction strength (MVC) and explosive muscle strength (Rate of force development: RFD) of the leg extensors was measured (1000 Hz) using a static adjustable leg press apparatus (Leg Force, Newtest, Finland). The participants were seated in the leg press with their knees at an angle of 120 degrees and asked to press as hard and as fast as possible against a fixed, strain-gauge-instrumented footplate using both legs for approximately 3 seconds. On-line feedback of the produced force was provided to the participant on a PC screen following each contraction [115]. The analogue strain-gauge signal (leg extension force) was sent through a linear instrumentation amplifier and subsequently digitally converted at 1 KHz using a 14-bit, 8-channel A/D converter and then stored on a personal computer.

During subsequent off-line analysis, the force signal was digitally filtered using a 4th order Butterworth filter (cut-off frequency 20 Hz) (Matlab 7.13, Mathworks, USA). Methodological details on the calculation of MVC and RFD, respectively, have been provided elsewhere [116]. Acceptable test-retest reproducibility has previously been demonstrated for the assessment of maximal isometric MVC and RFD for muscles in the lower limbs in middle-aged and older adults [117,118]. Prior to all test procedures, participants were asked to perform a series of 3-5 submaximal leg press maneuvers to get accustomed to the apparatus. After a small pause, participants performed three maximal trials (which later were averaged into a mean value) separated by a 30-s rest periods.

FORCE PLATE ASSESSMENTS

Postural balance was assessed by analyzing the magnitude and nature of horizontal excursion of the COP movement recorded (100 Hz) during static bilateral stance [80,81] using an instrumented force plate (Good Balance, Metitur, Finland) (Figure 7). The vertical ground reaction force signal from the force plate was sent through an amplifier and subsequently processed using a 24-bit, three-channel A/D converter and stored in a personal computer. The force signal was initially filtered on-line by the internal processing software (Good Balance) using a three-point median filter and secondly an IIR filter (cut-off frequency 20 Hz) to remove any high-frequency noise content in the signal.

FIGURE 7:



Metitur force plate with a superimposed COP path.

Prior to all force plate recordings participants were asked to remove their shoes, remain in a relaxed standing position with arms folded across the chest, and focus on a visual target positioned 3 meters away at eye-level. In study I participants were asked to place their feet in a narrow standing position (i.e. toes and heels together), as this would ease and help ensure an identical foot placement across the different time-points. In study II and III the distance between the participant's medial calcaneus and 1st metatarsal head was measured to ensure identical foot positions between successive test sessions, as this variable is known to influence reproducibility of collected data [119]. With respect to sampling time slightly different approaches were used for the three studies. In Study I and II three and four successive 30-s recording epochs were used, respectively, and in Study III two 60-s recording periods were used. In all tests the light intensity of the test room was controlled at 25 lux, room-temperature was held

at 22 degrees Celsius and the noise level never exceeded 55 db. Posturography is a widely used, reproducible and valid method of quantifying standing postural balance in various different populations [81,86,98-100]. Further, this notion is supported by case-control studies where patients and healthy controls can be readily separated by means of COP variables [90-92]. The selected COP variables used in this thesis comprised of velocity (mm/s), confidence ellipse (mm²), area (mm²) and velocity-moment (mm²/s)) and calculations are described in detail elsewhere [80,120].

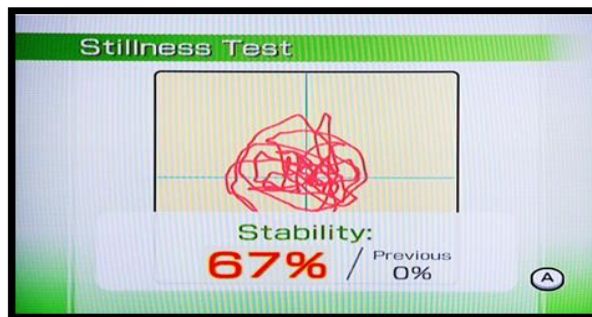
NINTENDO WII BALANCE TESTS

In both the Nintendo Wii Stillness and Agility test participants were positioned on a NWBB, which was connected to a standard Nintendo Wii console with the Wii Fit Plus software and a Samsung 40 inch (970 mm by 653 mm) LCD color television. In the tests participants were asked to remain relaxed in a comfortable bilateral standing position with their hands at their hips during the tests. For each participant the same (albeit individually adjusted) between-feet transversal distance (medial calcaneus to 1st metatarsal head) was used in all tests to ensure identical foot positions between measurements on the NWBB and the force plate.

Stillness Test

The Stillness Test is a static 30 seconds postural balance test which uses the NWBB to obtain the horizontal displacement of the COP in both the anterior-posterior and medial-lateral plane (Figure 8), and is projected and displayed on a connected TV screen. The main outcome from the test is given in percent ranging between 0 and 100% (0 being the worst score and 100 being the best score). In order to mimic force plate test conditions who instead were instructed to focus on a visual target positioned 3 meters away at eye-level on the wall. Participants performed four successive trials of the Stillness test separated by 30 seconds of rest between trials.

FIGURE 8:



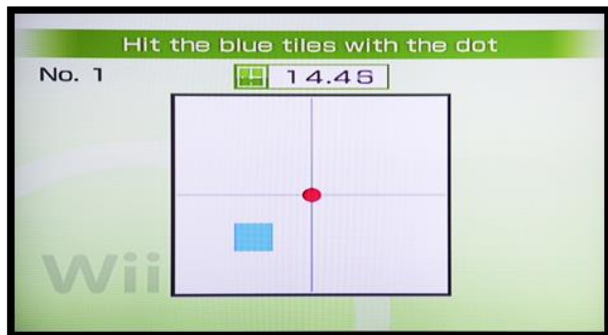
Still picture of the monitor-display provided at the end of the Wii Stillness Test

Agility Test

The Agility Test is a modulatory biofeedback 30 seconds postural balance test with outcome scores ranging between 0 and 30 (0 being the worst score and 30 being the best score) levels. The objective of this test is to hit blue squares displayed on the TV screen by moving a red dot representing COP over and across the squares (Figure 9), and as the squares are cleared on the screen, the test moves on to the next level. With every level the difficulty increases as the number of targets grow and start to move around on the TV screen in a random pattern. All visual effects were displayed on the TV screen and was placed three meters away from the participants at eye-level. For the Agility test six

successive trials were performed, separated by 30 seconds of rest. The higher number of trials performed in the Agility test was based on a priori assumption of a larger learning effect in this test compared to the Stillness test.

