Effects of real-time feedback in the form of biological cues on post-stroke gait symmetry

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Statement of authorship

I, Le Yu Liu, certify that I am the primary author of this thesis and all the manuscripts contained in this thesis. I claim full responsibility for the content and study of the text included herein.

Statement of originality

This thesis contains no material that has been published elsewhere, except where specific references are made. The manuscripts presented in Chapters 4, 5, 6, and 7 are original content, and the aim is to contribute to the field of feedback in the form of biological cues, sensorimotor integration, and post-stroke gait symmetry. In the studies of this thesis, a novel setup which included virtual reality and various motion capture systems was used to estimate the effects of visual and auditory real-time feedback on post-stroke symmetry, and to investigate the locomotor responses of healthy people to auditory feedback distortion presented in an error-augmentation paradigm. The results of these studies serve to advance the knowledge and understanding of the locomotor behavior quantified as spatiotemporal outcomes of individuals with stroke when they try to change their gait asymmetry, the relationship between gait symmetry and interlimb coordination, the differences between visual, auditory, and combined visual auditory feedback, and the potential application of an error-augmentation paradigm in gait symmetry training. Post-stroke gait asymmetry has always been a difficult aspect of gait to treat in rehabilitation and the findings of this PhD thesis contribute toward the design a novel intervention for clinicians and researchers to improve gait asymmetry.

All data presented in this thesis were collected at the Feil & Oberfeld Research Center of the Jewish Rehabilitation Hospital, which is affiliated to McGill University and to Centre Intégré de Santé et de Services Sociaux de Laval (CISSS de Laval). It is also a research site of the Center for Interdisciplinary Research in Rehabilitation of Greater Montreal (CRIR). All studies have been approved by the Ethics Board of CRIR (refer to Appendix. Consent forms for English and French consent forms used in the projects related to this dissertation).

Dedications

I dedicate this dissertation to my family, the pillar of my life. Without your love, support, and encouragement, this accomplishment would not have been possible. To my parents, I am eternally grateful for providing me with a joyful childhood filled with opportunities to learn and explore. You taught me to strive for excellence and to believe in myself, no matter the magnitude of the challenges. Your sacrifices and unconditional love have been instrumental to my success today. To my beloved wife, thank you for being my best cheerleader and my closest friend. You have consistently inspired me when I was stuck in my writing and motivated me when I felt lost or distracted. I am eager to embarking on a new chapter in our lives together with you. Finally, I dedicate this thesis to our soon-to-be-born son. Your mother and I love you deeply, and we are filled with anticipation as we welcome you into our family. May this thesis serve as a token of my best wishes for your happiness, health, and a life lived to the fullest.

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I also wish to thank the members of my supervisory committee, Dr. Joyce Fung (McGill University) and Dr. Kara K. Patterson (University of Toronto) for their guidance and critical feedback. Dr. Fung provided her laboratory for the data collection process, and without it the experiments presented in this thesis would not have been possible. Dr. Patterson offered her expertise and knowledge on post-stroke gait asymmetry as the foundation for this thesis to build upon.

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Contribution of authors

This thesis is presented in a manuscript format and includes four manuscripts. Two manuscripts are already published in peer-reviewed journals while the other two are in the process of submission. Additionally, information from one manuscript which is also published in a peer-reviewed journal is presented in the background under the 1.7.1.1 subsection. I, Le Yu Liu, am the main contributor and lead authors of all manuscripts included in this thesis. My contribution includes the research design, participants recruitment, data collection and analyses, interpretation of findings, preparation of figures/tables/appendices, submission for publication, revisions following peer review and resubmission, and writing of this dissertation.

Dr. Anouk Lamontagne, senior author on the manuscripts, is my PhD supervisor and she contributed to the research design, acquisition of laboratory equipment and provided guidance with data analysis and interpretation of findings. She also revised the different draft versions of the manuscripts; Dr. Samir Sangani contributed to the creation of avatars, footstep sound feedback and virtual scenes. He also helped with many programming related tasks and troubleshooting of the experiments; Dr. Joyce Fung contributed to the acquisition of equipment, laboratory setting adjustment, as well as data analysis and interpretation of findings. Dr. Kara K. Patterson contributed to the data analysis and interpretation of findings. All authors also read, revised, and approved the final version of manuscripts submitted to the peer-reviewed journals. This thesis was read, revised, and approved by Dr. Anouk Lamontagne.

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List of abbreviations

ACC: angular coefficient of correspondence

ADL: activities of daily living

CMSA: Chedoke-McMaster Stroke Assessment

CRIR: Center for Interdisciplinary Research in Rehabilitation of Greater Montreal

CV: coefficient of variation

DHI: dizziness handicap inventory

CRP: continuous relative phase

CVA: cerebrovascular accident

DRP: discrete relative phase

EA: error-augmentation

EHI: Edinburgh Handedness Inventory

EMG: electromyography

ER: error reduction

ETDRS: Early Treatment Diabetic Retinopathy Study

fMRI: functional magnetic resonance imaging

GEE: generalized estimating equation

lAdvance: large advance

lDelay: large delay

KP: knowledge of performance

KR: knowledge of results

MoCA: Montreal Cognitive Assessment

NparLD: non-parametric analysis of longitudinal data

RAC: rhythmic auditory cue

RCT: randomized controlled trial

sAdvance: small advance

SD: standard deviation

sDelay: small delay

SLR: step length ratio

SWR: swing time ratio

SW/ST: an intralimb ratio of swing to stance time

TMS: transcranial magnetic stimulation

VR: virtual reality

WHO: World Health Organization

Abstract

Gait asymmetry is a common gait dysfunction characterized by a prolonged swing phase on the paretic vs. non-paretic side and/or a larger or smaller step length on the paretic vs. non-paretic side. It can lead to negative consequences such as increased risk of injury on the non-paretic side, loss of bone density on the paretic side, and other issues. Biological feedback, that is feedback arising from human motion, was shown to be easily decipherable by the human brain. Delivered in the form of a real-time visual self-avatar, and/or via footstep sounds, it could enhance the ability of stroke survivors to minimize their gait asymmetry, although this remains to be explored.

In manuscript 1, we examined the effects of a virtual avatar displaying locomotor movements in real time on gait symmetry in stroke survivors, while focusing on the effects of different avatar views (back, front, and paretic side). Results indicated that avatar-based feedback is a feasible and acceptable approach to participants, and that only the paretic side view yielded a significant increase in walking speed and bilateral step length. For this condition, responders, who showed a larger initial step length on the paretic side, increased their step length to a larger extent on the non-paretic side during avatar exposure, causing improved step length ratios.

In manuscript 2, the effects of visual avatar-based feedback provided in the paretic side view on interlimb coordination during walking were examined. Results showed that participants who improved their step length ratio (SLR) also improved their continuous relative phase (CRP) magnitude, and that the changes in CRP magnitude were positively correlated with changes in SLR and walking speed. This manuscript also reaffirmed that changes in gait symmetry, coordination and walking speed are mediated by adaptations on the non-paretic side.

In manuscript 3, we investigated instantaneous changes in gait symmetry in stroke survivors exposed to real-time feedback provided as a visual avatar, auditory foot strike, and combined visual-auditory modalities. Findings showed that the combined modalities of feedback did not show advantage over the single-modality feedback to improve gait symmetry. Responders, who showed improved SLR, increased step length bilaterally but more so on the side displaying the shorter step initially.

In manuscript 4, the effects of distorted auditory feedback on gait symmetry, delivered in the form of delayed vs. advanced footstep sounds of small vs. large magnitude, were examined in healthy participants. Increased swing times on the perturbed side were observed in the advanced conditions, while swing time increased bilaterally in the delayed conditions but to a larger extent on the unperturbed vs. perturbed side. No significant changes in SLR were noted. Small vs. large magnitudes of distortion elicited similar spatiotemporal adaptations.

This dissertation deepens the knowledge on gait symmetry adaptations and underlying movement strategies in people with stroke. Results suggest that avatar feedback presented with a side view may be best to induce improvements in the spatial symmetry of gait post-stroke, providing a better perspective on step/stride length while walking. Results also showed that post-stroke temporal gait asymmetry remained unaffected regardless of the type of feedback. This result could be associated with the altered rhythm perception previously reported after stroke. In that regard, providing augmented feedback through distorted auditory feedback on foot strike events could be a promising avenue to enhance the perception and correction of post-stroke asymmetry, especially in the temporal domain. Collectively, results of this dissertation provide the foundation for the development and testing of an intervention incorporating a real-time, augmented feedback to improve post-stroke gait asymmetry.

Abrégé

L'asymétrie de la marche est un dysfonctionnement commun après l'accident vasculaire cérébral (AVC) qui est caractérisé par une phase d'oscillation prolongée du côté parétique et/ou une longueur de pas plus grande ou plus petite du côté parétique par rapport au côté non-parétique. Il a été démontré que le cerveau humain pouvait facilement déchiffrer une rétroaction (feedback) consistant en du 'mouvement biologique.' Présenté en temps réel sous la forme d'un avatar visuel et/ou de sons de pas, un tel feedback pourrait contribuer à minimiser l'asymétrie de la marche post-AVC, bien que cela reste à explorer.

Dans le premier manuscrit, nous avons examiné les effets d'un avatar virtuel en temps réel sur la symétrie de la marche après l'AVC, tout en nous concentrant sur les effets de différentes vues d'avatar (arrière, avant et côté parétique). Les résultats indiquent que le feedback par avatar est une approche faisable et acceptable pour les participants, et que seule la vue du côté parétique a produit une augmentation significative de la vitesse de marche et de la longueur de pas bilatéralement. De plus, les répondants à cette condition, qui montraient initialement un pas plus long du côté parétique, ont augmenté leur longueur de pas plus du côté non-parétique.

Dans le second manuscrit, les effets d'un feedback visuel par avatar présenté du côté parétique sur la coordination inter-jambes pendant la marche ont été examinés. Les résultats montrent que les participants qui amélioraient leur RLP amélioraient également la magnitude de leur phase relative continue (PRC), et que les changements de magnitude de la PRC étaient positivement corrélés avec les changements de RLP et de vitesse de marche. Ce manuscrit a également réaffirmé que les changements dans la symétrie de la marche, la coordination et la vitesse de marche sont médiés par des adaptations du côté non-parétique.

Dans le troisième manuscrit, nous avons étudié les changements instantanés de l'asymétrie de la marche lorsqu'exposé à un feedback en temps réel sous la forme d'un avatar visuel, d'un son de pas, ou encore d'une combinaison de ces deux modalités. Les résultats ont montré que le feedback incorporant les modalités combinées ne présentait pas d'avantage sur le feedback à modalité singulière pour améliorer la symétrie de la marche. Les répondants au feedback, ont augmenté leur longueur de pas bilatéralement, mais plus du côté où le pas était le plus court.

