ASSESSING BALANCE CONTROL AFTER MINOR STROKE

Moving from Laboratory towards Clinic

Ingrid Marjolein Schut

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ASSESSING BALANCE CONTROL AFTER MINOR STROKE

Moving from Laboratory towards Clinic

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Summary

In this thesis, we determined how system identification can be integrated in the clinic to assess human balance control. Adequately balance assessment is important in order to detect people with high fall risks and to optimize balance training, which would ultimately result in better rehabilitation and thus less falls. Current clinical tests suffer from ceiling effects, are subjective and do not provide insight in the underlying mechanisms. System identification techniques seem promising, but they depend on large, expensive and complex devices such as motion platforms and motion capture cameras, and are therefore less suitable for clinical use. In part 1, we first focussed on the technical and methodological characteristics of the system identification techniques. In part 2, we used the resulting system identification method, whereby the treadmill applied support surface perturbations, on a minor stroke population to evaluate subtle changes in balance control of the paretic leg.

System identification uses dedicated perturbations to unravel the underlying neurophysiological mechanisms of balance control. By applying support surface rotations, the sensory reweighting of proprioceptive information can be identified. Support surface translations enable the investigation of the stabilizing mechanism. In Chapter 2, system identification was implemented with the bilateral ankle perturbator (BAP), which applies support surface rotations around the ankle joint. A new application of the BAP was used investigate the effect of compliant support surfaces. Compliant surfaces, e.g. foam mats, are currently used in the training as tool for diagnosis and training. With the BAP continuous disturbance torques were applied in 9 trials; three levels of support surface compliance, combined with three levels of desired support surface rotation amplitude. The corrective ankle torques, in response to the rotations, were assessed in frequency response functions. Low frequency magnitude, i.e. the average frequency response function magnitudes in a lower frequency window, represents the sensory reweighting. As found previously, an increase in support surface rotation amplitude leads to a decrease in the lower frequency magnitude, i.e. down weighting of proprioceptive information. We found that this down weighting effect is less when the support surface is more compliant. In other words, the sensory reweighting of proprioceptive information due to support surface rotation amplitude is less on more compliant support surfaces. Therefore, it might be interesting to use foam mats with different compliances, since a wider range of sensory reweighting will be trained.

In Chapter 3 and 4, system identification is combined with a treadmill, which applies support surface translations. The methodological characteristics were studied in

Chapter 3, investigating the effect of the amplitude and number of repetitions of the perturbation signal on the identification of the neuromuscular controller (NMC). Chapter 4 focused on the treadmill characteristics. In chapter 3, healthy participants were asked to stand on a treadmill while small continuous support surface translations were applied in the form of a periodic multisine signal. The perturbation amplitude varied over seven conditions between 0.02 and 0.20 m peak-to-peak (ptp), where 6.5 repetitions of the multisine signal were applied for each amplitude, resulting in a trial length of 130 sec. For one of the conditions, 24 repetitions were recorded. The recorded external perturbation torque, body sway and ankle torque were used to calculate both the relative variability of the frequency response function of the NMC, i.e. a measure for precision, which depends on the noise-to-signal ratio and the nonlinear distortions. In general, the nonlinear contributions were low and, for the ankle torque did not vary with perturbation amplitude. Results showed that the perturbation amplitude should be minimally 0.05 m ptp, but higher perturbation amplitudes are preferred since they result in a higher precision, due to a lower noise-to-signal ratio. There is, however, no need to further increase the perturbation amplitude than 0.14 m ptp. More repetitions improves precision, but the number of repetitions minimally required, eventually depends on the perturbation amplitude and the preferred precision.

Chapter 4 validated the joint stiffness estimation of an inverted pendulum with known stiffness using system identification and support surface translations. Second, the contribution of horizontal ground reaction forces on the estimation was investigated. Ankle torque and resulting frequency response functions, which describes the dynamics of the stabilizing mechanism, were calculated by both including and excluding horizontal ground reaction forces. Results showed that the joint stiffness of an inverted pendulum estimated using system identification is comparable to the joint stiffness estimated by a regression method. Secondly, within the induced body sway angles, the ankle torque and frequency response function of the stabilizing mechanism dynamics calculated by both including and excluding horizontal ground reaction forces are similar. Especially for the lower frequencies, where stiffness dominates the frequency response function, the absolute relative errors are small (<1%). Therefore, the horizontal ground reaction forces can be omitted in calculating the ankle torque and frequency response function of the stabilizing mechanism dynamics. Chapter 3 and 4 show that the treadmill could be used to assess balance control, when minor adjustments are made to treadmills currently available in the clinic; vertical forces, i.e. vertical ground reaction forces and CoP in sagittal plane, should be recorded by a dual force plates, and continuous forward-backward translations of the belt should be possible.

In Part II, balance control of people with a minor stroke was assessed. In chapter 5, we indicated that people after minor stroke have an elevated fall risk, are less physically active, and show persistent balance impairments compared to their healthy counterparts, even though they have (almost) complete clinical recovery of leg motor impairments. Fugl-Meyer Lower extremity assessment and Mini-Balance Evaluation Systems Test (Mini-BESTest) were performed on a total of 64 minor stroke participants and 50 age-matched controls. Fall rates and daily physical activity levels were conducted in a follow-up period of six months. Minor stroke participants fell almost twice as often as controls (1.1 vs. 0.52 falls per person per year). The total time of physical activity was not significantly different for minor stroke participants compared to the controls, whereas the total intensity of physical activity was 6% lower for minor stroke participants. Minor stroke participants also scored significantly lower on the Mini-BESTest (24.2±2.3 vs. 26.1±2.1 points), indicating impaired static and dynamic balance, even when they scored maximal on the Fugl-Meyer Lower extremity assessment. There results indicate that individuals in the chronic phase after minor stroke with (almost) complete clinical recovery of leg motor impairments fall more often and show substantial impairments in dynamic balance control compared to healthy controls, pointing at an important unmet clinical need in this population.

Impaired balance and mobility of minor stroke participants, as shown in Chapter 5, might be caused by subtle changes in balance control of the paretic ankle, indicating an asymmetric balance control strategy. In Chapter 6, we investigated whether subtle control asymmetries can be demonstrated in minor stroke participants, in which balance measure these subtle changes in control asymmetries are most apparent and under which condition they could best be detected. Balance control of 54 minor stroke and 37 control participants was assessed. In static and perturbed conditions, both performed with eyes open and eyes closed, 11 balance measures were conducted: centre of pressure (CoP) related measures, torque related measures and the dynamic balance contribution, i.e. the contribution of the paretic leg to the total frequency response function, which describes the dynamics of the stabilizing mechanism in terms of a magnitude and phase. To investigate whether changes in control asymmetry are more apparent in a combination of the balance measure symmetry indices, principal component analysis was performed for each condition. Our results show that the individual balance measure symmetry indices were not significantly different between minor stroke and control participants. However, when the symmetry indices, measured during the perturbed condition with eyes closed, were combined according to principal component analysis, the resulting first principal component score was significantly higher for stroke participants. The first principal component includes symmetry indices of the mean dynamic balance contribution and root-mean-square of anterior-posterior CoP position and velocity,

i.e. symmetry indices indicating control in anterior-posterior direction. Replacing the dynamic balance contribution by the root-mean-square of the torque resulted in similar outcomes. This chapter indicates that subtle changes in control asymmetry of minor stroke participants cannot be demonstrated by measuring individual balance measures, but can be demonstrated by combining the dynamic balance contribution, CoP position and CoP velocity when measured during the perturbed trial with eyes closed.

In Chapter 7 we discuss the key findings and clinical implementation of this thesis, and elaborate on the considerations and future recommendations. Throughout this thesis we showed how the BAP and the treadmill can be used in combination with system identification to assess balance control, i.e. sensory reweighting and the stabilizing mechanism. This indicates that the large, expensive and complex motion platforms can be replaced, which makes it possible to assess balance control in the clinic. The advantage of treadmills is that they are already used in the clinic for training and can easily be adjusted such that our system identification method can be applied. First, the treadmill should be able to apply continuous forward-backward translations of the support surface with amplitudes in a range of 0.05-0.14 m ptp. This might require a stronger motor, if not already present, and small adjustments to the software. Second, vertical ground reaction forces should be recorded of both feet separately. This requires the replacement of a single force plate with dual force plates. We showed that using this setup, subtle changes in balance control of the paretic ankle of minor stroke patients can be demonstrated by combining the dynamic balance contribution, anterior-posterior CoP position and anterior-posterior CoP velocity, when measured during perturbed conditions with eyes closed. Future research should point out whether these methods could ultimately be used for the detection of people with high fall risks and assessment of training effects.

Samenvatting

In dit proefschrift hebben we vastgesteld hoe systeem identificatie geïntegreerd kan worden in de kliniek om menselijke balans control te beoordelen. Een goede balansbeoordeling is belangrijk om mensen met een hoog valrisico te detecteren en om balanstraining te optimaliseren, wat uiteindelijk zou leiden tot betere revalidatie en dus minder valpartijen. Huidige klinische testen hebben last van plafondeffecten, zijn subjectief en bieden geen inzicht in de onderliggende mechanismen. Systeemidentificatie lijkt veelbelovend, maar is afhankelijk van grote, dure en complexe apparaten zoals bewegingsplatformen en motion-capture camera's en is daarom minder geschikt voor klinisch gebruik. In deel 1 van dit proefschrift hebben we ons gericht op de technische en methodologische kenmerken van systeemidentificatie technieken. In deel 2 hebben we de resulterende systeemidentificatie methode, waarbij de loopband zorgde voor verstoringen van de ondergrond, toegepast bij mensen met een lichte beroerte om subtiele veranderingen in balanscontrole van het paretische been te evalueren.

Systeemidentificatie maakt gebruik van specifieke verstoringen om de onderliggende neurofysiologische mechanismen van balans controle te ontrafelen. Door rotaties van de ondergrond toe te passen, kan de sensorische herweging van proprioceptieve informatie worden geïdentificeerd. Translaties van de ondergrond maken het mogelijk om het stabilisatiemechanisme te onderzoeken. In hoofdstuk 2 werd systeemidentificatie geïmplementeerd met de 'bilateral ankle perturbator' (BAP), die rotaties van de ondergrond rond het enkelgewricht toepast. Een nieuwe toepassing van de BAP werd gebruikt om het effect van de ondergrond compliantie te onderzoeken. Flexibele ondergronden, b.v. balansmatten, worden vandaag de dag gebruikt als hulpmiddel voor diagnose en training. Met de BAP werden continue verstoringsmomenten toegepast in negen trials; drie ondergronden met een verschillende compliantie, gecombineerd met drie gewenste ondergrond amplitudes. De corrigerende enkelmomenten, als reactie op de rotaties, werden beoordeeld in frequentie responsiefuncties. De laagfrequente magnitude, d.w.z. de gemiddelde frequentie responsfunctie magnitudes in een laag frequentievenster, geeft de sensorische herweging aan. In overeenkomst met de literatuur, leidt een toename van de rotatie-amplitude van de ondergrond tot een afname van de laagfrequente, d.w.z. een lagere weging van proprioceptieve informatie. We hebben geconstateerd dat dit neerwaartse wegingseffect minder is naarmate de ondergrond een hogere compliantie heeft. Met andere woorden, de sensorische herweging van proprioceptieve informatie door de rotatie-amplitude van de ondergrond, is minder op een zachtere ondergrond. Het kan daarom interessant zijn om schuimmatten met verschillende stijfheden te gebruiken, aangezien een groter bereik van sensorische herweging wordt getraind.

In hoofdstuk 3 en 4 wordt systeemidentificatie gecombineerd met een loopband die translaties van de ondergrond toepast. De methodologische kenmerken werden bestudeerd in hoofdstuk 3, waarbij het effect van de amplitude en het aantal herhalingen van het verstoringssignaal op de identificatie van de neuromusculaire controller (NMC) werd onderzocht. Hoofdstuk 4 richtte zich op de karakteristieken van de loopband. In hoofdstuk 3 werd aan gezonde deelnemers gevraagd op een loopband te staan, terwijl kleine continue translaties van de ondergrond werden toegepast in de vorm van een periodiek multisinus signaal. De verstoringsamplitude varieerde over zeven condities tussen 0,02 en 0,20 m piek-tot-piek (ptp), waarbij 6,5 herhalingen van het multisinus signaal werden toegepast voor elke amplitude, resulterend in een trial lengte van 130 sec. Voor een van de condities werden 24 herhalingen opgenomen. Het gemeten externe moment, body sway, en enkel moment werden gebruikt om zowel de relatieve variabiliteit van de frequentieresponsfunctie van de NMC, wat een maat voor precisie is en die afhankelijk is van de ruis-signaalverhouding, als de niet-lineaire contributies te berekenen. Over het algemeen waren de niet-lineaire bijdragen laag en varieerde, voor het enkelmoment, niet met verstoringsamplitude. De resultaten toonden aan dat de verstoringsamplitude minimaal 0,05 m ptp zou moeten zijn, maar hogere verstoringsamplitudes hebben de voorkeur omdat ze resulteren in een hogere precisie vanwege een lagere ruis-signaalverhouding. Het is echter niet nodig om verstoringsamplitudes hoger dan 0,14 m ptp te gebruiken. Meer herhalingen verbeteren de precisie, maar het minimaal vereiste aantal herhalingen hangt uiteindelijk af van de verstoringsamplitude en de gewenste precisie.

Hoofdstuk 4 valideert de stijfheidsschatting van een omgekeerde slinger met bekende stijfheid, met behulp van systeemidentificatie en translaties van de ondergrond. Ten tweede werd de bijdrage van horizontale grondreactiekrachten aan de schatting onderzocht. Het enkelmoment en de daaruit voortvloeiende frequentie responsiefuncties, die de dynamiek van het stabilisatiemechanisme beschrijven, werden berekend door de horizontale grondreactiekrachten zowel binnen als buiten beschouwing te laten. De resultaten toonden aan dat de stijfheid van een omgekeerde slinger geschat met behulp van systeemidentificatie vergelijkbaar is met de stijfheid geschat met een regressiemethode. Ten tweede zijn, binnen de geïnduceerde body sway, het enkelmoment en de frequentie responsiefunctie van het stabilisatiemechanisme, berekend door de horizontale grondreactiekrachten zowel binnen als buiten beschouwing te laten, vergelijkbaar. Vooral voor de lagere frequenties, waar stijfheid de frequentie responsiefunctie domineert, zijn de absolute relatieve fouten klein (<1%). Daarom kunnen de horizontale grondreactiekrachten worden weggelaten bij de berekening van het enkelmoment en de frequentie responsiefunctie van de stabilisatiemechanisme dynamiek. Hoofdstuk 3 en 4 laten zien dat de loopband kan worden gebruikt om balans te meten wanneer kleine aanpassingen worden gedaan aan loopbanden die momenteel in de kliniek beschikbaar zijn; verticale krachten, d.w.z. verticale grond reactie krachten en CoP in het sagittale vlak, moeten worden gemeten door een dubbele krachtplaat, en continue voorwaartse-achterwaartse translaties van de belt moeten mogelijk zijn.

In deel II werd de balanscontrole van mensen met een lichte beroerte beoordeeld. In hoofdstuk 5 hebben we aangetoond dat mensen na een lichte beroerte een verhoogd valrisico hebben, fysiek minder actief zijn en aanhoudende balansstoornissen vertonen in vergelijking met hun leeftijdsgenoten, ook al zijn ze (bijna) volledig klinisch hersteld van motorische stoornissen in het been. De ‘Fugl-Meyer Lower extremity assessment’ en ‘Mini-Balance Evaluation Systems Test’ (Mini-BEST) werden uitgevoerd op een 64 deelnemers die een lichte beroerte hebben gehad en 50 leeftijdsgebonden controles. Valcijfers en dagelijkse fysieke activiteit niveaus werden in een follow-up periode van zes maanden bijgehouden. Deelnemers met een lichte beroerte vielen bijna twee keer zo vaak als gezonde controles (1,1 vs. 0,52 valpartijen per persoon per jaar). De totale tijd van lichamelijke activiteit was niet significant verschillend voor deelnemers met een lichte beroerte in vergelijking met de controles, terwijl de totale intensiteit van de lichamelijke activiteit 6% lager was voor deelnemers met een lichte beroerte. Deelnemers met een lichte beroerte scoorde ook significant lager op de Mini-BEST (24,2 ± 2,3 vs. 26,1 ± 2,1 punten), wat duidt op verminderde statische en dynamische balans, zelfs wanneer ze maximaal scoorden op de ‘Fugl-Meyer Lower extremity assessment’. De resultaten geven aan dat personen in de chronische fase na een lichte beroerte met (bijna) volledig klinisch herstel van motorische stoornissen aan het been vaker vallen en aanzienlijke stoornissen in dynamische balanscontrole vertonen in vergelijking met controles, wat wijst op een belangrijke onvervulde klinische behoefte in deze populatie.

Een verminderde balans en mobiliteit van deelnemers met een lichte beroerte, zoals weergegeven in hoofdstuk 5, wordt wellicht veroorzaakt door subtiele veranderingen in de balanscontrole van de paretische enkel, wat duidt op een asymmetrische balanscontrolestrategie. In hoofdstuk 6 hebben we onderzocht of subtiele control asymmetrie kan worden gedetecteerd bij deelnemers met ene lichte beroerte, in welke mate deze subtiele veranderingen in de control asymmetrie het meest zichtbaar zijn en in welke conditie ze het best kunnen worden gedetecteerd. Balanscontrole van 54 deelnemers met een lichte beroerte en 37 leeftijdsgebonden controles werd beoordeeld. In statische en verstoorde condities, beide uitgevoerd met open en gesloten ogen, werden 11 balansmaten gemeten: centre of pressure (CoP) gerelateerde maten, moment gerelateerde maten en de dynamic balance contribution, d.w.z. de bijdrage van het paretische been aan de totale frequentie responsiefunctie, die de dynamiek van het stabilisatiemechanisme beschrijft in termen van een magnitude en fase. Om te onderzoeken of veranderingen in de control asymmetrie duidelijker naar voren komen in een combinatie van de balansmaat symmetrie-indices, werd voor elke conditie een principal component analyse uitgevoerd. Onze resultaten tonen aan dat de individuele balansmaat symmetrie-indices niet significant verschilden tussen deelnemers met een lichte beroerte en controledeelnemers. Echter, wanneer de symmetrie-indices werden gemeten tijdens de verstoorde conditie met gesloten ogen, en werden gecombineerd volgens de principal component analyse, was de resulterende score van de eerste principal component significant hoger voor de deelnemers met een lichte beroerte in vergelijking met de controles. De eerste principal component bestond uit symmetrie-indices van de gemiddelde dynamic balance contribution en de root-mean-square van de anterior-posterior CoP-positie en snelheid, d.w.z. symmetrie-indices die de controle in anterior-posterior richting aangeven. Het vervangen van de dynamic balance contribution door de root-mean-square van het enkel moment resulteerde in gelijke resultaten. Dit hoofdstuk geeft aan dat subtiele veranderingen in de control asymmetrie van mensen met een lichte beroerte niet aangetoond kunnen worden door het meten van individuele balansmaten, maar wel aangetoond kunnen worden wanneer de dynamic balance contribution, CoP positie en CoP snelheid worden gemeten tijdens de verstoorde trial met gesloten ogen.

In hoofdstuk 7 bespreken we de belangrijkste bevindingen en de klinische implementatie van dit proefschrift, en gaan we dieper in op de overwegingen en toekomstige aanbevelingen. In dit proefschrift hebben we laten zien hoe de BAP en de loopband kunnen worden gebruikt in combinatie met systeemidentificatie om de balanscontrole, d.w.z. de sensorische herweging en het stabilisatiemechanisme, te evalueren. Hiermee geven we aan dat de grote, dure en complexe bewegingsplatformen vervangen kunnen worden, wat het mogelijk maakt om de balanscontrole in de kliniek te beoordelen. Het voordeel van loopbanden is dat ze al in de kliniek gebruikt worden voor training en eenvoudig kunnen worden aangepast zodat onze systeemidentificatiemethode kan worden toegepast. Ten eerste moet de loopband in staat zijn om continue voorwaartse en achterwaartse translaties van de belt toe te passen met amplitudes in een bereik van 0,05-0,14 m ptp. Dit kan een sterkere motor vereisen, als deze nog niet aanwezig is, en kleine aanpassingen aan de software. Ten tweede moeten de verticale grondreactiekrachten van beide voeten afzonderlijk gemeten kunnen worden. Dit vereist de vervanging van een enkele krachtplaat door een dubbele krachtplaat. We toonden aan dat met behulp van deze opstelling, subtiele veranderingen in de balans controle van de paretische enkel van mensen met een lichte beroerte aangetoond kunnen worden door het combineren van de dynami balance contribution, anterior-posterior CoP positie en anterior-posterior CoP velocity als deze gemeten worden tijdens de verstoorde conditie met gesloten ogen. Toekomstig onderzoek moet uitmaken of deze methoden uiteindelijk ook gebruikt kunnen worden om mensen met een hoog valrisico te detecteren en de trainingseffecten te beoordelen.

1 Introduction

Rationale

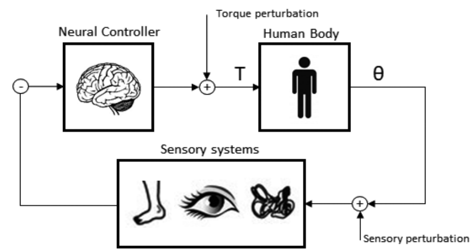
Balance control (Box 1) can be impaired due to aging or pathologies such as Parkinson's disease or stroke (Box 2), which increases the risk of falls [1,2,3]. The assessment of balance control in the clinical setting is important to detect people with high fall risk. If these people are adequately detected, proper rehabilitation can be provided. In addition, balance assessment is important to investigate the individual effect of balance training. The training can be adjusted to the individual needs, which is expected to ultimately result in better rehabilitation and thus less falls.

Currently, balance assessment in clinical settings consists of performance-based tests such as the Berg Balance Scale [15] and the Mini-BEST [16], which involve a variety of tasks, including transferring from sit-to-stance, standing still on one or two legs, normal walking and turning. These tests suffer from important limitations. First, some frequently used clinical tests, e.g. the Berg Balance Scale, have substantial ceiling effects [17], and are hence insensitive to more subtle impairments that still have an impact on functioning in more advanced activities of daily life. Second, the assessments are subjective, as the execution can differ from test to test and doctor to doctor or results might be influenced by the patient's fear of falling, leading to unclear results. Third, they do not provide insight into the neurophysiological mechanisms underlying impaired performance [4,18]. These mechanisms may differ greatly between individual patients and, consequently, warrant different treatment approaches. Therefore, there is a need for objective tests that do not suffer from ceiling effects and are capable of providing insight into the underlying mechanisms.

An alternative method to assess balance control is posturography. Posturography assesses the excursions of the center of pressure (CoP) which reflect the amount of body sway, as well as the generated corrective torques to keep the center of mass (CoM) above the base of support [19]. This makes it possible to detect balance or gait abnormalities in an objective assessment. In addition, impairments in the sensory system can be assessed by manipulation of the proprioceptive information, i.e. standing on a firm or compliant support surface, or by manipulation of vision, i.e. conditions with eyes open and eyes closed [18]. Although posturography is objective and has no ceiling effects, it still lacks the ability to distinguish between the underlying neurophysiological mechanisms due to the closed loop and compensation strategies used.

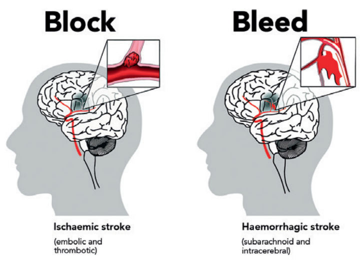
Box 1: Balance Control System

Human balance, i.e. keeping the body in an upright position, depends on the appropriate functioning of the balance control system, which comprises many subsystems, such as the sensory, nervous and motor systems, interacting with each other in a closed loop. In a simplified model of balance control the body, represented by an inverted pendulum, is constantly challenged by disturbances such as pushes (torque perturbations), or sensory noise (sensory perturbations) [4]. Information about changes in body position (body sway θ), is detected by the neuromuscular controller: the information is weighted in relation to its reliability by sensory systems, i.e. sensory reweighting, and then integrated by the neural controller which sends signals to the motor system, creating torques (T). The torques result in a change in body position, which is again detected by the sensory system. Depending on the disturbance, the balance control system is used in different strategies. When the perturbations are small, the motor system creates a corrective ankle torque, sufficient to keep the body in an upright position. This is known as the ankle strategy. When disturbances are larger, the created corrective ankle torque is not sufficient to keep the body in an upright position, an additional corrective hip torque is created, i.e. the hip strategy, or a corrective step is required, i.e. stepping strategy [5]. Another strategy is to counteract the disturbance by arm movements [6]. In this thesis we focus on the ankle strategy.



Recently, researchers have developed promising experimental tests that are objective, have no ceiling effects and are capable of revealing the mechanisms underlying impaired standing balance. System identification (Box 3) was used in combination with dedicated disturbance signals, which actively perturbed the body while standing [4,18,20-24]. In some studies using system identification, participants' stance was perturbed by small continuous random rotations of the ankle. The rotations, manipulating the proprioceptive information, are often combined with manipulations of the visual information, i.e. trials are repeated with eyes open and eyes closed [18,21]. By perturbing the sensory systems and measuring the sensitivity functions, i.e. the response of the body in terms of body sway and ankle torque to the perturbation, sensory reweighting can be identified.

Box 2: Stroke



Source: enableme.org.au

In the Netherlands, an estimated 41,000 people are affected by a stroke each year. A stroke is caused by a reduction of blood flow to the brain. There are two types of strokes: ischemic and hemorrhagic. The most common type is ischemic, occurring in 87% of the cases, and is caused by a blockage of the blood vessel. Hemorrhagic strokes, occurring in 13% of the cases, are caused by a ruptured blood vessel, causing intracranial swelling and pressure. Both types of stroke lead to the damaging or death of brain tissue. Due to combined sensori-motor and cognitive deficits such as paresis, sensory loss, defective coordination and perceptual and attentional problems, a stroke can lead to impaired balance control during standing and walking [7,8]. The impaired balance of stroke survivors not only has a great impact on independent mobility [9] but is also the most important risk factor for falls [3, 10,11]. Throughout the post-stroke life span, fall risk for people after stroke is three to ten times greater than for community-dwelling people of the same age [3]. The consequences of these falls are also more severe. For instance, individuals with stroke are three times more likely to sustain a hip fracture due to a fall than people without previous stroke, and they lose independent mobility or even die after a hip fracture more often [3,12]. Depending on the severity, a stroke can results in death, loss of specific abilities such as memory or muscle control, or best case scenario in no deficits at all. Almost half of the patients surviving a stroke have only minor or no obvious physical impairments during the acute phase (<6 months), and are therefore discharged from the hospital without receiving inpatient rehabilitation; subtle changes in their balance control were not evident [13]. Yet, preliminary findings show that these people may still have balance impairments during the chronic phase (>6 months), and are therefore more likely to fall [7, 14].

In other studies using system identification, perturbations were applied by small continuous random anterior-posterior translations in the range of 6-16 cm, delivered by a moveable platform on which the participants had to stand [20, 22]. The amplitude of the platform was based on the balance capacity of the participants; it was large enough to detect a response and small enough to maintain standing. By analyzing the corrective torques and sway as a response to the perturbations, the control of the central nervous system was identified [4,22]. Since previous research showed that system identification enables the estimation of neuromuscular control deteriorations in stroke and Parkinson's

disease [1,22], it is thought that system identification will be a powerful tool to detect the underlying balance control impairments of stroke patients, including those with minor residual impairments. Although system identification seems promising, there is one major drawback; it depends on large, expensive and complex devices such as motion platforms (Figure 2) and motion capture cameras, and are therefore not suitable for clinical use.