FIGURE 9:



Still picture of the monitor-display provided during the Agility Test

TIMED UP AND GO

The Timed Up and Go test (TUG) is a simple test used to assess a person's mobility and requires both static and dynamic balance control. The test records the time a person takes to rise from a chair (height of seat 46 cm), walk three meters, turn around, walk back to the chair, and sit down. During the test, the person is expected to wear regular footwear and if needed use any mobility aids that they normally would require. The TUG is frequently used in the elderly population, as the test is easy to administer, acceptable, feasible, valid and reproducible for evaluating short-range locomotive function in older adults [121].

Falls Efficacy Scale International short form (Short-FES-I)

The Short-FES-I is a seven-item questionnaire evaluating the concern of older adults with relation to falling while thinking of performing various daily activities. The Short-FES-I was developed to be more feasibly used in clinical practice [122] as it comprises 7 questions rather than the traditional 16 questions [123]. The Short-FES-I questionnaire has proven to be reliable, valid and sensitive to change in older adults with and without cognitive impairment [124], and a useful tool in the clinical practice [125].

30-S REPEATED CHAIR STAND' TEST

The 30-s repeated Chair Stand Test (30-CST) is a measure of functional strength and endurance in the lower extremities [126]. In the test participants are asked to stand upright from a chair with their arms folded across the chest, then to sit down again and repeat the movement pattern at a self-chosen speed for a period of 30 seconds (Figure 10). The main outcome is number of chair rises. It is important to point out that the test should be performed at a comfortable speed according to the subject's own rhythm. The same chair was used at both baseline and follow-up, as the score may be influenced by the height of the chair [127]. The 30-CST is considered a valid and reliable measure of functional strength and endurance in the lower extremities in older adults [128,128,129].

FIGURE 10:



Demonstrates the different postures of the '30-s repeated chair stand' test.

MOTIVATION EVALUATION

At 5- and 10-week time points, the Wii intervention group completed a small survey containing three statements (scores listed on a 5-point Likert scale) regarding their motivation towards Nintendo Wii training. The statements were: (1) "I find Nintendo Wii training both fun and motivating" (2) "I would like to continue using Nintendo Wii training in my own home" (3) "I would like to continue using Nintendo Wii training in a nearby senior center". The Likert scale operates on an ordinal scale expressing levels of agreement / disagreement (strongly disagree, disagree, agree or disagree, agree or strongly agree). The Likert scale is designed to measure attitudes or opinions and is considered a valid method in various study-populations [130].

Statistical analysis

SAMPLE SIZE CALCULATION

For study III sample size calculations were performed based on data from a pilot study. The calculations showed that in order to obtain a statistical power of 80%, 29 participants were needed in each group to detect at least a pre-to-post 15 mm²/s difference in group mean COP-VM delta (pre-to-post) changes between the Nintendo Wii group and the control group assuming an SD of 20 mm²/s.

Basic statistics

Overall, data are presented as mean \pm SD and was inspected for normality by histograms and q-q plots, and log transformed if distributions were skewed. Missing data were imputed in Study III with the use of last-observation-carried-forward in accordance with recommended guidelines [131]. Un-paired t-tests were used in study I to compare age, medicine use, body weight, height and BMI between the two samples from the two different occasions. Paired t-tests were used to evaluate test-retest differences for the Stillness and Agility test in study II. In study III Un-paired t-tests were used to compare the two samples (WII and CON) at baseline for selected variables. Intra Class Correlation coefficients (ICC) were calculated using a two-way mixed model (ICC3,1), where subject effects were random and measurement effects were fixed [132] to determine reliability of the two Nintendo Wii tests in study II. Moreover, for study II Coefficient of Variance (CV) was calculated using the following formula to evaluate agreement [133]:

$$CV = \left(200 \times \frac{SD}{\sqrt{2}}\right) \times (x_1 + x_2)^{-1}$$

Further, in study II 95% Limits of Agreement (LOA) were calculated ($\bar{d} - 1.96 sd$ and $\bar{d} + 1.96 sd$) [134]. Also, LOA% was calculated using the following formula:

$$LOA\% = \frac{LOA}{x_1 + x_2} \times 200$$

Finally, for study II Concurrent validity was determined by calculating the Pearson's correlation between selected force plate variables and the Nintendo Wii scores. The quality of the correlation was interpreted with the following definition: less than 0.50 indicated poor validity; 0.50 to 0.75 moderate to good validity; and higher than 0.75 excellent validity [135].

Advanced statistics

Study I

To assess if postural balance variables changed during a normal working day a linear mixed model with time-of-day being the fixed effect and subject id (number) as the random effect was applied. A general time effect on postural balance variables was initially outputted from the model, and if significant, the specific time-points which differed were reported.

Study III

Between-group differences in primary and secondary endpoints were analyzed using an analysis of covariance (ANCOVA) model adjusting for gender, age and baseline level. SPSS version 18 (IBM corporation, Armonk, New York, USA) was used to perform all

statistical analyses with a pre-specified level of significance at 5%. All tests were two-sided.

RESULTS

Study I

An overall time-of-day (09:00 – 16:00) effect on postural balance was observed for all of the selected COP variables: confidence ellipse area (mm²) (p<0.001), total sway length (mm) (p=0.037), total sway area (mm²) (p=0.001) and sway velocity-moment (mm²/s) (p=0.001). Mean and standard deviations values are presented for selected COP variables at different time-points in table 4.