Dans le dernier manuscrit, les effets d'un feedback auditif déformé sur la symétrie de la marche, sous la forme de sons de pas retardés ou avancés, de petite ou grande magnitude, ont été examinés chez des participants en bonne santé. Une phase d'oscillation plus longue du côté perturbé a été observée dans les conditions avancées, tandis que la durée de phase d'oscillation a augmenté bilatéralement dans les conditions retardées, mais plus du côté non-perturbé. Le RLP n'a pas été changé significativement. Les magnitudes différentes de distorsion ont provoqué des adaptations spatio-temporelles similaires.

Cette thèse approfondit les connaissances sur les adaptations et les stratégies de mouvement chez les personnes ayant eu un AVC. Les résultats suggèrent que le feedback par avatar présenté avec une vue latérale pourrait induire des améliorations de symétrie spatiale, en fournissant une meilleure perspective sur la longueur du pas pendant la marche. Les résultats ont également montré que l'asymétrie temporelle après l'AVC n'était pas modifiée par aucun type de feedback. Ce résultat pourrait être associé à une altération de la perception du rythme sonore rapportée après l'AVC. À cet égard, fournir un feedback augmenté via une distorsion temporelle du feedback pourrait améliorer la perception et la correction de l'asymétrie de la marche. Collectivement, les résultats de cette thèse servent à développer une intervention incorporant un feedback en temps réel afin d'améliorer l'asymétrie de la marche post-AVC.

Preamble

Stroke often results in a hemiparesis that impedes mobility, leading to limitations in community ambulation and restrictions to social participation [1, 2]. A hallmark of post-stroke locomotion is gait asymmetry, which is present in 49% to 59% of patients at admission and persists in the vast majority once rehabilitation is completed [3]. This asymmetry is associated with negative consequences such as gait inefficiency, poor dynamic balance and an enhanced risk of musculoskeletal injury on the non-paretic side [4, 5], which can impair the ability (speed, endurance, balance) to safely ambulate within a community setting [6].

While symmetrical gait is often an objective of rehabilitation [7], likely due to a lack of specificity, was shown to have little effects on it [3]. Gait training incorporating rhythmic auditory stimuli [8, 9] and split-belt treadmill [10] yields some improvements, but the gait remains largely asymmetrical compared to normative values. It is hypothesized that the mitigated results of existing approaches are explained, in part, by the impaired perception of individuals with stroke about their gait asymmetry [11] and a difficulty for therapists to provide timely, accurate and easily decipherable feedback about the gait pattern. A body of literature in psychophysics further indicates that humans have a remarkable ability to perceive and interpret biological sensory cues (i.e. cues arising from live beings). Perception of a pedestrian, including its orientation and direction, can be enhanced by multiple biological sensory cues, such as when footstep sounds (auditory cues) are added to an animated point-light figure mimicking locomotion (visual cues) [12, 13]. These observations concurred with the existence of a supramodal brain network that is specific to the perception of biological movement, including human locomotion [14-16]. In this PhD project, I was thus proposing, for the first time, ***to use virtual human-like avatars as a source of real-time, biological sensory feedback to enhance gait symmetry in stroke survivors. I also***

examined the possible additional benefits resulting from combining a visual avatar and auditory feedback in the form of footstep sounds on gait symmetry.

Evidence from upper and lower extremity training [17-19] and split-belt walking studies [10, 20] also suggests that increasing the perception of movement error through various sensory modalities such as visual or haptic feedback can enhance the potential for movement adaptations (e.g. larger change in arm trajectory, step length, etc.). However, as post-stroke gait asymmetry varies in type (spatial, temporal or both), direction (larger swing time on paretic side vs. non-paretic side) and magnitude [21, 22], the application of such error-augmentation paradigm needs to be tailored properly. In order to eventually apply an error-augmentation paradigm in stroke survivors, ***I thus examined, as a first step, the effects of distorted auditory feedback created by delaying or advancing footstep sound on gait symmetry in healthy young individuals***.

Chapter 1. Background

1.1 Disability and socio-economic consequences associated with stroke

Stroke, also referred to as cerebrovascular accident (CVA), is defined by the World Health Organization (WHO) as “caused by the interruption of the blood supply to the brain, usually because a blood vessel bursts or is blocked by a clot. This cuts off the supply of oxygen and nutrients, causing damage to the brain tissue [23]." Besides being one of the leading causes of death in Canada [24] and other countries in the western world [25], stroke is also one of the leading causes of disablement among adults [26, 27]. It is estimated that stroke costs the Canadian economy around $3.6 billion a year in medical services, personal care and lost productivity [28]. The disabilities resulting from stroke can affect all aspects of life including gross and fine motor ability, walking, activities of daily living (ADLs), speech and cognition [29].

According to a study of community-dwelling Canadians who were aged 65 or older, amongst those who had experienced a stroke, 87% had restrictions in their ADLs and 42% could not walk or required mechanical assistance to walk; in comparison, these proportions were 37% and 10%, respectively, among people who did not have a stroke [26]. As the Canadian population becomes older (the average age was 41.0 years in 2016 compared to 39.1 years in 2006 and 36.3 years in 1996 [30]), it is expected that the prevalence of stroke will increase as well. As a consequence, understanding and treating post-stroke disability and impairments is arguably a major priority for clinicians, researchers and decision makers [31].

1.2 Post-stroke locomotor impairments

Among all the impairments and activity limitations caused by stroke, gait dysfunction is amongst the most reported, and improving gait is the most important goal for the majority of people with stroke [32]. Immediately after stroke, more than half of individuals are not able to walk at all [33]. After 11 weeks of rehabilitation, 64% of stroke individuals regain independent walking function (Barthel subscore of 15 points), while 14% require assistance to walk and 22% remain unable to walk [33]. Among the individuals with stroke who can walk, gait has many characteristics that differ from those of healthy individuals. Studies have shown that the mean comfortable walking speed of people with chronic stroke is around 0.59 m/s [34-36] in comparison to 1.37m/s for healthy individuals in a similar age range [37]. The fast walking speed reaches an average of 0.77m/s in chronic stroke survivors [35, 36], compared to 1.91m/s in healthy elderly individuals [37]. This indicates that on average people with stroke not only walk much slower than healthy people, but they also cannot accelerate as much and reach higher speeds when it is needed.

The kinematic profile of post-stroke gait also deviates from that of healthy people. De Quervain and colleagues (1996) reported that among individuals with stroke, hip flexion on the paretic side usually occurs in the late pre-swing phase as opposed to the early pre-swing phase in healthy people [38]. They further observed that hip flexion on the paretic side progresses in the swing phase at a much slower rate compared to the non-paretic side. Moreover, the average paretic peak knee flexion during swing was shown to be around 42° [38] compared to 55° on the non-paretic side [39]. Most individuals with stroke show markedly reduced ankle plantarflexion during late stance and dorsiflexion during the swing phase on the paretic side, and the initial contact with the ground is often made with a flat foot instead of a heel contact [38]. Besides these deviations in the sagittal plane, many individuals with stroke also exhibit increased hip abduction angle from toe-off to swing phase, a phenomenon commonly referred as “hip circumduction [40].” Similarly, people with stroke also have problems with multi-segmental, intralimb and interlimb coordination that result in disrupted hip/knee movement patterns on the paretic side [41], unequal propulsive force of the two lower limbs [22], a poor coordination of upper and lower limbs [42] and an altered head stabilization during walking [43]. The non-paretic side also exhibits kinematic deviations, as the peak values of hip flexion, knee flexion, knee extension and plantarflexion were found to be lower on the non-paretic side in individuals with stroke versus healthy controls [39].

Abnormal muscle activation patterns shown in electromyographic (EMG) recordings is another characteristic of post-stroke gait. In a seminal study published in the 1970s, Knutsson and Richards described three types of muscle activation patterns of the paretic lower limb, which can be referred to as the ‘spastic’, ‘paretic’ and ‘abnormal co-contraction’ patterns of muscle activation. In the spastic pattern of muscle activation, the triceps surae muscle group was prematurely activated in the stance phase and its peak magnitude was lower than that of healthy controls. In the paretic pattern of muscle activation, there was almost no muscle activation in hip adductors, hamstrings, triceps surae and tibialis anterior throughout the gait cycle. The remaining pattern or muscle activation was characterized by a strong co-activation among the quadriceps, hip adductors, hamstrings and triceps surae from the end of the swing phase to the main part of the stance phase [44]. The non-paretic side generally demonstrated increased EMG magnitude and duration in different phases of stance phase, namely in the hamstrings, plantar flexors and quadriceps muscle groups [45]. This is believed to compensate for the reduced muscle activation of the paretic side, possibly to assist with propulsion and postural stability [45].

Key studies from Kim and Eng (2004) as well as Olney and Richards (1996) also showed that the kinetic aspect of post-stroke gait is different from healthy gait [40, 46]. In the sagittal plane, the paretic side shows abnormally high hip flexor moment in the late stance, as well as reduced knee extensor moment during weight acceptance concurrent with a knee hyperextension, reduced plantarflexion peak moment in late stance and a reduced or a lack of dorsiflexor moment at heel strike and during the swing phase swing [40, 46]. The abnormally large hip flexor moment mentioned above generates an early swing hip flexion pull-off which is thought to compensate for the lack of ankle plantarflexion moment or lack of ankle push-off in late stance, assisting with forward propulsion while walking, especially in slower walkers [47, 48]. As for the reduced ankle dorsiflexion moment, it results in the previously mentioned foot flat contact with the ground in early stance and a foot drag during swing [38]. On the non-paretic side, various moments at the hip, knee and ankle joints were also found to deviate from normative values, often being smaller compared to healthy gait [39]. In the frontal plane, people with stroke showed an additional hip abductor moment with a positive power burst from toe-off into swing phase on the paretic side, and a knee adductor moment on bilateral sides at the propulsion phase just prior to toe-off [40]. In the transverse plane, the kinetic profiles of people with stroke are highly variable compared to healthy controls, but many show a positive power burst on the paretic knee during push-off phase [40].

In terms of spatiotemporal parameters, post-stroke gait features decreased cadence [49, 50], shorter stride and step length [49, 50], increased time spent in double limb support and less time in single support on the paretic side [49], as well as a wider base of support [50] compared to healthy gait. Furthermore, walking after stroke is also portrayed by a number of interlimb differences such as prolonged swing phase on the paretic side vs. non-paretic side [51], as well as different step length on the paretic vs. non-paretic side, which are differences commonly referred to as ‘gait asymmetry’. The issue of post-stroke gait asymmetry, further elaborated on in the next section, is key to this PhD thesis which aims at examining different modalities of avatar-based feedback as a mean to promote the symmetry of spatiotemporal factors of gait and other gait parameters in stroke survivors.