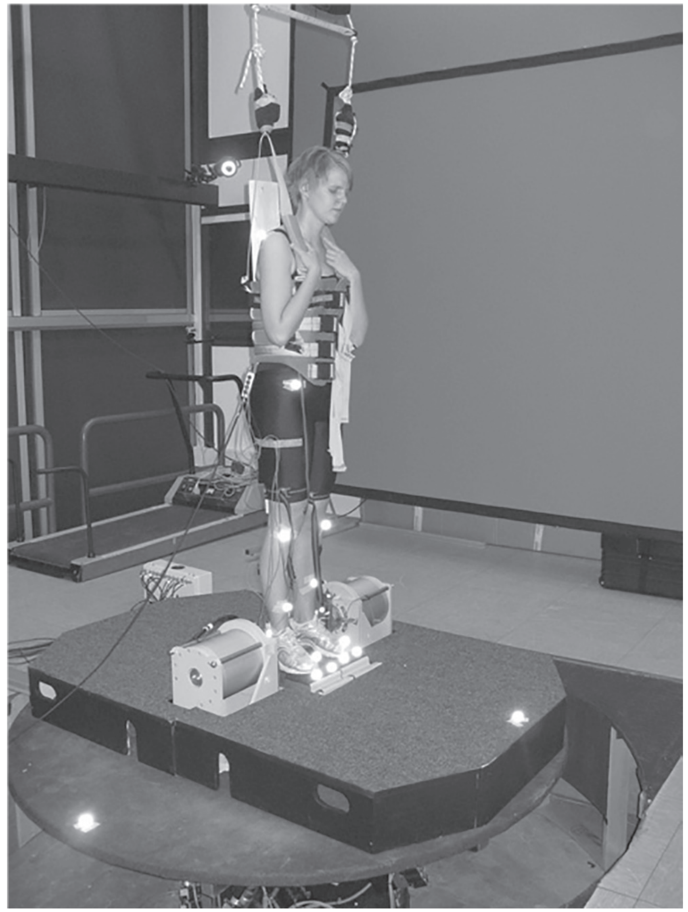
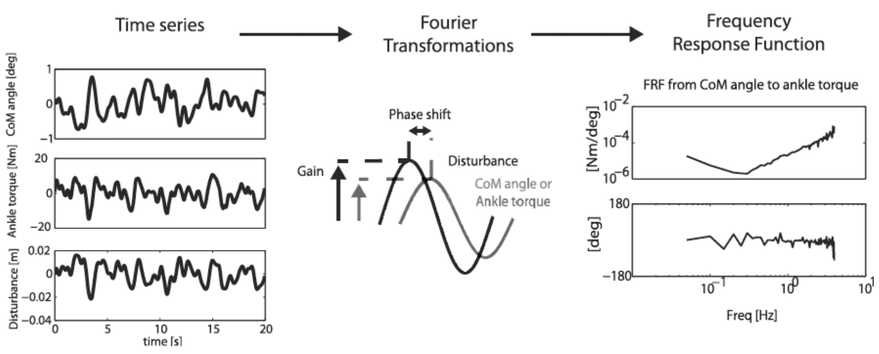


Figure 2: Motion platform used for system identification methods to assess balance control. Source: Journal of Neurophysiology - doi:10.1152/jn.01008.2011

Box 3: System identification to assess balance Control

Underlying mechanisms of balance control interact in a closed-loop, which makes it impossible to determine cause and effect. System identification is a method to open this loop by identifying the dynamics of each underlying system, thereby disentangling cause and effect. This requires dedicated perturbation signals such as sensory perturbations, e.g. perturbing proprioceptive information or eliminating vision, or force perturbations, e.g. pushes against the body. As humans respond differently to either fast (high frequency) or slow (low frequency) disturbances, the perturbation signals are often applied as unpredictable periodic multisines, including a wide range of frequencies. By transforming the measured signals (i.e. joint angles and joint torques) to the frequency domain using Fourier transformation, the system can be described by a frequency response function (FRF). The FRF described the dynamics in terms of a magnitude (amount) and phase (timing) of the response to the disturbances as a function of frequency.



Recently, the Bipedal Ankle Perturbator (BAP) has been developed to apply support surface rotations [2,24]. The BAP consists of two force plates that induce rotations around the ankle. As for the support surface translations, a possible solution would be to perform system identification in combination with a treadmill. Both the BAP and the treadmill are small, cheap and easy to use, thereby simplifying the integration of the laboratory into the clinic. This would make it possible to perform objective test unravelling the underlying neurophysiological mechanisms of impaired balance control in the clinic. However, the application of the BAP to apply specific compliances of the support surface to measure sensory reweighting is not yet tested. In addition, it is not yet known how to use system identification in combination with a treadmill. Furthermore, it is not yet known whether balance measures derived from system identification are more sensitive than

measures derived from posturography or clinical tests. As balance impairments in minor stroke patients could be underestimated due to compensation of the non-paretic leg, it is important to investigate what balance measure could best be used to evaluate subtle balance impairments in minor stroke patients and under which condition they should be measured.

Problem statement and aim

It is important to adequately assess balance in the clinic to detect people with high fall risks and to investigate the individual effect of balance training, which may ultimately result in better rehabilitation and fewer falls. For this purpose, system identification techniques seem promising, but they depend on large, expensive and complex devices such as motion platforms and motion capture cameras, and are therefore not yet suitable for clinical use.

Accordingly, the aim of this thesis, which is part of the Move On project (Box 4), is to determine how system identification can be integrated in the clinic to assess balance control of minor strokes. First we investigate how we can use system identification to assess balance control, thereby opening the closed-loop by applying perturbations. Second, we apply the results to evaluate subtle changes in the stabilizing mechanism of the paretic leg of people after minor stroke.

Outline

In Part I, we investigated how system identification can be used to assess human balance control. Chapter 2 focuses on the assessment of the contribution of sensory systems to balance control. We use support surface rotations applied by a bilateral ankle perturbator (BAP) to study the effect of compliant support surfaces such as foam mats to sensory reweighting. Chapter 3 and 4 investigate the methodology when using a treadmill in combination with system identification. In Chapter 3, focusing on the perturbation signal characteristics, we investigate the effect of amplitude and the number of repetitions of the perturbation signal on the precision and nonlinear distortions of the frequency response function, thereby providing guidance when choosing appropriate perturbation settings.

Box 4: Move On Project

The work of this thesis was part of the Move On project, a project within the IMDI NeuroControl consortium, which was funded by The Netherlands Organization for Health Research and Development (grant number: 104003014). Move On was a collaboration among Delft University of Technology and Radboud University Medical Center working in close collaboration with industrial partners (Motek Medical, 2MEngineering) and clinical partners (Sint Maartenskliniek, Tolbrug Specialistische Revalidatie, Pieter van Foreest, Amstelland Fysiotherapie). In a cohort of people after a minor stroke, the aim was to investigate whether balance tests assessing standing balance, stepping balance and step adjustment capacity, are sensitive enough to detect subtle balance impairments. During the project, several balance tests were implemented on the N-Mill. The N-Mill is a treadmill instrumented with a servomotor, two embedded force plates, and a single belt. Belt movements enable both large discreet perturbations as small continuous perturbations.

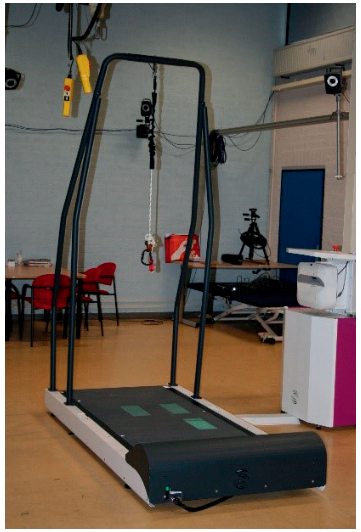


Figure 1: N-Mill. Treadmill designed for the Move On project

Chapter 4, focusing on the treadmill features, validates the use of this device to measure human balance by identifying the dynamics of an single inverted pendulum with fixed characteristics, representing the human body. In addition, this chapter investigates the contribution of horizontal ground reaction forces and debates whether they can be neglected.

In Part II we use the results of Part I to assess subtle changes in balance control after minor stroke. First (Chapter 5), we emphasize that for minor strokes, although discharged from the hospital with few or no obvious impairments, balance performance and gait capacity, physical activity and fall rates are affected. Second (Chapter 6), we use the setup resulting from Chapter 3 and 4 to objectively determine in which balance measure the subtle changes in balance control of the paretic leg in people after stroke are most apparent and under which condition they can best be measured in the clinic, by assessing static balance and balance perturbed by translations of a treadmill belt.

Chapter 7 discusses the key findings and clinical implementation of this thesis, and elaborates on the considerations and future recommendations.

1

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1

PART I

Assessment of balance control using system identification

2

Compliant support surfaces affect sensory reweighting during balance control

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Gait & Posture, 2017, 53: 241-247

**These authors contributed equally to this work.*

Abstract

To maintain upright posture and prevent falling, balance control involves the complex interaction between nervous, muscular and sensory systems, such as sensory reweighting. When balance is impaired, compliant foam mats are used in training methods to improve balance control. However, the effect of the compliance of these foam mats on sensory reweighting remains unclear. In this study, eleven healthy subjects maintained standing balance with their eyes open while continuous support surface (SS) rotations disturbed the proprioception of the ankles. Multisine disturbance torques were applied in nine trials; three levels of SS compliance, combined with three levels of desired SS rotation amplitude. Two trials were repeated with eyes closed. The corrective ankle torques, in response to the SS rotations, were assessed in frequency response functions. Lower frequency magnitudes (LFM) were calculated by averaging the frequency response function magnitudes in a lower frequency window, representative for sensory reweighting. Results showed that increasing the SS rotation amplitude leads to a decrease in LFM. In addition there was an interaction effect; the decrease in LFM by increasing the SS rotation amplitude was less when the SS was more compliant. Trials with eyes closed had a larger LFM compared to trials with eyes open. We can conclude that when balance control is trained using foam mats, two different effects should be kept in mind. An increase in SS compliance has a known effect causing larger SS rotations and therefore greater down weighting of proprioceptive information. However, SS compliance itself influences the sensitivity of sensory reweighting to changes in SS rotation amplitude with relatively less reweighting occurring on more compliant surfaces as SS amplitude changes.

Introduction

Human balance control during stance is continuously challenged by the gravitational field. To maintain an upright posture and prevent falling, balance control involves the complex interaction of nervous, muscular and sensory systems. The central nervous system (CNS) receives feedback about the body orientation from three main sensory systems: the visual, proprioceptive and vestibular system. For each sensory system, the feedback is compared to its reference. The CNS integrates this information and generates an ‘error’, representing deviations of body orientation from upright stance. The error signal of each sensory system is weighted in relation to its reliability; the CNS prefers reliable over less reliable sensory information within an adaptive weighting process termed sensory reweighting [1-3]. Subsequently, the neural controller (NC) generates with a time delay, a corrective, stabilizing torque by selective activation of muscles. This stabilizing torque (together with a torque caused by the intrinsic dynamics of the muscle properties) keeps the body in upright position.

In elderly and in people with neurological, sensory or orthopedic disorders, balance control might be impaired, leading to postural instability and falls [4,5]. People with impaired balance control often undergo functional balance training that is specifically oriented to improve steadiness while standing on compliant surfaces like foam mats [6,7]. It is assumed that sensory reweighting will be trained using these foam mats, since proprioceptive information is disturbed by the compliant support surface [8]. However, the effect of the compliance of these foam mats on sensory reweighting and balance control remains unclear due to a causality problem. The compliant support surface, i.e. the surface in contact with the feet, might have an effect on sensory reweighting induced by the compliance itself, but on the other hand also might have an effect on sensory reweighting provoked by support surface rotations induced by the compliance. System identification techniques in combination with specifically designed external disturbances provide a way to disentangle cause and effect in balance control. By externally exciting the system with an unique input that is not related to the internal signals of the system, a causal relation between the external disturbances and output signals can be created. This ‘opens’ the closed loop and generates informative data about a dynamic system such as balance control [9].

In this paper we investigated the effect of compliant support surfaces, comparable to foam mats, on sensory reweighting of proprioceptive information in balance control using system identification techniques, independent of the effect caused by the change in support surface rotation amplitude. Previous studies showed that increasing the amplitude of support surface rotations result in a decrease of the proprioceptive weight (i.e. down weighting), since the proprioception becomes less reliable [1,3,10]. Therefore, we hypothesize that increasing the amplitude of the support surface rotations lowers the reliability of the proprioceptive information and thus results in down weighting of proprioceptive information [11]. Due to the compliance effect of the support surface, an increase in compliance might affect this sensory weighting. If a compliance effect is present, sensory reweighting due to increasing support surface rotation will change for different levels of compliance.

Methods

Subjects

Eleven healthy young volunteers (age: 20-30 years, 8 women, weight: 67.4 ± 8.2 kg, height: 1.85 ± 0.09 m), without any history of balance disorders, musculoskeletal injuries or neurological disorders, participated in this study and gave written informed consent prior to participation. The study was performed according to the principles of the Declaration of Helsinki and approved by the Medical Ethics Committee of Medisch Spectrum Twente, Enschede, the Netherlands.

Apparatus

The Bilateral Ankle Perturbator (BAP, Forcelink B.V., Culemborg, The Netherlands)(Figure 1) consists of two pedals with similar SS rotations around the ankle axis [10]. The BAP was used to mimic compliant support surfaces and to evoke sensory reweighting by rotations of the support surface (SS). The control scheme (Figure 1) shows the control of each compliant support surface of the BAP and the implementation in the human balance control scheme as a torque controlled device; the input is a disturbance torque resulting in a disturbance rotation amplitude as output. For each leg, the reference torque ($T_{r,L/R}$) comprises a disturbance torque ($T_{d,L/R}$) and an exerted ankle torque by the human ($T_{h,L/R}$) and is translated via the BAP dynamics to a SS rotation amplitude ($\theta_{SS,L/R}$). The BAP dynamics consist of a virtual inertia (I_V), a virtual damping (B_V) and an adjustable virtual stiffness, from here on called the SS stiffness (K_{SS}). A high SS stiffness mimics stiff (i.e. less compliant) support surfaces and a low SS stiffness mimics more compliant support surfaces.

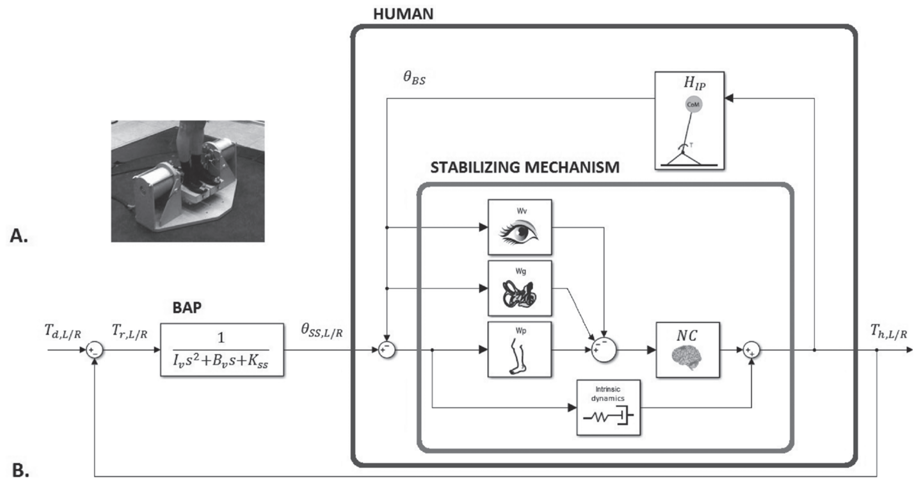

Figure 1: The Bilateral Ankle Perturbator (BAP) consists of two pedals, each driven by an electromotor. The two pedals together form the support surface (SS) which can be controlled using a SS stiffness such that it mimics standing on foam. Rotating the SS with specific SS rotation amplitudes around the subjects ankle can evoke sensory reweighting of proprioceptive information. (B) The control scheme of each support surface of the Bilateral Ankle Perturbator (BAP) is shown in combination with the human. The BAP dynamics include a virtual inertia I_v, a virtual damping B_v and a virtual stiffness (i.e. support surface stiffness K_{SS}). The human is represented by the dynamics of the rigid body (H_{IP}) and the stabilizing mechanism. The stabilizing mechanism contains the vestibular (W_g), visual (W_v) and proprioceptive system (W_p), the neural controller (NC) (including a time delay) and intrinsic dynamics due to the muscle properties.

Disturbance signal

A 20-second multisine disturbance was generated with frequencies in the range of 0.05-10 Hz containing 41 logarithmically distributed frequencies. Signal power was constant up to 3 Hz after which signal power decreased exponentially with frequency. The disturbance torque (T_d) was divided into two and applied to both pedals simultaneously (Figure 2). Previous studies found that in normal stance, humans lean slightly forward and exert a total ankle torque of approximately 40 Nm [12]. Therefore, an additional torque of 20 Nm was added to the disturbance signal for each pedal of the SS, resulting in normal stance of the subjects when standing on the SS.

Process

Subjects were asked to stand on the BAP, without shoes and their arms crossed over their chest. Subjects wore a safety harness to prevent falling, which did not constrain movements or provided support in any way.

The experiment consisted of eleven trials, each containing 9 repetitions of the disturbance signal resulting in trials of three minutes (9 times 20 seconds). In the first nine trials, performed with eyes open, a combination of three levels of SS stiffness and three levels of SS rotation amplitude were applied.

The level of SS stiffness was chosen such that a high level ($K_{SS,H}$ = 700 Nm/rad) is comparable to the required stiffness to maintain an upright stance [13], a low level ($K_{SS,L}$ = 100 Nm/rad) is the minimum stiffness on which subjects are able to maintain balance (as determined in a pilot experiment) and a medium level ($K_{SS,M}$ = 300 Nm/rad) is set between the two extremes. Virtual damping and inertia were set to low values (i.e. B_V of 24.2, 76.7 and 117.1 Nms/rad and virtual inertia I_V of 0.2 kgm^2).

Sensory reweighting of proprioceptive information was evoked by applying different levels of disturbance torques (T_d), equal for all subjects. Three levels of disturbance torques were applied to generate three levels of rotations of the SS around the ankle axis (i.e. SS rotations (θ_{SS})). These levels differed for each level of simulated SS stiffness, such that the resulting SS rotations had a peak-to-peak amplitude of approximately 0.03 ($\theta_{SS,L}$), 0.07 ($\theta_{SS,M}$) and 0.13 rad ($\theta_{SS,H}$). These SS rotation amplitudes were comparable to previous sensory reweighting studies [1,3].

After the nine randomly performed trials with eyes open, the trial with medium SS rotation amplitude ($\theta_{SS,M}$) combined with medium SS stiffness ($K_{SS,M}$) and high SS stiffness ($K_{SS,H}$) were performed with eyes closed resulting in a total of eleven trials. The combination of medium SS rotation amplitude ($\theta_{SS,M}$) with low SS stiffness ($K_{SS,L}$) was not included since pilot experiments indicated that most subjects were unable to perform this condition.

Data recording and processing

The applied torques to both support surfaces were summed to result in the disturbance torque (T_d). The angles of both SS rotations (i.e. BAP motor angles) were measured and averaged to give the SS rotation amplitude (θ_{SS}). Total corrective ankle torque (T_h) was obtained by the summation of the recorded torques (i.e. BAP motor torques) of both support surfaces. Two draw wire potentiometers (Celesto SP2-25, Celesto, Chatsworth, CA, United States) were attached to the right upper leg and the subjects' trunk, measuring the translations of the upper and lower body segments. All signals were recorded at a sample frequency of 1 kHz and processed in Matlab (The MathWorks, Natick, MA).

The height of the Center of Mass (CoM) was calculated according to the equations of Winter et al. using the measured distance between the ground and ankle joint (lateral malleolus), the ankle and hip joint (greater trochanter), the hip and shoulder joint (acromion), and the subject's height [14]. Body sway angle (θ_{BS}), i.e. angle of the Center of Mass (CoM) with respect to vertical was calculated based on potentiometer data and the height of the CoM.

Data analysis

The time series were segmented into data blocks of 20 seconds (i.e. the length of the disturbance signal) after which the first cycle was discarded because of transient effects, resulting in eight data blocks. Subsequently, for each subject and each trial, data were transformed to the frequency domain using the Fourier transform and averaged across the eight data blocks in the frequency domain. Cross spectral densities (CSD) between disturbance torque and body sway were calculated according to

$$\Phi_{T_d\theta_{BS}}(f) = \frac{1}{N} \cdot T_d(f) \cdot \theta_{BS}{}^*(f) \qquad (1)$$

in which T_d(f) and θ_{BS}*(f) represent the Fourier transform of the disturbance torque and body sway. The asterisk indicates the complex conjugate. Similarly, CSDs were calculated between disturbance torque and corrective ankle torque and disturbance torque and SS rotation amplitude. CSDs were used to calculate the frequency response functions (FRFs) (equation 2 and 3). Two FRFs were estimated using closed-loop system identification methods [1,9]

$${}^{SS}\hat{S}_{Th}(f) = \frac{\Phi_{T_dT_h}(f)}{\Phi_{T_d\theta_{SS}}(f)} \qquad (2)$$

$$\hat{H}_{IP}(f) = \frac{\Phi_{T_d\theta_{BS}}(f)}{\Phi_{T_dT_h}(f)} \qquad (3)$$

The FRFs were only evaluated on the excited frequencies in the disturbance signal (f) up to 3 Hz. Equation (2) is the FRF of the torque sensitivity function (${}^{SS}\hat{S}_{Th}(f)$) to the disturbance, which describes the dynamic relation between the proprioceptive disturbances (θ_{SS}) and the torque exerted by the ankles (T_h) in terms of amplitude (magnitude) and timing (phase) as function of stimulus frequency [3]. The FRF of the sensitivity function contains dynamics of the rigid body and the stabilizing mechanism which comprises the visual (W_v), proprioceptive (W_p) and vestibular system (W_g), neural controller (NC) (including a time delay) and the intrinsic dynamics (Figure 1). The estimated FRF of the sensitivity function (${}^{SS}\hat{S}_{Th}(f)$) was normalized for the gravitational stiffness, i.e. participants mass and the distance from the ankles to the CoM multiplied by the gravitational acceleration (mgl_{CoM}), which influences the FRF magnitude. A change in the FRF magnitude implies a relative change of responsiveness to the proprioceptive perturbations, i.e. sensory reweighting. The effects of SS stiffness and SS rotation amplitude on the FRF magnitude are most pronounced at the lower frequencies as the influence of sensory reweighting is most evident at low frequencies where system dynamics are dominated by sensory influences and are minimally affected by other factors such as inertia [1,3,10]. Therefore, the FRF magnitudes were averaged over the five lowest frequencies (0.05-0.25 Hz) resulting in a low frequency magnitude (LFM).

$\hat{H}_{IP}(f)$ (equation 3) is the estimated FRF of the rigid body dynamics, describing the relation between the body sway (θ_{BS}) and the torque exerted by the ankles (T_h) (Figure 1). To check whether this FRF was constant across all the trials for each subject and to validate the identification, the experimentally obtained FRF was compared to the theoretical transfer function of the rigid body dynamics (*$H_{IP}(s)$)*, which is representative of an inverted pendulum and can be described with a moment of inertia (I_{IP}), and a gravitational stiffness (mgl_{CoM})

$$H_{IP}(s) = \frac{1}{I_{IP}s^2 - mgh} \qquad (4)$$

in which *s* denotes the Laplace operator, with s=i2πf, m is the mass of the subject, h the subjects height of the CoM relative to the ankle and g the gravitational acceleration [2]. Both the inertia and the CoM are derived according to Winter et al.[14].

Statistical Analysis

Linear mixed models were used statistically compare differences in LFM due to SS rotation amplitude and level of SS stiffness. SS rotation amplitude, SS stiffness and their interaction were included as covariates and set as fixed effects. The subject was included as a random effect to correct for differences in SS rotation amplitude due to variations in subjects corrective ankle torque and to take the measurement repetitions into account. For illustration purposes, regression lines were plotted between individual LFM and SS rotation amplitude for all levels of SS stiffness, together with the means and standard errors of both LFM and SS rotation amplitudes. To investigate the effect of closing the eyes, similar linear mixed models were used with eyes condition as additional covariate and fixed effect. For all tests, the significance level (α) was set at 0.05. All analyses were performed with SPSS version 22.0 (SPSS, Chicago, IL).

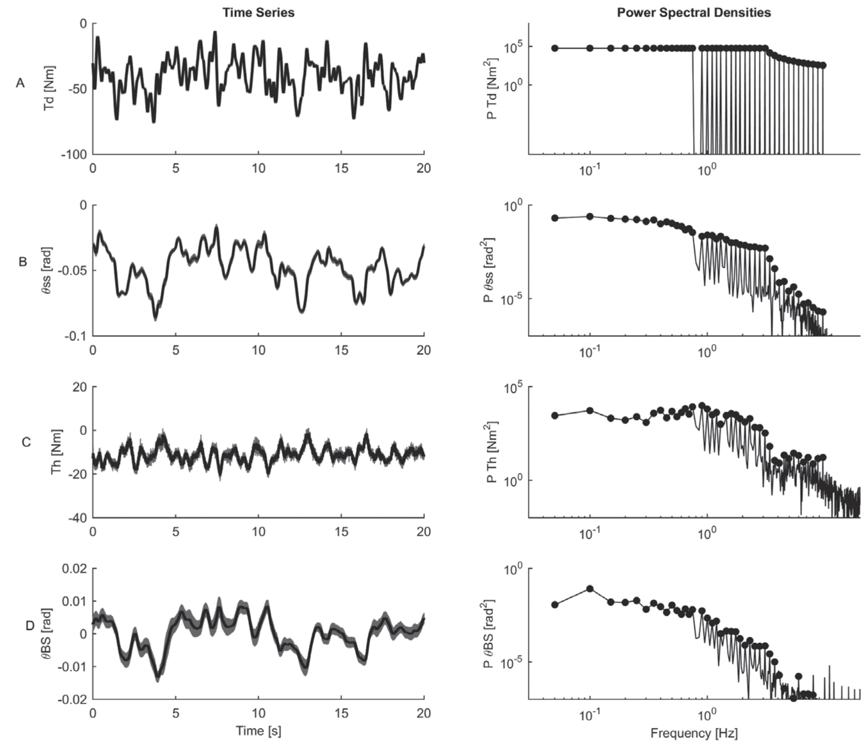

Figure 2: (Left) Time series of a typical subject for the trial with medium support surface (SS) stiffness and medium SS rotation amplitude, in which the disturbance torque (T_d), SS rotation amplitude (θ_{SS}), corrective ankle torque (T_h) and body sway angle (θ_{BS}) are shown. The mean of the time series is displayed in black and the standard errors in grey. For display purposes, signals were filtered with a phase preserving fourth order low pass digital Butterworth filter with cut-off frequency of 20 Hz. (Right) The associated power spectral densities are shown with the excited frequencies as dots.

Results

Time series

Figure 2 shows the time series as response to the disturbances of a typical subject in the medium K_{SS} – medium θ_{SS} condition with eyes open. The standard error of the SS rotation amplitude is relatively low. The responses of body sway angle and corrective ankle torque are slightly more variable. The power spectral densities corresponding to the time series show that the excited frequencies are present in all signals.

Rigid body dynamics

Figure 3 shows the mean FRF and standard error of the FRF of the rigid body dynamics ($\hat{H}_{IP}$) of one typical subject, averaged over all trials with eyes open. Other subjects showed similar results. In addition, the theoretical FRF (H_{IP}) according to the transfer function described in the section 'Data Analysis' which is based on the subject's anthropometries, is shown. The experimental FRF shows (up to 3 Hz) similar characteristics as the theoretical FRF although the magnitude is somewhat lower. Also, the standard error of the experimental FRF is low.

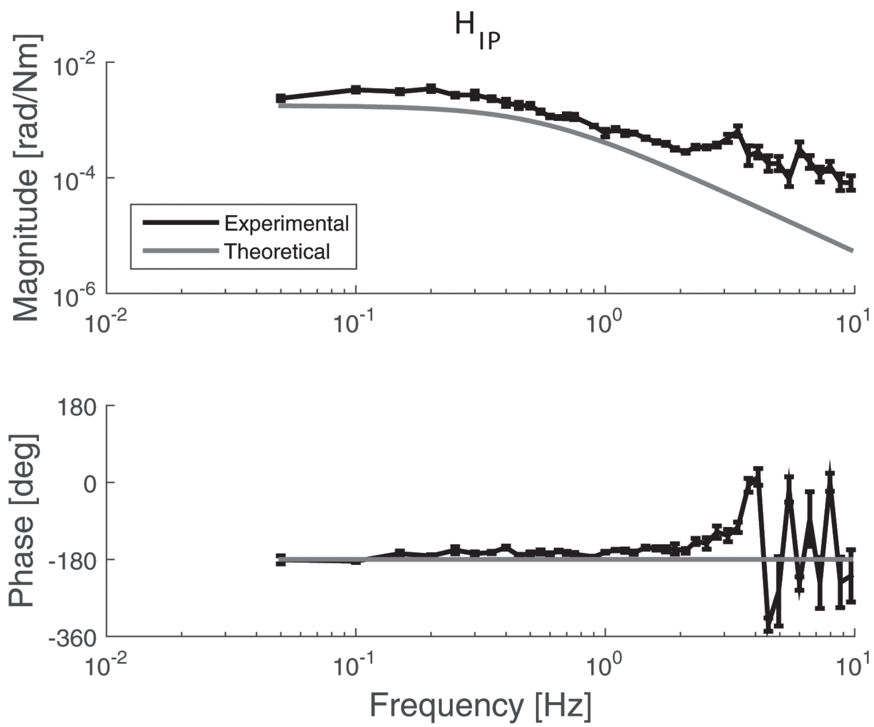

Figure 3: Frequency Response Function (FRF) of the rigid body dynamics (H_{IP}) for one typical subject is shown. The mean and standard error in the nine experimental trials with eyes open are show in black. The theoretical transfer function of the inverted pendulum, based on the body mass and height of the subjects Centre of Mass, is shown in grey.