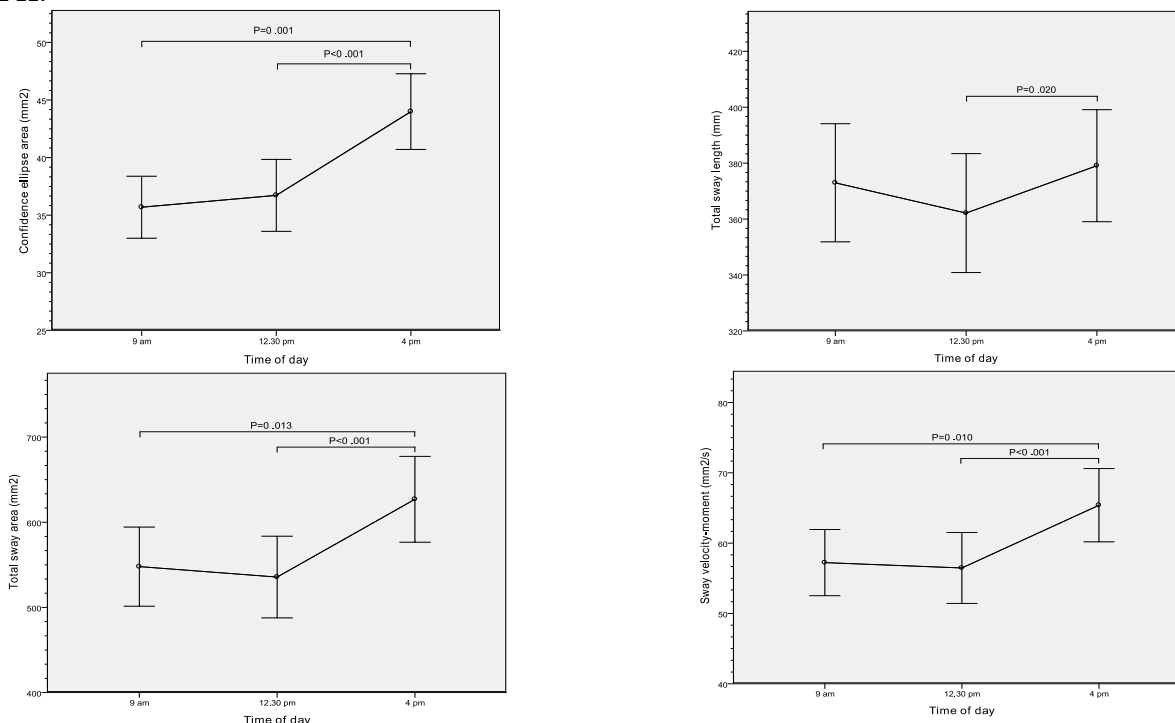
TABLE 4:

COP variables	Time-of-day			P-value
	09:00	12:30	16:00	
Confidence ellipse area (mm ²)	36 ± 16	37 ± 18	44 ± 19	p<0.001
Total sway length (mm)	373 ± 120	362 ± 118	379 ± 113	p=0.037
Sway area (mm ²)	548 ± 263	532 ± 268	627 ± 285	p=0.001
Velocity moment (mm ² /s)	57 ± 27	56 ± 28	65 ± 29	p=0.001

Mean ± SD values calculated from raw-data for confidence ellipse area (mm²), total sway length (mm), sway area (mm²) and velocity moment (mm²/s) recorded at different time-points throughout a single day. P-values represent an overall time-of-day (09:00-16:00) interaction with the selected COP variable.

Post-hoc evaluation revealed a primary systematic impairment in postural balance from midday (12:30) to the afternoon (16:00) as indicated in all COP variables obtained. No differences were observed between 09:00 and 12:30 in any of the COP variables (Figure 11). Expressed in percent these differences between the midday (12:30) and the afternoon (16:00) measurements were 18.5%, 4.6%, 17.1% and 15.8% for confidence ellipse area, total sway length, total sway area and velocity-moment, respectively.

FIGURE 11:



Selected COP sway parameters (Mean values ± SE) obtained at 09:00 in the morning, at 12:30 and at 16:00 in the afternoon. Statistical significant differences (p<0.05) between measurements at the various time-points are indicated where present.

TABLE 5:

Stillness	Test 1	Test 2	P-value	ICC	CV	LOA	LOA
Test	Mean (SD)	Mean (SD)		ICC (95% CI)	(%)	(Absolut)	(%)
Trial 1	59.7 (12.3)	58.6 (14.0)	0.37	0.75 (0.52-0.87)	11	18.5	31
Trial 1+2	61.2 (10.8)	60.2 (12.0)	0.43	0.83 (0.68-0.92)	7.7	13	21
Trial 1+2+3	62.3 (10.1)	61.3 (11.5)	0.33	0.86 (0.74-0.93)	6.4	11	18
Trial 1+2+3+4	62.7 (10.3)	62.1 (10.9)	0.51	0.87 (0.75-0.94)	6.1	10.5	17

Agility	Test 1	Test 2	P-value	ICC	CV	LOA	LOA
Test	Mean (SD)	Mean (SD)		ICC (95% CI)	(%)	(Absolut)	(%)
Trial 1	10.2 (2.0)	12.9 (1.5)	<0.001	0.49 (0.17-0.72)	11	3.4	30
Trial 1+2	11.3 (1.5)	13.2 (1.2)	<0.001	0.62 (0.33-0.80)	7	2.4	20
Trial 1+2+3	11.9 (1.4)	13.2 (1.1)	<0.001	0.73 (0.50-0.86)	5.3	1.8	15
Trial 1+2+3+4	12.1 (1.4)	13.3 (1.1)	<0.001	0.70 (0.45-0.84)	5.4	1.9	15
Trial 1+2+3+4+5	12.3 (1.4)	13.4 (1.0)	<0.001	0.65 (0.39-0.82)	5.5	2	15
Trial 1+2+3+4+5+6	12.5 (1.4)	13.5 (1.1)	<0.001	0.69 (0.44-0.84)	5.2	1.9	14

Data for the Stillness and the Agility tests are presented as Mean(SD), P-values, Intra-class Correlation Coefficient and 95% CI, Coefficient of Variance, Limits of Agreement and Limits of Agreement in percent.

Study II

Intra-rater intra-day reproducibility measures, including P-values, ICC, CV, LOA and LOA% were calculated for both the Wii Stillness and Agility test outcomes (Table 5). No systematic test-retest difference was observed for the Stillness test between Test 1 and Test 2 whether averaging 1, 2, 3 or 4 trials. In contrast, a systematic test-retest effect was observed in the Agility test, since statistically significant differences emerged between Test 1 and Test 2 when averaging 1 to 4 trials. Intra-day reliability for the Stillness test expressed as ICC using a single trial (1st trial) was 0.75 (95% CI 0.52-0.87) and increased to 0.87 (95% CI 0.75-0.94) when averaging trials 1 to 4. A similar trend was observed for the CV, LOA and LOA% by averaging an increasing number of trials in the Stillness Test. Intra-day reliability for the Agility test measured by ICC using a single trial (1st trial) was 0.49 (95% CI 0.17-0.72), and increased to 0.69 (95% CI 0.44-0.84) when all 6 trials were averaged. A similar pattern emerged for the agreement measures (CV, LOA and LOA%).