1.3 Post-stroke gait asymmetry

Similar to other post-stroke gait impairments, gait asymmetry results from the muscle weakness, also referred to as hemiparesis, that follows the brain lesion. Several negative consequences associated with stroke can be linked to gait asymmetry. First, the proportion of people who have experienced at least one fall per year among the community-dwelling stroke individuals is 1.5 to 2 times higher than the general healthy elderly population, and the people with stroke are also prone to have multiple falls [52]. It was hypothesized that the asymmetrical loading between the paretic and the non-paretic limbs associated with temporal gait asymmetry causes compensatory stepping behaviour to occur, thus creating difficulty to maintain dynamic balance [31]. Gait asymmetry could also cause musculoskeletal injury to the non-paretic limb due to repetitive high loading forces [31], and other complications such as a loss of bone mineral density on the paretic side [5]. Post-stroke gait is also associated with a higher energy cost compared to the gait of healthy individuals [53]. The increased energy expenditure is associated with the increased mechanical work done by the muscles [54], which could be due to the asymmetrical gait pattern [31]. Finally, the levels of ambulatory activity of community-dwelling people with chronic stroke are extremely low (2837 steps/day) when compared to sedentary healthy older adults (5000-6000 steps/day)[55]. It is possible that the impairments and disabilities resulting from the persisting gait asymmetry contribute, in part, to the restriction of overall activity and participation levels in people with stroke [31].

Spatiotemporal parameters of gait are the most common gait variables used for symmetry analysis [31]. Temporal symmetry calculations typically involve swing time, stance time or an intralimb ratio of swing to stance time (SW/ST), while spatial symmetry calculations mainly use step length [31]. Different equations and parameters have been used to calculate symmetry which makes the comparison of the value of symmetry between studies difficult [31]. Among the studies that used a simple ratio (expressed as paretic/non-paretic values), reported values for swing time symmetry in people with stroke ranged from 1.24 to 1.61 [21, 49], and the mean step length symmetry ratio ranged from 1.13 to 1.33 [56]. As for healthy individuals, the mean step length ratio and swing time ratio are around 1.02 [57]. The threshold value for asymmetry in swing time ratio was determined to be 1.06 and 1.08 for swing time ratio and step length ratio respectively [57]. Patterson and colleagues (2010) analyzed four different equations of symmetry: (1) symmetry ratio ($Variable_{paretic}$ / $Variable_{non\text{-}paretic}$), (2) symmetry index ([($Variable_{paretic}$ - $Variable_{non\text{-}paretic}$)/0.5*($Variable_{paretic}$ + $Variable_{non\text{-}paretic}$)]*100), (3) log-transformed symmetry ratio (│100*(ln($Variable_{paretic}$ / $Variable_{non\text{-}paretic}$)│) and (4) symmetry angle (based on angles of vectors on a Cartesian plane) ([45°- arctan($Variable_{paretic}$ / $Variable_{non\text{-}paretic}$)* 100%]/90). Their results have shown that all four equations were highly correlated and had similar distributions [57]. Other kinetic and kinematic variables have been reported to measure gait symmetry, namely trunk movement symmetry along the antero-posterior and mediolateral axes [58] and vertical ground reaction force symmetry [22]. However, since the most common measures of symmetry involve spatiotemporal parameters [57], other symmetry measures will not be the focus point of this research project.

When comparing the gait of healthy people versus stroke using symmetry measures, it is reported that the gait of healthy people is almost symmetrical in spatiotemporal parameters as the interlimb difference of temporal symmetry index and was found to be less than 6% [59], while post-stroke gait usually exhibits a temporal asymmetry which is described as a prolonged (18% longer) paretic swing time and/or a prolonged (30% longer) non-paretic stance time compared to the contralateral side [21, 22, 49, 51, 60, 61]. The interlimb difference of step length in post-stroke gait is less consistent because some individuals with stroke may have longer paretic step lengths while others have longer non-paretic step lengths [21, 22, 62, 63]. It has been shown in one study of Patterson and colleagues (2008) that 55.5% participants of a group of individuals with chronic stroke exhibited temporal asymmetry, but spatial asymmetry was less prevalent, affecting 33.3% of the same group [56]. Although some of participants with spatial asymmetry also presented temporal asymmetry, the overall spatial asymmetry was not correlated with the temporal asymmetry (r=.03) [56]. The temporal asymmetry was found to have a nonlinear association with walking speed and motor impairment, where greater severity of asymmetry (ratio≥1.5) was linked with slower speed (≤60 cm/s) and more pronounced motor impairment [56]. In summary, post-stroke gait asymmetry can vary in types (temporal, spatial or both), directions (larger step length on paretic or non-paretic side) and magnitude.

Despite the negative consequences and prevalence of post-stroke gait asymmetry, it has been shown that most people with stroke don’t significantly improve their gait symmetry during rehabilitation [3]. The possible reasons for this lack of improvement could be an altered perception of gait symmetry after stroke, a lack of interventions that target gait symmetry specifically, and the feedback on gait symmetry provided by clinicians during therapy sessions which could be difficult to understand.

1.4 Perception of gait asymmetry

Post-stroke gait asymmetry has been found to be difficult to change in the course of rehabilitation [64]. A potential explanation could be that people with stroke have impaired perception of their gait symmetry, which makes its detection and remediation difficult. In fact, the motor and sensory systems closely interact when learning a task. Studies on post-stroke individuals with impaired proprioception [65] and on the disruption of somatosensation among healthy individuals [66] revealed that impaired sensory perception negatively affects the acquisition of a new motor task. Learning an upper extremity task was also shown to enhance the perception of limb position (proprioception) in healthy adults [67]. Somatosensory deficits, which are common after stroke [68], could thus lead to difficulty in perceiving gait asymmetry and, consequently, in re-learning how to walk symmetrically.

In support of this hypothesis, a study on temporal gait asymmetry post stroke indicated that around half of the participants incorrectly perceived the presence and/or direction of their temporal asymmetry [69], although the study was carried out in a small sample of participants (n=13). Crosby and colleagues (2021) further conducted a study where a temporal gait asymmetry was induced in healthy people by attaching cuff weight to the thigh and ankle on the non-dominant side. Their results showed that only a portion of the participants correctly perceived the presence and direction of asymmetry, while most of them overestimated the magnitude of asymmetry [70]. Their results suggest that the detection and correct estimation of gait asymmetry could be a difficult task even for the healthy population.

Additional evidence on the perception of gait asymmetry arises from the studies that utilized split-belt treadmills. Hoogkamer (2017) hypothesized that the perception of gait asymmetry is based on the processing and ability to detect differences in temporal afferent inputs between the left and right side, while the influence and impact of spatial inputs remain unknown [71]. This hypothesis is supported by a study that examined the ability of healthy older adults to detect different belt speeds during split-belt treadmill walking, which showed that the perception threshold was inversely correlated with the magnitude of stance time asymmetry [72]. Moreover, Hoogkamer and colleagues (2015) showed that healthy people and individuals with ataxia following a cerebellar lesion had similar ability to detect belt-speed differences. Participants who displayed a better perception of belt-speed differences were those with the smallest stance time asymmetry; these individuals, however, also showed the largest limb excursion (a measure of spatial aspect of gait) asymmetry [73].

As for the perception of gait asymmetry post stroke, Wutzke and colleagues (2015), in a study involving split-belt treadmill walking, initially hypothesized that post-stroke gait asymmetry would partly be a consequence of sensory deficits that prevent people with stroke from recognizing the asymmetry as a movement error [11]. Their results, however, rather showed that people with large stance time asymmetry still used stance time symmetry values to detect belt-speed differences, while those with large limb excursion asymmetry used limb excursion symmetry values [11]. Therefore, the authors argued that people with stroke do not lose the ability to perceive gait asymmetry and that instead their perception of asymmetry is 'recalibrated' as the spatiotemporal parameters of their current gait become their 'new symmetrical gait [11].' A potential limitation of the studies that so far examined the perception of gait symmetry in stroke survivors, however, is that the only sensory modality available to participant to detect symmetry was proprioception. It is possible that through other sensory modalities (e.g., visual and auditory) used as augmented feedback, that individuals would be able to better perceive and modify their spatiotemporal parameters of gait, leading to enhanced gait symmetry.

1.5 Post-stroke gait coordination

Coordination is an important measure of the quality of movement, and it can provide information about the inter-joint or inter-segment movement relationships while walking that cannot be revealed by spatiotemporal outcomes [74, 75]. It has been argued that the coordinated movement leads to a reduction in the dimensionality of the degree of freedom in gait [76]. Furthermore, the coordination of multiple body segments would be crucial to achieve stability without excessive energy expenditure during gait [77]. Krasovsky and Levin (2010) defined gait coordination as "an ability to maintain a context-dependent and phase-dependent cyclical relationship between different body segments or joints in both spatial and temporal domains [75]." In fact, similar to the spatiotemporal properties of gait symmetry, gait coordination also has spatial and temporal components. The spatial component of gait coordination refers to the spatial relationship between positions of segments and joints across gait cycles, while the temporal component refers to the relative timing of movement of these different joints and segments throughout a gait cycle [75]. Furthermore, gait coordination at the lower limb level (or upper limb) can be broadly divided into two categories, namely 'intralimb coordination' which involves two or more joints/segments in the same limb (e.g., hip-knee, thigh-shank) and 'interlimb coordination' which involves the same joints/segments on both sides (e.g., hip-hip, knee-knee) [78]. The term 'inter-segmental coordination' is also used to refer to movement across different body segments, such as the head, trunk, and pelvis [79]. This thesis will focus mainly on interlimb coordination as it describes the movement relationship between paretic and non-paretic lower limbs, which is relevant in the context of gait symmetry.

The spatial component of gait coordination can be measured using cyclograms or covariance of sagittal elevation angles of the lower limbs. Cyclograms are created by plotting two joint angles against each other on a plane [80]. For interlimb coordination, it has been suggested that hip-hip and knee-knee cyclograms could be compared to perfectly symmetric cyclograms to describe gait in a qualitative way [81]. In order to provide a quantitative measure of cyclograms, an 'angular coefficient of correspondence' (ACC) can be used to describe the variability of cyclograms across gait cycles by using vector coding technique [82]. Another means to quantify spatial coordination is to calculate the covariance of sagittal elevation angles of the lower limbs which are formed by a body segment and a vertical axis in the sagittal plane [83]. In healthy gait, the sagittal elevation angles of the lower limbs was shown to closely covaried across gait cycles [83]. Neither planar covariance or ACC has been used to describe post-stroke gait [75], as existing studies in this population have focused exclusively on temporal coordination.