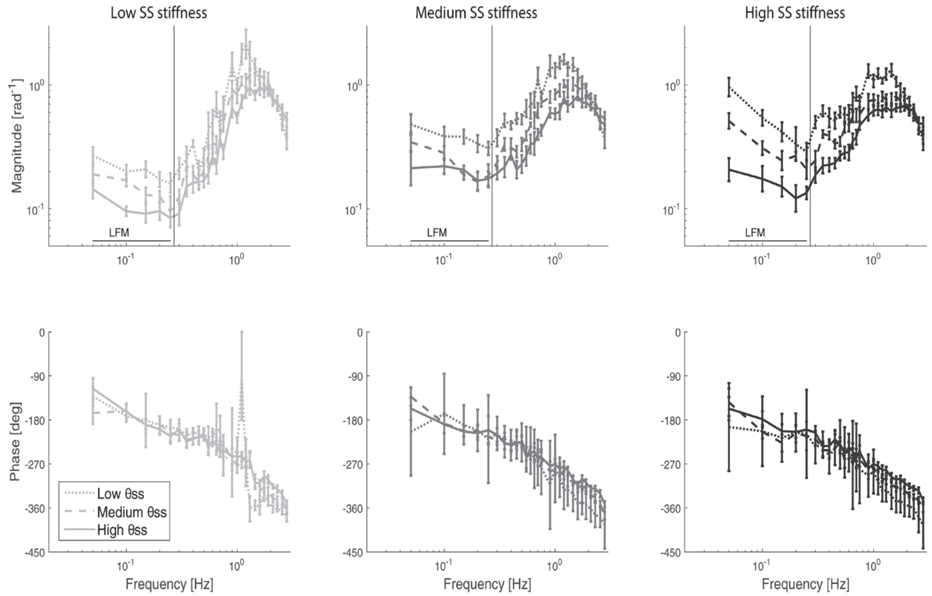

Figure 4: Mean and standard error of the Frequency Response Functions (FRF) of the sensitivity function (${}^{SS}S_{TH}$), averaged over all subjects, normalized by gravitational stiffness. For each level of support surface (SS) stiffness (low, medium and high K_{SS}), the effect of SS rotation amplitude (low, medium and high θ_{SS}) on the FRF is shown. The vertical line indicates the lower frequency window over which statistical analysis is performed. The lower frequency magnitude (LFM) was calculated by averaging the magnitude of the five lowest frequency magnitudes from 0.05-0.25 Hz.

Sensitivity function

Figure 4 shows the estimated FRFs for each level of SS stiffness describing the sensitivity functions (${}^{SS}\hat{S}_{Th}(f)$), as an average across subjects with the SS rotation amplitude (in trials with eyes open). Figure 5 shows, for all trials, the corresponding mean LFM and SS rotation amplitude averaged over all subjects with corresponding standard error of both SS rotation amplitude and LFM. In addition the regression line as function of the SS rotation amplitude is shown for each SS stiffness. The SS rotation amplitude is given as Root Mean Square (RMS) to eliminate the effect of outliers on the peak-to-peak amplitude. Due to the torque exerted by the human, the RMS of the SS rotation amplitude of all trials deviated from the three desired SS amplitude levels. Statistical analysis showed a significant interaction effect of SS rotation amplitude and SS stiffness on the LFM ($p < 0.001$) as shown in the slope of the regression lines. The slope of the regression line becomes smaller as the SS stiffness decreases, i.e. less sensory reweighting for a given change in SS amplitude. For each level of SS stiffness, linear mixed models showed a significant main effect of SS rotation amplitude ($p < 0.001$) on the LFM; by increasing SS rotation amplitude the LFM decreases.

Looking at the effect of closing the eyes, mean LFM and standard errors are shown in Figure 5. Linear mixed models showed a significant effect of closing the eyes ($p<0.001$) on the LFM. Closing the eyes resulted in a higher LFM. In addition, there was a significant effect of SS rotation amplitude ($p=0.005$) on the LFM similar to the previous trials. There was no significant effect of stiffness ($p=0.088$) and no interaction effect between SS stiffness and SS rotation amplitude ($p=0.811$).

Discussion

Sensory reweighting

As in previous studies, sensory reweighting is most pronounced at low frequencies where system dynamics are dominated by sensory influences and are minimally affected by other factors such as inertia [1,3,10]. In this study, we found a comparable effect of the SS rotation amplitude on the LFM; by increasing the SS rotation amplitude, the LFM decreased. This indicates that the stabilizing mechanism was down weighting the proprioceptive information accompanied by up weighting the vestibular and/or visual information as proprioceptive information was less reliable.

In addition, the trials with eyes closed showed a significant increase in LFM compared to eyes open conditions. This implies that closing the eyes (i.e. eliminating visual information) results in an up weighting of the proprioceptive information [1,3,10].

The effect of compliant support surfaces

Standing on compliant support surfaces, such as foam mats, is believed to disturb the proprioceptive information of the ankles by producing a time varying SS angle and making this information less reliable [7]. Due to the existence of the interaction effect of SS rotation amplitude and SS stiffness, the independent effect derived from SS stiffness is hard to interpret.

As for the interaction effect of SS stiffness and SS rotation amplitude, results showed that by decreasing SS stiffness, the slope of the regression line becomes smaller. This means that sensory down weighting of proprioceptive information as a response to increasing SS rotation amplitude is less when standing on more compliant support surfaces.

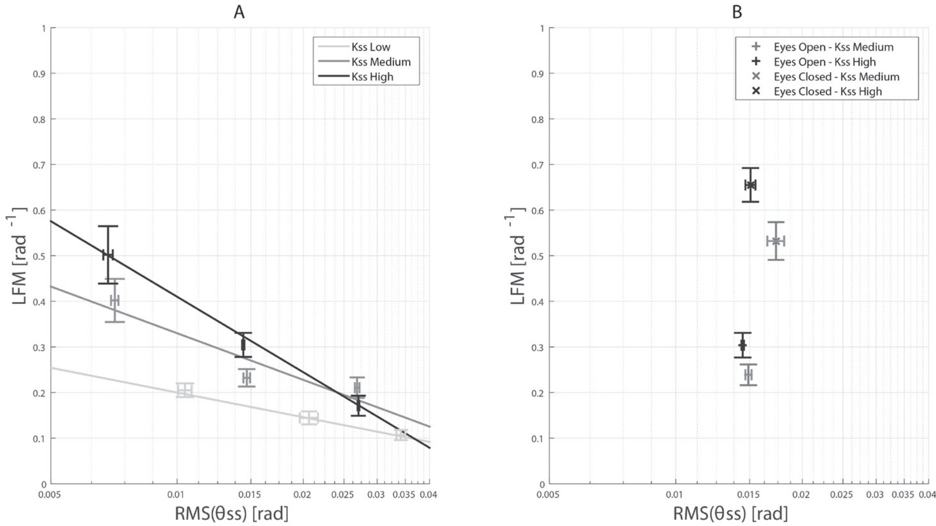

Figure 5: (A) Mean and standard errors of both lower frequency magnitude (LFM) of the sensitivity function (${}^{SS}S_{TH}$) and support surface (SS) rotation amplitudes, averaged over all subjects for each level of SS stiffness (K_{SS}). In addition, three regression lines, fitted on all individual data, are plotted for each level of SS stiffness. (B) Mean and standard errors of both LFM and SS rotation amplitudes, averaged over all subjects as function of SS rotation amplitude for the condition with medium (K_{SS} Medium) and high (K_{SS} High) SS stiffness combined with medium SS rotation amplitude with eyes closed and open.

Thus, sensory reweighting is relatively less when the proprioceptive information is already perturbed by a compliant SS independent of the effect of changes in SS rotation amplitude. The overall results of this study imply that when balance control is trained using foam mats, two different effects should be kept in mind. A foam mat with higher compliance (lower stiffness) leads to larger SS rotations and thus down weighting of proprioceptive information. However, the amount of down weighting for a given amount of SS rotation will also depend on the compliance of the foam mat itself.

Methodological considerations

The experimental FRF shows (up to 3 Hz) similar characteristics as the theoretical FRF although the magnitude is somewhat lower; humans behave more or less as an inverted pendulum. Also, the standard error of the experimental FRF of the rigid body dynamics is low, indicating that the rigid body dynamics do not change over the conditions within a subject. This implies that the changes in the FRF of the human (${}^{SS}\hat{S}_{Th}(f)$) are solely due to changes in the stabilizing mechanism. In this study we applied disturbance torques, which resulted in SS rotation amplitudes of approximately 0.03, 0.07 and 0.13 rad peak-to-peak. However, the SS rotation amplitude could not be fully controlled due to the closed loop nature of the experimental setup where SS rotation amplitude was determined not only by the applied disturbance torque (which was controlled), but also by the torque applied by the subject (which was not experimentally controlled). In contrast to the levels of stiffness, it was therefore not possible to compare the LFM within one level of SS rotation amplitude due to the variabilities within each level of SS rotation amplitude. Therefore, data were statistically analyzed with linear mixed models in which the real SS rotation amplitude was used as an independent variable.

Based on the study of Peterka (2002) [1], the assumption was made that changes in the LFM are caused by changes of sensory reweighting. However, the neural controller also might have changed, thereby influencing the LFM.

Conclusion

In this study we investigated the effect of compliant support surfaces by changing the level of stiffness on sensory reweighting of proprioceptive information in human balance control during stance using closed loop system identification techniques. Results indicate sensory down weighting of proprioceptive information occurs with increasing SS rotation amplitude, but this sensory down weighting is also affected by the level of SS stiffness resulting in relatively less sensory reweighting on more compliant surfaces. When balance control is trained using compliant foam mats, therapists should be aware that the compliance of the foam mat will influence the relative amount of sensory reweighting and thus perhaps the training effect. It may be advantageous to use foam mats with different compliances to provide more comprehensive exercises of the sensory reweighting mechanism.

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3

Effect of amplitude and number of repetitions of the perturbation on system identification of human balance control during stance

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Abstract

To unravel the underlying mechanisms of human balance control, system identification techniques are applied in combination with dedicated perturbations, like support surface translations. However, it remains unclear what the optimal amplitude and number of repetitions of the perturbation signal are. In this study we investigated the effect of the amplitude and number of repetitions on the identification of the neuromuscular controller (NMC). Healthy participants were asked to stand on a treadmill while small continuous support surface translations were applied in the form of a periodic multisine signal. The perturbation amplitude varied over seven conditions between 0.02 and 0.20 m peak-to-peak (ptp), where 6.5 repetitions of the multisine signal were applied for each amplitude, resulting in a trial length of 130 sec. For one of the conditions, 24 repetitions were recorded. The recorded external perturbation torque, body sway and ankle torque were used to calculate both the relative variability of the frequency response function of the NMC, i.e. a measure for precision, depending on the noise-to-signal ratio and the nonlinear distortions. Results showed that the perturbation amplitude should be minimally 0.05 m ptp, but higher perturbation amplitudes are preferred since they resulted in a higher precision, due to a lower noise-to-signal ratio. There is, however, no need to further increase the perturbation amplitude than 0.14 m ptp. Increasing the number of repetitions improves the precision, but the number of repetitions minimally required, depends on the perturbation amplitude and the preferred precision. Nonlinear contributions are low and, for the ankle torque, constant over perturbation amplitude.

Introduction

Human balance control is essential to keep the human body upright in the gravitational field. Deviations from the upright position can be caused by internal and external disturbances, such as breathing and pushes against the body respectively. The central nervous system (CNS) receives sensory information about deviations from the upright position and generates stabilizing corrective ankle torques by sending motor commands to the muscles. Balance control is often described using a simplified model consisting of a single inverted pendulum representing the human body (B), pivoting around the ankle axes, controlled by a neuromuscular controller (NMC) representing the CNS and the muscles, forming a closed loop control system [1-3].

To quantify the contribution of the NMC to balance control, system identification techniques are used, thereby typically applying continuous anterior-posterior translations of the support surface to perturb the human body, while measuring the response in terms of body sway and ankle torque [1,2,4-10]. Alternatively, pushes against the body at the hip and/or shoulders are used as perturbations while measuring the EMG response and body sway [11-14]. The perturbation signal is repeated several times in one or more trials. However, no consistency exists on the perturbation amplitude and the number of repetitions required. The used peak-to-peak (ptp) perturbation amplitude ranges from 0.05 to 0.23 m for support surface translations, from 1 to 16 Nm for torques at the ankle joint or from 0.04 to 0.15 m for displacements of the hip or shoulder pushes. The used number of repetitions varies from 4 to 54. The length of one perturbation signal depends on the lowest excited frequency, resulting in recording lengths of 10 to 720 s in total. However, there are no studies investigating the effect of the perturbation amplitude and the number of repetitions on the quality of the estimated NMC. On one hand, the perturbation amplitude must be high enough to reach a low noise-to-signal ratio (NSR), and the number of repetitions must be high enough to allow for averaging, thereby both improving the quality of the estimated NMC. On the other hand, the perturbation amplitude must be low enough so participants can withstand the perturbation without stepping, and the number of repetitions must be low enough to avoid artefacts due to fatigue.

Another important aspect to consider is the nonlinear behavior of human balance control. Since human balance control is often considered as linear feedback control [1][15-19], linear system identification techniques can be used. However, nonlinear responses affect the linear estimation of the NMC since parts of the signal are transferred to other frequencies [20].

Table 1: Seven conditions (Con.) of the perturbed trials with corresponding peak-to-peak (ptp) position (Pos.), participants mean maximal acceleration (Acc.), participants mean maximal perturbation torque (D_{ext}), participants mean ptp body sway (BS), number of recorded trials (Nr. Tr. Rec.), number of recorded repetitions of the perturbation signal (Nr. Rep. Rec.) and number of repetitions available for analysis (Nr. Rep. An.).

Con.	Pos. ptp (m)	Acc. max (m/s²)	D_{ext} max (Nm)	BS ptp (°)	Nr. Tr. Rec.	Nr. Rep. Rec.	Nr. Rep. An.
A2	0.02	0.87	48.67	1.09	1	6.5	6
A5	0.05	1.39	80.88	2.17	1	6.5	6
A8	0.08	2.25	151.84	3.12	4	26	24
A11	0.11	3.22	205.20	3.92	1	6.5	6
A14	0.14	3.88	257.23	4.80	1	6.5	6
A17	0.17	4.41	291.35	5.59	1	6.5	6
A20	0.20	4.79	340.01	6.56	1	6.5	6

Nonlinearities can be either odd, which generate power on odd harmonics of the excited frequency, or even, which generate power on the even harmonics of the excited frequencies. By using linear system identification techniques in combination with random perturbation signals however, nonlinearities are often not accurately characterized because they cannot be separated from the noise. Therefore, it is important to know how the nonlinear distortions change with perturbation amplitude. Using periodic perturbation signals, van der Kooij et al. [1] showed that the linear response of both body sway and ankle torque increased with increasing perturbation amplitude. However, only two moderate perturbation amplitudes were used.

In this study, we separated the nonlinear contributions from the noise using linear system identification techniques with specific periodic perturbation signals according to the methods of Pintelon and Schoukens [21] on healthy participants; a method that is not often used in the field of human balance control. This method allows us to 1) estimate the NMC, 2) quantify the relative variability of the estimation, i.e. a measure for precision, as a function of perturbation amplitude and number of repetitions, and 3) quantify both odd and even nonlinear contributions as a function of perturbation amplitude. The results of this study will help researchers to select an appropriate perturbation amplitude and number of repetitions to estimate the NMC, allowing for the investigation of the underlying changes in balance control due to ageing or pathologies, such as Parkinson's disease and stroke.

Methods

Participants

Twelve healthy volunteers (six women, median age 26 years, range 24-65 years, height 1.73±0.09 m, weight 73.67±14.19 kg) participated in the study. The study was approved by the Human Research Ethics Committee of the Delft University of Technology (the Netherlands) and was in accordance with the Declaration of Helsinki (59th WMA General Assembly, Seoul, Republic of Korea, October 2008). All participants gave written informed consent.

Apparatus and recording

Standing balance was perturbed in anterior-posterior direction with support surface translations applied by an instrumented split belt treadmill (GRAIL, Motekforce Link, Amsterdam, the Netherlands), where both belts moved in synchrony. Participants wore comfortable flat shoes and a safety harness to prevent fall injuries, without constraining normal body sway or providing support or body-oriented information. Two 6-DOF force plates embedded in the treadmill recorded ground reaction forces of each foot at a sample frequency of 1000 Hz. Eight retroreflective markers were attached to the participants' acromioclavicular joints, major trochanters, lateral epicondyles and lateral malleoli of both left and right side. Additional markers were placed on each treadmill belt. Ten motion capture cameras (Vicon Bonita, Vicon Motion Systems, Oxford, United Kingdom) surrounding the treadmill recorded the marker positions at a sample frequency of 100 Hz. Approximately 2 m in front of the treadmill a grid of 0.2 by 0.2 m was projected on a semi-cylindrical screen, at which participants could focus their gaze.

Perturbation signal

The perturbation was a random-phase multisine signal with a period of 20 s, designed to excite 18 specific odd frequencies between 0.05 and 5 Hz at an interleaved logarithmic frequency grid, since changes in human balance control are most pronounced in the frequency range of 0-3 Hz [5]. The multisine has a flat velocity spectrum, except for the magnitude of the first excited frequency (0.05 Hz), which was 1/3 of the magnitude of the second excited frequency (0.15 Hz), to prevent dominance of the lowest frequency in the belt movement. The unexcited odd and even harmonics enable analysis of the nonlinear contributions [20,22-24]. The amplitude and the number of repetitions of the 20 s multisine varied between conditions, see procedures.

Procedures

Participants were instructed to stand as normal as possible without moving their feet, with eyes open and the arms crossed in front of the chest. Prior to the perturbation trials, a static trial of 5 s was recorded to calculate the length of the pendulum, i.e. the height of the center of mass (CoM) above the ankle joint. Subsequently, participants performed three practice trials of 60 s, with a low, middle (mid) and high perturbation amplitude of 0.02, 0.08 and 0.2 m ptp respectively.

To study the effect of the amplitude of the perturbation signal to the relative variability of the NMC estimation, the perturbation amplitude varied over seven conditions, ranging from 0.02 m ptp (A2) to 0.2 m ptp (A20) (Table 1). For each condition, 6.5 periods of the multisine were recorded, resulting in a trial length of 130 s. All conditions were recorded once, except for the A8 condition which was recorded 4 times to study the effect of the number of repetitions on the relative variability of the NMC estimation. All 10 trials were presented in random order. Between each trial, participants could take an optional break of 1 minute.

Data processing

Data were processed in Matlab version R2016b (MathWorks, Natick, MA, USA). Force plate data were resampled to 100 Hz to match the sample frequency of the marker data.

The marker and force plate data from the static trial were used to calculate the length of the pendulum according to Winter et al. [25], and the mass of the participant respectively.

The first 10 s of the data from the perturbation trials were discarded to remove transient effects, leaving 120 s of data. The data were cut in 6 segments of 20 s, i.e. the length of one period of the multisine. Position of the CoM was derived from the marker positions. Body sway (BS), i.e. the angle of the CoM with respect to the vertical, was calculated using the CoM position in anterior-posterior direction and the length of the pendulum. The Centre of Pressure with respect to the ankle position (CoP) of both feet was used to calculate the left and right ankle torque with inverse dynamics [26]. Total ankle torque was calculated by the sum of both left and right ankle torque.

Translations of the belt position resulted in an external torque perturbing human standing balance according to [5]

$$D_{ext}(t) = -m_{com} l_{com} \ddot{x}_{ss}(t) \quad (1)$$

in which $\ddot{x}_{ss}(t)$ is the acceleration of the support surface derived from the belt markers, 1_{com} is the length of the pendulum and m_{com} is the mass of the pendulum, i.e. the mass of the participant minus the mass of the feet [25].

Data analysis

For the data analysis, the Matlab toolbox provided by Pintelon and Schoukens [21] was used. The perturbation torque $D_{ext}(t)$, body sway BS(t) and ankle torque T(t) were transformed to the frequency domain using the fast Fourier transform (FFT) and divided into periodic responses and nonperiodic noise. The periodic response $D_{ext}(f)$, BS(f) and T(f) respectively, were obtained by averaging the FFT over all segments. The nonperiodic noise $D_{ext',n}(f)$, $BS_n(f)$ and $T_n(f)$ are different for each segment and are defined as the remnants after subtracting the mean FFT from each segment. The power spectral densities (PSDs) were calculated for both the periodic responses and the nonperiodic noise. The dynamics of the NMC are described by the frequency response function (FRF), i.e. the relation between body sway and ankle torque, in terms of a magnitude and phase [2,5,6,27]. The FRF can be defined as

3

$$G(f) = G_0(f) + G_B(f) + G_S(f) + N_G(f) \quad (2)$$

in which G0(f) is the underlying linear system, GB(f) is the bias due to the nonlinear distortions, GS(f) are the stochastic nonlinear contributions and NG(f) are the errors due to the output noise [20].

Best Linear Approximation

The underlying linear system combined with the bias due to nonlinear distortions defines the best linear approximation (BLA)

$$G_{BLA}(f) = G_0(f) + G_B(f) \quad (3)$$

Since the perturbation signal is periodic, the $G_{BLA}(f)$ of the NMC can be estimated by

$$G_{BLA}(f_{ex}) = -\frac{T(f_{ex})}{BS(f_{ex})} \quad (4)$$

in which f_{ex} are the excited frequencies [1,28].

Relative variability of the Best Linear Approximation

The sample variance of the estimated BLA is defined as [22]

$$\sigma_G^2(f_{ex}) = \frac{|G_{BLA}(f_{ex})|^2}{P}\left(\frac{\sigma_{T_n}^2(f_{ex})}{|T(f_{ex})|^2} + \frac{\sigma_{BS_n}^2(f_{ex})}{|BS(f_{ex})|^2} - 2Re\,\frac{\sigma_{T_nBS_n}^2(f_{ex})}{T(f_{ex})BS(f_{ex})}\right) \qquad (5)$$

where P is the number of repetitions, $\sigma_{X_n}^2(f_{ex})$ is the variance of the nonperiodic noise of the body sway or ankle torque and $\sigma_{T_nBS_n}^2(f_{ex})$ is the covariance of the body sway and ankle torque according to

$$\sigma_{X_n}^2(f_{ex}) = \frac{1}{P-1}\sum_{p=1}^{P}\left|X_n^p(f_{ex})\right|^2 \qquad (6)$$

$$\sigma_{T_nBS_n}^2(f_{ex}) = \frac{1}{P-1}\sum_{p=1}^{P}T_n^p(f_{ex})\cdot conj(BS_n^p(f_{ex})) \qquad (7)$$

where p denotes the repetition index. The first and second term within the brackets of (5) represent the NSR of the nonperiodic noise of the ankle torque (NSR_T) and body sway (NSR_{BS}) respectively. The third term represents the correlation between both signals (NSR_{TBS}).

Equation (5) was rewritten to define the relative variability ε, which is described by the ratio between the sample standard deviation ($\sigma_G(f_{ex})$) and $G_{BLA}(f_{ex})$

$$\varepsilon = \sqrt{\frac{\sigma_G^2}{|G_{BLA}|^2}} = \sqrt{\frac{1}{P}\overline{\sum NSR}} \qquad (8)$$

with ∑NSR the sum of the three terms between brackets in (5), i.e. NSR_T, NSR_{BS} and NSR_{TBS}. The bars indicate averaging over the excited frequencies and participants. ε indicates how much nonperiodic noise is left after averaging the segments, relative to $G_{BLA}(f_{ex})$. An ε of 0 indicates a perfect estimator without noise, i.e. no relative variability and thus high precision. An ε of 1 indicates a poor estimator with a high relative variability where the noise level is of the same order as the magnitude of $G_{BLA}(f_{ex})$, i.e. low precision. According to (8), the relative variability of the estimated $G_{BLA}(f_{ex})$ can be influenced by both the number of repetitions and the NSR, which itself can be influenced by the perturbation amplitude.

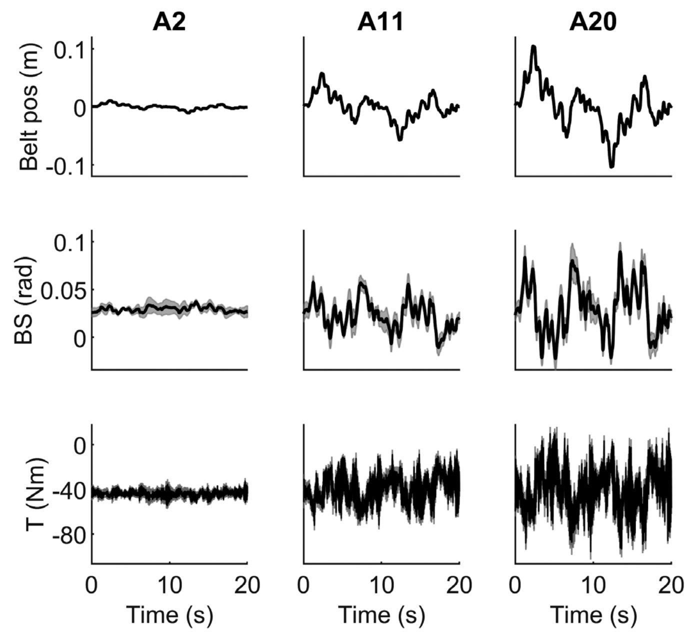

Figure 1: Time series of a typical participant. Mean (black) and standard deviation (grey) over 6 segments of the belt position (upper row), body sway (BS) (middel row) and ankle torque (T) (bottom row) are shown for the A2, A11 and A20 condition.

Equation (8) was used to calculate the required number of repetitions P_ε to reach given ε of 0.02, 0.05, 0.10 and 0.15

$$P_\varepsilon = \frac{\sqrt{\sum NSR}}{\varepsilon^2} \qquad (9)$$

P_ε was calculated for each perturbation amplitude on a low frequency range of 0.05-0.95 Hz, mid frequency range of 1.00-2.35 Hz and high frequency range of 2.40-4.95 Hz.

To check the calculated number of repetitions required to reach ε of 0.02, 0.05, 0.10 and 0.15, a technique called bootstrapping was used [28]. For each number of repetitions, ε was calculated according to (8) using x randomly chosen repetitions, with x ranging from 1-23, out of the recorded data of 24 repetitions at the A8 conditions. This process was repeated 100 times, over which the mean and standard deviation were calculated.

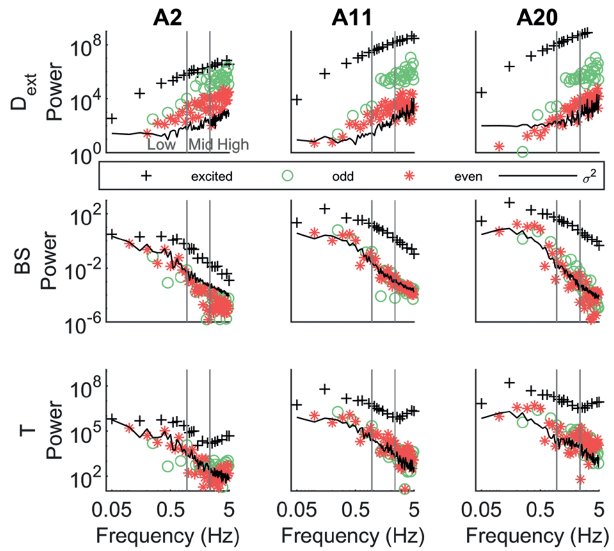

Figure 2: Power spectral densities (PSDs) of the perturbation torque (upper row), body sway (middle row), corrected for impurities in the perturbation torque, and ankle torque (bottom row), corrected for impurities in the perturbation torque, for the A2, A11 and A20 condition of one typical participant, presented by the mean power over the 6 segments of the excited (+, black), unexcited odd (o, green) and unexcited even (*, red) frequencies. The solid black line represents the variance over the 6 segments of the excited and unexcited frequencies. The three areas between the two vertical grey lines represent the three frequency groups.