TABLE 6:

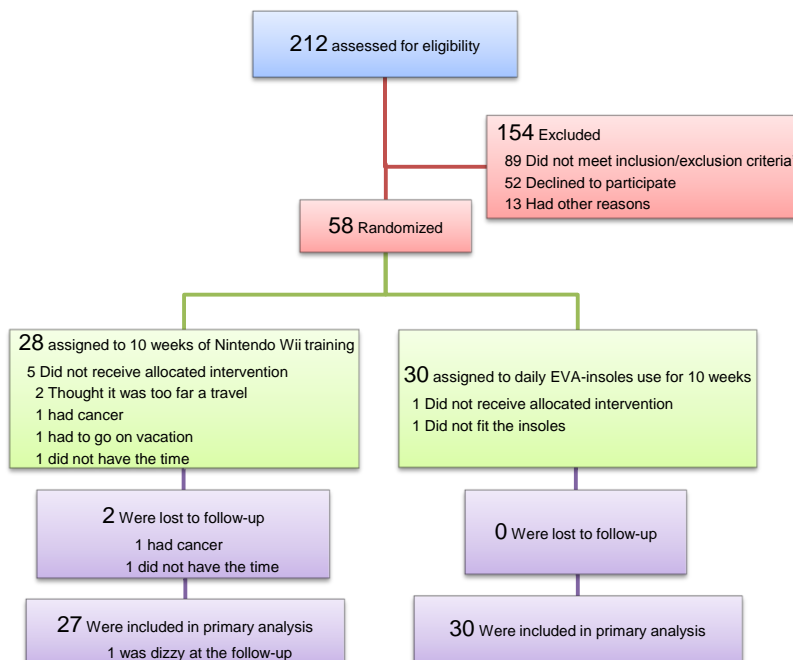
Pearson's correlations	CoP velocity (mm/s)	CoP confidence ellipse (mm ²)	CoP area (mm ²)	CoP velocity-moment (mm ² /s)
Stillness Test	-0.65*	-0.82*	-0.76*	-0.74*
Agility Test	-0.29	-0.23	-0.29	-0.29

Relationships between the Wii Stillness test outcomes (mean of 4 trials) and Wii Agility Test outcomes (mean of 6 trials) vs. selected force plate variables (mean of 4 trials) (Pearson r-values: * p<0.05).

Study III

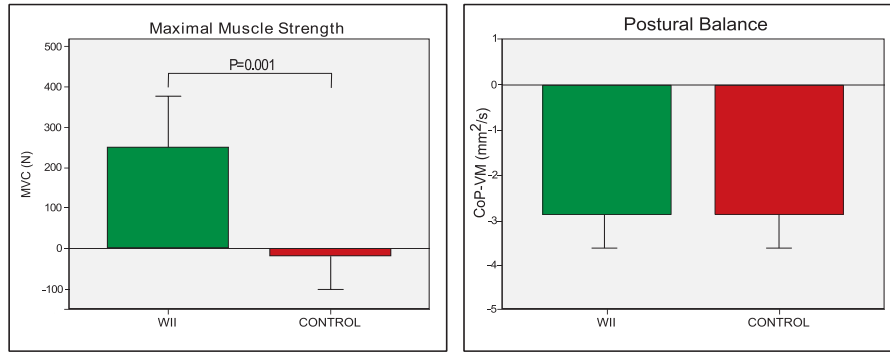
Of the 212 people screened for eligibility in this study, 154 (73%) were ineligible or did not wish to participate; thus, 58 underwent randomization with 28 assigned to Wii training while 30 served as controls (Figure 12). In the Wii group, five individuals never showed up for training. Thus, Wii training was never started nor completed by 18% of the participants. The remaining participants (82%) took part in 76.7% of the scheduled training sessions.

FIGURE 12:



Enrollment and randomization of participants.

FIGURE 13:



Pre-to-post intervention changes in maximal leg extension strength (MVC; left panel) and postural balance (COP-velocity moment, right panel) adjusted for gender, age and baseline level in the Nintendo Wii group (Green bars) and the control group (Red bars). I bars indicate 95% confidence intervals. Statistical significant differences ($p < 0.05$) are indicated where present.

Leg press MVC improved from 1470 N to 1720 N in the WII group (+250 N; +17%) and decreased from 1533 N to 1514 N in the CON group (-19 N; -1%) following the period of intervention corresponding to an absolute between-group difference adjusted for gender, age and baseline level of 269 N (95% [CI] = 122;416, $P=0.001$). PRE-to-POST changes in COP-VM went from 22.2 mm²/s to 20.6 mm²/s in the WII group (-1.6 mm²/s; -7%) and from 20.7 mm²/s to 19.1 mm²/s in the CON group (-1.6 mm²/s; -8%), corresponding to an absolute between-group difference adjusted for gender, age and baseline level of 0.23 mm²/s (95% [CI] = -4.1;4.6, $P=0.92$) (Figure 13). A sensitivity analysis was performed by excluding those individuals who never received a single session of Wii training ($n=5$). This analysis did not alter any of the main findings.

PRE-TO-POST intervention changes in secondary outcomes were greater in the WII group than in the CON group for RFD ($P=0.03$), TUG ($P=0.01$), short FES-I ($P=0.03$), and 30-CST ($P=0.01$; Table 7). In relative terms, the difference at post-intervention between WII and CON groups were 24.6% for RFD, 13.4% for TUG, 4.9% for Short FES-I and 7.7% for the 30-CST.

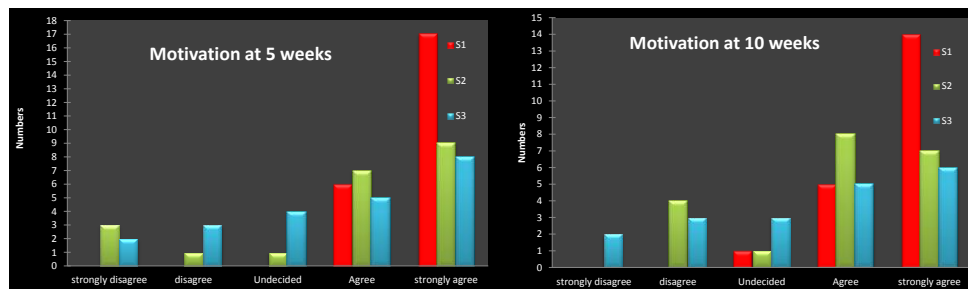
Psycho-social assessments in the WII group at weeks 5 and 10 showed that participants who undertook the Wii program either agreed or strongly agreed with the statement that Wii training is fun and motivating (Figure 14). A similar trend of agreement was observed for statements 2 and 3, however, the data showed a split opinion within the WII group as to whether to continue using the Wii system in their own home or at a nearby seniors center.