The temporal component of gait coordination is studied mainly by examining the phase relationship between joints and limbs. Although there are many different measures being used to quantify the phase relationship in the literature, most studies used the 'continuous relative phase' (CRP), which is calculated by subtracting the phase angles of two joints or segments at every time point during the gait cycle [84], or the 'discrete relative phase' (DRP), which compares the timing of a gait event such as heel strike with respect the same event on the opposite side [85]. In both CRP and DRP, a value of 180° indicates that the joints are moving in an antiphase manner while 0° indicates an in-phase movement pattern [84, 85].

Both CRP and DRP have been used in studies that examined post-stroke gait to describe interlimb or intersegmental coordination. It has been found, for instance, that the CRP values for the thorax and pelvis was similar between people with stroke and healthy controls [86], and that in both groups those two segments moved in a more antiphase manner when gait velocity was increased [86, 87]. Kwakkel and Wagenaar (2002) also examined the arm-leg CRP of people with stroke during walking and concluded that the arm-leg CRP on both the paretic and non-paretic sides improved (became more anti-phase) and reduced in variability following both upper-extremity and lower-extremity rehabilitation sessions [88]. Through cross-covariance analyses, it has also been shown that bilateral arm-leg coordination in high functioning stroke survivors did not differ from that of healthy people [89], suggesting that arm-leg coordination deficits depend on the severity of motor impairment and the level of motor/gait recovery.

As for intralimb coordination post-stroke, a study characterizing the coordination of thigh-shank elevation angles via CRP revealed asymmetrical intralimb coordination between the paretic and non-paretic side and overall CRP values that differed from that observed in healthy people [90]. Hip/knee intralimb coordination was also found to be altered bilaterally in stroke survivors vs. healthy controls [91]. In terms of interlimb coordination, studies on the phase relationship between bilateral heel strike events showed that while healthy people have a near anti-phase heel-strike pattern with high consistency, people with stroke have a more in-phase heel-strike pattern with a large variability, indicating altered interlimb coordination [92, 93]. Furthermore, Haddad and colleagues (2010) examined in healthy individuals the impact of a weight wrapped around the non-dominant ankle that created gait asymmetry on interlimb coordination between different segments of lower extremity (i.e., thigh-thigh, shank-shank, foot-foot) [94]. Their results indicated that CRP values for all segment pairs became more in-phase when an asymmetry was induced, as opposed to a typical out-of-phase pattern [94]. In stroke survivors, a recent study also showed that asymmetry was significantly associated with impaired interlimb coordination during walking (R^2=0.79) [92], adding further support to the hypothesis that defective interlimb coordination plays a role in post-stroke gait asymmetry. It should be noted, however, that above-mentioned studies described the temporal aspect of interlimb coordination and gait symmetry, such that it remains unclear if results would extend to the spatial aspect of gait coordination and symmetry.

1.6 Most studied interventions for post-stroke gait asymmetry

As mentioned previously, more than half of the people with chronic stroke exhibit temporal asymmetry and about one third of them have spatial asymmetry [56]. Therefore, improving gait symmetry is an important treatment goal for patients and clinicians [32, 95]. The following section focusses on the three most well-studied and commonly used intervention approaches for gait asymmetry, including conventional treadmill training, split-belt training, and rhythmic auditory cueing.

1.6.1 Conventional treadmill training on post-stroke gait

Treadmill training is a common approach in post-stroke gait rehabilitation. It has the advantage of providing task-specific, repetitive practice of walking [96] within a confined space. Treadmill training has been shown to help people with stroke to improve walking speed [64], endurance [64] and cardiovascular fitness [97]. In addition, many studies and clinical trials coupled treadmill training with body weight support to improve walking speed, balance, and other outcomes [98-100].

For the spatiotemporal parameters specifically, a systematic review showed that treadmill training could lead to an increase in paretic step length, stride length and cadence among people with stroke [101]. In terms of temporal gait asymmetry, an RCT which involved 2 weeks of treadmill training with visual feedback showed that stroke participants in both groups (with or without visual feedback) did not change their swing time ratio at the end of training program, nor at the 6-month follow-up [102]. In another study that compared treadmill training to prosthetic gait training among people with stroke, the participants who received treadmill training did not change their stance time nor stance time ratio at the end of 3-weeks training [103]. Furthermore, Gama and colleagues (2015) conducted a controlled randomized trial (RCT) which demonstrated that among people with chronic stroke, those who received 12 sessions of treadmill training with partial weight support at 10% inclination did not have greater improvement in swing time ratio compared to those who received treadmill training with partial weight support at level surface [104]. The within-group improvements in swing time ratio were not significant either [104].

In terms of spatial asymmetry, Kahn and Hornby (2009) showed that by performing a unilateral step training on a treadmill using the paretic side, participants with chronic stroke were able to improve their step length ratio by 13% after 10 sessions, and the retention effect lasted for about 2 weeks before vanishing [105]. In a previously mentioned RCT where treadmill training with vs. without visual feedback was examined, participants in both groups improved their step length ratio while the inter-group difference was not significant [102]. Hase and colleagues (2011) also showed that the step length ratio of people with stroke was improved with a 3-weeks treadmill training, but they did not report the significance level [103]. However, in the work of Gama and colleagues (2017), it was shown that people with stroke only improved their step length ratio in the overground training group and not in the treadmill group after 6 weeks of training [106]. Overall, while conventional treadmill training failed to show positive effects on temporal gait symmetry so far, current literature suggests that it has the potential to improve the spatial aspect of gait symmetry.

1.6.2 Split-belt training on post-stroke gait

Many studies have demonstrated that split-belt treadmill could be a useful tool to improve post-stroke gait symmetry [10, 107-112]. A systematic review on neural control involved in split-belt treadmill adaptations indicated that although people with stroke might be slower to adapt their gait patterns to split-belt treadmill initially, but after a few days of training their extent of adaptation is not different than healthy people [113]. Moreover, another systematic review that examined the effects of split-belt treadmill on post-stroke step length asymmetry concluded that split-belt treadmill could lead to improvement of step length symmetry following long-term training (more than one session) only, which support the postulate that people with stroke would need more practice to display the desired gait adaptations [114]. Reisman and colleagues (2013) and Lewek and colleagues (2018) have shown in their studies that the step length asymmetry was improved after a respective 12 and 18 sessions of split-belt treadmill training, but the stance time ratio did not change [10, 111]. Tyrell and colleagues (2011) showed, however, that individuals with chronic stroke walking at their fastest speed on a split-belt treadmill immediately (in one session) improved their step length ratio by a very large effect size compared to walking at their comfortable speed [115]. There was also no significant change on the temporal symmetry measure, similar to the two studies mentioned above [115]. In brief, like the conventional treadmill training, split-belt treadmill training also appears to be effective at improving spatial symmetry only.

Besides conventional and split-belt treadmills, rotational treadmills have also been used to study post-stroke gait asymmetry. Chen and colleagues (2014) showed that participants with chronic stroke who received 12 sessions of turning-based treadmill training over 4 weeks significantly improved their stance time ratio by a small effect size, while those who received regular treadmill training did not improve significantly [116]. The effect persisted after 1 month of follow-up [116]. However, the step length ratio was not significantly changed. It is to be noted that rotational treadmill has not been widely used in clinical setting, possibly due to its high cost and requirement of large space to be installed.

1.6.3 Rhythmic auditory cueing on post-stroke gait

Rhythmic auditory cueing (RAC) is an intervention where a person is walking with either metronome or musical cueing, and the objective is for the person to align his/her foot strikes with the cueing [117]. The mechanism behind RAC is that there is neural connectivity between auditory and motor areas in the brain, and perception of auditory rhythm can lead to rhythmic movement [118, 119]. This phenomenon of synchronization of motor responses to the frequency of external rhythm is called 'entrainment [120].' Based on the findings of two systematic reviews with meta-analyses, RAC has shown beneficial effects at improving spatiotemporal parameters of post-stroke walking, namely increasing walking speed, stride length and cadence [121, 122]. However, these systematic reviews did not report the findings on gait symmetry, nor analyzed the differences between spatiotemporal parameters of paretic and non-paretic sides.

Upon further examination of the literature, however, there are studies that examined the impact of RAC on gait symmetry. Thaut and colleagues (2007) conducted a randomized controlled trial that compared the effects of RAC to neurodevelopmental technique/Bobath and their results showed that RAC was better at improving the swing time ratio [8]. In another study where RAC was compared to conventional physical therapy, RAC did not show statistical significant superiority at improving swing time ratio [117]. Although RAC demonstrated potential at improving the temporal aspect of gait asymmetry among people with stroke, Patterson and colleagues (2018) argued that there is a large variability in terms of responsiveness to RAC among the stroke population, which is possibly due to people with stroke having reduced rhythm perception abilities compared to the healthy population [123].

In terms of spatial component of gait asymmetry, the literature shows mixed results on the effectiveness of RAC. In a study that compared the use of home-made metronome beat to conventional gait training among people with stroke, the group that received metronome training improved their stride length ratio significantly more than the other group [124]. In another study that compared RAC to overground training among people with stroke, the authors only mentioned that the stride length of both paretic and non-paretic sides were increased in the RAC group, and the spatial gait asymmetry was not directly reported; however, based on my own calculation using their results, the stride length ratio seemed to become worse after training in the RAC group (pre: 1.01 vs. post: 1.06) [125]. Moreover, many studies confirmed that the stride length appear to be larger after RAC training, but they also did not report on the spatial gait symmetry [8, 117, 126, 127].

Overall, it seems that treadmill training shows mixed results in terms of improving temporal symmetry but promising effects on spatial symmetry, while RAC training shows the opposite trend, with demonstrated positive effects for temporal symmetry only. However, it is to be noted that among all the studies examined, none of the interventions utilized extrinsic feedback, which will be discussed in the following section.

1.7 Feedback in motor learning/relearning

The development of contemporary interventions, including those targeting locomotor impairments post-stroke, rely on principles of motor learning and motor control [128]. Motor learning has been defined by Schmidt (1988) as “a set of processes associated with practice or experience that leads to relatively permanent changes in the ability to produce skilled action" [129]. Many models and theories have been proposed to analyze motor learning in the rehabilitation setting. Kleim and Jones (2008) proposed that the motor learning in the intact brain and relearning following brain damage relies on 10 principles of experience-dependent neural plasticity: use it or lost it; use it and improve it; specificity; repetition matters; intensity matters; time matters; salience matters; age matters; transference; interference [130]. Schmidt (1988) further defined four factors that contribute to motor learning, namely the stages of learning, types of tasks, practice and feedback [129]. Regarding skill acquisition, practice and feedback are believed to be the most important factors [129]. Learning relies on intrinsic sensory feedback experienced by the performer (e.g. somatosensory, visual, etc.) and the therapists can facilitate this process by using augmented (extrinsic) feedback (e.g. verbal or manual guidance, etc.), which supplements the performer's intrinsic feedback [131, 132].