Quantifying nonlinear distortions

Since it is not possible to quantify the bias due to nonlinear distortions ($G_B(f)$), which affects the estimation of $G_{BLA}(f)$, the stochastic nonlinear contributions ($G_S(f)$), which are of the same order as $G_B(f)$, were calculated according to Pintelon and Schoukens [21].

First, the relative stochastic nonlinear contributions on the perturbation torque, body sway and ankle torque were calculated, by looking at the odd and even unexcited harmonics. When the power on the unexcited harmonics was twice as large as the variance on those frequencies, the stochastic nonlinear contributions were detectable [22]. Stochastic nonlinear contributions in the perturbation torque indicate nonlinearities due to the treadmill. The periodic responses of the body sway and ankle torque were corrected at the unexcited harmonics for those impurities in the perturbation torque by

$$BS_c(f_u) = BS(f_u) - D_{ext}(f_u) \cdot \frac{B(f_u)}{1+B(f_u)NMC(f_u)} \qquad (10)$$

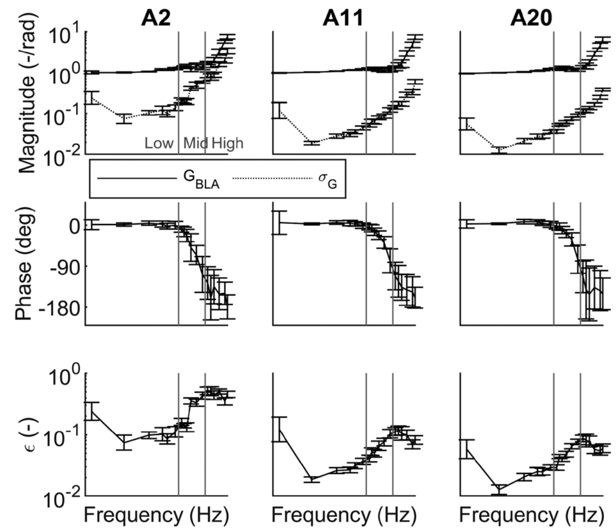

Figure 3: Mean and standard deviation over all participants of the magnitude of G_{BLA} (upper row, solid) and square root of the sample variance (σ_G) (upper row, dotted), both normalized for the gravitation force, phase of G_{BLA} (middle row) and relative variability ε (bottom row) for the A2, A11 and A20 condition. The three areas between the two vertical grey lines represent the three frequency groups.

$$T_c(f_u) = T(f_u) - D_{ext}(f_u) \cdot -\frac{B(f_u)NMC(f_u)}{1+B(f_u)NMC(f_u)} \qquad (11)$$

where f_u represents the unexcited frequencies and $B(f_u)$ represents the rigid human body dynamics [21]. Any remaining power on the unexcited frequencies is caused by the human. The relative stochastic nonlinear contributions of the body sway and ankle torque were calculated as a percentage by respectively averaging the power of the corrected body sway and corrected ankle torque over low, mid and high frequencies, dividing to the total power, and multiplying by 100.

Second, the relative stochastic nonlinear contributions on the body sway and ankle torque were used to calculate $G_S(f_{ex})$, which was compared to $N_G(f_{ex})$, both calculated according to Pintelon and Schoukens [21].

Variance Accounted For

To study the effect of both the relative variability and nonlinear distortions ($G_B(f_{ex})$), we calculate how well the estimated linear model $G_{BLA}(f_{ex})$ describes the measured data, using the variance accounted for (VAF). The modelled ankle torque was calculated according

$$T_{mod}(f_{ex}) = \frac{1}{P}\sum_{p=1}^{P}(BS(f_{ex}) \cdot G_{BLA}(f_{ex})) \quad (12)$$

and converted to the time domain using the inverse Fourier transform

$$T_{mod}(t) = \mathcal{F}^{-1}(T_{mod}(f_{ex})) \quad (13)$$

The VAF was calculated according

$$VAF = \left(1 - \frac{var(\overline{T(t)} - \overline{T_{mod}(t)})}{var(\overline{T(t)})}\right) \cdot 100\% \quad (14)$$

where $\overline{T(t)}$ and $\overline{T_{mod}(t)}$ are the recorded ankle torque and modeled ankle torque respectively, both averaged over 6 segments and filtered with a second order butterworth lowpass filter with a cutoff frequency of 5 Hz. A VAF of e.g. 100% indicates that 100% of the measured data can be explained by the linear system $G_{BLA}(f_{ex})$. The VAF values can be decreased by the bias due to nonlinear distortions ($G_B(f_{ex})$) or remaining noise after averaging over 6 segments.

Results

The time series and corresponding PSD of the perturbation torque, corrected body sway and corrected ankle torque of a typical participant are shown in Figure 1 and Figure 2.

Relative variability of the Best Linear Approximation

Figure 3 shows the estimated FRF of $G_{BLA}(f)$ and σ_G averaged over the participants, both normalized for the gravitational stiffness, i.e. mass of the pendulum multiplied by the length of the pendulum and the gravitational constant ($m_{com}l_{com}g$), to eliminate the effect of participants mass and height. The ratio between σ_G and $G_{BLA}(f)$, i.e. ε, decreases by increasing the perturbation amplitude (Figure 3) due to lower NSR of the nonperiodic noise on those perturbation amplitudes (Figure 4). However, at higher perturbation amplitudes, ΣNSR seems to flatten out.

Table 2 shows, for each frequency group, the required values for $P_ε$, given a certain perturbation amplitude and ε of 0.02, 0.05, 0.10 and 0.15. Both higher perturbation amplitudes, i.e. due to the decreasing NSR, and higher numbers of $P_ε$ result in a lower ε. Note however that at the higher perturbation amplitudes, a lower ε can only be obtained by increasing $P_ε$ and not by further increasing the perturbation amplitude due to the flattened NSR.

Figure 5 shows the calculated ε using the bootstrap method ($ε_b$) together with the calculated ε corresponding to Table 2 ($ε_t$). Both ε are comparable although $ε_b$ is around 0.02 lower than $ε_t$ at the high frequency range.

Table 2: Calculated number of repetitions ($P_ε$) required to obtain a certain relative variability ε, given a specific perturbation amplitude and frequency range.

Frequency group	Amplitude (m ptp)	ΣNSR (-)	Nr. repetitions to obtain relative variability ε of			
			.02	.05	.10	.15
Low	A2	0.199	497	80	20	9
[0.05-0.95] Hz	A5	0.038	94	15	4	2
	A8	0.021	52	8	2	1
	A11	0.029	74	12	3	1
	A14	0.010	26	4	1	-
	A17	0.007	18	3	1	-
	A20	0.008	21	3	1	-
Mid	A2	0.548	1370	219	55	24
[1.00-2.35] Hz	A5	0.099	247	40	10	4
	A8	0.042	105	17	4	2
	A11	0.032	79	13	3	1
	A14	0.027	67	11	3	1
	A17	0.020	50	8	2	1
	A20	0.018	44	7	2	1
High	A2	1.404	3510	562	140	62
[2.40-4.95] Hz	A5	0.263	657	105	26	12
	A8	0.084	209	33	8	4
	A11	0.072	180	29	7	3
	A14	0.065	162	26	6	3
	A17	0.044	110	18	4	2
	A20	0.038	95	15	4	2

Quantifying nonlinear distortions

Figure 6 shows the estimated relative stochastic nonlinear contributions on the unexcited odd and even harmonics for the corrected body sway and corrected ankle torque. The relative stochastic nonlinear contributions are only shown for those perturbation amplitudes where the stochastic nonlinear contributions were detectable.

For the corrected body sway the power on the odd and even unexcited harmonics is too low to detect any stochastic nonlinear contributions. Only at A20 stochastic nonlinear contributions could be detected in the lower and mid frequencies, although not contributing more than 0.1% for odd and 2.3% for even harmonics.

In the corrected ankle torque, both odd and even relative stochastic nonlinear contributions are highest on the high frequencies (1.1-1.5% and 2.4-3.4% respectively), but they are also present on the mid frequencies (0.7-1.2%). For the lower frequencies, the stochastic nonlinear contributions could only be detected for the A20 condition, where the contributions are 1.5% (odd) and 2.4% (even). When increasing the perturbation amplitude, both odd and even relative stochastic nonlinear contributions do not change.

$G_S(f_{ex})$, i.e. the stochastic nonlinear contributions of body sway and ankle torque together, was as large as $N_G(f_{ex})$ (both not shown) for almost all perturbation amplitudes, meaning that $G_S(f_{ex})$ is of the same level as noise. Moreover, $G_S(f_{ex})$ was for none of the perturbation amplitudes twice as large as the noise $N_G(f_{ex})$ and thus not detectable.

Variance Accounted For

Figure 7 shows the filtered ankle torque and modeled ankle torque, averaged over the segments of the A2, A11 and A20 condition for one typical participant. The averaged VAF over all participants increases from 63±15% to 95±2% by increasing the perturbation amplitude (Figure 7, bottom row) and flattens out at A14.

Discussion

In this paper we used a specific periodic perturbation signal to study the effect of the perturbation amplitude and the number of repetitions on the estimation of the NMC with respect to the precision and nonlinear contributions. Since both perturbation amplitude and the number of repetitions have an effect on the precision of the estimator, the required number of repetitions to reach a certain relative variability was calculated given a specific perturbation amplitude. In addition, the relative stochastic nonlinear contributions were quantified and the variance accounted for was calculated, indicating how well the linear estimator of the NMC explained the measured data.

Precision of the Best Linear Approximation

Both increasing the perturbation amplitude and the number of repetitions of the perturbation signal resulted in a higher precision, indicating an improvement of the estimation of the NMC.

Table 2 shows that the minimal perturbation amplitude that can be used is A5 since ΣNSR is too high for amplitudes lower than A5, thereby requiring hundreds of repetitions of the perturbation signal. Higher perturbation amplitudes result in a lower ΣNSR and are therefore preferred over lower perturbation amplitudes. However, since the ΣNSR flattens out above A14, it is better to increase the number of repetitions than to increase the perturbation amplitude in order to further improve the precision of the estimator.

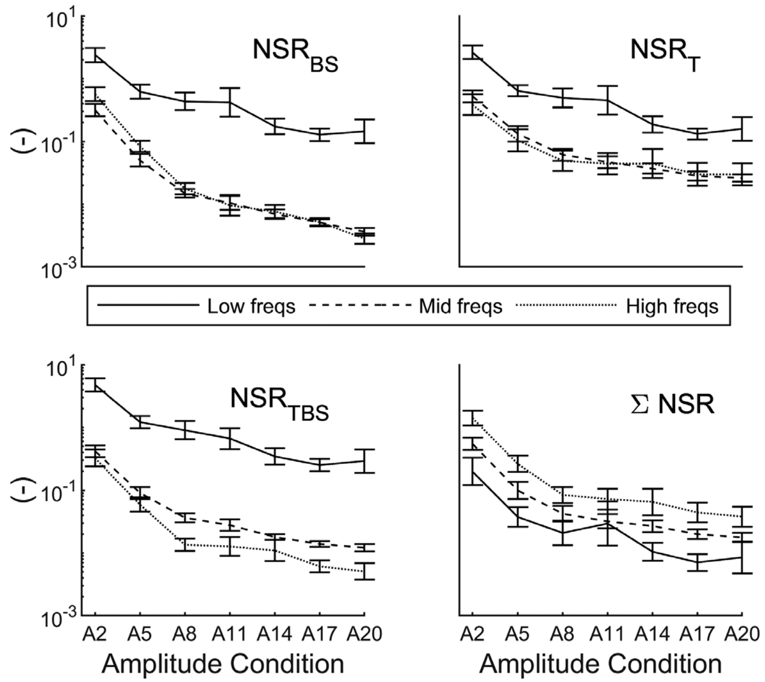

Figure 4: Mean and standard deviation over all participants of NSR_{BS} (top left), NSR_T (top right), the correlation term (bottom left) and the summation of the three terms (NSR_{BS}+NSR_T-NSR_{TBS}) (bottom right) for all amplitude conditions. For each term, the results are plotted for the low (solid), mid (dashed) and high (dotted) frequency range.

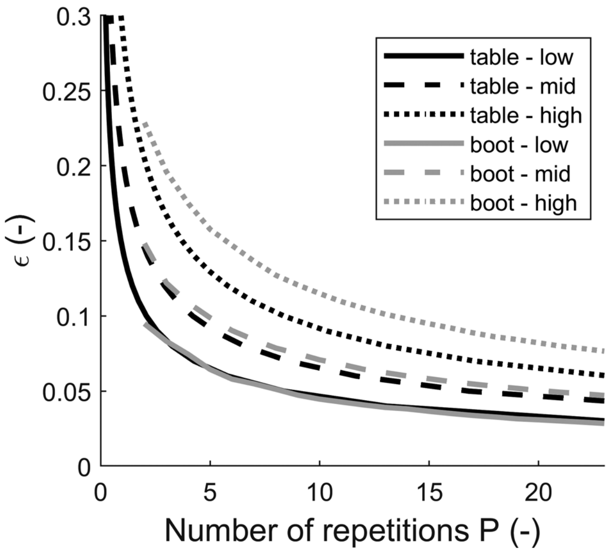

Figure 5: Mean over 100 relative variabilities (ε) calculated with the bootstrap method (ε_b)(grey) for low (solid), mid (dashed) and high (dotted) frequencies. The calculated ε corresponding to Table 2 (ε_t) are shown in black for low (solid), mid (dashed) and high (dotted) frequencies.

Unfortunately, researchers are often limited to lower perturbation amplitudes due to physical limitations of the participants such as fatigue or the inability to withstand higher perturbation amplitudes. To still reach an acceptable precision, more repetitions of the perturbation signal are required. Table 2 helps the researcher selecting the required number of repetitions. Researchers have to decide what ε is acceptable in a low, mid or high frequency group, depending on the expected changes in the NMC of the participant group of interest, and in what frequency group those changes are most pronounced.

Researcher should keep in mind that for each perturbation amplitude, the ΣNSR of the nonperiodic noise is different for the low, mid and high frequencies. Therefore, when choosing a proper number of repetitions to obtain a certain precision in one frequency range, the precision might be worse in another frequency range.

The measured ε using the bootstrap method were 0.02 lower than calculated in Table 2 at the high frequencies. This difference could be explained by higher variance of the FRF in the high frequency range. Since the variance at these frequencies is large, it is important to keep in mind that it seems that even more repetitions than stated in Table 2 are required to reach a certain ε in this frequency range.

Our findings are comparable with van der Kooij et al. [1] showing more power in the PSD of the body sway and ankle torque and a decrease in NSR_{BS} and NSR_T when increasing the perturbation amplitude from 0.06 m ptp to 0.08 m ptp. In addition, the correlation between the nonperiodic noise of the body sway and ankle torque (not shown) was high up to 1 Hz, with similar values to van der Kooij et al. This correlation suggests that the dominant source of the noise occurred inside the feedback loop, i.e. the human. The physiological cause could be the imperfect processing of noisy sensory signals, time variant behavior due to fatigue or adaption, or to other discontinuous control mechanisms [1].

The used peak-to-peak perturbation amplitudes of other studies ranging from 0.05 to 0.23 m for the support surface translations [1,2,4-10] and perturbation amplitudes ranging from 0.04 to 0.15 m for hip or shoulder pushes [11,12] are comparable with our perturbation amplitudes. The perturbation torques at the ankle joint ranging from 1 to 16 Nm [13,14] are also comparable with our induced perturbation torque, when assuming the mass of the participant was not taken into account. This shows that in general the used perturbation amplitudes in previous studies seem acceptable.

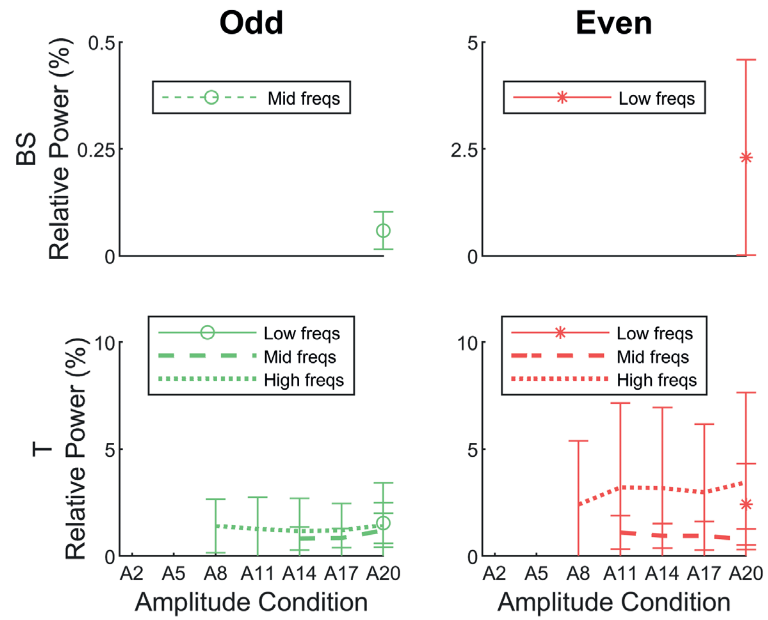

Figure 6: Mean and standard deviation over all participants of the relative stochastic odd (left) and even (right) nonlinear contributions in the corrective body sway (top) and corrective ankle torque (bottom). The results are plotted for low (solid), mid (dashed) and high (dotted) frequencies. Note the different scales on the y-axis.

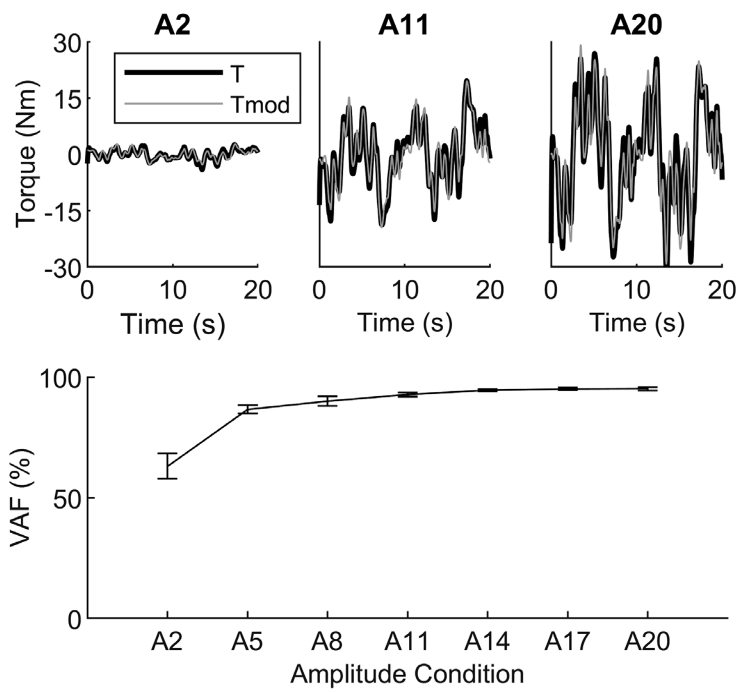

Figure 7: (Top) Filtered measured ankle torque (black) and filtered modeled ankle torque (grey) of one typical participant for the A2, A11 and A20 condition. (Bottom) Mean and standard deviation over all participants of the Variance Accounted For (VAF) for all amplitude conditions.

Quantifying nonlinear distortions

Since it is not possible to directly measure the bias due to nonlinear distortions ($G_B(f)$) on the estimation of the NMC, we calculated the stochastic nonlinear contributions ($G_S(f)$), which are of the same order as $G_B(f)$ [22].

Our results showed that the relative stochastic nonlinear contributions in the body sway due to nonlinear behavior of the NMC are only 2.3% for the even low frequencies and even lower (0.1%) for the odd mid frequencies, when detectable. Note that when stochastic nonlinear contributions are undetectable, the nonlinearities are small compared to the noise, which does not necessarily mean that they are not present. For the ankle torque, the relative stochastic nonlinear contributions due to nonlinear behavior of the NMC are only around 2% for the odd and even low frequencies and around 1% for the odd and even mid frequencies, when detectable. The odd and even high frequencies, however, showed more relative stochastic nonlinear contributions of 1.1-3.4%. The relative stochastic nonlinear contributions in the ankle torque do not change by increasing the perturbation amplitude.

Based on the results of van der Kooij [1], we expected the relative stochastic nonlinear contributions to be higher at high perturbation amplitudes. Especially at the higher perturbation amplitudes at which participants could not withstand the perturbation by keeping their feet in place. However, the relative nonlinear contributions did not increase at higher perturbation amplitudes. Since the relative nonlinear contributions did not increase at higher perturbation amplitudes, we assume that the nonlinear behavior due to a change in strategy, i.e. stepping, did not play a role yet. The fact that all participants could withstand the A20 condition supports this idea. The nonlinearities could be introduced by the nonlinear properties of a single inverted pendulum. However, the relative stochastic nonlinear contributions corresponding to the measured ptp body sway are too small to explain our results. Other explanations for the nonlinearities could be the nonlinear dynamics of the muscle such as short range stiffness or tendon stiffness, or the existence of thresholds in the NMC [1,29,30].

Variance Accounted For

To study the effect of both the relative variability, i.e. precision, and nonlinear distortions (G_B) on $G_{BLA}(f)$, the VAF was calculated to show how well the estimated linear model G_{BLA} describes the measured data. The VAF increased from 61±15% to 93±2% by increasing the perturbation amplitude. It remains unclear whether the VAF increases due to better NSR or due to the reduction of nonlinear distortions (G_B). Nevertheless, the VAF shows that up to 93% of the data could be explained by a linear model when using a perturbation amplitude of A17 or A20.

Limitations

The treadmill introduces nonlinear distortions in the perturbation torque (Figure 2, upper row). Nonlinear distortions in the perturbation torque due to nonlinear behavior of the treadmill might be interfering with the linear system identification techniques. However, with the method of Pintelon and Schoukens [20], the body sway and ankle torque are corrected for the impurities. As the correction is not perfect, it would be best to limit the amount of nonlinear distortions in the perturbation torque.

The experiments in this study were performed with mainly healthy young participants. When studying populations with balance deficits, the variability between participants would probably be higher. In this case, we suggest a larger study population rather than higher perturbation amplitudes or higher number of repetitions. The within-subject variability for these populations is harder to predict and should first be investigated which can be done using the method presented in this paper.

Conclusions

In this study, we provide guidance to choose the appropriate amplitude and number of repetitions of the perturbation signal used in system identification approaches. The minimal perturbation amplitude should be 0.05 m peak-to-peak, since lower perturbation amplitudes require too many repetitions. However, higher perturbation amplitudes are preferred because the precision of the estimation is better, i.e. the relative variability is lower, resulting in a better explanation of the data by a linear model. There is however no need to further increase the perturbation amplitude than 0.14 m peak-to-peak. Using more repetitions always results in better precision, but the minimal required number of repetitions depends on the chosen perturbation amplitude and the desired precision. Nonlinear contributions are not higher than 3.5% in the range of 0.02-0.20 m peak-to-peak and nonlinear contributions to the ankle torque do not change with perturbation amplitude. To conclude, when investigating changes in underlying mechanisms of balance control due to ageing or pathologies, such as Parkinson's disease and stroke, the NMC could be estimated with the use of linear system identification techniques despite the presence of nonlinearities.

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4

Estimating ankle torque and dynamics of the stabilizing mechanism

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Abstract

Changes in human balance control can objectively be assessed using system identification techniques in combination with support surface translations. However, large, expensive and complex motion platforms are required, which are not suitable for the clinic. A treadmill could be a simple alternative to apply support surface translations. In this paper we first validated the estimation of the joint stiffness of an inverted pendulum using system identification methods in combination with support surface translations, by comparison with the joint stiffness calculated using a linear regression method. Second, we used the system identification method to investigate the effect of horizontal ground reaction forces on the estimation of the ankle torque and the dynamics of the stabilizing mechanism of 12 healthy participants. Ankle torque and resulting frequency response functions, which describes the dynamics of the stabilizing mechanism, were calculated by both including and excluding horizontal ground reaction forces. Results showed that the joint stiffness of an inverted pendulum estimated using system identification is comparable to the joint stiffness estimated by a regression method. Secondly, within the induced body sway angles, the ankle torque and frequency response function of the joint dynamics calculated by both including and excluding horizontal ground reaction forces are similar. Therefore, the horizontal ground reaction forces play a minor role in calculating the ankle torque and frequency response function of the dynamics of the stabilizing mechanism and can thus be omitted.

Introduction

Assessing changes in human balance control, due to aging or pathologies such as Parkinson's disease and stroke, is important to provide for appropriate rehabilitation therapies which reduce the fall risk. Often, the ankle torque is used to assess unperturbed balance [1-3] or perturbed balance using perturbations such as platform translations [4-8]. Platform translations could also be combined with system identification techniques where the body sway and ankle torque are used to obtain the frequency response function (FRF), describing the dynamics of the stabilizing mechanism (STM) [9,10]. However, in experimental settings, large, expensive and complex motion platforms are often used to perturb the body, which hampers clinical implementation.

A treadmill could be a simple alternative to apply support surface translations, which could be used in the clinic, but brings with it two main questions. The first question is whether the STM stiffness, i.e. the low frequency magnitudes of the frequency response function [10-14], could correctly be estimated using a treadmill in combination with system identification methods. The STM stiffness is required to keep the body upright in a gravitational field, and consists of the passive muscle stiffness and active neural stiffness. No previous studies, however, validated the estimation of the STM stiffness using a treadmill in combination with system identification methods. The second question is what the effect of horizontal ground reaction forces is on estimation of the ankle torque and thereby on the STM dynamics. Although it is generally known that horizontal ground reaction forces are substantially lower than vertical ground reaction forces, it is not clear what errors are made when the horizontal ground reaction forces are omitted in calculating the ankle torques and the stabilizing mechanism. The ankle torque is calculated by summing the vertical ground reaction forces multiplied by the centre of pressure (CoP) and the horizontal ground reaction forces multiplied by the height of the ankle joint (Figure 1). However, measuring horizontal ground reaction forces with a treadmill requires a complex and expensive construction.

In this study we assessed human balance control with support surface translations and system identification using a treadmill. Firstly, we validated the STM stiffness estimation using an inverted pendulum, i.e. a single inverted pendulum with fixed STM stiffness. The fixed STM stiffness was measured by applying several forces and measuring the deviation, where theslope indicates the spring stiffness. The derived STM stiffness was compared with a dynamic system identification approach. Secondly, we investigated the effect of horizontal ground reaction forces on the estimation of the ankle torque and STM dynamics.

Table 1: Mean and standard deviation of the body sway and VAFs for all conditions, averaged over participants. The SD represents the standard deviation.

Amplitude (m ptp)	Body sway (° ptp)		VAF (%)	
	Mean	SD	Mean	SD
0.02	1.1	0.3	99.9	0.1
0.05	2.1	0.4	99.8	0.2
0.08	3.1	0.5	99.8	0.2
0.11	3.8	0.4	99.8	0.2
0.14	4.7	0.6	99.8	0.3
0.17	5.4	0.6	99.8	0.2
0.20	6.4	0.7	99.8	0.2

Methods

Subjects

To validate the STM stiffness estimation, an inverted pendulum (length 1.00 m) was used, consisting of a stick mounted on a brick via a piece of rubber. To investigate the effect of horizontal forces on the ankle torque and STM dynamics, twelve healthy volunteers participated (six women, median age 26, range 24-65 years, length 1.73 ± 0.09 m, weight 73.67 ± 14.19 kg). The study was approved by the local Human Research Ethics Committee and performed according to the principles of the Declaration of Helsinki.

Apparatus and recording

Balance was perturbed using a dual-belt treadmill (GRAIL, Motekforce Link, Amsterdam, The Netherlands) by anterior-posterior translations of both belts synchronously. A 6-DOF force plate under each belt recorded ground reaction forces (1kHz).

Twelve cameras captured (Bonita, Vicon motion Systems, United Kingdom) marker positions (100 Hz). Seven retroreflective markers were attached on the inverted pendulum: three on the stick, one on the rubber and three on the brick. Eight markers were attached to the participants' acromioclavicular joints, major trochanters, lateral epicondyles, and lateral malleoli of both left and right side. Two markers were placed on both belts.

Perturbation signal

The perturbation signal was a multisine signal with a period of 20 s, exciting 18 frequencies in the range of 0.05-5 Hz at a logarithmic frequency grid.