TABLE 7:

Variable	Wii (n=27)		CON (n=30)		Between group difference	95% CI	P Value
	Pre	Post	Pre	Post			
RFD - N/s	3266±2271	4143±2831	3704±2627	3622±2423	811	65;1556	0.03
TUG - s.	10.3±3.8	9.0±3.2	11.0±5.0	10.9±5.1	-1.4	-2.5;-0.4	0.01
FES-I (short) - score.	11.3±3.5	10.5±3.0	11.3±4.3	11.6±3.8	-1.2	-2.2;-0.1	0.03
30-s Chair Stand Test - no.	11.5±3.8	13.3±3.2	11.2±3.0	12.1±3.0	1.1	0.3;2.0	0.01

Data is presented as pre and post intervention means and standard deviations. Absolute between group difference, 95% confidence interval and P-values are derived from an analysis of covariance (ANCOVA), adjusting for gender, age and baseline level. RFD = Rate of Force Development, TUG = Timed Up & Go, Short FES-I = shortened Falls Efficacy Scale, 30-CST = 30-s repeated Chair Stand Test. The means were computed with reference age=75, gender=female and baseline RFD=3000; TUG=10; FES-I=10; 30-s Chair Stand Test=10

FIGURE 14:



Motivation data obtained at 5 weeks (left panel) and 10 weeks (right panel) into the Wii training on a 5-point Likert scale. S1 denotes the statement "I find Nintendo Wii training both fun and motivating"; S2 denotes the statement "I would like to continue Nintendo Wii training in my own home"; S3 denotes the statement "I would like to continue Nintendo Wii training in a nearby Senior center"

DISCUSSION

Main findings

This thesis presents data related to selected methodological aspects (Study I) and novel experimental approaches (Study II) of relevance for the assessment of static PB in older adults, while also addressing the effects of biofeedback-based Nintendo Wii training (Study III) on physiological, psychological and functional measures in community-dwelling older adults.

Time-of-day appeared to have an overall systematic effect on static PB in older adults, which should be accounted for in future assessments of static PB in old adults. Specifically, the results showed that selected postural balance control variables (confidence ellipse area, total sway area, velocity-moment) were elevated in the afternoon compared to mid-day and the morning measures. In addition, total COP sway length demonstrated a trend towards a time-of-day effect as a statistically significant difference appeared between mid-day and afternoon (Study I). Both the Nintendo Wii Stillness and Agility tests demonstrated high reproducibility and appear feasible in clinical settings. However, a systematic learning effect between test sessions was found for the Agility test. Therefore, a familiarization period is

necessary for this test to avoid systematic differences between successive test sessions. A moderate-to-excellent concurrent validity was seen for the Stillness test, which is in contrast to the Agility test in which a poor concurrent validity was found. Initial steps have been taken towards the use of low-cost objective evaluation tests of static PB for older adults by utilising the Stillness and Agility tests (Study II).

Finally, marked improvements in maximal leg muscle strength (MVC), rapid force capacity (RFD) and functional performance were observed following the period of biofeedback-based Nintendo Wii training. Unexpectedly, however, static bilateral postural balance remained unaltered following the Nintendo Wii intervention. The older adults found the Nintendo Wii training highly enjoyable and motivating, which suggests that this exercise modality might be successfully adapted to senior citizens' clubs or in their own home.

Time-of-day effects on Postural balance control (Study I)

It is well-known that the circadian rhythm affects a number of physiological variables throughout the day i.e. temperature, blood pressure, hormone levels [136]. Despite a broad use of posturography in scientific and clinical settings on many different study-populations, there is a lack of consensus on when (i.e. time-of-day, time-of-week) and how to use this technique (i.e. sampling-frequency and time, number and pauses between trials etc.) [98]. Thus, Study I was designed to examine to which extent time-of-day would affect PB performance in community-dwelling older adults.

EXTERNAL VALIDITY

The effect of time-of-day on PB has previously been examined in younger subjects with [102-105] or without sleep deprivation [106,107]. Without sleep deprivation, selected sway parameters (Fractal dimension of sway, most common sway amplitude and time interval for open-loop stance control) were impaired during the later time points of the day (recordings at 8:30, 10:30 and 13:30 o'clock) in 30 younger subjects [106]. Moreover, the differences in balance performance were greater between 10:30 and 13:30 compared to 8:30 and 10:30. This finding corresponds well with the present results, which also revealed a greater impair-

ment in balance performance towards to afternoon. A similar time-of-day trend was found by Gribble et al. in 30 healthy young subjects, when measuring static PB at 10:00, 15:00 and 20:00 (on day 1 of 2) [107]. However, on the second day of testing (day 2 of 2) no time-of-day effect on static PB control was observed, which could be the result of a learning effect from two consecutive days of performing this task. Gribble et al. also examined time-of-day effects on dynamic PB control, and found that this type of balance performance was impaired during later time points on both day 1 and 2. Collectively, the above studies indicate that impairments in PB performance may exist past midday in young healthy individuals. The current study is the first to demonstrate a similar impairment in PB late in the day among older adults.

Throughout the last decades numerous studies have evaluated changes in PB control utilizing posturography in response to exercise based intervention protocols in older adults [137]. Some studies have shown clinical relevant improvements from these exercise protocols [51] while others have failed [138].

These inconsistent findings might be explained by heterogeneity of the cohort, small sample sizes, inadequate dose/intensity or duration of training, insufficient compliance to the frequency of training, and a lack of commonly accepted standardized balance testing paradigms. In terms of the latter factor, the present data suggest that a strong bias could potentially arise from using non-controlled time-of-day measurements. If time of baseline and follow-up testing were not matched in some of these studies, this could potentially influence the results in a systematic manner. Inconsistent results have also been found in studies trying to predict fallers from non-fallers from posturography measures. In their comprehensive review from 2006 Piirtola & Era reported that 5 out of 9 prospective studies (55%) on older adults were capable of predicting fallers from non-fallers within the next year using force plate assessments only, while 4 studies (45%) failed to do so [139]. These disparate findings may result from the etiological complexity of fall accidents, or from the current perspective be the result of using non-standardised test time points throughout the day, consequently leading to an impaired ability to discriminate fallers from non-fallers.