There are two broad categories of augmented or extrinsic feedback commonly used in clinical settings: knowledge of results (KR) and knowledge of performance (KP) [129]. In contrast to KR which gives information about whether a goal is successfully attained, KP is more concerned with the movement pattern and the aspects of the human system that leads to the movement [131]. It has been suggested that KP can lead to less motor impairments and better motor function among severely impaired stroke survivors comparing to KR [133].

1.7.1 Distortion of feedback

Feedback can be modified and does not have to reflect reality in order to be effective. Two main paradigms, arising mainly from the literature on robotics, were proposed and tested as means to facilitate motor learning and relearning: the error augmentation (EA) paradigm and error reduction (ER) paradigm. The ER paradigm is to reduce the performance errors of a subject during a motor task [18], usually via the haptic assistance or visual cues. This paradigm is based on the hypothesis that a demonstration of the correct movement trajectory enables a person to learn this movement by imitation [134]. Moreover, the discovery of "mirror neurons" that were first identified using microelectrode recordings of single neurons in area F5 of monkey premotor cortex [135] prompted researchers to hypothesize that such mirror neuron system could support learning through imitation [136] and, by extension, the learning occurring under the ER paradigm. The ER paradigm further assumes that there is a unique, optimal movement trajectory and any deviation from it should be considered as an error. Other motor control principles such as the principle of abundance, however, argue that having variance in how a motor action is performed does not necessarily impede the overall motor performance [137].

A whole body of literature also suggests that motor learning is actually an error driven process, a postulate that can be explained and supported by motor control theories such as the internal model theory [138] and the equilibrium point hypothesis [139]. In the internal model theory, it is hypothesized that subjects form an 'internal model' based on their anticipation of the effects of the environment on their motor actions, therefore the internal model acts as a feed-forward component of the motor control [138]. The detection of errors that occur during the motor performance play the role of a feedback component, as errors prompt the existing internal model to adapt in order to reduce errors [140-143]. In the equilibrium point hypothesis, the errors occur in the subsequent movements following a change in the environment, but the motor system is able to correct these errors by adjusting the control variables based on information about the current motor state, joint positioning of the limbs, etc., thus resetting the activation thresholds (λ) of muscle and forming a new equilibrium point [139, 144]. The notion that the motor system is constantly adjusting itself to minimize performance errors is also central to other motor control theories, such as the back-propagation theory in neural networks [145]. Given the role of errors in motor learning, it was hypothesized that artificially increasing the performance error would cause learning to occur more quickly [134], an idea that is the foundation of the EA paradigm.

1.7.1.1 EA and ER in upper-extremity rehabilitation

Until this day, most of the literature on the use of EA and ER paradigms comes from research on upper-extremity recovery. For this reason, I collaboratively conducted a systematic review aimed to examine the effects of distorted haptic feedback on the performance of reaching tasks among people with chronic stroke [146]. In this review, we included thirteen studies (n=13) where 6/13 studies compared EA to conventional training, 3/13 compared ER to conventional training, and 4/13 compared EA to ER. The results showed that the EA paradigm was more effective than unmodified feedback at improving upper-extremity impairments, disabilities and kinematic performance while ER did not show any significant better results than unmodified feedback [146]. Moreover, EA was more effective than ER at improving reaching trajectory smoothness, but was not significantly better than ER at improving impairment and disabilities [146].

A previous systematic review that only compared EA to conventional training also showed that EA can be used to enhance motor performance in upper extremity after stroke [147], which is in agreement with our findings. EA also showed potential at improving the quality of movement [148, 149], but additional studies with larger sample size and more rigorous methodology would be needed to confirm this.

1.7.1.2 EA and ER in lower-extremity rehabilitation

As for gait training, fewer studies with similar paradigms that involve modified feedback were tested. Using robotics, it was shown that reducing movement error among healthy participants while walking with the use of force field that provides assistance 'as needed' has potential to improve gait outcomes such as step height [150, 151]. Other studies have applied force field resistance while walking to amplify movement error [148, 152-154]. The after-effect seen upon removal of the force field has been proposed as necessary to train correct movement patterns following neurological dysfunction [18, 148]. In 2013, Kao and colleagues compared the effects of EA versus ER approach in enhancing step height among healthy participants performing a stepping task using robotic exoskeletons [18]. In this study, the exoskeleton provided either an assistive force field that brought the ankle path near the desired (heightened) ankle path (ER) or a resistive force field pulling the ankle path down, away from the desired ankle path (EA). Results of that study showed that the EA training protocol yielded better short-term effects in step height modification than the ER protocol [18]. Kao and colleagues (2015) conducted a pilot study on the use of force field in the EA and ER paradigms among people with stroke, and their results also showed that EA is more effective than ER at modifying gait patterns and ankle trajectories during stepping [19].

Reisman and colleagues have conducted a few studies in the past exploring the effects of EA paradigm on post-stroke gait asymmetry with the use of split-belt treadmill [10, 155, 156]. Their training paradigm consisted of having participants placing their foot with a longer step length on the belt with slower speed, thus increasing the spatial asymmetry even further during the training [10, 155, 156]. However, the results indicated that although the spatial asymmetry was increased initially during the adaptation period, it would eventually decrease, leading to an improvement effect, and the improvement would persist for several minutes after the adaptation [10, 155, 156]. It is to be noted that only step length had a significant change while stance time did not change [10, 155]. In summary, it was suggested that post-stroke asymmetry is not necessarily permanent, and that people with stroke could potentially still produce a symmetrical movement pattern [10]. In addition, feedback provided in the EA paradigm has the potential to improve step length and spatial asymmetry [10, 155, 156].

1.7.2 Timing of feedback

According to Cech and Martin (2012), extrinsic feedback can be categorized either as terminal and concurrent feedback based on the timing at which it is delivered [157]. Concurrent feedback is defined as a feedback given "during task performance" while terminal feedback is given "at the completion of a motor task" [157]. The main advantage of concurrent feedback would be to guide the learner in order to achieve a desired movement pattern and to activate certain musculature [157]. On the one hand, it is argued that providing concurrent feedback too frequently may cause the learner to become overly dependent on it and, as a result, motor learning would be less than when providing terminal feedback [157]. A solution to this problem was proposed in Yamamoto and Ohashi's study where healthy people were to perform an acceleration task using shoulder and wrist movement[158]. They showed that by adjusting the accessibility of concurrent feedback according to participants' needs, the kinematic performance was improved to a greater extent with a large effect size than when simply providing terminal feedback [158]. On the other hand, a study showed that providing terminal feedback frequently (100% of the trials) significantly reduced temporal gait asymmetry among people with stroke, while feedback provided at 50% of the trials did not have a significant effect [159]. In summary, for the concurrent feedback the ideal frequency depends on the participants' needs. For the terminal feedback, some studies suggested that it should be provided as often as possible [159-161], while other studies pointed out that providing too much terminal feedback could lead to dependency [162, 163]. Therefore, the ideal frequency of terminal feedback for individuals with stroke is still being debated.

Real-time feedback is an example of concurrent feedback which was only recently explored in gait training research. It consists of providing an instantaneous KP about the gait pattern of the individuals [164, 165]. It can provide information about almost every aspect of gait. One systematic review examined the effectiveness of real-time kinematic, spatio-temporal, and kinetic biofeedback in gait training among stroke survivors [166]. The authors concluded that real-time feedback offered greater improvement than conventional therapy in the participants' base of support, walking speed, step length, as well as other parameters of gait. This suggests that providing feedback instantaneously may have superior effects in post-stroke gait training than providing feedback after the movement [166]. Studies have shown that the real-time visual feedback on weight bearing can lead to larger improvement in stride length ratio and single support time ratio versus conventional overground training among people with stroke [167, 168]. Thus, the use of real-time feedback showed potential at improving spatiotemporal outcomes of gait symmetry after stroke, but current studies only used real-time feedback on weight bearing while direct feedback on gait pattern, especially in other sensory modalities besides visual modality, remains to be investigated.

1.7.3 Sensory modalities of feedback

The sensory modality through which sensory feedback is conveyed to the participant also vary from one study to the other. As mentioned in the previous sections, haptic feedback is a modality that is often used in robotic-based therapy and which can guide a participant towards the desired trajectory of a movement by providing kinesthetic and tactile information [148, 150-154, 169]. Some disadvantages associated with the use of robotic devices which could make them impractical to be applied in the clinical setting are that the devices can be very expensive, the preparation phase can be time consuming, and the operators need to have the proper expertise to ensure the safety of participants.

In rehabilitation, visual feedback is commonly used given that vision is the sensory modality that is the most relied upon in humans to perceive spatial information in general and given the important role of vision in learning the spatial aspects of a movement [170]. Chunduru and colleagues (2019) compared the effects of visual feedback to split-belt treadmill at inducing asymmetrical walking pattern among healthy participants and the results indicated that participants who trained with visual feedback showed the longest gait asymmetry aftereffects [171]. The authors concluded that people may show a greater implicit learning process when exposed to visual feedback versus relying on the proprioceptive feedback provided by split-belt treadmill [171]. This observation of visual feedback about one's own movement causing implicit gait modulation was also reported in another study, which reported that with gradual distortion of visual feedback on bilateral step length among healthy people, the step length ratio of participants could be modulated toward asymmetry [172].

Auditory feedback has also been shown to be an effective method to be used in motor learning in stroke rehabilitation [173]. According to Sigrist and colleagues (2013), auditory feedback could provide information about the temporal aspect of a movement and help performers in the advanced stages of learning to fine-tune their movement execution [174]. The authors also suggested that auditory feedback is most effective in fast repetitive tasks such as walking [174]. For the stroke population, locomotor studies in the past mainly utilized auditory feedback to improve weight bearing symmetry through the lower extremities [175, 176], except in the study of Kim and colleagues (2021) where they showed that auditory feedback was not only effective at improving weight bearing symmetry, but also superior over conventional gait training to improve the symmetry of spatiotemporal features such as step time, single stance time and step length in individuals with stroke [177].