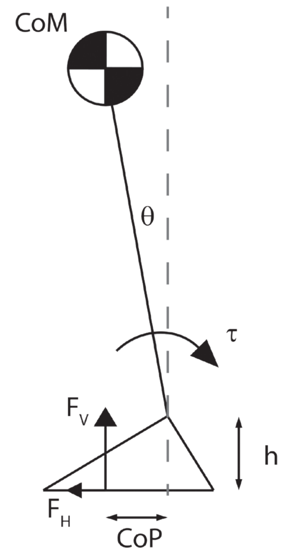

Figure 1: Free body diagram of an inverted pendulum. The joint torque (τ) is calculated by summing the vertical ground reaction forces (F_V) multiplied by the centre of pressure (CoP) and the horizontal ground reaction forces (F_H) multiplied by the height of the joint (h).

The signal had a flat velocity spectrum, except for the magnitude of the first frequency (0.05 Hz), which was 1/3 of the magnitude of the second frequency (0.15 Hz), to prevent dominance of the lowest frequency in the translations. The signal was repeated 6.5 times resulting in trials of 130 s.

Procedures

To validate the estimation of the STM stiffness, the inverted pendulum's STM stiffness estimated using system identification was compared with the STM stiffness estimated using a regression method. In the regression method, the STM stiffness was measured by placing the inverted pendulum horizontal on a table allowing the stick to rotate freely without gravity interacting. Forces were applied perpendicularly on the most distal side of the stick and measured using a spring scale (Salter, Super Samson, range 0-1 kg), such that the stick was gradually loaded and unloaded 5 times over a displacement range of -0.35 to 0.35 m in steps of 0.05 m, thereby compensating hysteresis. In the system identification method, the inverted pendulum stood on the left belt such that the stick could pivot around the rubber in anterior-posterior direction.

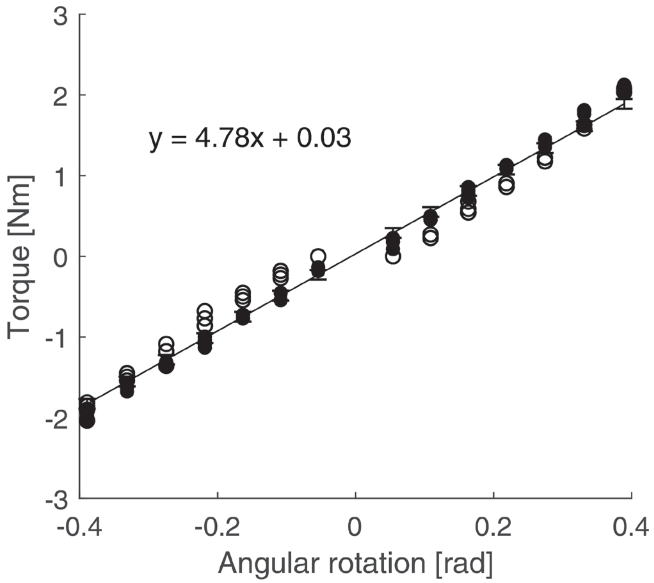

Figure 2: Torque versus angular rotation. Black dots represent loading, white dots represent unloading. The black line represents the linear fit with function y=4.78x+0.03. The hysteresis can be seen by the difference in required torque for loading (black dots) and unloading (white dots).

A static trial of 5 s was recorded to obtain the distance between the centre of mass (CoM) and the joint, i.e. the distance between the stick centre and pivot point. Four perturbed trials were recorded with perturbation amplitude of 0.08 m peak-to-peak (ptp).

To study the effect of horizontal ground reaction forces on the estimation of the ankle torque and STM dynamics, participants stood on the treadmill as normal as possible without moving the feet and with arms crossed in front of the chest. First, a 5 s static trial was performed to obtain the participants weight and distance between the CoM and ankle joint. Four trials with perturbation amplitude of 0.08 m ptp were recorded. To study whether the relative effect of horizontal ground reaction forces is independent of perturbation amplitude, six additional trials with amplitudes of 0.02, 0.05, 0.11, 0.14, 0.17 and 0.20 m ptp were recorded. All perturbed trials were presented in random order.

Data Pre-processing

Data were processed in Matlab (MathWorks, USA). Force plate data were resampled to 100 Hz to match the sample frequency of the marker data. For visualization, force plate data and marker data were zero-phase filtered by applying a 2nd order 5 Hz low pass Butterworth filter in forward and time-reversed direction. The static trials were used to obtain the mass and distance between the CoM and the (ankle) joint, according to Winter et al. [15].

For each perturbed trial, the first 8 and last 2 s were discarded to remove transient effects, leaving 120 s, and subsequently cut in 6 segments of 20 s, i.e. the period length of the multisine. The segments of the four trials with amplitude 0.08 m ptp were combined, resulting in 24 segments. For the analysis regarding the influence of perturbation amplitude, only the first trial with amplitude 0.08 m ptp was used.

Belt and subject marker positions were used to respectively obtain the perturbation torque according to [9] and the body sway (BS), which was defined as the angle of the CoM with respect to vertical, using the anterior-posterior CoM position, and the distance between the CoM and the (ankle) joint.

For the CoP calculations of the validation measurements, vertical ground reaction forces were corrected for the force due to the mass of the brick, since the mass of the brick is large compared to the mass of the CoM. The CoP on each belt with respect to the joint was corrected for CoP displacements due to the mass of the brick according to

$$CoP = CoP_r - \frac{m_b \cdot \ddot{x}_{ss} \cdot 0.5z}{m_b \cdot 9.81} \qquad (1)$$

with CoP_r the CoP with respect to the joint, i.e. the CoP derived from the force plates minus the joint marker position, m_b the mass of the brick and z the height of the brick, i.e. 0.5z represents the height of the brick's CoM. For the human experiments, the CoP was calculated with respect to the joint.

For the validation, the joint torque was calculated with inverse dynamics [16,17] according to

$$T = -F_V CoP - F_H h \qquad (2)$$

with F_H and F_V the horizontal and corrected vertical ground reaction forces, respectively. To investigate the effect of horizontal ground reaction forces, the participants' joint torques of both feet were calculated by 1) including F_H which is stated by equation 2, and 2) neglecting F_H which results in equation 3

$$T_{NH} = -F_V CoP \qquad (3)$$

The ankle torque was obtained by adding the joint torques of both feet.

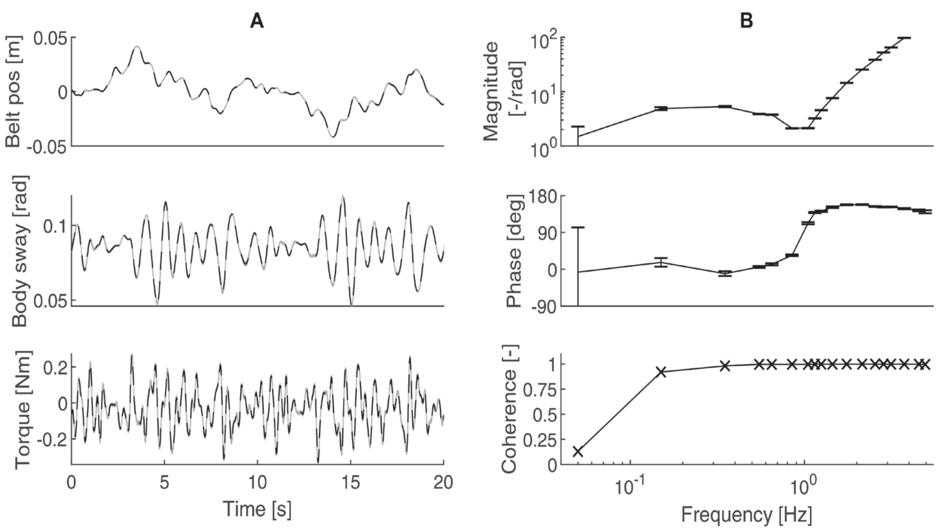

Figure 3: A. Mean (black) of the inverted pendulums belt position (top), body sway (middle) and torque (bottom) time series. The grey areas represent the standard deviation, which is small. B. Mean magnitude normalized for gravitational stiffness (top), phase (middle) and coherence (bottom) of the frequency response function of the inverted pendulum, averaged over the 24 segments. The error bars indicate the standard deviation. Crosses indicate the excited frequencies.

Data Analysis

For the validation, the regression method was used to calculate the applied joint torque by multiplying the measured force with the length of the stick. The angular displacement was obtained from the stick displacements using goniometry. The slope of a fitted linear line represented the rotational stiffness, i.e. the STM stiffness.

The STM stiffness calculated with the regression method was compared with the stiffness calculated using the system identification method. The body sway and joint torque were transformed to the frequency domain using the fast Fourier transform resulting in T(f) and BS(f), which were averaged and used to calculate the FRF, describing the STM dynamics in terms of a magnitude and phase, according to [18,19]

$$FRF(f) = -\overline{T(f)}/\overline{BS(f)} \quad (4)$$

The bars indicate averaging over the segments. STM stiffness of the inverted pendulum was calculated by averaging the second and third excited frequencies (0.15-0.35 Hz), as the coherence and signal-to- noise ratio of the first excited frequency were low (see results). Coherence was calculated according to

$$COH(f) = \frac{|\overline{S_{uy}(f)}|^2}{\overline{S_{uu}(f)}\,\overline{S_{yy}(f)}} \quad (5)$$

with S_{uu} and S_{yy} representing the spectral densities of body sway and joint torque respectively and S_{uy} the cross spectral density from body sway to torque.

The variance accounted for (VAF) was calculated according to

$$VAF = \left(1 - \frac{var(\overline{T(t)} - \overline{T_{NH}(t)})}{var(\overline{\overline{T(t)}})}\right) \cdot 100\% \quad (6)$$

The bars indicate averaging over the segments to reduce measurement noise. A VAF of 100% means that 100% of the ankle torque (T) is explained by T_{NH}, i.e. the horizontal ground reaction forces do not contribute.

Two FRFs and their coherences were calculated by 1) including F_H (FRF), and 2) neglecting F_H (FRF_{NH}) according to the method described above. For each FRF the STM stiffness was calculated by averaging the first three excited frequencies. In addition, the magnitudes were averaged over a low (0.05-0.95 Hz), mid (1.00-2.35 Hz) and high (2.40-4.95 Hz) frequency group, in which the stiffness, damping and inertia respectively dominate the magnitude. Relative errors (RE) were calculated for the STM stiffness and frequency groups by subtracting the FRF_H magnitude from the FRF_{NH} magnitude and dividing by the FRF_{NH} magnitude.

Table 2: Relative errors (RE) expressed as percentage, averaged over participants for the stiffness [0.05-0.35 Hz], low frequencies [0.05-0.95 Hz], mid frequencies [1.00-2.35 Hz] and high frequencies [2.40-4.95 Hz]. The SD represents the standard deviation.

	RE [%]	SD
Stiffness	-0.38	0.35
Low freqs	-0.68	1.16
Mid freqs	0.66	7.55
High freqs	-14.7	25.5

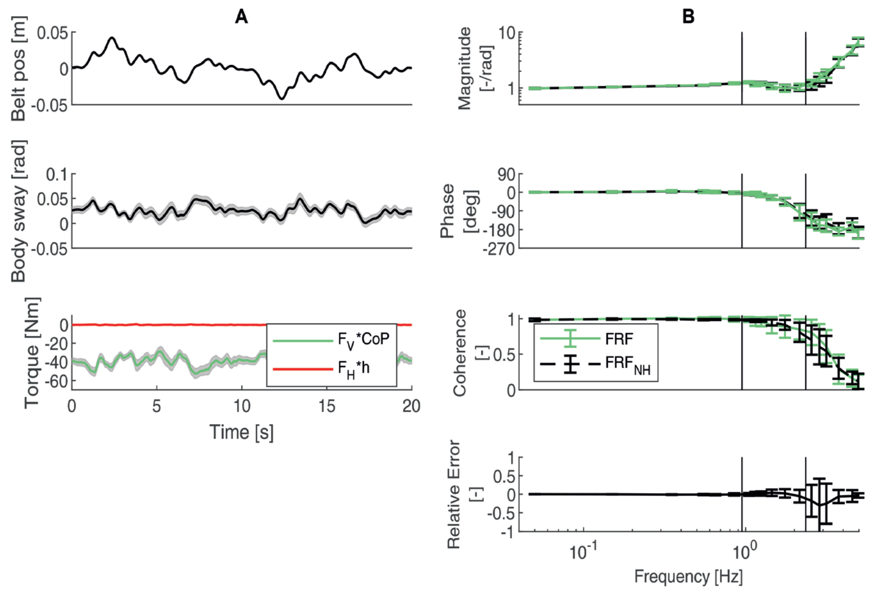

Figure 4: A. Mean belt position (top), body sway (middle) and torque (bottom) time series calculated by neglecting horizontal ground reaction forces (green) and neglecting vertical ground reaction forces (red) of one typical participant, averaged over 24 segments. The grey areas represent the standard deviation. B. Mean normalized magnitude (top), phase (2nd row), coherence (3rd row) and relative error (bottom) of the frequency response function, calculated by including horizontal ground reaction forces (black) and by neglecting horizontal ground reaction forces (green), averaged over participants. The error bars indicate the standard deviation.

Results

Validation

Linear regression on the data resulted in

$$T = 4.78\theta + 0.03 \quad (7)$$

with θ the angular rotation and 4.78 representing the STM stiffness in Nm/rad, with a standard error of (±0.06) (Figure 2). The time series of the belt position, body sway and torque were as expected (Figure 3). The STM stiffness of 5.08±0.22 Nm/rad, estimated using system identification, was within 6% of the joint stiffness calculated with the regression method (4.78 Nm/rad).

Effect of horizontal ground reaction forces

All participants showed a low contribution of F_H and h to the calculation of the ankle torque compared to the contribution of F_V and CoP (Figure 4). This resulted in a high VAF of 99.9±0.2% averaged over participants. Body sway increased with perturbation amplitude and resulted in larger F_H and CoP (not shown). The relative contribution of F_H to the ankle torque was constant over amplitude, resulting in VAFs between 99.8±0.3% and 99.9±0.1% (Table 1).

The FRF magnitudes, normalized for the gravitational stiffness (gravitational constant multiplied by mass and distance between CoM and ankle joint) and averaged over participants, were as expected, with high coherence for the low frequencies (Figure 4). The low frequencies, representing the stiffness, had values around 1, indicating that the stiffness provided by the human was sufficient to compensate the pull of gravity. There was a small dip within the mid frequencies, representing the damping, and the magnitudes increase at the high frequencies, representing the inertia. The FRF_{NH} magnitude is almost identical to the normalized FRF_{NH} magnitude, especially for the lower frequencies. There is no difference in STD stiffness between the STD stiffness of FRF_{NH} and FRF (error relative to FRF_{NH} (RE) = -0.38%)(Table 2). The RE is -0.68, 0.66 and -14.7% for the low, mid and high frequencies respectively. The phases of FRF_{NH} and FRF are similar (Figure 6). REs were similar over different perturbation amplitudes (not shown).

Discussion

Validation

The STM stiffness of the inverted pendulum estimated with the regression method was similar to the STM stiffness estimated with the system identification method (difference 6%). This indicates that the STM stiffness could be estimated using the system identification method in combination with support surface translations.

Effect of horizontal ground reaction forces

The effect of horizontal ground reaction forces on the ankle torque was negligible as more than 99.8% of the ankle torque was explained by the vertical ground reaction forces and CoP. This effect is independent of the perturbation amplitude as long as the induced body sway stays within a range of 1.1-6.4° ptp, a common range in literature [9,10,20-23]. The effect of horizontal ground reaction forces on the FRF of the STM dynamics were small (|RE|<15%), especially for the STM stiffness (|RE|<0.5%), and the low and mid frequencies (|RE|<1%).

To conclude, the STM stiffness of an inverted pendulum can be estimated using support surface translations in combination with system identification. Secondly, within the induced body sway angles, the horizontal ground reaction forces play a minor role in human balance and can be omitted to calculate the ankle torque, thereby still resulting in a reliable estimation of the STM stiffness and dynamics. This allows for the use of less complex treadmills that only measure vertical ground reaction forces and the centre of pressure.

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PART II

Balance assessment in minor strokes

5

Minor stroke, serious problems: the impact on balance and gait capacity, fall rate, and physical activity

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To be submitted

Abstract

Importance. Recent findings suggest that even after minor stroke persistent balance problems may occur. This notion deserves further investigation, because poor balance is a risk factor for falls and reduced activity levels. *Objective.* To test the hypothesis that people with minor stroke show persistent balance and gait problems, elevated fall risk, and decreased physical activity levels compared to healthy controls. *Design.* Longitudinal observational cohort study with 6-month follow-up period. *Setting.* General hospitals and community in the Netherlands. *Participants.* Participants were included if they had sustained a unilateral supratentorial transient ischemic attack (TIA) or stroke longer than 6 months ago that resulted in motor and/or sensory loss in the contralesional leg. They needed to have shown (near-)complete motor recovery as indicated by a score ≥24 points on the Fugl-Meyer Assessment – Lower Extremity (FMA-LE; range: 0-28). *Exposure.* None. *Main Outcomes.* Mini-Balance Evaluation Systems Test (mini-BESTest), Timed Up and Go test (TUG), 10-Meter Walking Test (10-MWT), 6-item short version of Activity-specific Balance Confidence scale (6-ABC), fall rate, daily physical activity (total time and intensity). *Results.* 245 eligible persons with stroke and 88 healthy controls were screened for eligibility. Of these, 64 participants with minor stroke and 50 healthy age-matched controls were included. Thirty-six participants with minor stroke (56%) showed full leg motor recovery (FMA-LE: 28 and Motricity Index – Lower Extremity: 100). Compared to controls, participants with minor stroke scored significantly lower on the mini-BESTest (24.2±2.3 vs. 26.1±2.1 points), were slower on the TUG (10.0±2.0 vs. 8.6±1.1 seconds), had lower walking speed (1.31±0.22 vs. 1.45±0.16 m/s), and lower 6-ABC scores (79±19 vs. 89±10%). All statistical differences persisted in the subgroup of full recoverers. Participants with minor stroke fell more than twice as often as healthy controls (1.1 vs. 0.52 falls per person-year). No between-group differences were found for total time of physical activity, but intensity of physical activity was 6% lower in participants with minor stroke. *Conclusions.* Individuals in the chronic phase after minor stroke with (near-)complete clinical motor recovery of the paretic leg may still demonstrate deficiencies in balance and gait capacities, a relatively high fall frequency, and lower intensities of physical activity. These results may point at an unmet clinical need in this population.

Introduction

Approximately 1.1 million persons in Europe suffer a stroke each year [1]. Despite improvements in acute treatment over the last decades, a stroke still contributes to a significant loss in disability-adjusted life years [2]. Currently, post-stroke rehabilitation is mainly aimed at improving functional status in stroke survivors, focusing on disabilities that are visible to the naked clinical eye. Nevertheless, a large part (i.e., 79%) of all stroke patients initially present with motor symptoms – such as a paresis of the contralesional arm and/or leg – that resolve relatively quickly, ultimately resulting in (near-)absent motor symptoms [3]. Generally, these individuals have sustained a so-called ‘minor stroke’. Compared to more severely affected individuals, persons after minor stroke have received very little attention in the scientific literature or clinical guidelines with regard to the possible sensorimotor consequences.

Post-stroke motor impairments often lead to a decline in balance and gait capacities that subsequently increase the risk of falling in daily life [4]. Falling is a major problem in moderately to severely affected individuals after stroke, as their fall risk is two to ten times higher compared to healthy individuals [4]. So far, it is unknown whether persons with (near-) complete clinical recovery of motor impairments after stroke also have an increased fall risk. This deserves further investigation, because falls can have serious physical and psychological consequences such as fractures and fear of falling. Fractures were reported in 0.6 to 8.5% of the post-stroke falls [4], whereas 88% of the individuals who had received inpatient stroke rehabilitation developed fear of falling following a fall [5]. Both consequences often lead to daily life activity limitations [4], thereby contributing to restricted social participation and reduced cardiovascular fitness after stroke. As physical activity levels in community-dwelling chronic stroke survivors are already low in terms of both duration and intensity [6], further deconditioning can easily contribute to loss of independence. Thus far, it is unknown whether physical activity levels are also reduced in persons after minor stroke.

Preliminary studies found that persons after minor stroke may have persistent balance and gait problems [7-9]. Since these studies included rather small groups of minor stroke individuals [7,8] or specifically focused on balance control [8,9], an extensive and comprehensive evaluation of the long-term effects of a minor stroke on balance, gait, falls, and daily physical activity levels is still lacking. We therefore conducted a longitudinal observational cohort study of individuals in the chronic phase after minor stroke to test the hypothesis that these persons have persistent balance and gait problems, elevated fall risk, and decreased physical activity levels compared to healthy age-matched controls.

Methods

Design, setting and participants

We conducted a longitudinal observational cohort study with a baseline clinical assessment and 6 months follow-up. Potential participants who had sustained a minor stroke were recruited from the outpatient departments of Rehabilitation and Neurology at several general hospitals in the Netherlands (Radboud university medical center in Nijmegen, Rijnstate Hospital in Arnhem, Reinier de Graaf in Delft), and through advertisements in local newspapers. They needed to be in the chronic phase (> 6 months) after a minor stroke. In this study, a minor stroke was defined as a unilateral supratentorial transient ischemic attack (TIA) or stroke that had resulted in motor and/or sensory loss in the contralesional leg at stroke onset, with (near-)complete clinical motor recovery of the paretic leg as defined by the Fugl-Meyer Assessment – Lower Extremity score ≥ 24 (FMA-LE; range: 0-28, motor selectivity items only) at study inclusion. Participants were excluded if they 1) suffered from other neurological or musculoskeletal (e.g., joint arthrosis or replacement) problems; 2) had severe cognitive problems (Montreal Cognitive Assessment (MoCA) < 24) [10]; 3) used psychotropic medication; or 4) had persistent unilateral spatial neglect (Behavioral Inattention Test – Star Cancellation Test < 44) [11]. Age-matched healthy control participants were recruited from the community and from a database available at the department of Rehabilitation that contains contact details of healthy persons interested to participate in research. At inclusion, the following demographics and clinical characteristics were determined for the characterization of both study groups: sex, age, Body Mass Index (BMI), MoCA as a measure of cognition, Quantitative Vibration Threshold (QVT; range: 0-8) of the medial malleolus and first metatarsophalangeal joint as a measure of deep sensibility of the paretic leg (minor stroke) or the average of both legs (healthy control) [12,13], and Functional Ambulation Categories (FAC; range: 0-5) as a measure of ambulation capacity [14]. Specifically for the participants with minor stroke, we additionally recorded duration of initial hospital admission, location of discharge, prescription of home-based physiotherapy, time since stroke, type of stroke, affected body side, FMA-LE as a measure of selective motor control of the paretic leg, and the Motricity Index – Lower Extremity score (MI-LE; range: 0-100) as measure a of strength of the paretic leg. Written informed consent was obtained from all participants. The study protocol was approved by the Medical Ethical Board of the region Arnhem-Nijmegen and all procedures were conducted in accordance with the Declaration of Helsinki.

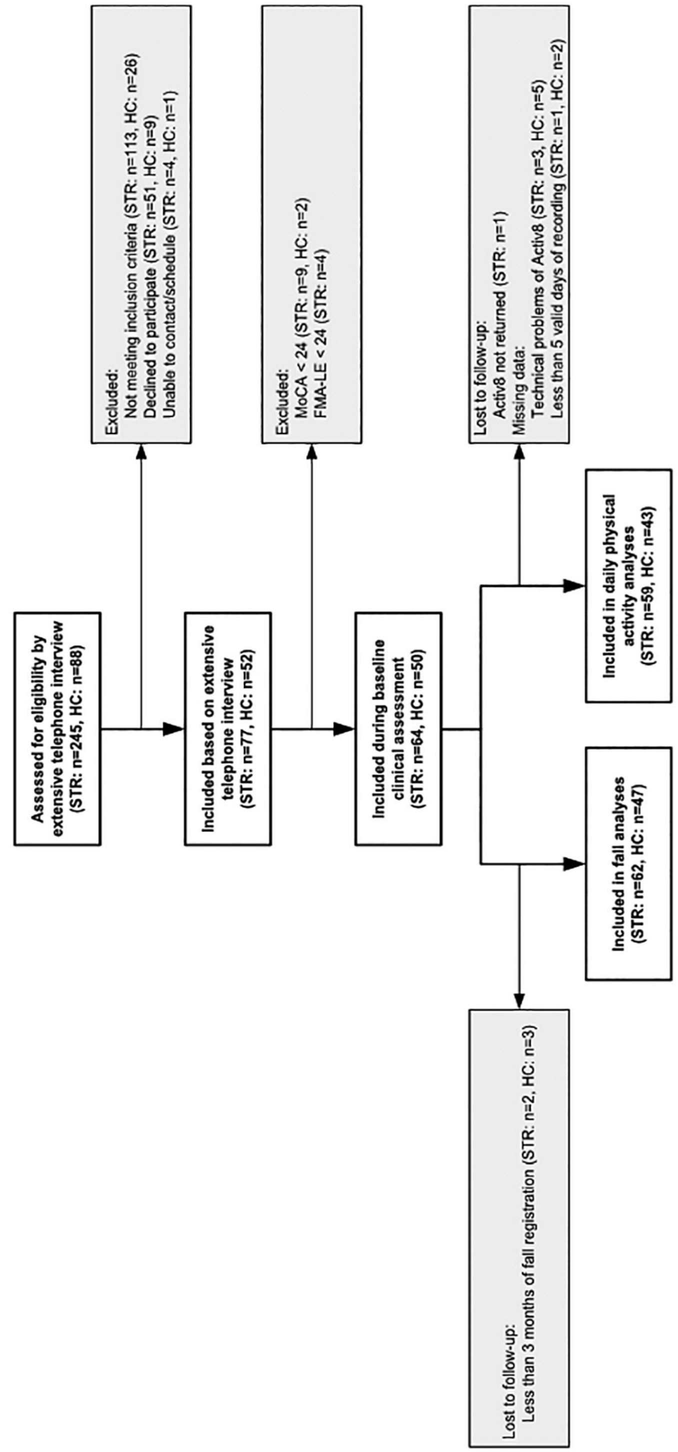

Figure 3: Flow of participants. STR: participant with minor stroke; HC: healthy control participant; MoCA: Montreal cognitive Assessment; FMA-LE: Fugl-Meyer Assessment – Lower Extremity; Activ8: Activ8 Physical Activity Monitor.

5

Outcome measures

Balance and gait

At baseline, participants performed the following clinical tests: 1) the mini-Balance Evaluation Systems Test (mini-BESTest; range: 0-28) that focuses on static and dynamic balance [15]; 2) the Timed Up and Go test (TUG) to quantify functional performance [16]; 3) the 10-Meter Walking Test (10-MWT) to assess comfortable walking speed; and 4) the 6-item short version of the Activity-specific Balance Confidence scale (6-ABC; range: 0-100%) to assess balance confidence [17].

Falls

Falls were prospectively registered for 6 months on a monthly basis using fall calendars [18]. Each fall calendar was provided with a stamped and addressed envelope. Participants who did not return the fall calendar within 2 weeks were called to determine if any falls had occurred. A fall was defined as an unexpected event which resulted in body contact with the ground, floor or a lower level surface [19]. Falls during sports or caused by a high-energy external force (e.g., a collision) or loss of consciousness were excluded. The primary outcome for falls was fall rate per person-year. As secondary outcomes we included the proportion of fallers and the number of injurious falls during the 6-month follow-up.

Daily physical activity

Daily physical activity levels were registered during the week following baseline assessment for 24 hours a day using the professional version of the Activ8 Physical Activity Monitor (Activ8; Remedy Distribution Ltd., Valkenswaard, The Netherlands). The Activ8 is a small (30x32x10 mm) and lightweight (20 g) one-sensor device with a triaxial accelerometer that has previously been validated in stroke patients [20]. It was attached with Tegaderm™ skin tape to the thigh of the non-paretic (minor stroke) or dominant (healthy control) leg. This waterproof attachment allowed participants to swim and shower while wearing the device. Participants received no feedback about their daily physical activity levels. The measures of activity were total time (minutes/day) of daily physical activity (i.e., minutes of classified walking, cycling, and high-intensity activities (i.e., mainly running)), and the intensity of daily physical activity (counts/minute during periods of walking, cycling, and high-intensity activities).