A possible explanation for the time-of-day effect on PB that was observed in the present study could relate to sleepiness, which in turn is affected by circadian rhythms, time awake, and diurnal endogenous release of various hormones [140]. It is well-known that sleepiness peaks at night (02:00-7:00) and in the afternoon (14:00-17:00) [104,141,142], thus, as participants become sleepy in the afternoon PB may be relatively impaired compared to morning conditions [102-104]. General muscle fatigue is another possible explanation for the impaired PB observed in the afternoon. General muscle fatigue typically progress in the late afternoon as a result of having performed a large number of daily functions and work tasks. In support of this notion, studies have shown that individuals tend to sway to a greater extent (demonstrating larger COP excursion paths) following an 8-hour work shift [143]. Finally, impaired PB in the afternoon could be caused by daily alterations in hormone secretion, especially for the female participants in the present study. Several studies have reported that PB control was positively affected by increased levels of plasma oestrogen [144-146]. It is well-known that plasma oestrogen secretion follows a diurnal pattern with elevated plasma levels in the morning that gradually decreases throughout the day [146]. This diurnal pattern could in part explain some of the variation seen in PB for the women in the present study.

INTERNAL VALIDITY

In the present study there were some methodological limitations. For instance, participants were allowed to leave the hospital unit between the various time-points of testing, meaning that their behaviour in terms of eating and drinking could not be fully controlled. However, to minimize this potential bias, participants were strictly informed not to exercise, and not to perform any heavy work or consume food or beverages, other than water 1½ hours prior to each testing session. Secondly, participants could have been randomized to be tested on three different days each at a different time-of-day, in an attempt to eliminate onset of fatigue at the end of each day of testing. However, this approach would have caused other confounders to interact with the outcome measures, while also imposing a greater burden on the participants as testing would have lasted for more days. Finally, participants were not accustomed to the test procedures on separate occasions prior to actual sway testing. Instead, within-trial familiarization procedures were employed on the day of testing (cf. Methods). The possibility exists that even more marked changes in sway performance would have been observed (due to less pronounced learning effects) if separate familiarization trials had been employed.

Reproducibility and validity of Nintendo Wii balance tests (Study II)

Impaired PB with aging represents a major risk factor for fall accidents [69,147]. A common way of assessing static PB in older adults is by use of instrumented force platform recordings [79-81,100]. However, force platforms are often expensive, highly immobile and technically difficult to use. Thus, a need seems to exist for developing low-cost objective quantitative valid and reliable assessment tools for clinical evaluation of PB in the elderly population. Such a tool might be provided by the Nintendo Wii balance board combined with its standard software (Wii Fit Plus).

EXTERNAL VALIDITY

At this point in time, a total of 116 peer-reviewed scientific studies have examined or utilized the Nintendo Wii console, the supplied Wii balance board or a combination of both. However, only few studies have focused on reproducibility and validity aspects [108,148-150]. Of these limited reproducibility studies, only two have focused on using standard Nintendo Wii software analysis [148,150], while the remaining have explored reproducibility of COP assessment based on raw data extracted directly from the Wii board [108,149]. Wikstrom (2012) examined concurrent validity by comparing twelve different Nintendo Wii balance tests with selected COP variables measured on a force platform (Bertec Corp.) and the Star Excursion Balance Test (SEBT) in 45 young adults (mean age 27.0±9.8) [150]. Poor concurrent validity was observed for all variables when compared to the both the COP variables and the SEBT. Furthermore, low intra- and inter-session reproducibility as observed for the twelve standard software balance tests. These findings seem in contrast with the present data, which demonstrated good-to-excellent inter-session reproducibility and concurrent validity for the Stillness test, while a good reproducibility was observed for the Agility Test. Potentially, these disparate findings may arise from Wikstrom studying a homogenous study-population of young individuals presumably with a high level of postural control. By recruiting a homogenous study-population participants might have received more compressed scores on the different balance tests, which in result means that strong correlation scores (high ICC values) would be

difficult to achieve [134]. This was not the case in the present study where a more heterogeneous group of older adults were recruited with a larger range of PB, which may have influenced the relatively high ICC values presently observed. The poor validity between force plate derived COP measures, SEBT data and the Nintendo Wii balance test outcomes in Wikstroms study (2012) likely was caused, at least in part, by a ceiling effect during Nintendo Wii testing, as this type of young study-population normally demonstrates a very high level of PB. In a study from 2012 Reed-Jones et al. focused solely on validity aspects of two Nintendo Wii balance tests (Basic balance and Prediction Tests) in a group of older adults (age 67.2±5.2 yrs.), and found a poor concurrent validity ($r=0.01-0.31$) when compared (correlated) to standardized test outcomes of various fitness, balance, mobility, and self-reported balance confidence measures [148]. This lack of concurrent validity may be a result of comparing tests of different nature (i.e. dynamic vs. static; cognitive vs. non-cognitive), or that some of these tests have a large magnitude of biological and/or methodological noise (stochastic variability). In accordance with this notion, no or only poor relationships were observed in the present study between Wii Agility test scores and selected COP sway variables ($r=0.23-0.29$). This lack of validity might also be related to different nature of tests, as the posturography measures inherently were static (quite bilateral stance) compared to the highly modulatory nature of the Wii Agility test (subjects continuously performing rapid self-perturbations of COM in order to hit specific visual targets displayed on the Wii screen). In contrast to these negative findings, good-to-excellent validity ($ICC=0.77-0.89$) between a 'gold standard' force plate (AMTI model) and raw COP data obtained from a standard Nintendo Wii balance board (using custom build software) was reported during quiet bilateral standing in young adults (age 23.7 ± 5.6 yrs.) [108]. Good-to-excellent reproducibility ($ICC=0.66-0.94$) was also found between multiple successive tests occasions using the Wii board. The present results and the findings by Clark et al. (2010) are not readily comparable since Clark and coworkers examined the reproducibility and validity of the raw output of the Wii-board itself, whereas the present study examined these aspects in relation to the standard build-in Wii software.

Numerous studies addressing reliability and agreement of PB assessment based on force plate analysis have been conducted thru the years [81,100,151]. Bauer et al. (2008) i.e. examined the reproducibility of four different force plate variables in older adults ($n=63$, age ~ 78.7 yrs.) and found ICC values of 0.87 for COP sway area (CI 0.80-0.92) during bilateral stance with eyes open [100]. Examining a much smaller group ($n=7$, age ~ 62-73 yrs.), Lafond and co-workers (2004) reported an ICC value for COP sway area of 0.47 when analyzing a single trial of 60-s duration [151]. Their data further indicate that to obtain an ICC value above 0.90, a total of 10 trials would need to be averaged [151], partly as a potential consequence of their small sample size. Finally, Swanenburg et al. (2008) reported ICC values of 0.75 (95% CI 0.57-0.86) and a relative LOA% of ~46 for COP sway ellipse area when calculating the mean of four 20-s trials in community-dwelling old adults ($n=37$, 73 ± 6 yrs.) [81]. Compared to these previous reports, the present study observed similar and/or stronger reliability and agreement measures for the Stillness and Agility test, which implies a fairly good external validity to the existing literature.