Combining different sensory modalities may offer additional advantages for motor learning as in daily lives, people are constantly processing different modalities simultaneously. It has been argued that multimodal compared to unimodal stimuli are perceived more precisely and faster [178, 179], a phenomenon described as intersensory facilitation [180]. In fact, the presence of a stimulus in one modality (e.g. auditory stimulus) can amplify the neuronal processing of a similar construct displayed in another modality (e.g. visual stimulus) [169]. For instance, an auditory stimulus, which originates at approximately the same time and place as does a visual stimulus, can significantly affect the likelihood that a visual-auditory neuron will fire, and can also profoundly affect its firing frequency [181]. It is to be noted that combining different sensory modalities can only be beneficial if they deliver congruent (as opposed to incongruent or conflictual) information. In fact, incongruent multimodal stimuli can cause reduced perception of each of the modalities [182]. Visual feedback has been combined with proprioceptive feedback as a dual-learning paradigm for people with stroke in a study where participants received real-time visual feedback on their paretic knee flexion angle while walking on a split-belt treadmill versus a tie-belt treadmill [112]. After split-belt treadmill training with visual feedback, participants had their paretic knee flexion increased and step length asymmetry reduced, while only the paretic knee flexion increased following tied-belt training session with visual feedback [112]. This shows that processing two modalities at the same time is a feasible task and can lead to larger benefits in motor learning for people with stroke. Such an approach, however, is yet to be examined for the visual and auditory modality. Combining those two modalities could be advantageous as people with stroke often present with both temporal and spatial gait asymmetry [3], and visual and auditory feedback were shown to have potential at improving spatial and temporal aspects of asymmetry, respectively [172, 177].

1.7.4 Feedback in biological cues

Feedback in the form of biological cues is a recent topic of interest in motor learning research [165]. Visually, it could consist of human-like moving figures or avatars while auditory wise, it could be footstep sounds being heard as someone walks. A study done by Grosbras et al. (2012) showed that the posterior superior temporal sulcus plays a special role in integrating information arising from human movement [183]. In fact, people are remarkably good at recognizing the biological motion of a live being by looking at it, even when the kinematic patterns of the movements are portrayed by point-light displays which are nothing more than a handful of light points attached to the head and major joints of the body [184, 185]. Individual, static frames look like meaningless clusters of dots, but when the frames are animated, one immediately perceives a biological organism engaged in a readily identifiable activity [184]. Furthermore, people are adept at judging the direction in which animate objects are moving [186-189] and can detect slight differences in the speed at which animate objects are moving [187]. Therefore, KP feedback in the form of biological motion could be used to provide additional and more easily decipherable information about one's spatiotemporal aspects of movement compared to conventional feedback delivered in the forms of numbers or bar graphs.

In recent literature on gait training, an approach to apply biological feedback is to use virtual self-avatars [190], which allows individuals to obtain visual feedback about their own walking pattern in real time which can be useful for postural and locomotor rehabilitation [191]. A feeling of agency and embodiment can be created over the avatar when the movement of the avatar is synchronized with the user's movement, [192, 193] and this can facilitate the user's perception of the cues on his/her body location provided via the avatar [194]. Compared to feedback provided by a video camera, feedback in the form of avatars could enhance the sense of immersion and be implemented as part of a virtual environment to simulate daily activities. Additionally, by providing muscle vibration that mimics muscle activation during walking in conjunction with a visual avatar, the sense of embodiment can be further enhanced provided that the multimodal congruency is kept [195]. Kannape and Blanke (2013) showed that the sense of agency was affected by the temporal delay of the avatar feedback [190], thus in order to maximize the sense of agency the avatar feedback would need to be provided in real time. In the same study, the authors concluded that when the avatar feedback was provided with a temporal delay, participants decreased their stride time (faster gait cycles) in an attempt to resynchronize their gait to that of their avatar [190]. In a pilot study involving 9 healthy participants, it was also observed that increasing the stride length of avatars by modulating the hip flexion angles could lead to increased stride length in the participants, although the differences were not significant [192]. It is important, however, to distinguish visual feedback in the form of avatars from the phenomenon of 'gait synchronization' which is characterized by unintentional walking speed modifications and phase locking of rhythmic movements between two individuals walking together [196-200]. In other words, gait synchronization is based on the mechanism of cueing, while self-avatars used as feedback allows one to observe their own gait movements. In the Willaert et al. (2020) study [192], although instructions given to participants were not described in their proceedings paper, it appears that participants attempted to synchronize their gait to the observed avatar (i.e. tended to increased their step length in response to the avatar showing larger step length), as opposed to reducing their step length in response to a step length that would be visually perceived as ‘too large’. In the paragraph below, the very few studies that involve avatar feedback during gait or stepping movements, i.e. self-avatars used with the purpose of providing feedback on one’s movements, are being described.

A study that involved the use of virtual avatars was to investigate the influence of visual feedback on stepping movements among healthy people [201]. While this study showed that visual feedback was superior to visual cueing at improving spatial and temporal hip motion tracking, the spatiotemporal parameters of gait were not assessed [201]. In addition to the visual feedback, the authors also provided auditory ‘pacing’ with a whistle sound, but because it was auditory cueing and not feedback, the biological visual-auditory feedback interaction could not be investigated [201]. To my knowledge, only two studies have used feedback in the form of virtual avatars to improve gait features in patient populations. A first one, conducted by Darter and Wilken (2011), is a case study on a 3-week gait training using virtual reality-based real-time feedback on full body kinematics in the form of an avatar in one individual with transfemoral amputation. Their results suggest that this type of feedback could be effective at improving various kinematic parameters, as well as at increasing bilateral step length and reducing bilateral stance time, although this would need to be examined in a larger sample of individuals [165]. In 22 children with cerebral palsy, Booth et al. (2019) compared the instantaneous effects of visual feedback in the form of a self-avatar to no feedback and showed that the avatar feedback led to increased hip and knee sagittal joint excursion as well as larger step length [202].

Based on the very few existing studies on the topic, it appears that visual feedback provided in the form of virtual self-avatars shows potential at improving different parameters of gait. The use of such paradigm to improve gait symmetry in patient populations such as stroke, however, is yet to be examined. In addition, different view angles of avatar could lead to different effects on gait adaptations. A side view, for instance, could hypothetically be more advantageous for detecting interlimb differences in step length, while frontal and back views could be better at detecting hip circumduction. Furthermore, psychophysical studies that used biological motion information showed that combining a visual point-light walker to footstep sounds leads to enhanced perception of specific features of the walking pattern compared to when the visual point-like walker is devoid of footstep sounds [203, 204]. Thus, combining biological visual and auditory cues as sources of real-time feedback on lower limb movements during gait could lead to better perception and correction of the walking symmetry in stroke survivors. This hypothesis, however, remained to be verified.

Chapter 2. Rationale and research question

To date, the interventions on post-stroke gait symmetry have either shown mixed results or effects that were only short-term based [87, 96, 99-101, 103, 106-111, 114, 122, 124, 125, 155, 159, 167, 168]. Therefore, in order to help people with stroke to improve their gait symmetry in the long term, clinical interventions would need to target specifically gait symmetry and provide feedback that is augmented and easily decipherable to accommodate their altered gait symmetry perception. Feedback in the form of biological cues has the potential to be incorporated in such interventions because humans not only have the remarkable ability to perceive and interpret biological motion information, but also are able to detect even the slightest deviation when observation a walking pattern [185, 191]. When compared to established interventions such as split-belt treadmill training, feedback in the form of biological could further facilitate the implicit learning process [171]. In addition, virtual reality (VR) can be used as the ideal platform to provide such feedback as it can facilitate the integration of different sensory information and allow the real-time feedback to be augmented or modulated [191, 205]. As a result, feedback in the form of biological cues presented in a VR environment can be a valuable approach to improve gait symmetry.

Until now, there is very limited research done on real-time feedback in the form of biological cues (i.e., avatars, footstep sound) in general, and existing studies were conducted amongst healthy participants and populations other than stroke, while not focussing on gait symmetry [165, 192, 201, 202]. Furthermore, there is a need to examine which viewing angles of avatar may provide the best effects in terms of gait symmetry, as different views (side or sagittal view vs. frontal view) might provide a different perspective on existing gait deviations. There is also a lack of evidence on how avatar-based feedback may influence interlimb coordination of lower extremities, which was found to be closely related to gait symmetry [92, 93]. Feedback that combines different sensory modalities also showed an enhanced effect on gait symmetry compared to single-modality feedback when applied to split-belt walking [112]. As people with stroke who have gait asymmetry can present with either or both temporal and spatial asymmetry [3], and given that visual vs. auditory feedback may respectively impact the spatial vs. temporal aspects of gait [172, 177], it is highly relevant to study the impact of those modalities of feedback, provided individually vs. as a combination, on the spatial and temporal symmetry of gait. Lastly, an EA paradigm provided via a differential in belt speed during split-belt walking was shown to improve step length and spatial asymmetry in stroke survivors [10, 155, 156], but whether such approach could also be used with auditory feedback to modify the temporal aspect of gait symmetry in either a healthy or stroke population remains unknown.

Thus, the main research question I sought to address in my PhD project was as follows: Among *people in the chronic phase of stro*ke performing a walking task, to what extent does avatar-based feedback on their gait pattern impact on gait asymmetry? More specifically, I explored the effects of different types of avatar feedback in terms of presentation view (avatar presented with a paretic side, back and front view) and sensory modality (footstep sounds, visual avatar, and a combination of both). In *healthy individuals*, I also examined the effects of distorted auditory feedback on gait symmetry, focussing on the type (delayed vs. advanced feedback) and extent of distortion (small vs. large). Through the different studies presented in this thesis, I opted for an *instantaneous adaptation paradigm,* whereby every experiment would take place in a single session with the goal of testing the feasibility and applicability of the different feedback approaches, before conducting longer trials in the future. Specific research objectives and hypotheses are detailed in the following chapter.

Chapter 3. Research objectives and hypotheses

The short-term goals of the research projects presented in this thesis are: (1) to explore the immediate effects of avatar feedback (presented in three different view angles as frontal, back and paretic side) on post-stroke gait asymmetry; (2) to determine the optimal combination of sensory modalities (visual avatar, auditory footstep sound) for an avatar-based gait training paradigm; (3) to examine the immediate effects of distorted auditory feedback on gait symmetry in healthy participants. Results gathered in this thesis will serve the long-term goal of developing a VR-based intervention involving real-time avatar-based feedback that can be applied as part of a post-stroke rehabilitation program to improve gait symmetry in stroke survivors.

This thesis comprises of four manuscripts, each exploring specific objectives and hypotheses that are further detailed below.

3.1 Manuscript 1: "Real-time avatar-based feedback to enhance the symmetry of spatiotemporal parameters after stroke: instantaneous effects of different avatar views"

The specific objectives of this manuscript were:

1. To examine the feasibility of real-time visual feedback in the form of virtual avatars as an approach to improve post-stroke gait symmetry and other gait parameters.
2. To compare the effects of the frontal, back and paretic side view of avatar feedback on gait symmetry.
3. To investigate whether responders to the avatar feedback differed in terms of their level of motor recovery and gait capacity.

In relation to these objectives, it was hypothesized that: (1) real-time visual feedback in the form of avatars is a feasible approach to improve gait symmetry and other parameters of gait in people with stroke; (2) the paretic side view provides the largest improvement in gait symmetry when compared to the frontal and back view of avatar because the side view has been shown to elicit fastest movement recognition [206]; (3) participants with higher gait capacity and better motor recovery are more likely to improve the symmetry of spatiotemporal parameters with the avatar-based feedback because studies of post-stroke gait recovery suggested that people with faster gait speed, higher level of balance and motor recovery generally showed higher potential for recovery [3, 207].