Table 1: Participants' characteristics. MoCA: Montreal Cognitive Assessment (range: 0-30); QVT: Quantitative Vibration Threshold (range: 0-8); MTP: metatarsophalangeal joint; FAC: Functional Ambulation Categories (range: 0-5); FMA-LE: Fugl-Meyer Assessment – Lower Extremity (range: 0-28); MI-LE: Motricity Index – Lower Extremity (range: 0-100). [a] Subgroup of participants with minor stroke with complete clinical motor recovery of the paretic leg (i.e., FMA-LE=28 and MI-LE=100). [b] p=0.022.

	All participants with minor stroke (n=64)	Minor stroke full recoverers (n=36)[a]	Healthy control participants (n=50)
Sex (male/female); *n*	39/25	20/16	24/26
Age (years); *mean (range)*	63.8 (40-85)	61.2 (40-76)	63.6 (42-82)
Body Mass Index; *mean (range)*	26.8 (19.0-39.0)[b]	26.4 (19.0-39.0)	25.0 (19.5-33.5)[b]
MoCA; *median (range)*	27 (24-30)	27 (24-30)	29 (24-30)
QVT-affected medial malleolus; *median (range)*	5.4 (0-8)	5.4 (0-8)	5.8 (2.5-8)
QVT-affected first MTP; *median (range)*	5.3 (0-8)	5.4 (0-8)	5.6 (0-8)
FAC; % FAC 5	100	100	100
Duration of hospital admission (≤3 days/>3 days/unknown); *n*	38/23/3	21/13/2	
Location of discharge (home/inpatient rehabilitation center); *n*	61/3	35/1	
Home-based physiotherapy (yes/no); *n*	35/29	16/20	
Time since stroke (months); *mean (range)*	38 (6-186)	45 (6-186)	
Type of stroke (ischemic/hemorrhagic); *n*	59/5	34/2	
Affected body side (left/right); *n*	34/30	18/18	
FMA-LE; *median (range)*	28 (24-28)	28	
MI-LE; *median (range)*	100 (63-100)	100	

Statistical Analysis

The Mann-Whitney U test was used to compare demographic and clinical characteristics between groups. To determine whether balance and gait outcomes and daily physical activity measures differed between the participants with minor stroke and healthy controls, we conducted analysis of covariance (ANCOVA) with age as covariate. To determine whether fall rates differed between participants minor stroke and healthy controls, we used Poisson regression analyses with number of falls as dependent variable and group (minor stroke / healthy control) as independent variable. All participants with ≥3 months fall registration were included in the analyses. We conducted a Chi-square analysis to compare the proportion of fallers between groups.

Furthermore, we repeated the above analyses on a subgroup of participants with complete clinical motor recovery of the paretic leg (i.e., FMA-LE=28 and MI-LE=100; further referred to as the *full recoverers*). Note that this secondary analysis was not applied to the fall data because of insufficient power.

As tertiary analysis we studied static and dynamic balance control and daily physical activity in more depth. A Chi-square test was used to compare the percentage of participants with minor stroke, full recoverers, and healthy controls that obtained the maximal score on each item of the mini-BESTest. To determine whether total time and intensity of each physical activity sub category (i.e., walking, cycling, high-intensity activities) differed between groups, we conducted analysis of covariance (ANCOVA) with age as covariate.

All statistical analyses were performed in SPSS (version 25.0). P-values <0.05 were considered statistically significant.

Results

Between August 2016 and July 2018, a total of 245 community-dwelling persons in the chronic phase (> 6 months) after minor stroke and 88 healthy controls were assessed for eligibility. After an extensive telephone interview and physical examination for verifying the inclusion and exclusion criteria, 64 participants with minor stroke and 50 healthy controls were included. Figure 1 shows the flow diagram with the numbers and reasons of participants who were excluded, who were lost to follow-up, and who showed missing data. Table 1 shows the participant characteristics. Following their acute stroke, 95% of the participants with minor stroke were discharged home following a short (median ≤ 3 days) hospital admission, and 55% subsequently received home-based physiotherapy. Thirty-six of the participants with minor stroke (56%) were identified as full recoverers, as they had obtained maximal scores on both the FMA-LE and MI-LE. All participants were able to stand and walk independently on an irregular surface without supervision (FAC 5). No significant differences in sex, age, cognition, or deep sensibility were found between groups, but the BMI was higher for participants with minor stroke compared to controls.

Table 2: Balance and gait, falls, and daily physical activity outcomes of all participants. *Values are presented as mean (standard deviation). Mini-BESTest (range: 0-28): mini-Balance Evaluation Systems Test; TUG: Timed Up and Go test; 10-MWT: 10-Meter Walking Test; 6-ABC (range: 0-100): 6-item short version of the Activity-specific Balance Confidence scale. [a] Comparison between all participants with minor stroke and healthy control participants; [b] Subgroup of participants with minor stroke with complete clinical motor recovery of the paretic leg; [c] Comparison between full recoverers and healthy control participants.

	All participants with minor stroke	Healthy control participants	P-value[a]	Minor stroke full recoverers[b]	P-value[c]
Balance and gait					
Mini-BESTest*	24.2 (2.3)	26.1 (2.1)	**<0.001**	24.8 (2.1)	**0.001**
TUG (s)*	10.0 (2.0)	8.6 (1.1)	**<0.001**	9.4 (1.4)	**0.002**
10-MWT (m/s)*	1.31 (0.22)	1.45 (0.16)	**<0.001**	1.37 (0.16)	**0.009**
6-ABC*	79 (19)	89 (10)	**0.001**	80 (21)	**0.003**
Falls					
Number of falls (per person-year)	1.1	0.52	**0.023**		
Proportion of fallers (%)	37	21	0.094		
Number of falls (n)	33	12			
Injurious falls (no/minor/severe)	15/17/1	4/7/1			
Daily physical activity					
Total time active (minutes/day)*	171 (55)	179 (44)	0.499	183 (51)	0.871
Total intensity active (counts/minute)*	1498 (200)	1598 (239)	**0.030**	1553 (221)	0.260

5

Balance and gait

Participants with minor stroke scored significantly lower on the mini-BESTest than healthy control participants (24.2±2.3 vs. 26.1±2.1 points, F(1)=24.647, p<0.001; Table 2). In fact, 73% of the persons after minor stroke did not reach near-maximal scores (i.e., 26-28 points), whereas this was the case for only 26% of the healthy control participants (Figure 2). These results were paralleled by a 10% lower balance confidence score (as measured with the 6-ABC) in the participants with minor stroke (F(1)=12.387, p=0.001). Likewise, to complete the TUG, participants with minor stroke were on average 1.4 seconds slower than controls (F(1)=21.854, p<0.001), and their comfortable walking speed was slower by on average 0.13 m/s (F(1)=14.496, *p*<0.001). All these statistically significant differences persisted in subgroup analyses of the full recoverers (Table 2). Supplementary Table 1 shows for each item of the mini-BESTest the percentage of all participants with minor stroke, healthy controls, and full recoverers that obtained the maximal item score. The percentages of participants with minor stroke who obtained the maximal score on the items standing on one leg, compensatory stepping in the backward direction, compensatory stepping in the sideward direction, stance with eyes closed on foam surface, pivot turn, and TUG with and without dual task were lower compared to healthy control participants ($\chi^2(1) \geq 4.907$, $p \leq 0.027$).

Falls

Participants with minor stroke fell more than twice as often as healthy control participants (1.1 vs. 0.52 falls per person-year, *p*=0.023; Table 2). A trend was found for a higher percentage of fallers in the minor stroke compared to the control group (37 vs. 21%, $\chi^2(1)=3.170$, *p*=0.094). More than half of the falls (i.e., 52% in the minor stroke and 58% in the control group) resulted in injuries like cuts, bruises, pain and joint sprains. Severe injuries (i.e., dislocated joint and fracture) were rare with only one case in each group.

Daily physical activity

Table 2 shows the daily physical activity outcomes for all participants with minor stroke, healthy controls, and full recoverers. No between-group differences were found for the total time of physical activity (F(1)=0.461, *p*=0.499), whereas the intensity of physical activity was 6% lower in participants with minor stroke compared to controls (F(1)=4.870, *p*=0.030). In addition, no between-group differences were found in the total time or intensity of physical activity for the subgroup of full recoverers compared to controls (F(1)≤1.289, p≥0.260). Supplementary Table 2 shows the total time and intensity for each physical activity subcategory for all participants with minor stroke, healthy controls, and full recoverers. Except for a lower intensity of cycling in the total minor stroke group compared to the healthy control group (F(1)=5.462, *p*=0.021), no between-group differences were found in total time or intensity for each physical activity subcategory (F(1)≤3.286, *p*≥0.073).

Discussion

To the best of our knowledge, this is the first longitudinal cohort study that investigated balance and gait outcomes as well as falls and daily life physical activity in a group of carefully selected individuals in the chronic phase after minor stroke

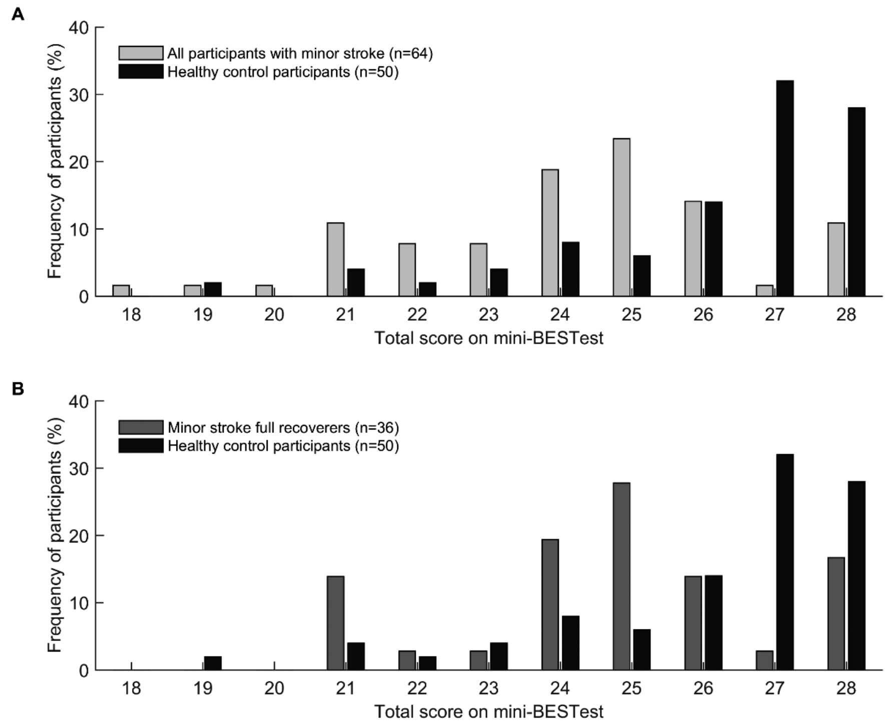

Figure 1: Frequencies of each score obtained on the mini-BESTest for **(A)** all participants with minor stroke vs. healthy control participants; and for **(B)** the subgroup of participants with minor stroke with complete clinical motor recovery of the paretic leg vs. healthy control participants.

(i.e., individuals who had some motor and/or sensory loss in the contralesional leg at stroke onset and showed (near-) complete motor recovery at inclusion as indicated by a score ≥24 points on the FMA-LE). We found that the vast majority of individuals after minor stroke had balance and gait problems. Remarkably, these problems were also present in the subgroup of full recoverers (i.e., individuals after minor stroke with maximal scores on both the FMA-LE and MI-LE). In addition, participants with minor stroke fell more than twice as often as healthy age-matched controls and performed daily life activities at a lower intensity.

Balance and gait

Not only were balance scores on the mini-BESTest moderately but significantly lower in participants with minor stroke compared to healthy controls, we also found that 73% of the individuals with minor stroke did not reach near-maximal scores. These balance problems were accompanied by worse performance on the TUG and lower comfortable walking speed in participants with minor stroke compared to healthy controls. In a previous study, Batchelor et al. also found deficits on the TUG with and without dual task, lower comfortable and fast walking speeds, increased sway during turning, increased turn time, and deficits in stepping in a less-strictly selected group of 12 individuals after minor stroke [7]. Merely three of these 12 persons (i.e., 25%) suffered from stroke-related motor impairments of the lower extremity at stroke onset, with only two persons reporting lower limb weakness or numbness. In contrast to our study, a substantial proportion of their participants had severe cognitive impairment as shown by a mean MoCA score of 22.2±3.1 points. In the present study, we included 64 individuals with minor stroke who *all* showed motor and/or sensory loss in the paretic leg at stroke onset and *none* of whom had serious cognitive problems at study inclusion. This careful selection of participants with minor stroke makes it more likely that the observed balance problems are indeed related to the clinically identified stroke itself and not to pre-existent vascular cerebral microlesions or white matter disease. Coherent with the current findings, a previous study of our group has shown that individuals after stroke with (near-)complete clinical recovery of leg motor impairments may still show an asymmetric kinetic contribution of the legs to standing balance control in favor of the non-paretic leg [9]. Also this observation points at persistent balance problems being caused by the stroke itself rather than by diffuse white matter lesions. Importantly, in the present study, we found that even a subgroup of full recoverers (as defined by maximum FMA-LE and MI-LE scores) demonstrated lower balance and gait test scores than healthy control participants, which indicates that our results were not merely driven by individuals with residual – clinically identifiable – leg motor impairments. Together, these findings suggest that complete clinical motor recovery of the non-paretic leg – as assessed with common clinical measures such as the FMA and the MI – does not prove that the leg motor control needed for balance and gait is entirely restored.

Falls

Our participants with minor stroke showed an elevated fall rate of 1.1 falls per person-year, which is within the range of fall rates previously reported for more severely affected individuals in the chronic phase after stroke [21-23]. In addition, 37% of our participants with minor stroke fell at least once during the 6-month observation period. This proportion of fallers is also within the range of 26% to 51% as observed for more severely affected individuals during the same time period in various phases post stroke [24]. The finding that people with minor stroke appear to have a similar risk of falling compared to more affected individuals may be explained by their relatively high level of physical activity. Indeed, in terms of duration of daily physical activity, our participants with minor stroke were as active as healthy controls and, therefore, had a larger exposure to risky situations

compared to more affected stroke survivors that are less physically active [25]. In our study population, the reported falls generally did not have serious physical consequences, since no or relatively ‘minor’ injuries were reported as a result of 96% of the falls. Yet, a history of falls is a strong predictor for future falls [24], thus causing an incremental risk of fall-related injuries. In addition, the psychological consequences of falling should not be underestimated. Many individuals who have fallen after discharge from inpatient rehabilitation develop fear of falling [5]. Coherent with this notion, our participants with minor stroke had on average 10% lower balance confidence scores compared to healthy controls. Importantly, a lower balance confidence may lead to avoidance of daily life activities, which may lead to a vicious circle of deconditioning, loss of balance capacity, and increased fall risk.

Daily physical activity

Although no between-group differences in total time of physical activity were found, the intensity of physical activity was 6% lower in our participants with minor stroke compared to the healthy control participants. The lower intensity in the minor stroke group could be the consequence of their poorer balance and functional performance (i.e., lower scores on mini-BESTest and TUG), forcing them to perform activities more carefully. In addition, their lower comfortable walking speed may also partly explain the lower intensity of daily life activities. The lack of differences in total time of physical activity – despite deficits in balance and gait and an increased fall rate – seems to suggest that people with minor stroke do not avoid daily life activities. This was, however, not true for high-intensity activities (mainly running), since both the proportion of participants with minor stroke who performed any high-intensity activities (i.e., 36% vs. 72% in controls), as well as the proportion of participants with minor stroke who performed high-intensity activities for more than one minute per day (i.e., 8% vs. 33% in controls) were considerably lower compared to the healthy control participants (see supplementary Table 2). As people after minor stroke already have an increased cardiovascular risk profile [26] (also indicated by their BMI-values in Table 1), being physically active at sufficiently high intensity is of particular importance for reducing systolic blood pressure and other cardiovascular risk factors [27]. Furthermore, it has previously been shown that a higher intensity of leisure time activities is associated with a lower incidence of cardiovascular diseases [28]. Taken together, individuals after minor stroke should be stimulated to perform more high-intensity activities, but always with a particular eye for safety because of their increased fall risk.

Clinical implications

This study highlights the potential impact of a minor stroke on balance and gait capacity, fall risk, and (intensity of) daily life physical activity. Noteworthy, balance and gait problems after minor stroke were found on all clinical tests, i.e., the mini-BESTest, TUG, and 10-MWT. Currently, the Berg Balance Scale (BBS) is frequently used in clinical practice for assessing balance [29], but this test is not sensitive enough to detect balance deficits in relatively well-recovered individuals after stroke due to well-known ceiling effects [30]. Therefore, instead of the BBS, we recommend using the mini-BESTest as an alternative test for assessing balance capacity in the population with (minor) stroke as well as in other neurological populations with relatively mild motor problems.

Balance and gait deficits are the key risk factors for falling [4]. Given the double fall rates in our minor stroke population, these balance and gait deficits – that were present in all four subdomains of the mini-BESTest (see supplementary Table 1) – appear to be clinically relevant. Therefore, persons with minor stroke may potentially benefit from training programs aimed at improving balance and/or gait. A systematic review and meta-analysis found that improvements in balance capacity following exercise therapy are particularly achieved by challenging and task-specific balance training, functional weight-shifting and/or gait training [31]. A promising example is the training of dynamic balance responses to external perturbations, so-called perturbation-based balance training [32-34].

Our participants with minor stroke were as active as controls, but performed activities at a lower intensity. To optimize daily activity patterns and reduce the cardiovascular risk profile after minor stroke, life style interventions in this population should especially focus on increasing the intensity of physical activity [27,28].

Limitations

We used a ‘minor stroke’ definition that was based on clinically absent or limited residual motor impairments in the paretic leg (as determined by the FMA-LE), as well as on the absence of severe cognitive problems (as determined by the MoCA) at study inclusion. As we included our participants at a minimum of 6 months after stroke onset, our criteria should not be confused with the criteria that are commonly used for classifying stroke severity on admission or at discharge from hospital, such as a score of ≤ 3 on the National Institute of Health Stroke Scale (NIHSS) (35) or ≤ 2 on the modified Ranking Scale (mRS) [36]. Due to our community-based recruitment of participants with minor stroke, we did not have insight into their initial mRS scores or NIHSS scores. Nevertheless, given the fact that 95% of our participants were discharged home following a short (median ≤ 3 days) hospital admission after stroke onset, it is likely that the majority had been classified as ‘minor stroke’ according to these commonly used rating scales for stroke severity [35,36].

An important finding was that even individuals in the chronic phase after minor stroke were still more prone to falling than age-matched healthy controls. Ideally, we would have collected more specific information about fall circumstances and precipitating factors to gain insight into the etiology of falls in this population and to identify specific targets for intervention. Therefore, the determinants of falling need to be established in future studies.

Final remarks

Even individuals in the chronic phase after minor stroke, characterized by (near-)complete clinical motor recovery of the paretic leg, may show substantial deficits in balance and gait performance, increased fall risk, and lower intensity of daily life activities. To optimize care for these seemingly well-recovered individuals, a comprehensive assessment of balance and gait capacities during a regular follow-up visit would be helpful for identifying those who are in need of task-specific balance and/or gait training to reduce their fall risk. In addition, assessment of both the time and intensity of individual physical activity may identify those who may benefit from a targeted lifestyle intervention.

Supplement

Supplementary Table 1: Percentage of participants with maximal scores on each item of the mini-Balance Evaluation Systems Test (mini-BESTest). [a] Comparison between all participants with minor stroke and healthy control participants; [b] Subgroup of participants with minor stroke with complete clinical motor recovery of the paretic leg; [c] Comparison between full recoverers and healthy control participants.

Subdomain	Item	All participants with minor stroke	Healthy control participants	P-value[a]	Minor stroke full recoverers[b]	P-value[c]
Anticipatory postural adjustments	1. Sit to stand	100	100	-	100	-
	2. Rise to toes	90.6	92.0	0.797	100	0.082
	3. Stand on one leg	50.0	82.0	**<0.001**	61.1	**0.031**
Postural responses	4. Compensatory stepping – forward	70.3	80.0	0.239	61.1	0.054
	5. Compensatory stepping – backward	39.1	62.0	**0.015**	36.1	**0.018**
	6. Compensatory stepping – sideward	51.6	72.0	**0.027**	47.2	**0.020**
Sensory orientation	7. Stance, eyes open, firm surface	100	100	-	100	-
	8. Stance, eyes closed, foam surface	64.1	94.0	**<0.001**	86.1	0.214
	9. Stance, eyes closed, incline	93.8	98.0	0.272	97.2	0.813
Balance during gait	10. Change in gait speed	95.3	100	0.121	94.4	0.092
	11. Walk with head turns	98.4	96.0	0.420	100	0.225
	12. Pivot turn	65.6	86.0	**0.013**	72.2	0.113
	13. Step over obstacle	93.8	96.0	0.593	94.4	0.735
	14. Timed Up and Go test with and without dual task	43.8	66.0	**0.018**	50.0	0.136

Supplementary Table 2: Total time and intensity of walking, cycling, and high-intensity activities. Values are presented as mean (standard deviation). [a] Comparison between all participants with minor stroke and healthy control participants; [b] Subgroup of participants with minor stroke with complete clinical motor recovery of the paretic leg; [c] Comparison between full recoverers and healthy control participants. [d] Not all participants performed high-intensity activities during the monitoring week; the percentage of participants who did perform these activities were 36%, 72%, and 50% for all participants with minor stroke, healthy controls, and full recoverers, respectively. Of the participants who performed high-intensity activities, only 8% of all participants with minor stroke, 33% of the healthy controls, and 15% of the full recoverers spent more than one minute per day on such activities.

	All participants with minor stroke	Healthy control participants	P-value[a]	Minor stroke full recoverers[b]	P-value[c]
Total time (minutes/day)					
Walking	151 (52)	153 (39)	0.897	162 (51)	0.458
Cycling	19 (24)	24 (18)	0.282	20 (19)	0.172
High-intensity activities	1 (5)	2 (5)	0.379	2 (7)	0.804
Total intensity (counts/ minute)					
Walking	1442 (177)	1508 (166)	0.073	1485 (185)	0.406
Cycling	1695 (198)	1787 (183)	**0.021**	1721 (225)	0.114
High-intensity activities[d]	4809 (310)	4841 (385)	0.734	4859 (324)	0.852

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6

Detection of balance control asymmetries in people with minor stroke

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To be submitted

Abstract

Stroke survivors often have impaired balance and mobility. Their impaired balance may (at least partly) be caused by subtle changes in balance control, where the nonparetic leg compensates for the paretic leg, resulting in an asymmetric balance control strategy. In this paper we investigated whether subtle control asymmetries around the ankle joint can be detected in minor stroke participants, in which balance measure these subtle changes in control asymmetries are most apparent and under which condition they could best be measured. Balance control of 54 minor stroke and 37 control participants was assessed. In static and perturbed conditions, both performed with eyes open and eyes closed, 11 different balance symmetry measures were assessed. The balance symmetry measures included centre of pressure (CoP) related measures, torque related measures and the dynamic balance contribution. To maximize between-group contrasts in the symmetry measures, principal component analysis was performed for each condition. Our results show that none of the balance symmetry indices were significantly different between stroke and control participants. However, when the symmetry indices, measured during the perturbed condition with eyes closed, were combined according to principal component analysis, the resulting first principal component score was significantly higher for stroke participants. The first principal component includes symmetry indices of the mean dynamic balance contribution or torque root-mean-square and root-mean-square of anterior-posterior CoP position and velocity, i.e. symmetry indices indicating control in anterior-posterior direction. These results indicate that subtle changes in control asymmetry of minor stroke participants may not be demonstrated by measuring individual balance measures, but can be detected when the dynamic balance contribution or torque and CoP position and velocity are measured during the perturbed trial with eyes closed.

Introduction

Stroke survivors often have impaired balance, which severely impacts mobility. Our recent study (Chapter 5) indicated that even minor stroke participants, i.e. people in the chronic phase (> 6 months) after a stroke who did not receive inpatient rehabilitation, still have serious balance impairments. They scored lower on functional balance and mobility tests such as the Mini-BESTest (assessing static and dynamic balance and gait), Timed Up and Go test (quantifying functional mobility), and the 10-Meter Walking Test (assessing comfortable walking speed) and were more likely to fall, even when motor recovery of the paretic leg was (near-)complete. Impaired balance and mobility might be caused by subtle deficits in balance control around the paretic ankle, which could not be detected by Fugl-Meyer Assessment scores [1-6]. This indicates an asymmetric balance control strategy, where the non-paretic leg compensates for the paretic leg.

A recent study by Roelofs et al. (2018) indicated that 21% of participants with a mild paresis had an asymmetry in the root-mean-square (RMS) of the centre of pressure (CoP) velocity [5]. However, differences in control asymmetry between minor stroke participants and control participants might be more apparent in other asymmetry measures. In the literature, many measures indicating control asymmetry have been used. In addition to body-weight asymmetry, studies often used CoP position and velocity under both feet in either medio-lateral (ML) and/or anterior-posterior (AP) direction [3-7]. CoP data was used to derive the mean, peak or RMS of the CoP data [3-6], and/or to calculated the CoP entropy, i.e. CoP regularity [6], between-limb-synchronisation of the CoP data [3], CoP stability indices [4], or CoP mean frequency and amplitude in the frequency domain [7]. All these studies show significant asymmetry between both legs, with the non-paretic leg contributing more to balance than the paretic leg.

All the above studies used posturography methods to assess static standing balance. Using these methods, a clear asymmetry can be detected, but due to the closed-loop characteristics, the control contribution of each leg to balance cannot be identified [1,8]. System identification techniques using perturbations can disentangle a closed-loop system [9,10]. To quantify the contribution of each leg to balance control in people after stroke, Van Asseldonk et al. (2006) used system identification and support surface translations, thereby identifying the dynamic balance contribution (DBC), i.e. the ratio of ankle torque and body sway, expressed in the frequency domain [1]. The DBC indicated the contribution of each leg to balance control. It was found that the DBC did not show a clear relation with weight bearing. The DBC of the paretic leg was significantly smaller than its relative contribution to weight bearing, i.e. although people put weight on their paretic leg, the contribution of the paretic leg to balance control was relatively low.

Roelofs et al. (2018) previously reported asymmetries in CoP velocity in a subgroup of minor stroke participants. Here we investigated whether the asymmetries in control could also be found in other balance measures. In addition, we investigated in which measure these subtle changes in control asymmetries are most apparent and under which condition they could best be measured. In this study, posturography and system identification measures assessing standing balance of minor stroke participants were determined and compared to control participants in both static and perturbed trials.

Methods

Participants

This study is part of a population-based cohort study with a baseline clinical assessment (at Radboud University Medical Center in Nijmegen or Pieter van Foreest in Delft) and 6 months follow-up regarding falls and physical activity (see Chapter 5). In this paper, only data from the baseline clinical assessment were evaluated. A total of 245 community-dwelling persons in the chronic phase (> 6 months) after a minor stroke and 88 control participants were assessed for their eligibility. These potential participants were recruited from the outpatient departments of Rehabilitation and Neurology at several hospitals in the Netherlands (Radboud University Medical Center in Nijmegen, Rijnstate in Arnhem, Reinier de Graaf Gasthuis in Delft), and through advertisements in local newspapers, between august 2016 and July 2018.

After an extensive telephone interview and physical examination, inclusion and exclusion criteria were verified. Potential participants were included if they had sustained a minor stroke, which was defined as a unilateral supratentorial transient ischemic attack or stroke that had resulted in motor and/or sensory loss in the contralesional leg at minor stroke onset with (almost) complete clinical recovery of leg motor impairments at study inclusion, as defined by the Fugl-Meyer Assessment lower-extremity score without the coordination domain ≥ 24 (FMA-LE; range: 0-28). Potential participants were excluded if they had other neurological or musculoskeletal (e.g. hip or knee replacement) impairments, had severe cognitive problems (Montreal Cognitive Assessment < 24) [11], used psychotropic medication, were not able to stand or walk independently (Functional Ambulation Categories ≥ 4), or had a persistent unilateral spatial neglect (Behavioral Inattention Test – Star Cancellation Test < 44, minor stroke participants only) [12]. Thereafter, 76 minor stroke participants and 51 control participants were included. Participants were included in analysis when the follow-up was completed before December 2018.

Written informed consent was obtained from all participants. The study protocol was approved by the Medical Ethical Board of the region Arnhem-Nijmegen (file number: 2015-2125) and all procedures were conducted in accordance with the Declaration of Helsinki.

Following definitive inclusion, clinical tests were conducted for characterization of the study population. These clinical tests included the Quantitative Vibration Threshold (range: 0-8) of the medial malleolus and hallux as measure of deep sensibility [13,14], and the Motricity Index lower-extremity score (range: 0-100, minor stroke participants only) as measure of leg strength [15].