INTERNAL VALIDITY

In terms of methodological strengths, Study II reported several measures of reproducibility including absolute and relative outcome measures as recommended by previous guidelines [111]. Secondly, the study did not report reproducibility aspects only, but also evaluated validity aspects of the two Nintendo Wii balance tests. Such an extensive approach is warranted when evaluating a novel test modality as seen in the present study. Thirdly, no signs of ceiling or flooring effects were detected for the Wii Stillness Test or the Agility Test in the current population of community-dwelling older adults. The absence of a ceiling and floor effect suggests that the tests may be applicable to well-functioning or frail older individuals.

A limitation to study II was the absence of data on inter-day reproducibility, particularly considering the learning effect that was observed for the Wii Agility test. Consequently, a third test session on a separate day might have served to overcome the learning effect (causing a level-off in test outcomes). This notion is supported by data from a recent pilot study performed in our Lab although focused on a younger study-population ($n=20$, 18-50 years of age). These data indicated that the learning effect for the Agility test could be abolished with a familiarization protocol consisting of 6 within-session trials performed prior to the actual test (Jorgensen MG, unpublished observations). Another limiting factor in present study was the choice of measure for validating the Agility test, which in retrospective could have been more dynamic in nature. A solution could have been to validate the Agility test against i.e. the Timed Up and Go test, as the latter test is more dynamic than the quiet bilateral stance test on the force plate. Finally, Study II examined community-dwelling older adults (~70 yrs.) only and the current findings, therefore, may not readily be transferred to younger or older study-populations, respectively.

Efficacy of Nintendo Wii intervention (Study III)

The risk of falling increases as people get older [152,153] and major causes for this elevated risk are associated with reduced lower extremity muscle strength [7,43,44] including loss of rapid force capacity (rate of force development: RFD) [44] that, among other factors, contribute to impaired PB [69]. To counteract this age-related decline in physiological function, specific types of exercise and training can be employed to achieve improvements in the neuromuscular system of older adults [154,155] and very old frail individuals [35,137] in order to reduce the risk and incidence of falls [156]. Nevertheless, traditional balance and muscle training regimes may be perceived as monotonous to participants leading to poor compliance, which in turn prevents participants from reaching their full physiological and/or rehabilitative adaptive potential [157,158]. Several studies have indicated that the Nintendo Wii system is enjoyable [159-162] (Franco et al. 2012, Griffin et al. 2012, Meldrum et al. 2012, Williams et al. 2010b), motivating and acceptable as a training tool in older adults [159-162]. However, currently the Wii system has only rarely been applied as a training device including a single non-RCT experiment [110], few pilot studies [162,163], a case report [164], short communication report [165] and a study protocol presentation [166].

EXTERNAL VALIDITY

Study III is the first RCT to utilize biofeedback-based Nintendo Wii exercise in community-dwelling older adults. The Wii training performed in Study III was expected to result in improved PB accompanied by gains in lower limb mechanical muscle function

(increases in MVC, RFD). However, this a priori assumption was not met for PB performance. This finding was unexpected as we assumed a positive response on PB measures, given that the game playing exercises require participants to perform rapid yet controlled shifts in COP position in a variety of directions. However, it should be recognized that deviating findings have been reported in middle-aged women and older individuals showing improved [110,163] and unaltered [109,165] PB following this type of training. These different results may have been caused by small sample sizes, lack of control groups, insufficient randomization procedures, or use of subjective balance scales without blinding the assessor. Biofeedback-based training involving movements similar to the Nintendo Wii exercises - only using a conventional force plate with visual feedback of COP excursion - has previously been shown to improve PB and lead to reduced fall incidence in older adults [167-169]. In Study III, the evaluation of PB by means of static bilateral testing might not have been sufficiently challenging to participants to allow detection of potential improvements in these measures. The Wii training comprised of highly dynamic balance exercises and the possibility therefore exists that the use of more dynamic and challenging balance test modalities could have revealed improvements in PB in the Wii group. Thus, future studies in well-functioning older adults should (also) employ challenging postural balance tests to minimize ceiling effects on PB outcome variables.

Very limited data exist on the potential effect of Nintendo Wii training on mechanical muscle function in older adults. Nitz et al. (2010) reported a 14% improvement in quadriceps MVC for the right leg and a 17% improvement for the left leg, respectively, following 10 weeks of Nintendo Wii training in 10 women (30-58 yrs. of age) [163]. As a novel finding, Study III demonstrated a substantial gain (~20%) in rapid force capacity (RFD) of the leg extensors following the period of biofeedback-based Wii training, which was accompanied by a corresponding increase in maximal isometric muscle strength (MVC). This improvement in mechanical leg muscle function as a result of Wii training was likely to be the result of training-induced gains in neuromuscular function, which may have involved an adaptive increase in lower extremity muscle size as well [170,171]. In addition, these clinically relevant improvements in mechanical muscle function were presumably caused by the strengthening exercises within the Nintendo Wii training regime. Finally, the observed improvements in mechanical leg muscle function may represent a reduction in the risk of falling in this study-population, as impaired mechanical muscle function in the lower extremities consistently has been identified as one of the primary risk factors for fall accidents [43,69,172]. For a given exercise-based intervention program to be successfully implemented in everyday living as well as in senior citizens' clubs and organizations, it is essential that older people find it effective, enjoyable, and motivating. Likewise, it is essential that the intervention is integrated with social activities in elderly communities to ensure long-term sustainability in this population group. The current findings showed that older adults found this modality of biofeedback-based training motivating and enjoyable, which is in line with previous reports [109,110,159-162].

INTERNAL VALIDITY

Some potential limitations may be observed with Study III. Five individuals were non-attenders in the Wii group prior to the first training session, which suggests that the participants could have benefited from receiving more thorough information about the conditions of the study prior to enrollment. Secondly, the partici-

pants recruited for this study could be characterized as fairly well-functioning in terms of physiological and functional performance. Thus, the findings in Study III may not be generalized to other elderly populations' i.e. frail older individuals or very old adults. Thirdly, the Wii training intervention period of 10 weeks may have been too short to elicit detectable pre-to-post training differences in postural balance. Finally, trained participants and control subjects did not receive equal amounts of personal attention (i.e. examiner interaction) during the study period, which might limit comparability between the two groups. As a methodological strength, Study III followed established consort guidelines [131] on RCT experiments. Furthermore, Study III comprised a novel combination of various physiological, functional and psychological outcome measures. This approach of combined bio-psychological measures might facilitate a more successful and sustainable implementation of physical exercise as a tool in fall prevention and rehabilitation in older adults.