3.2 Manuscript 2: "Instantaneous effects of real-time avatar visual feedback on interlimb coordination during walking post-stroke"

The specific objectives of this manuscript were:

1. To explore whether avatar-based feedback which aims to improve gait symmetry can also improve interlimb coordination among people with stroke.
2. To examine the relationship between the changes in coordination and step length symmetry, as well as between the changes in coordination and walking speed.

In relation to objective 1 of this study and manuscript, it was hypothesized that (1) the avatar-based feedback improves interlimb coordination of lower extremities. As for the objective 2, it was hypothesized that (2) the improvement in interlimb coordination is correlated with the improvement in gait symmetry, and; (3) the improvement of the interlimb coordination is also correlated with the improvement in walking speed.

3.3 Manuscript 3: "Immediate effects of visual avatar, auditory foot strike and combined feedback on gait symmetry post stroke"

The specific objectives of this manuscript were:

1. To compare the effects of visual only, auditory only, and combined visual-auditory feedback on post-stroke gait symmetry.
2. To investigate the motor strategies leading to improvements in gait symmetry.
3. To examine the relationship between the improvements in gait symmetry and the individual characteristics of stroke participants.

It was hypothesized that (1) the combined visual-auditory feedback would provide the largest improvements in post-stroke gait symmetry; (2)) individuals would improve their symmetry by adapting their spatiotemporal factors primarily on the non-paretic side, as seen previously with a single-modality visual avatar [208] and; (3) individuals with a smaller initial gait asymmetry, due to better sensorimotor functions, would show larger improvements in gait symmetry.

3.4 Manuscript 4: "Application of an auditory-based error-augmentation paradigm to modify gait symmetry in healthy individuals"

In this fourth and last manuscript, which involved healthy individuals, I aimed to address the following specific objectives:

1. To determine changes in step length and swing time ratios in response to distorted footstep sound feedback of different directions (delay vs. advance) and magnitudes (small vs. large) applied to either the right or left lower limb.
2. To examine changes in sagittal plane joint kinematics of the lower limbs associated with the different variations in auditory feedback.

In relation to objective 1, it was hypothesized that (1) participants would modify their gait pattern by increasing their swing time and step length on the perturbed side in the advanced feedback conditions, and on the unperturbed side in the delayed feedback conditions, leading in both instances to altered swing time and step length symmetry. It was also hypothesized that (2) a large feedback distortion would lead to larger alterations in spatiotemporal factors and gait symmetry in comparison to a small distortion. As for objective 2, it was hypothesized that (3) changes in swing time and step length symmetry would be accompanied by changes in sagittal joint excursion at multiple lower limb joints (hip, knee, and ankle), and possibly changes in maximum toe height during swing.

Chapter 4

4.1 Preface

Gait asymmetry is common and persists in most individuals with stroke once rehabilitation is completed [3]. As part of this PhD project, a VR-based paradigm that involved real-time avatar-based feedback on locomotion was developed and tested in individuals with stroke and healthy participants. Manuscript 1 of this dissertation investigates the feasibility and acceptability of the real-time avatar feedback as an approach to improve post-stroke gait symmetry as this VR-based feedback paradigm is implemented for the first time among people with stroke. In addition, Manuscript 1 also aims to address the first short-term goal which is to *explore the immediate effects of avatar feedback (presented in three different view angles as frontal, back and paretic side) on post-stroke gait asymmetry*. The view angle that proves to be the most effective at improving post-stroke gait symmetry would be selected and used for future experiments.

Manuscript 1: Real-time avatar-based feedback to enhance the symmetry of spatiotemporal parameters after stroke: instantaneous effects of different avatar views

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4.2 Abstract

Gait asymmetry, one of the hallmarks of post stroke locomotion, often persists despite gait rehabilitation interventions, impacting negatively on functional mobility. Real-time feedback and biological cues have been studied extensively in recent years, but their applicability to post-stroke gait symmetry remain questionable. This proof-of-concept study examined the feasibility and instantaneous effects of real-time visual feedback provided in the form of an avatar in twelve participants with stroke on gait symmetry and other gait-related outcomes. The visual avatar was presented via three different views from the back, front and paretic side. Avatar feedback from the paretic side view showed significant increase in bilateral step length, paretic swing time ratio and treadmill walking speed, but no significant differences were found in symmetry measures in any of the three views. Those who had changes in symmetry ratio>0 were grouped as responders to spatial symmetry improvement in the side view. The responders had a significantly higher Chedoke-McMaster Stroke Assessment foot score and presented with a larger initial step length on the paretic side. Furthermore, all participants provided positive feedback and no adverse effects were observed during the experiment. Overall, these findings suggest that real-time avatar-based feedback can be used as an intervention to improve post-stroke gait asymmetry.

4.3 Introduction

Stroke is one of the leading causes of death and disabilities worldwide. Among all the impairments and limitations in activities of daily living caused by stroke, gait dysfunction is the most reported, and improving gait is the most important goal for the majority of people with stroke [1]. Immediately after stroke, more than half of the patients are not able to walk at all [2], and among those who can walk, their gait has many characteristics that differ from the gait of healthy individuals. Post-stroke gait not only features slow walking speed [3-5] but it is also characterized by deviations in kinematic/kinetic [6-8] and spatiotemporal parameters. Spatiotemporal deviations consist of decreased cadence [9, 10], shorter stride length [9, 10], increased time spent in double limb support [9], and wider base of support [10] compared to healthy gait. Walking after stroke is also portrayed by a number of inter-limb differences including prolonged swing phase on the paretic side and prolonged stance phase on the non-paretic side, which is commonly referred to as temporal asymmetry [11]. Spatially, some people with stroke exhibit a longer paretic step length while others exhibit longer non-paretic step length [12, 13]. These temporal and spatial asymmetries are commonly referred as gait asymmetry.

Gait asymmetry can lead to many negative consequences, including poor balance control [14], gait inefficiencies [15], increased risk of musculoskeletal injury to the non-paretic limb [16] and decreased overall physical function [17]. A longitudinal study on the changes in gait asymmetry over the course of inpatient rehabilitation indicated that even though the therapists were aware of the presence and magnitude of the gait asymmetry among their stroke clients, these clients did not significantly improve their gait asymmetry at discharge [18]. It was suggested that there was a lack of specificity of the gait interventions on gait asymmetry in the rehabilitation setting [18].

The development of contemporary interventions, including those targeting locomotor impairments post-stroke, rely on principles of motor learning and motor control [19]. Feedback is known to be one of the most important factors that contribute to skill acquisition and motor learning [20]. Feedback can be categorized either as terminal or concurrent feedback based on the timing at which it is delivered [21]. Concurrent feedback is defined as a feedback given "during task performance" while terminal feedback is given "at the completion of a motor task" [21]. The main advantage of concurrent feedback would be to guide the learners in order to feel the desired movement pattern and activation of certain musculature, so that ultimately the learners could improve their movement pattern in the subsequent trials [21]. Real-time feedback is an example of concurrent feedback which was only recently explored in gait training research. It consists of providing instantaneous information about almost every aspect of gait of the subjects [22, 23]. One systematic review examined the effectiveness of real-time kinematic, spatio-temporal, and kinetic biofeedback in gait training among stroke survivors [24]. We concluded that real-time feedback resulted in greater short-term improvement to biomechanical parameters (e.g. narrower base of support, and faster walking speed than conventional therapy, while the retention effects were unclear. Furthermore, the immediate and retention effects of real-time feedback on outcomes of gait symmetry after stroke remain to be examined.

Feedback in the form of biological cues (i.e. cues that arise from live beings or animate objects) is a recent topic of interest in motor learning research [23], and it can be used to create human-like moving figures. An imaging study showed that the posterior superior temporal sulcus plays a special role in integrating information arising from human movement [25]. In fact, people are remarkably adept at recognizing the biological motion of a live being by looking at it, even when the kinematic patterns of the movements are portrayed by nothing more than a handful of light points attached to the head and major joints of the body [26, 27]. Furthermore, people are also adept at judging the direction in which animate objects are moving [28-31] and can also detect slight differences in the speed of animate objects [29]. Therefore, feedback in the form of biological cues could be used as a means to provide additional and more easily decipherable information about one's spatiotemporal aspects of movement compared to conventional feedback delivered in the forms of verbal explanations, numbers and bar graphs. Recently, virtual avatars were used as a novel approach to investigate the influence of external visual biological cueing and/or feedback on locomotion and stepping movement [32, 33]. It is believed that virtual avatars could also elicit 'gait synchronization,' a phenomenon characterized by unintentional walking speed modifications and phase locking of rhythmic movements between two individuals walking side-by-side [34-37]. Studies which explored the use of avatars on post-stroke locomotion, however, were restricted to stepping activities [33] and/or had a very short exposure to the avatar (3s) [32], hence providing no information on short- and longer-term walking adaptations. Additional limitations included the use of a fixed-speed treadmill that hindered speed adaptations [32].

In the present study, we are proposing for the first time to explore the use of visual feedback in the form of virtual avatars (biological cues) displaying locomotion in real time to improve the symmetry of gait spatiotemporal parameters in people with stroke. In this proof-of-concept study that involved a single-time exposure to avatar-based feedback, we hypothesized that: (1) real-time visual feedback provided by avatars is a feasible and acceptable approach to improve gait symmetry and other parameters of gait in people with stroke; (2) the paretic side view provides the largest improvement in gait symmetry when compared to the frontal and back view of avatar because the side view has been shown to elicit fastest movement recognition [38]; (3) participants with higher gait capacity, and better motor recovery are more likely to improve the symmetry of spatiotemporal parameters with the avatar-based feedback because studies of post-stroke gait recovery suggested that people with faster gait speed, higher level of balance and motor recovery generally showed higher potential for recovery [18, 39]. Thus, the relationship between the level of initial gait asymmetry and the improvement in gait symmetry should also be examined.

4.4 Methods

4.4.1 Experimental design

A cross-sectional within-subjects design with repeated measures was used for this study.