Table 1: Participant characteristics. MoCA: Montreal Cognitive Assessment (range: 0-30); FMA-LE: Fugl-Meyer Assessment lower-extremity (range: 0-28); QVT: Quantitative Vibration Threshold (range: 0-8); FAC: Functional Ambulation Categories (range: 0-5); MI-LE: Motricity Index lower-extremity (range: 0-100); TUG: Timed Up and Go test; 10-MWT: 10 meter walking test; Mini-BESTest: Mini Balance Evaluation Systems Test (range: 0-28). 'nonpar' and 'par' indicate the non-paretic and paretic leg respectively. N.A.: not applicable. * p < 0.05 was considered significant.

	Control participants (n=37)	Minor stroke participants (n=54)
Affected body side (n: left/right)	N.A.	31 (57%) / 23 (43%)
Sex (n: male/female)	19 (51%) / 18 (49%)	32 (59%) / 22 (41%)
	Mean ± STD	*Mean ± STD*
Age *(years)*	63 ± 10	63 ± 9
Body Mass Index	24.8 ± 2.8	27.0 ± 4.2
MoCA	28.4 ± 1.5	N.A.
FMA-LE	N.A.	27.2 ± 1.3
QVT malleolus *(nonpar/right)*	5.6 ± 2.0	5.2 ± 2.0
QVT malleolus *(par/left)*	5.2 ± 2.2	4.7 ± 2.4
QVT hallux *(nonpar/right)*	5.7 ± 1.6	5.2 ± 1.8
QVT hallux *(par/left)*	5.6 ± 1.6	4.9 ± 2.2
FAC	5 ± 0	5 ± 0
MI-LE *(nonpar/right)*	N.A.	100 ± 0
MI-LE *(par/left)*	N.A.	96.0 ± 8.5
TUG no dual task *[sec]*	8.7 ± 1.1	9.8 ± 1.8 (p=0.007)*
TUG dual task *[sec]*	9.4 ± 1.4	10.9 ± 2.3 (p=0.002)*
10-MWT *[sec]*	6.9 ± 0.7	7.7 ± 1.2 (p=0.003)*
Mini-BESTest	26.0 ± 2.3	24.4 ± 2.1 (p=0.003)*

In addition, several balance and mobility tests were conducted during the clinical assessment: 1) the Mini-Balance Evaluation Systems Test (Mini-BESTest; range: 0-28) to examine static and dynamic balance and gait [16], 2) the Timed Up and Go test to quantify functional mobility [17], 3) the 10-Meter Walking Test to assess comfortable walking speed. Table 1 shows the participant characteristics.

Apparatus and recording

Static and perturbed standing balance was assessed using an instrumented single belt treadmill (N-Mill, Motek Medical, Amsterdam, the Netherlands). During static trials the belt did not move. During perturbed trials, standing balance was perturbed by translations of the belt in anterior-posterior direction. The perturbation was a multisine signal with a period of 20 s, designed to excite 18 specific odd-frequencies between 0.05 and 5 Hz at an interleaved logarithmic frequency grid. The perturbation amplitude was 0.06 m peak-to-peak. Participants wore a safety harness to prevent falling, without constraining normal body sway or providing support or body-oriented information.

Two force plates embedded in the treadmill each recorded two torques around the horizontal AP and ML axes and vertical ground reaction forces under each foot at a sample frequency of 1000 Hz. Eight retroreflective markers were attached to the participants' acromioclavicular joints, major trochanters, lateral epicondyles and lateral malleoli of both left and right side. Additional markers were placed on each treadmill belt. For the measurements in Nijmegen 13 motion capture cameras (Vicon Bonita, Vicon Motion Systems, Oxford, United Kingdom) surrounding the treadmill recorded the marker positions at a sample frequency of 100 Hz; in Delft 8 cameras were used.

Procedure

Participants were instructed to stand, with their feet placed on projected rectangles (0.3 m centre to centre), as normal as possible without moving their feet and with the arms crossed in front of the chest. Static trials of 30 s were recorded for the eyes open condition (EO) (looking straight forward) and eyes closed condition (EC). This was repeated in reversed order, resulting in 2 trials per condition. After two 20 s practice trials with perturbation and eyes open and closed, perturbed trials of 120 s, i.e. 6 periods of the multisine, were recorded for the eyes open condition (EO_P) and eyes closed condition (EC_P). This was repeated in reversed order.

Data analysis

Pre-processing

Data were processed in Matlab version R2016b (MathWorks, Natick, MA, USA). Force plate data were resampled to 100 Hz to match the sample frequency of the marker data. Force plate data and motion capture data were filtered with a second order butterworth lowpass filter with a cutoff frequency of 10 Hz. From the static data, the first and last second were discarded to remove transient effects, leaving 28 s of data for each trial. From the perturbed trial data, the first 15 s and last 5 s were discarded, leaving 100 s of data. Each perturbed trial was cut in 5 segments of 20 s, i.e. the length of one period of the multisine.

Body sway (BS), i.e. the angle of the centre of mass (CoM) with respect to the vertical, was calculated according to Winter et al. [18]; The CoM position in anterior-posterior direction was derived from the marker positions, and the length of the pendulum, i.e. the length of the CoM to the ankle joint, was derived from the static data of the first EO trial. Vertical ground reaction forces of each leg were calculated as percentage of the total vertical ground reaction forces of both feet. The CoP with respect to the ankle position of each foot was calculated in both AP and ML direction. CoP velocities in AP and ML direction of each foot were calculated by taking the derivatives of corresponding CoP positions. The torque of each ankle was calculated with inverse dynamics [19]. Total ankle torque was calculated by the sum of both ankle torques. To calculate outcome measures in time domain the time series were averaged over the 10 segments.

The segments of body sway and ankle torques were transformed to the frequency domain using the fast Fourier transform. Fast Fourier transforms were averaged over the 10 segments. For the perturbed trials, the fast Fourier transforms were used to calculate the frequency response function, which describes the dynamics of the stabilizing mechanism in terms of a magnitude and phase [1,9,10,20,21]. The frequency response function of the total stabilizing mechanism and the frequency response function of the stabilizing mechanisms of each leg were calculated by dividing the fast Fourier transforms of the total ankle torque and ankle torque of each leg respectively to the fast Fourier transform of the body sway. To determine the contribution of each leg to the generation of the total ankle torque, the contribution of the magnitude and phase of each leg to the magnitude of the total body was calculated according to van Asseldonk et al. [1], representing the dynamic balance contribution (DBC).

Outcome measures

As a balance measure for weight bearing in ML direction, the percentage ground reaction forces were averaged over time (F_{perc_mean}). As a balance measure for the forward lean torque, the ankle torques were averaged over time (T_{mean}). As a balance measure for control in ML direction, the CoP position and velocity in ML direction were centred, i.e. the mean over time was subtracted, and the RMS was calculated ($COP_{ML,rms}$, $vCOP_{ML,rms}$ respectively). As a balance measure for control in AP direction, the RMS of the centred CoP position and velocity in AP direction ($COP_{AP,rms}$ and $vCOP_{AP,rms}$ respectively) and RMS of centred ankle torques (T_{rms}) were calculated. In addition, the DBC was averaged over frequencies in the range 0.05-2.55 Hz (DBC_{mean}).

As a balance measure for combined control in AP and ML direction, the phase plane indices (PPI) were calculated according to Pilkar et al. [4] using the standard deviations of the CoP positions and velocities in both AP and ML directions.

$$PPI = \sqrt{\sigma^2_{COP_{AP}} + (\sigma^2_{COP_{ML}} + \sigma^2_{vCOP_{ML}})} \quad (1)$$

$$PI = \sqrt{\sigma^2_{COP_{AP}} + \sigma^2_{COP_{ML}}} \quad (2)$$

$$VI = \sqrt{\sigma^2_{vCOP_{AP}} + \sigma^2_{vCOP_{ML}}} \quad (3)$$

in which PI represents the position index and VI the velocity index.

For all balance measures the symmetry indices (SI) between the left and right leg were calculated according to [5,6,22]

$$SI_x = \frac{2(x_{right} - x_{left})}{(x_{right} + x_{left})} \cdot 100\% \quad (4)$$

where x represents the balance measure. A symmetry index of 0% represents perfect symmetry. A symmetry index of 200% indicates complete asymmetry towards the right leg. A symmetry index of 100% indicates that the measure of the right leg is three times bigger than that of the left leg.

Theoretically, left paretic participants and right paretic participants show opposite shifts in symmetry indices compared to control participants, i.e. the right paretic participants would show a shift towards the non-paretic left leg (negative symmetry indices) and the left paretic leg participants would show a shift towards the non-paretic right leg (positive symmetry indices). Therefore, all symmetry indices were calculated relative to the mean symmetry index of the control participants (given in Appendix A) and for the right paretic participants multiplied with -1, such that for all stroke participants positive symmetry indices indicated a shift towards the non-paretic leg and negative symmetry indices indicated a shift towards the paretic leg, relative to control participants.

Statistical Analysis

Statistical procedures were conducted with SPSS (IBM SPSS Statistics, Version 25, Chicago, Ill., USA).

Linear regression analyses were performed on the balance and mobility tests, i.e. Timed Up and Go, 10 meter walking test and Mini-BESTest, with adjustment for weight, length, age and gender, to test for significant differences between stroke and control participants. P-values <0.05 were considered significant. Higher coefficients indicate larger differences of the balance measure symmetry index between stroke participants and control participants.

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Table 2: Coefficients (coeff) and p-values (p) of balance measure symmetry indices for the static eyes open (EO), static eyes closed (EC), perturbed eyes open (EO_P) and perturbed eyes closed (EC_P) conditions. N.A.: not applicable. *p < 0.005 was considered significant after Bonferroni correction.

Symmetry index	EO		EC		EO_P		EC_P	
	Coeff	p	Coeff	p	Coeff	p	Coeff	p
F_{perc_mean}	3.066	0.366	4.427	0.177	3.563	0.374	4.591	0.212
T_{mean}	-6.994	0.319	-2.933	0.671	-4.694	0.378	-2.781	0.591
$COP_{ML,rms}$	10.886	0.362	2.362	0.843	2.981	0.739	-6.903	0.485
$vCOP_{ML,rms}$	9.135	0.335	-0.001	1.000	0.179	0.982	-3.017	0.752
$COP_{AP,rms}$	9.846	0.209	1.573	0.832	5.985	0.267	7.653	0.119
$vCOP_{AP,rms}$	8.578	0.283	3.609	0.662	2.502	0.568	6.802	0.135
T_{rms}	7.226	0.368	2.966	0.712	9.713	0.142	13.107	0.039
DBC_{mean}	N.A.	N.A.	N.A.	N.A.	9.475	0.209	12.500	0.060
PI	4.953	0.221	0.708	0.850	2.958	0.281	3.107	0.215
VI	4.251	0.294	1.520	0.717	1.219	0.596	3.113	0.183
PPI	4.340	0.266	0.151	0.968	1.751	0.547	1.218	0.699

To test significant differences in symmetry indices between stroke and control participants, linear regression analyses were performed for each condition on relative symmetry indices of the balance measures, with adjustment for weight, length, age and gender. To correct for Type I errors due to the number of dependent variables, Bonferroni correction was applied. P-values <0.005 were considered significant. When symmetry indices of the stroke participants were significantly different from control participants, the coefficients were compared.

To investigate whether changes in control asymmetry are more apparent in a combination of the balance measure symmetry indices, principal component analysis was performed for each condition with the symmetry indices of F_{perc_mean}, T_{mean}, $COP_{ML,rms}$, $vCOP_{ML,rms}$, $COP_{AP,rms}$, $vCOP_{AP,rms}$, T_{rms} (for EO and EC) and DBC_{mean} (for EO_P and EC_P). PI, VI and PPI were excluded due to high correlations with the other balance measures. Orthogonal rotation was applied (using 'varimax' in SPSS). Components with eigenvalues over Kaiser's criterion of 1 were extracted. Each component, explaining a certain percentage of the variance in the data, consists of specific loadings of the balance measure symmetry indices. First principal component scores, i.e. the scores explaining the most variance in the data, were calculated relative to control participants. For each condition, linear regression was performed on the relative first principal component scores.

To test whether the symmetry index of DBC_{mean} could be replaced by T_{rms} in the principal component analysis of the perturbed conditions, the principal component analysis of those conditions was repeated including T_{rms} instead of DBC_{mean}.

Results

Participant characteristics

From the 65 stroke participants and 50 control participants who completed the follow-up before December 2018, data of 11 stroke participants and 13 control participants could not be included in the present study due to a broken force plate sensor (n=9) or missing data in motion capture recordings (n=15), leaving data from 54 minor stroke participants and 37 control participants available for analysis. Stroke participants scored significant lower on the Mini-BESTest (p=0.003), 10 meter walking test (p=0.003) and Timed Up and Go without dual task (p=0.007) and with dual task (p=0.002) (Table 1).

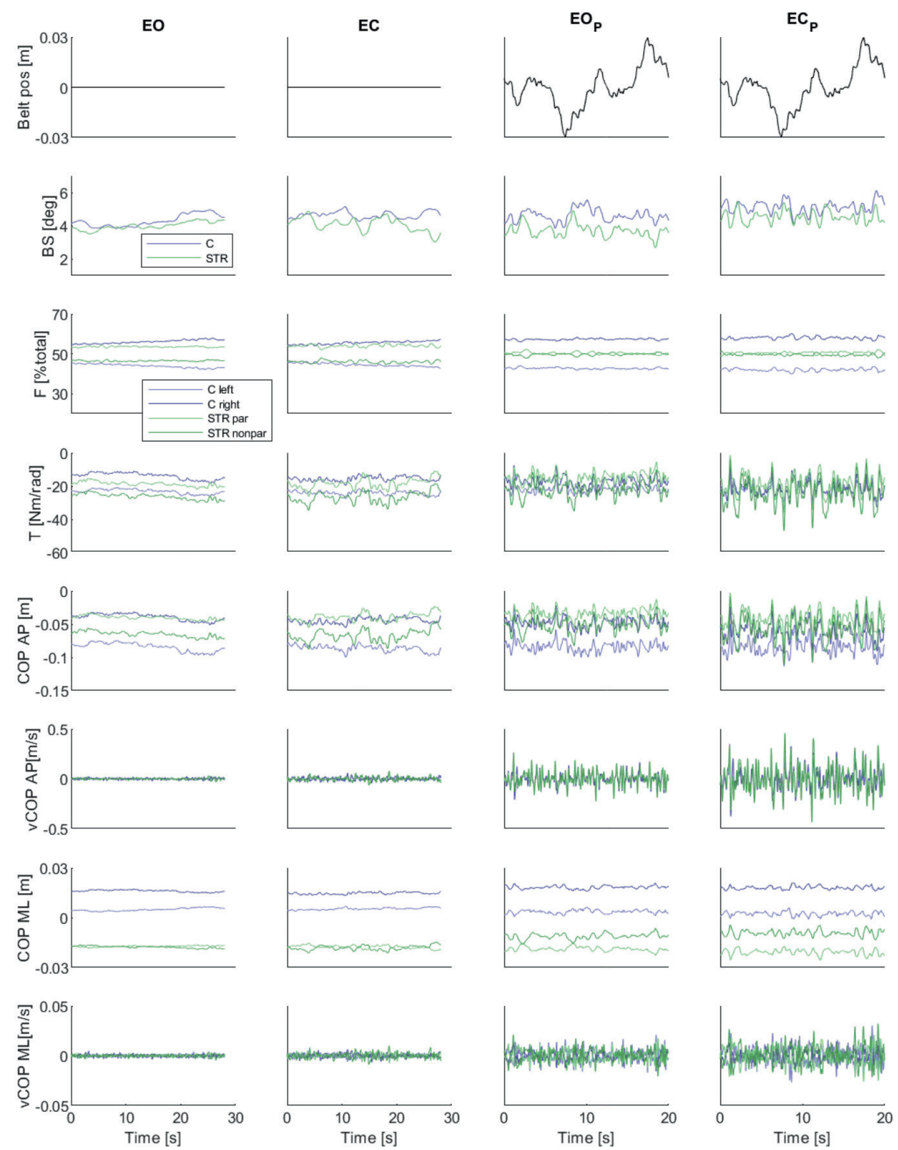

Figure 1: Time series of one typical stroke participant (STR) and control participant (C) for static eyes open (EO), static eyes closed (EC), perturbed eyes open (EO_P) and perturbed eyes closed (EC_P) conditions: Belt position (Belt pos)(black), body sway (BS), percentage ground reaction force (F), ankle torque (T), centre of pressure (CoP) position in anterior-posterior direction (COP AP), CoP velocity in anterior-posterior direction (vCOP AP), CoP position in medio-lateral direction (COP ML) and CoP velocity in medio-lateral direction (vCOP ML) for the paretic (par)/left and non-paretic(nonpar)/right leg.

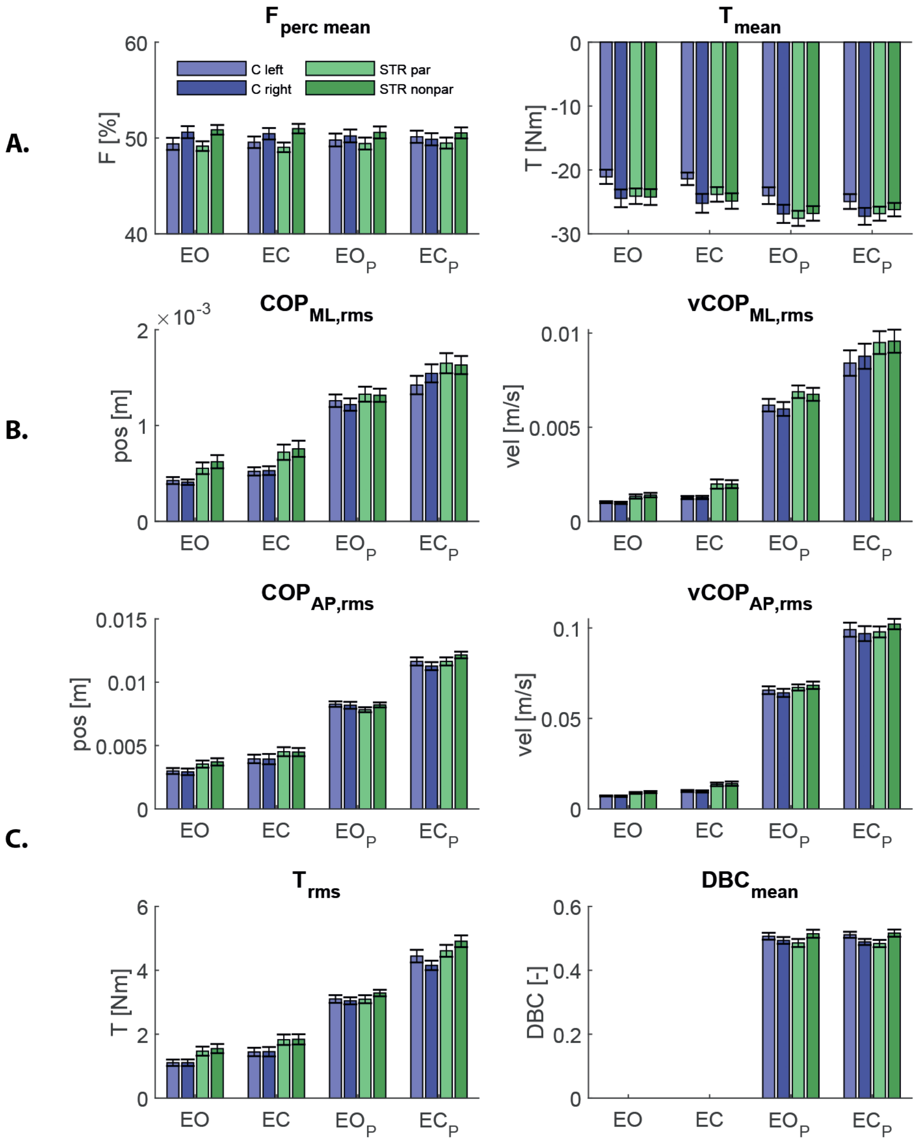

Figure 2: Balance measures for the paretic(par)/left and non-paretic(nonpar)/right leg, averaged over stroke participants (STR) and control participants (C) for static eyes open (EO), static eyes closed (EC), perturbed eyes open (EO_P) and perturbed eyes closed (EC_P) conditions. Error bars indicate standard errors. A. Balance measures indicating weight bearing (F_{Perc_mean}) and forward lean torque (T_{mean}). B. Balance measures indicating control in medio-lateral direction ($COP_{ML,rms}$, $vCOP_{ML,rms}$). C. Balance measures indicating control in anterior-posterior direction ($COP_{AP,rms}$, $vCOP_{AP,rms}$, T_{rms}, DBC_{mean}).

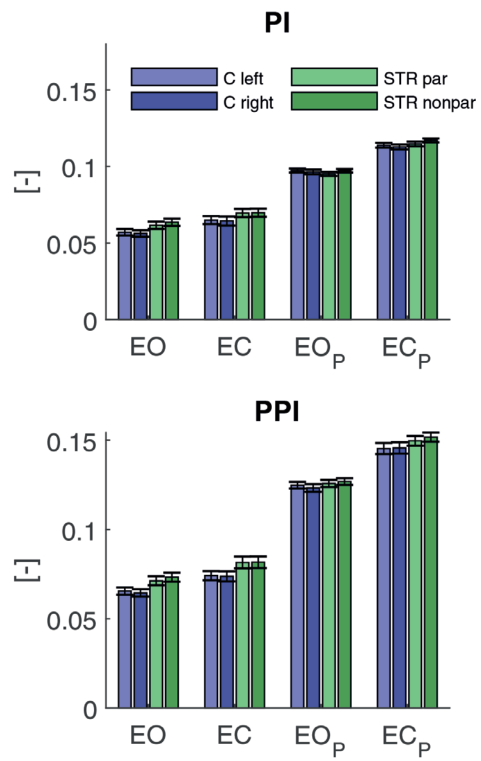

Figure 3: Balance measures PI, VI and PPI for the paretic(par)/left and non-paretic(nonpar)/right leg, averaged over stroke participants (STR) and control participants (C) for static eyes open (EO), static eyes closed (EC), perturbed eyes open (EO_P) and perturbed eyes closed (EC_P) conditions. Error bars indicate standard errors.

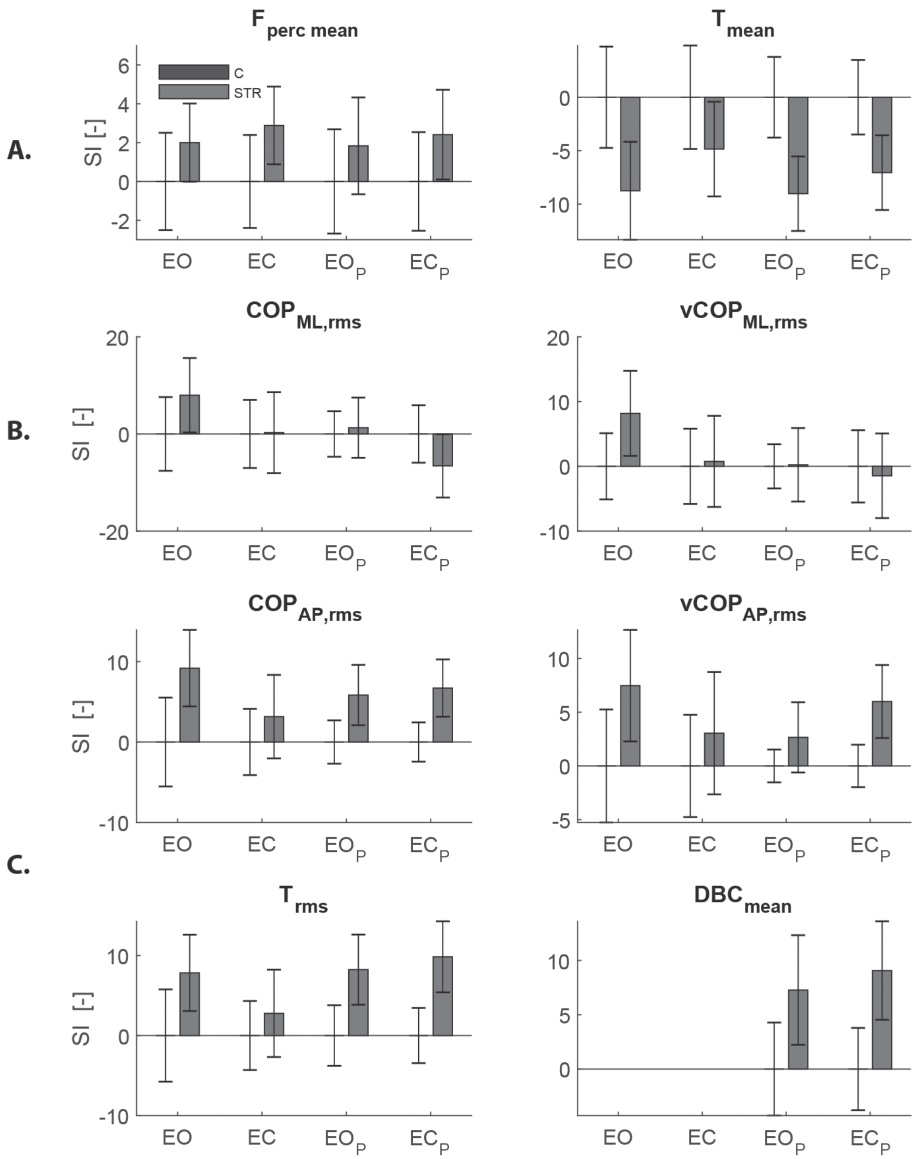

Figure 4: Relative symmetry indices (SI), averaged over stroke participants (STR) and control participants (C) for static eyes open (EO), static eyes closed (EC), perturbed eyes open (EO_P) and perturbed eyes closed (EC_P) conditions. Error bars indicate standard errors. A. Weight bearing symmetry index and forward lean torque symmetry index (F_{Perc_mean}, T_{mean}). B. Medio-lateral control symmetry indices ($COP_{ML,rms}$, $vCOP_{ML,rms}$). C. Anterior-posterior control symmetry indices ($COP_{AP,rms}$, $vCOP_{AP,rms}$, T_{rms}, DBC_{mean}). *p<0.005 was considered significant.

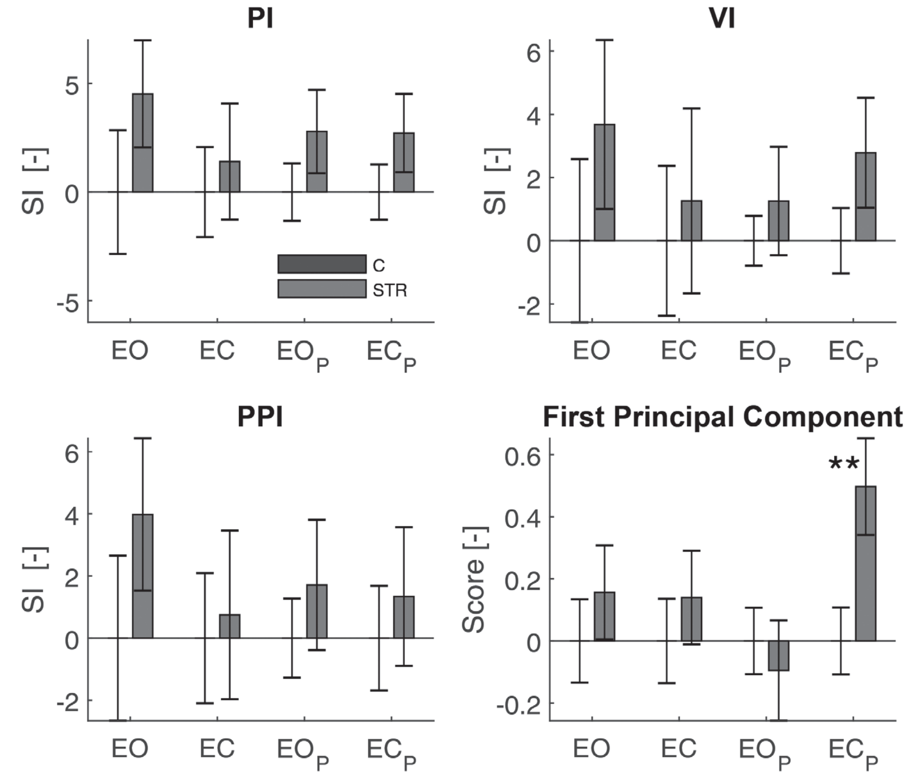

Figure 5: Relative symmetry indices (SI) of PI, VI and PPI and first principal component score, averaged over stroke participants (STR) and control participants (C) for static eyes open (EO), static eyes closed (EC), perturbed eyes open (EO_P) and perturbed eyes closed (EC_P) conditions. Error bars indicate standard errors. *p<0.05 was considered significant for symmetry indices of PI, VI and PPI.**p<0.05 was considered significant for the first principal component.