Clinical implications

- * The present findings suggest that time-of-day influence static PB in older adults. Thus, the findings imply that repeated (i.e. pre-to-post intervention) measurements of postural balance in older adults should be performed at the same time-of-day (Study I).
- * The first steps towards developing low-cost objective, reproducible and valid tests of static PB have been taken with the Nintendo Wii Stillness test. The present results show that this test is highly reproducible, valid and appear feasible in a clinical setting (Study II).
- * Ten weeks of Biofeedback-based Nintendo Wii training among community-dwelling old adults led to clinically relevant improvements in key factors known to influence the risk of fall accidents. In addition, participants perceived the Nintendo Wii training highly enjoyable and motivating, which may ensure a high degree of compliance to home and/or community-based training using this system in community-dwelling older adults (Study III).

CONCLUSIONS

Time-of-day appears to influence static postural balance in older adults as reflected by enlarged COP oscillations in the afternoon relative to mid-day and the morning. Thus, time-of-day should be controlled when assessing static postural balance in older adults (Study I). The Nintendo Wii Stillness test demonstrated a high reproducibility, a moderate-to-excellent concurrent validity and appears feasible in clinical settings. In contrast, a systematic difference between successive test sessions was observed for the Wii Agility test, thus more intense familiarization procedures are necessary for this test. The initial steps towards developing low-cost objective and valid evaluation tests of static postural balance for older adults have been taken with the Stillness and Agility tests (Study II). Biofeedback-based Nintendo Wii training led to substantial improvements in maximal leg muscle strength, rapid muscle force capacity and functional performance in community-dwelling older adults. Unexpectedly, however, static bilateral postural balance remained unaltered following the period of Nintendo Wii intervention. Finally, participants perceived the Nintendo Wii training as enjoyable and highly motivating, which may ensure a high degree of compliance to home and/or com-

munity-based training using this exercise modality in community-dwelling older adults (study III).

PERSPECTIVES

An increased emphasis on methodological aspects in relation to evaluation of PB in older adults, including prophylactic biofeedback-based intervention and more effective regimes of post-injury rehabilitation seem highly relevant in both clinical and basic research settings. The results from the present thesis can be seen as a step in this direction. Still, numerous questions remain unanswered and need to be addressed in future studies as elaborated below.

Methodological aspects of postural balance evaluation

Future studies should focus on verifying the results obtained in study I and secondly examine the variation of PB at later time points of the day (18:00, 21:00 and 24:00 etc.) in order to get a better understanding of the diurnal variation in PB in older adults. Additionally, the potential effects of seasonal variation on PB could be studied, as PB might be enhanced/weakened dependent on the time-of-year.

With respect to the Nintendo Wii balance tests (Stillness and Agility) the ability of these tests to discriminate between cases and controls need to be addressed, as this ability is important for successful clinical implementation. Moreover, studies to identify the specific familiarization procedures needed to minimize a learning effect for the Agility test between successive test sessions should be conducted. Finally, custom user-friendly low-cost software extracting COP data from the NWBB should be developed and validated, as low-cost tools operating on a continuous scale could be useful in the future.

Biofeedback Interventions

The intervention study in the present thesis showed that biofeedback-based Nintendo Wii training represents a motivational type of training intervention in the older population. Future studies examine if this type of training is equally well suited in home or community-based settings, respectively. Demographic and economic projections anticipate that the number of older people will grow substantially along with increased medical costs in the future years. Also, an overwhelming amount of documentation on the positive effects of physical activity is available, however, compliance and implementation of many of these exercise interventions is often low and lacking, respectively. Thus, research is needed to develop motivating biofeedback-based interventions (such as the Nintendo Wii, Microsoft Xbox Kinect etc.) that may effectively facilitate lifestyle changes in old and relatively physically inactive individuals.

SUMMARY

The overall purpose of this thesis was to examine selected methodological aspects and novel approaches for measuring postural balance in older adults, and to examine the effects of biofeedback-based Nintendo Wii training on selected physiological, psychological and functional outcome variables in community-dwelling older adults.

In Study I balance control was investigated using force plate analysis of Centre of Pressure (COP) excursion during static bilateral standing in 32 community-dwelling older adults at three different time-points (09:00, 12:30, and 16:00) throughout the day. An overall significant time-of-day effect was observed for all selected COP variables. The greatest change in all COP variables was ob-

served (on average ~15%) between midday (12:30) and the afternoon (16:00), indicating that a systematic time-of-day influence on static postural balance exists in community-dwelling older adults. Consequently, longitudinal (i.e. pre-to-post training) comparisons of postural balance in older adults with repeated assessments should be conducted at the same time-of-day.

In Study II a novel approach for measuring postural balance (using the Nintendo Wii Stillness and Agility tests) was examined for reproducibility and concurrent validity in 30 community-dwelling older adults. While the Nintendo Wii Stillness test showed a high reproducibility, a systematic learning effect between successive sessions was observed for the Agility test. Moderate-to-excellent concurrent validity was seen for the Stillness test. In contrast, the Agility test revealed a poor concurrent validity. In conclusion, the Wii Stillness test seems to represent a low-cost objective reproducible test of postural balance in community-dwelling older adults and appears feasible in various clinical settings. A habituation (familiarization) period is necessary for the Wii Agility test to avoid a systematic learning effect between successive test sessions.

Study III investigated the effect of 10 weeks of biofeedback-based Nintendo Wii training on static postural balance, mechanical lower limb muscle function, and functional performance in 58 community-dwelling older adults. Additionally, the study investigated the participant motivation for this type of training (Exergaming). Marked improvements in maximal leg muscle strength, rapid force capacity and functional performance were observed following the period of biofeedback-based Nintendo Wii training. Unexpectedly, static bilateral postural balance remained unaltered following the period of intervention. The study participants perceived the Nintendo Wii training as enjoyable and highly motivating, which suggests that this type of exercise may be successfully implemented at senior citizens' centers and/or in the home of the elderly.

The results presented in this thesis suggest that strict control of time-of-day is an important methodological aspect when evaluating postural balance in older adults, and an assessment protocol using the Nintendo Wii Balance Board is reproducible and valid. Biofeedback-based Nintendo Wii exercise intervention appeared unsuccessful in improving static bilateral postural balance, most likely due to a test ceiling effect in the selected outcome measures, but the intervention elicited marked positive changes in various key risk factors associated to fall accidents. Notably, Wii based biofeedback exercise was perceived by the older adults as a highly motivating type of training.

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