Balance measure time series

Time series of a typical stroke and control participant are plotted in Figure 1. In general, the balance measures, averaged over participants into a stroke and control group (Figure 2 and 3), seem higher for the eyes closed condition and even higher for the perturbed conditions, which is in accordance with previous literature [23,24].

Balance measure asymmetries

Mean symmetry indices of control participants are shown in Appendix A. Figure 4 and 5 show the symmetry indices of the stroke participants relative to the control participants. Positive values indicate a shift towards the non-paretic leg relative to the mean symmetry index of control participants. Corresponding significance and coefficient of each symmetry index are given in Table 2. Since none of the symmetry indices of the stroke participants were, after Bonferroni correction, significantly different from control participants, coefficients were not compared. Although not significant, the $COP_{AP,rms}$, $vCOP_{AP,rms}$, T_{rms}, DBC_{mean} and VI symmetry indices were closest to significance when measured during the EC_P condition. These symmetry indices seemed to be slightly higher for stroke participants compared to control participants, indicating a shift towards the non-paretic leg.

Principal Component Analysis

For the EO condition, one component was extracted. For the EC, EO_P and EC_P, three components were extracted. The first principal component for the EO, EC, EO_P and EC_P conditions explained 48.13, 50.40, 46.00 and 45.43% of the variance respectively. Table 3 shows the loadings of each symmetry index onto this component. The first principal component score (Figure 5) was significantly higher for stroke participants during the EC_P condition (p=0.028)(Table 3).

Principal component analysis of the perturbed condition with eyes closed including T_{rms} instead of $DBC_{mean,}$ resulted in a component score explaining 46.21% of the variance. The component score, explaining 46.21% of the variance, was significantly larger for stroke participants than for control participants (p=0.026, coefficient=0.492). Symmetry indices of $COP_{AP,rms}$, $vCOP_{AP,rms}$ and T_{rms} loaded on the first principal component with loading scores of 0.949, 0.936 and 0.895 respectively.

Discussion

In this paper we investigated whether control asymmetries are present in minor stroke participants, in which measure these subtle changes in control asymmetries are most apparent and under which condition they could best be measured. Posturography and system identification measures were conducted in both static and perturbed trials assessing standing balance and compared.

Minor stroke participants scored significantly lower than control participants on clinical balance test. One of the underlying causes might be subtle changes in control asymmetry. Yet, none of the individual balance measures yielded significant balance control asymmetries (symmetry indices were not significantly different for stroke participants compared to control participants). However, the balance control asymmetries could be demonstrated when the symmetry indices, measured during the perturbed condition with eyes closed, were combined using principal component analysis, i.e. the first principal component was significantly higher for stroke participants compared to control participants. The first principal component consists of symmetry indices of the DBC mean, RMS of anterior-posterior CoP position and RMS of anterior-posterior CoP velocity, i.e. symmetry indices indicating control in anterior-posterior direction, all loading similarly onto the component.

Results of previous studies, investigating stroke participants with more severely affected leg motor function, showed significant differences between stroke and control participants in RMS of symmetry indices of anterior-posterior CoP position [3-5] and velocity [25], DBC [1] and balance measures PI, VI and PPI [4]. All these symmetry indices indicate significantly more asymmetry in stroke participants with a larger relative contribution of the non-paretic leg to balance control. It was to be expected that, when investigating participants with less severe strokes, the balance impairments are smaller and subtle changes in balance control asymmetries may not be apparent in the individual balance measure symmetry indices during static conditions. Our results, however, show that it is possible to demonstrate the existence of such subtle control asymmetries, when the individual balance measures are measured during perturbed conditions with eyes closed and combined into a first principal component score.

Minor stroke participants score significantly lower on the miniBESTest (p=0.003). These results are obtained with a subset of the minor stroke population reported in Chapter 5, where the results were similar (p<0.001). 73% of the minor stroke participants did not reach near-maximal scores, whereas this was the case for only 26% of the control participants. These results persisted in subgroup analysis of participants who scored maximal on the Fugl-Meyer Assessment (lower extremities) and the motricity index (lower extremities), i.e. full recoverers. The relatively low p-value of the miniBESTest in Chapter 5 could suggest that differences in balance between minor stroke and control participants are more pronounced in the miniBESTest than in the first principal component score ($p=0.028$), although effect sizes should be compared, rather than p-values. However, the lower miniBESTest scores in the minor stroke participants may not only be due to subtle deficits in paretic leg motor control, but may be related to other confounding factors as well (e.g. the lower balance confidence or higher body mass index in the minor stroke participants compared to the controls).

The strength of our system identification approach is that differences in symmetry indices are due to subtle deficits in paretic leg motor control only, as it is likely that symmetry indices are mildly related to cofounding factors. Taken together, the miniBESTest appears to be a sensitive clinical tool to detect people with impaired balance, but future research should point out whether system identification could be used in addition to the miniBESTest to give insight in the underlying cause of impaired balance, thereby accounting for confounding factors.

Table 3: Loadings of the balance measure symmetry indices on the first principal component and significance and effect size of the first principal component for the static eyes open (EO), static eyes closed (EC), perturbed eyes open (EO_P) and perturbed eyes closed (EC_P) conditions. N.I.: not included. *p<0.05 was considered significant.

		EO	EC	EO_P	EC_P
Symmetry index loading score	F_{perc_mean}				
	T_{mean}				
	$COP_{ML,rms}$	0.785	0.625	0.875	
	$vCOP_{ML,rms}$	0.883	0.800	0.953	
	$COP_{AP,rms}$	0.764	0.904		0.948
	$vCOP_{AP,rms}$	0.754	0.895	0.584	0.933
	T_{rms}	0.463	0.749	N.I.	N.I.
	DBC_{mean}	N.I.	N.I.		0.860
Significance	P-value	0.411	0.599	0.720	0.028*
Effect size	Coefficient	0.184	0.119	-0.082	0.492

Methodological Considerations

Here we performed a principal component analysis per condition and on a selected subset of the symmetry indices. A next step would be to combine the symmetry indices of all conditions together in the principal component analysis instead of running the analysis for each condition separately. However, more participants are required since for each variable about 10 participants should be assessed to reach stable component solutions [26].

The results of the principal component analysis depended on which symmetry indices were included. In the principal component analysis of the perturbed condition with eyes closed, the symmetry index of the torque RMS was excluded as previous studies showed that the DBC, another symmetry index indicating control in AP direction, is a more promising variable [1]. When the principal component analysis is performed with the RMS of the torque instead of the DBC, the symmetry indices loading on the component are similar, i.e. loadings higher than 0.85 on the symmetry indices indicating control in AP direction. The effect size of the first principal component was also similar (coefficient of 0.499 when including T_{rms} vs. 0.492 when including DBC_{mean}). Although including the symmetry index of the torque RMS requires a less complex setup, i.e. motion caption recordings are not necessary and less complex data analysis, including the symmetry index of the DBC mean has the advantage that the control contribution of each leg to balance can be identified.

The individual symmetry indices of control in AP direction were not significantly different between stroke and control participants. However, these symmetry indices were closest to significance during the perturbed condition with eyes closed, i.e. the most demanding condition. Possibly, potential differences in symmetry indices may be enhanced by examining these measures while maintaining an imposed amount of weight bearing between the legs. Van Asseldonk et al. [1] showed that not only the DBC by itself was an interesting asymmetry measure, but that also the ratio between weight bearing asymmetry and DBC differed between stroke and control participants. Control participants showed a 1:1 ratio whereas for stroke participants, the contribution of the paretic leg to balance control was relatively smaller than its contribution to weight bearing. Although our results did not show significant differences in this ratio (not shown in paper), the effect might be amplified when participants are instructed to adopt an asymmetrical weight bearing where the paretic leg is highly loaded. This might also hold for other control measures such as RMS of CoP position and velocity and torque. Another method to possibly enlarge the contrast between stroke and control participants is to measure during even more demanding conditions [27]. An example is standing on one leg, which is the most extreme asymmetrical weight bearing condition. However, this might be too difficult to perform for the participants. Another example is a smaller stance width or tandem stance, potentially with eyes closed, yet these conditions might also be too difficult. It remains to be investigated how differences in control asymmetry between stroke and control participants can be amplified.

In this study, the symmetry indices were calculated by subtracting left from right. Since we are interested in a shift towards the non-paretic or paretic leg, compared to a 'baseline' preference, i.e. in our study the mean symmetry index of the control participants, it would have been better to calculate the symmetry index by subtracting preferred from non-preferred leg. By subtracting left from right, the resulting mean symmetry index of the control participants, which we use as a baseline, is biased since participants with a preference for the left leg, show opposite symmetry indices compared to participants with a preference for the right leg. However, we did not obtain these data and it is debatable for both stroke and control participants how the individual preference could be assessed. Assuming that both groups have equal ratios of left and right preferred participants, the bias has no effect on the results.

A next step would be to correlate the component score resulting from the principal component analysis to the Mini-BESTest or falls. This allows for individual assessments in which the principal component would act as a predictor for impaired balance control and people at high fall risk. However, larger number of participants are required for correlation analysis.

Conclusion

Impaired balance and mobility of stroke patients might be caused by subtle changes in balance control of the paretic ankle, indicating an asymmetric balance control strategy. In this paper we investigated whether subtle control asymmetries can be detected in minor stroke participants, in which balance measure these subtle changes in control asymmetries are most apparent and under which condition they could best be measured. In both static and perturbed trials assessing standing balance, posturography and system identification measures were conducted and compared. Our results show that subtle changes in balance control asymmetries cannot be demonstrated by individual balance measure symmetry indices. However, subtle control asymmetries can be demonstrated when the symmetry indices are measured during the perturbed condition with eyes closed, and combined into a first principal component score. The first principal component consists of symmetry indices of the DBC mean or torque RMS and RMS of anterior-posterior CoP position and velocity, i.e. symmetry indices indicating control in anterior-posterior direction, all loading similarly onto the component. These results indicate that subtle changes in control asymmetry of minor stroke participants cannot be demonstrated by measuring single balance measures, but can be demonstrated when combining the anterior-posterior centre of pressure (CoP) position, anterior-posterior CoP velocity and dynamic balance contribution, when measured during the perturbed conditions with eyes closed.

Appendix A

Table 4. Symmetry indices and principal component score (PC) of control participants for static eyes open (EO), static eyes closed (EC), perturbed eyes open (EO_P) and perturbed eyes closed (EC_P) conditions. Mean and standard deviation (STD) are given for all balance measure symmetry indices.

	EO		EC		EO_P		EC_P	
Symmetry index	Mean	STD	Mean	STD	Mean	STD	Mean	STD
F_{perc_mean}	2.44	15.24	1.78	14.56	0.84	16.32	-0.52	15.44
T_{mean}	14.68	28.82	14.44	29.47	11.26	22.96	8.73	21.23
$COP_{ML,rms}$	1.18	46.18	2.38	42.65	-3.24	28.52	8.50	35.99
$vCOP_{ML,rms}$	-6.12	31.10	-0.88	35.33	-4.27	20.77	3.66	33.95
$COP_{AP,rms}$	-3.77	33.60	-3.94	25.03	-1.92	16.37	-3.16	14.84
$vCOP_{AP,rms}$	-4.86	31.98	-4.00	28.94	-2.49	9.30	-2.62	12.02
T_{rms}	-1.14	35.08	-1.03	26.25	-1.50	23.03	-5.34	20.97
DBC_{mean}	n.a.	n.a.	n.a.	n.a.	-2.65	26.02	-4.46	23.03
PI	-1.56	17.32	-1.52	12.61	-1.04	8.02	-0.95	7.73
VI	-2.49	15.68	-1.78	14.42	-1.32	4.78	-1.09	6.29
PPI	-1.65	16.16	-0.92	12.75	-1.37	7.74	0.15	10.24
PC	-0.09	0.82	-0.08	0.83	0.06	0.65	-0.29	0.66

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7

General discussion

General conclusions and discussion

In this thesis we developed and evaluated system identification techniques enabling assessment of reactive balance capacity by applying balance perturbations. Balance is important to keep the body in an upright position, thereby preventing falls, but is difficult to measure experimentally. By applying perturbations and assessing the response of the body, i.e. a typical system identification approach, the corrective actions of the neuromuscular controller to maintain balance can be identified. This thesis investigated how system identification may be of use for clinical evaluation of balance control in minor stroke patients. First, we show how system identification can be implemented using the Bilateral Ankle Perturbator (BAP) or a treadmill to assess different aspects of balance control, i.e. sensory reweighting and the stabilizing mechanism, by focusing on the technical features and the methodological characteristics of the support surface perturbations (Part I). Second, we focused on balance assessment of a minor stroke population, using both clinical test and system identification techniques based on continuous support surface translations while standing on a treadmill (Part II). We found that both approaches could demonstrate persistent balance impairments in minor stroke participants, with the system identification technique revealing subtle changes in the stabilizing mechanism of the paretic leg.

Main findings

The work presented in this thesis resulted in the following main findings:

- To assess the stabilizing mechanism of balance control, system identification can be used in combination with a treadmill applying support surface translations.
- When using continuous forward-backward translations of the treadmill belt in combination with system identification to assess the stabilizing mechanism, the perturbation amplitude should be minimally around 0.05 m peak-to-peak, but higher amplitudes are desired as they require fewer repetitions of the perturbation signal. There is, however, no need to increase the perturbation amplitude beyond 0.14 m peak-to-peak as the noise-to-signal ratio saturates.
- During standing balance, the horizontal ground reaction forces have a minor contribution to the ankle torque and frequency response function of the stabilizing mechanism. These can therefore be omitted in the calculations, which simplifies the technical requirements of the instrumented treadmill design (i.e. the embedded force plate only needs to measure vertical forces).

- Individuals in the chronic phase after minor stroke with (near-)complete clinical motor recovery of the paretic leg may still demonstrate deficiencies in balance and gait capacities, a relatively high fall frequency, and lower intensities of physical activity.
- Subtle changes in balance control around the paretic ankle can be found in a group of minor stroke patients (compared to a control group) when using a combined measure of the root-mean-square (RMS) of the anterior-posterior centre of pressure (CoP) position, RMS of the anterior-posterior CoP velocity and mean dynamic balance contribution, as recorded during the perturbed conditions with eyes closed.

Clinical implications

It is important to adequately assess balance in the clinic, as impaired balance is a key risk factor of falls. Currently used clinical balance tests suffer from important limitations; they do not provide insight into the neurophysiological mechanisms underlying impaired performance [1,2], they are subjective, and some also have substantial ceiling effects [3] and are hence insensitive to more subtle impairments. The alternative method of posturography [4] is objective and has no ceiling effects, but still lacks the ability to distinguish between underlying neurophysiological mechanisms and compensation strategies [2]. With system identification using dedicated perturbations, it possible to objectively assess balance control, thereby identifying the contribution of the neuromuscular controller to impaired balance control [5-10]. There is however one major drawback; current system identification methods depend on large, expensive and complex devices such as motion platforms and motion capture cameras, and are therefore not suitable for clinical use.

System identification implementation

In this thesis we introduce a new application of the BAP (chapter 2) to measure sensory reweighting by applying a specific compliance to the support surface. The BAP is a relatively small and easy-to-use device that enables rotations around the ankles [9]. The compliance of the BAP can be adjusted such that foam mats currently used in the clinic can be mimicked. Foam mats are often used as a diagnostic tool whereby people stand on the foam mats with either eyes closed or open while body sway is measured [11-19]. When used for training, participants often perform several balance exercises on the foam mats [12, 16, 20-22]. However, the identification of the sensory systems and the effect of training with foam mats on the sensory systems remained unknown. We show that using the application of the BAP in combination with system identification, allows for the objective assessment of balance control, thereby giving insight in changes in sensory reweighting when standing on compliant surfaces. Future research should indicate whether the BAP could also be used for objective evaluation of balance training effects.

In chapter 3 and 4, we used a treadmill with two 6 DoF force plates (M-gait, Motek Medical, Amsterdam, The Netherlands) that allows to measure the ground reaction forces of both feet, combined with system identification methods, to specify the technical characteristics for a smaller and simplified novel instrumented treadmill (N-Mill) that may be more clinically usable. When using continuous forward-backward translations, the perturbation amplitude should be within the range of 0.05-0.14 m peak-to-peak, whit preference for an amplitude of 0.14 m (chapter 3). The horizontal ground reaction forces have a minor contribution to the ankle torque and frequency response function of the stabilizing mechanism. These can therefore be omitted in the calculations (chapter 4). Using these proposed system identification methods, the contribution of the stabilizing mechanism to balance control can objectively be assessed. Based on this information, a new treadmill was developed along with a specific perturbation protocol that could be used for evaluating impairments in stabilizing mechanisms in several populations with a high prevalence of balance impairments (e.g. stroke or elderly) [7, 23, 24].

The advantage of using instrumented treadmills for evaluating balance impairment is that they are relatively small, cheap, and easy-to-use compared to motion platforms, and are already used in the clinic for training. Our system identification method could be integrated on the C-Mill, i.e. an instrumented treadmill in which the surface of the belt can be augmented with visual context (targets, obstacles) via a projector for training of gait adaptability [25, 26]. This would require two adjustments of the current C-mill technology. First, the treadmill should be able to apply continuous forward-backward translations of the support surface with amplitudes in a range of 0.05-0.14 m ptp. This might require a stronger motor, if not already present, and small adjustments to the software. This requires an application procedure for a new CE marking. Second, when assessment of the stabilizing mechanism of each leg separately is required, for instance when assessing stroke participants, vertical ground reaction forces should be recorded of both feet separately. This requires the replacement of a single force plate with dual force plates. However, when the combined stabilizing mechanism of both legs should be identified, for instance when assessing elderly or Parkinson's disease patients, the force plate already present in the C-Mill should be sufficient.

Assessment of balance control in people with minor stroke

In Chapter 5 we show that minor stroke participants are more likely to fall than control participants. We also found that these individuals had lower scores on the miniBESTest, which test assesses balance and gait capacity in four subdomains. Since balance and gait deficits are the key risk factors for falling [27], assessment of balance and gait could be of use in the clinic for evaluating people's fall risk. Currently, clinicians often

use the Berg Balance Scale (BBS) [28], but this test has well-known ceiling effects that preclude identifying residual balance deficits in relatively well-recovered individuals after stroke [3]. Based on our findings in chapter 5, we therefore recommend using the miniBESTest instead of the BBS as a clinical test for assessing balance capacity in individuals with stroke who have relatively mild motor problems. The miniBESTest takes the same administration time as the BBS and only requires an additional incline board and foam mat. Future research should indicate whether the miniBESTest also has added value for other populations with neuromuscular impairments.

Chapter 5 shows that the miniBESTest is a promising tool to detect balance impairments in minor stroke participants. To gain insight in the cause of these impairments, i.e. the contribution of either leg to balance control, system identification might be a solution. Although we found in Chapter 6 that our system identification measure contributed to the principal component that yielded greater balance control asymmetries in people with minor stroke compared to healthy control subjects, this measure had to be combined with conventional posturography measures. Thus, system identification measures and the posturography measures complement each other and they should both be assessed when identifying control asymmetries in this population. In addition, the between-group differences in balance control asymmetries (as identified from this principal component) were modest and only significant during the most demanding condition, i.e. perturbed with eyes closed. Therefore, the added value of the system identification approach remains debatable. Future research should indicate whether system identification is of clinical use for individual assessment of people with high fall risk (see considerations and future research). Furthermore, the assessment of standing balance alone may not be sufficient to capture impairments in balance control at large. The miniBESTest has the advantage of assessing different aspects of balance, i.e. anticipatory, reactive postural control, sensory orientation and dynamic gait. The fact that minor stroke participants scored lower on at least one task of each subdomain, might hint at the importance of assessing all subdomains. To sum up, although system identification might give more insight in the cause of balance impairments, i.e. changes in control contribution, future research should focus on its additional clinical value, e.g. for estimating fall risk.

Considerations and future recommendations

Treadmill integration in the clinic

The proposed treadmill setup for assessment of balance control consist of the treadmill and a motion capture system. This thesis shows that the treadmill protocol could be used when adjustments are made to C-Mills currently available in the clinic, i.e. when continuous forward-backward translations of the belt are possible and when ground reaction forces are recorded by a dual force plates. Although the results show that such a treadmill may be a promising device to objectively assess balance control, the current setup still relies on expensive motion capture camera's that also require a lot of space. It would be very beneficial if these motion capture cameras could be replaced with smaller and simpler camera's. System identification for the assessment of standing balance requires the measurement of body sway during the whole trial, which should also be synchronised with the force plates. In Chapter 6 we showed that for demonstrating balance control asymmetries, the dynamic balance contribution might be replaced by the ankle torque for which motion caption recordings are not necessary, which is supported by recent research of Van der Kooij [29]. However, the ankle torque lacks the ability to analyse the control contribution of each leg to balance. It remains to be investigated whether accelerometers, laser displacement sensors [30], center of pressure sensors or multiple 2D cameras, e.g. DeepLabCut, could replace the currently used motion cameras, thereby enabling the identification of the control contribution of each leg to balance.

Assessment of asymmetries in balance control of people with minor stroke

In Chapter 6 we indicate that by using system identification, while applying support surface translations, subtle changes in balance control of the paretic leg of minor stroke participants can be found when the dynamic balance contribution, i.e. a system identification measure, is combined with posturography measures. Future research may focus on the question whether other test conditions could be applied for magnifying the observed differences in balance control asymmetry between minor stroke and control participants. Measuring balance control asymmetries under more demanding conditions, e.g. more asymmetric weight-bearing posture, might lead to more apparent deteriorations of the underlying balance control of the paretic leg [2]. The study of van Asseldonk et al. showed the largest differences in dynamic balance contribution between the stroke and control participants when the weight-bearing on the paretic leg was high [7]. To identify the potential added value of testing under conditions of asymmetric weight-bearing, future studies could systematically compare differences in control asymmetries between stroke and control participants using a protocol with varying degrees of imposed weight-bearing asymmetries.

Additional balance assessment methods

In this thesis, we show how standing balance can be assessed using system identification in combination with a treadmill. Yet, falls often occur during walking [31], so measures of balance (i.e. dynamic stability) during gait may provide important additional insight into the full spectrum of balance impairments in various clinical populations. It is a matter of ongoing debate how balance during gait can best be tested and quantified. On the one hand, several tasks can be performed such as unperturbed walking on a treadmill or overground [32-34], obstacle avoidance [35,36] or perturbed balance in which participants react on perturbations such as trips, slips or pushes [37-40]. On the other hand, several dynamic balance measures can be assessed. Some studies investigate performance-based outcomes such as success rates or number of falls [35]. Some studies assess balance measures such as margin of stability or Lyaponov exponent [41,42]. Other studies assess spatiotemporal or kinetic outcome measures [32,33,35,37,41]. Interestingly, all these tests can potentially be performed on the treadmill proposed in this thesis, thereby enlarging the future possibilities of the treadmill.

Training of people with poor balance and high fall risk

For those people with impaired balance and high fall risk, the next step would be to offer individual rehabilitation. Recent studies have shown the benefits of currently used C-Mill training with visual perturbations [25, 43]. During the Move On project, we originally aimed to also conduct a training study for exploring the potential benefit of adding mechanical perturbations to the training protocol. The study was designed in such a way that it could evaluate differential effects of specific types of training on the various domains of balance capacity. The training protocols for the study have been designed early in the project, but since the treadmill development took longer than anticipated and the inclusion rate was lower than expected, we focused on the balance assessment study when the first participant was assessed, leaving no time for the training study. From the participants of the pilot, we learned that the different types of training on a treadmill, including training with visual and mechanical perturbations, were well-tolerated. Participants enjoyed the training sessions, especially when the session contained a broad variety of perturbations, but the perceived difficulty was different for each participant. It is an interesting topic for future studies to compare the effects of various training regimes on a range of balance tests for providing insight into their mode of action and for informing evidence-based exercise prescription for people with different types of balance impairments.

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Appendix

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About the author

Ingrid Schut was born in 1989, in Delft, The Nethderlands. In 2006 she got her high school diploma from the 'Stanislas College' in Delft, and started studying biomedical engineering at the University of Twente in Enschede. She received her bachelor's diploma after finishing the bachelor assignment at the department of Biomedical Signals and Systems thereby focussing on the detection of slip by analysis of the frequency spectrum of the Biotac sensor. For the internship during the master, she went to Northwestern University in Chicago, to temporarily join the lab of prof. dr. Jules Dewald at the department of Physical Therapy & Human Movement Sciences where she studied the kinematics and muscle activity during ballistic movements of post stroke patients. Back at the University of Twente, she started her master assignment at the department of Biomechanical Engineering, studying the effect of compliant sufaces on sensory reweighting and intrinsic/reflexive control in human balance control. In January 2015, Ingrid graduated with a Master's degree in Biomedical Engineering. In line with the master assignment Ingrid started her PhD research at the Delft Technical University at the department of Biomechanical Engineering. The MoveOn project was part of the NeuroControl Consortium, and resulted in this PhD thesis entitled: 'Assessing balance control after minor stroke', under the supervision of prof. dr. ir. H. van der Kooij. In this thesis she investigates the assessment of balance control after minor stroke using system identification techniques, and how these techniques could be used in the clinic. Currently, Ingrid is working as procedure coordinator at the department 'Toetsing en Onderzoek' of UMC Utrecht.

List of Publications

Published papers

M.D. Ellis, I.M.Schut, J.P.A. Dewald. Flexion synergy overshadows flexor spasticity during reaching in chronic moderate to severe hemiparetic stroke. Clinical Neurophysiology. 2017; 128: 1308-1314.

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J.M.B. Roelofs, F. Hulzinga, I.M. Schut, A.C. Schouten, V. Weerdesteyn. Backward leg angles at stepping-foot contact can accurately be determined from a 2D video frame.

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I.M. Schut, J.M.B. Roelofs, J.H. Pasma, A.C.H. Geurts, V. Weerdesteyn, H. Van Der Kooij, A.C. Schouten. Detection of balance control asymmetries in people with minor stroke.

Conference contributions

I.M. Schut, D. Engelhart, R.G.K.M. Aarts, H. van der Kooij, A.C. Schouten. Effect of compliant support surfaces on sensory reweighting of proprioceptive information in human balance control. NeuroControl symposium 2015, Zeist. Abstract and poster.

International Posture Symposium, 2015, Smolenice Castle, Slovakia. Abstract and oral presentation.

I.M. Schut, J.M.B. Roelofs, N. Keijsers, J.H. Pasma, A.C. Schouten, V. Weerdesteyn. Move On: balance capacity in people after stroke – project update. NeuroControl symposium 2016, Egmond aan Zee. Abstract and oral presentation.

I.M. Schut, J.M. Roelofs, J.H. Pasma, V. Weerdesteyn, H. van der Kooij, A.C. Schouten. Influence of horizontal forces when measuring balance control on a treadmill. NeuroControl symposium 2016, Zeist. Poster. SMALLL congress 2016, Enschede. Abstract, oral presentation and poster. ISEK congress 2016, Chicago, US. Abstract and oral presentation. BME congress 2017, Egmond aan Zee. Abstract and oral presentation.

J.M.B. Roelofs, I. Kolenbrander, E. Smulders, I.M. Schut, A.C. Schouten, V. Weerdesteyn. Can foot placement errors accurately be derived from center of pressure data? ISGPR congress 2017, Fort Lauderdale, Amerika. Abstract and oral presentation. DCNR congress 2017, Maastricht. Abstract and poster. SMALLL congress 2017, Leuven, België. Abstract and poster.

I.M. Schut, J.M.B. Roelofs, J.H. Pasma, V. Weerdesteyn, H. van der Kooij, A.C. Schouten. Detecting subtle balance changes in minor stroke survivors. SMALLL congress 2017, Leuven, België. Abstract and poster.

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J.M.B. Roelofs, I.M. Schut, J.H. Pasma, A.C. Schouten, V. Weerdesteyn. Balance problems in the chronic phase after a minor stroke: from scientific research to a clinical application. NeuroControl symposium 2018, Soesterberg. Oral presentation.

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Press

- De Telegraaf. Beroertepatiënten vaak aan hun lot overgelaten. October 2017.
- Gemeentenieuws Lingewaard. February and March 2017.
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