4.4.2 Participants

Participants were included in this study if they met the following inclusion criteria: (1) having a first time sub-acute or chronic stroke (>6 months) supratentorial stroke; (2) age between 45 to 79 years; (3) being able to walk for 2 minutes independently while supervised, with or without a walking aid; (4) having a deficit in motor recovery of the lower limb, as indicated by stage scores ranging from 2 to 6 on the leg and foot components of the Chedoke-McMaster Stroke Assessment (CMSA); (5) having either temporal asymmetry (swing time ratio >1.06) or spatial asymmetry (step length ratio >1.08) [40] or both. Participants were excluded if they had (1) a stroke affecting brainstem or cerebellum; (2) co-morbid conditions such as cardiovascular, respiratory, musculoskeletal or other neurological conditions affecting locomotion; (3) dementia or cognitive deficits as indicated by scores < 24 on the Montreal Cognitive Assessment (MoCA); (4) severe aphasia or apraxia based on medical charts and initial screening; (5) non-corrected visual deficits; (6) a history of motion sickness or perceived handicap caused by dizziness, as indicated by a score > 16 on the Dizziness Handicap Inventory (DHI).

Participants were recruited from the Jewish Rehabilitation Hospital located in Laval, Quebec, Canada, which is a McGill University-affiliated teaching hospital and a research site of the Montreal Centre for Interdisciplinary Research in Rehabilitation (CRIR). This study received ethics approval from the Research Ethics Board of CRIR and all participants understood and signed the consent form prior to the first session of experiment.

4.4.3 Experimental setup and procedure

The data collection consisted of two sessions. The first session included habituating participants to a self-paced treadmill (described below) and evaluating them with the 10-Meter Walk Test, CMSA, MoCA and DHI in order to determine their overground comfortable speed, stroke severity, presence of cognitive deficits and history of motion sickness, respectively. These tests have demonstrated excellent psychometric properties [41-44].

In the second session, the participants performed the walking task on a custom-built self-pace treadmill (0.6 m x 1.5 m). The motor of the treadmill is driven by PID servo-control based on the real-time distance and velocity feedback obtained with a potentiometer tethered to the participant [45]. A safety harness system suspended overhead was used to prevent the participants from falling. The treadmill is fitted with sliding handrails to assist with balance. The use of handrails, if applicable, was determined during habituation and was kept constant throughout the experiment. The participants who needed to use the handrails were instructed to only use it for balance, and not to put body weight on it during the habituation and the experiment. A screen (2.44 m × 3.05 m) was mounted in front of the treadmill for rear-projection of the virtual environment representing a long street with an avatar located 3.5 m ahead of the participant. Maya LT™ 2016 (Autodesk, USA) was used to design avatars of similar appearance and anthropometric characteristics to those of the participants. During the experiment, real-time tracking of the limb movement was provided by Tracker™ (Vicon, UK) based on the displacement of the 15 rigid bodies markers placed on the participant on specific body landmarks specified in Vicon Tracker™, which were tracked by the 6-camera Vicon™ (Vicon, UK) motion capture system. Pegasus Advanced™ (Vicon, UK) was used to retarget the limb positions onto a virtual avatar which would then be displayed on the screen and controlled using Unreal Engine 4 (Epic Games, USA). Kinematic data of participants were collected at 120 Hz in Vicon Tracker.

The participant performed two walking trials of each of the following conditions in a random order (Figure 4.1): (1) avatar viewed from the back; (2) avatar displayed with a paretic side view and; (3) avatar facing the participant. The paretic side was chosen because most gait deviations happened on the paretic side, and a clearer view of their gait deviations was preferred. The duration and number of trials were determined based on a previous study performed in healthy participants [46], while taking into account the limited endurance of stroke participants. Each trial had three phases which included 30s of comfortable walking without the avatar (pre-adaptation phase), followed by 1 min of walking while visualizing the avatar replicating the exact walking pattern of the participant in real time (adaptation phase), and finally 1 min of walking without the avatar (post-adaptation phase). Prior to the start of each trial, the following verbatim was given to participants: "*Please wait for the "Go" sign on the screen before starting walking. When the trial starts, always walk with your comfortable speed and keep looking at the screen. For the first 30 secs, you will be looking at an empty street, then an avatar will appear. He (she) will mimic your way of walking in real-time, so please look at his (her) legs and feet for feedback and pay attention to your walking symmetry in at the same time. The avatar will disappear after 1 min, and you will be looking into at the empty street again. Keep walking until you see the "Stop" sign*.". Participants were allowed to rest by sitting between the walking trials.

4.4.4 Data analysis

Kinematic data were processed and exported using Vicon Nexus^{TM} 1.8.5, before being analyzed in Matlab R2017b. To avoid the effects of acceleration and deceleration, data in the first and last 10 seconds of each trial were excluded. Data were normalized to 100% of the gait cycle, then filtered with a 4th order Butterworth low-pass filter at a cut-off frequency of 10 Hz.

The primary outcomes were step length ratio and swing time ratio, respectively, for the spatial and temporal components of gait symmetry. These two outcomes were calculated in the following way: first, rigid body markers were placed on the dorsum of feet along with additional reflective markers being put on the big toes and heels. This allows us to measure the distance between toe/heel and the rigid body makers. The reflective markers were then removed prior to the start of walking trials because they could interfere with the capturing of the movement of rigid body markers. The position data of rigid body markers plus the pre-determined distance between toes and heels were used for the calculation of swing time and step length. The ratios were calculated using the values of left and right side with the larger value in the numerator regardless of which side was the paretic [40]. A resulting value of '1.0' indicated perfect symmetry.

Secondary outcomes included paretic and non-paretic step length and swing time and treadmill walking speed. The feasibility was evaluated using in-trial observations on whether a participant was able to complete all trials, whether there was pain or fatigue involved while performing the walking task, whether the handrail was used and if loss of balance/fall occurred. The acceptability was examined with a short interview post-experiment composed of the following questions: 1) overall, how do you like this avatar intervention? 2) do you feel that this avatar intervention changes the way you walk? 3) would you like to see this type of avatar intervention be implemented in the rehabilitation program in the future? 4) do you have a preferred view of the avatar (e.g. front, back or side)?

4.4.5 Statistical analysis

Gait outcomes were averaged for each of the three phases (pre-adaptation, adaptation), separately for each avatar view. As for the primary outcomes of spatial and temporal symmetry, only data from participants who were considered 'asymmetric' were included for analysis. Since the data could not be assumed to follow a normal distribution, Friedman test was used to assess differences in gait symmetry and other outcomes across phases (pre-adaptation, adaptation, post-adaptation) for each avatar view separately. Wilcoxon signed-rank test was then used to conduct post-hoc pairwise analysis between phases, with Bonferroni-Holm correction adjustments. To calculate the effect size, the formula proposed by Rosenthal (1994) '$r=z/\sqrt{N}$' was used [47]. If r was between 0.1 and 0.3, the effect size was considered small; between 0.3 and 0.5, it was medium and above 0.5, it was large [48].

Responders vs. non-responders to the avatar-based feedback during adaptation phase were further compared on their overground comfortable walking speed, CMSA leg and foot scores, initial step length ratio using Mann-Whitney U tests. In the context of this study, responders were defined as participants showing an improvement in symmetry (ratio change > 0) and were considered separately for spatial and temporal symmetry. Since people with stroke can present with one of two directions of step length asymmetry, i.e., a longer paretic step length or a longer non-paretic step length [12, 13], the directions of step length asymmetry was also examined as an explanatory variable for responders vs. non-responders. The statistical analyses were performed in SPSS v.24 (IBM Inc, USA), and the significance level needed to reject the null hypothesis was set at $p \leq 0.05$.

4.5 Results

Twelve participants with stroke were recruited after the clinical screening process in the period between December 2017 and February 2019. Table 4.1 outlines the demographic and clinical results for all participants. The participants consisted predominantly of people who are males (ratio: 9:3), affected on right hemisphere (ratio: 9:3), and who had an ischemic stroke (ratio: 10:2). Also, 3/12 participants wore ankle-foot orthosis during the experiment. 3/12 participants had an overground comfortable speed that was considered below 'most-limited community ambulation level' (<0.4m/s) and 6/12 participants were considered above 'community ambulation level' (>0.8m/s) [3]. 10/12 participants presented temporal asymmetry and 9/12 presented spatial asymmetry. Among those who had spatial asymmetry, 5/10 had a larger non-paretic step length while the other 4/10 had a larger paretic step length.

4.5.1 Feasibility and acceptability

All participants successfully completed both the clinical and experimental sessions and there is no missing data to be reported. No adverse effects such as shortness of breath, cybersickness or other discomfort were observed during the experimental trials. No participant reported pain or fatigue during the walking trials, but two participants stated that they felt tired after the experiment session ended. None of the participants experienced loss of balance or a fall while walking.

In response to the questions included in the post-experiment interview, all participants expressed enjoyment and eagerness to participate in other avatar-based interventions. All participants also reported that this walking training with an avatar made them more aware about their gait abnormalities such as asymmetrical step length (10/12, only 9 actually had an initial step length ≥ 1.08 ratio which deemed to be asymmetrical), hip hiking (2/10), and hip circumduction (2/10). Furthermore, 10/12 participants also reported that they felt more confident in walking with this avatar-based training. In addition, they all believed that this type of intervention would have the potential to be implemented in a stroke rehabilitation program and that it could be beneficial for other people with stroke. Finally, when asked which view they preferred the most, 5/12 reported preferring the side view, 4/12 the back view and 3/12 the frontal view.

4.5.2 Symmetry and spatiotemporal parameters

When considering the group results, neither swing time ratio (n=10) nor step length ratio (n=9) showed statistically significant differences across the three phases for all three views (Figure 4.2A right and left). From pre-adaptation to adaptation, however, a trend for increased swing time ratio (worsened symmetry) was observed for all three views while step length ratio tended to improve in the side view only. A large inter-subject variability that was reflected by large standard deviations were also observed in terms of the participants' outcomes across phases, especially for step length ratios in the adaptation phase to the side view. Given these observations, an analysis of individual results was performed for the side view specifically and the results are presented in the next section on responders vs. non-responders.

Analysis of group results also revealed that for the side view only, both the paretic (χ^2=9.23, p =0.01) and non-paretic step lengths (χ^2=15.17, $p \leq 0.001$) varied across walking phases (Figure 4.2B). For the paretic step length, post-hoc analyses revealed a significant increase between adaptation and pre-adaptation (0.020±0.022 m, CV: 110%; Z=2.432, p =0.015) but no significant difference between post-adaptation and pre-adaptation (Z=1.337, p =0.181). On the non-paretic side, step length was found to be larger in the adaptation vs. pre-adaptation (0.033±0.020 m, CV: 61%; Z=3.061, p =0.002) and post-adaptation vs. pre-adaptation phase (0.034±0.038 m, CV: 112%; Z=2.510, p =0.012). A significant effect of walking phase was also observed for swing time on the paretic side only in the side view (χ^2=6.83, $p \leq 0.033$), due to a larger swing time in adaptation vs. pre-adaptation (0.012±0.014 s, CV: 117%; Z=2.847, p =0.004). Treadmill walking speed (Figure 4.2C) was also found to significantly differ across walking phases for the side view only (χ^2=9.44, p =0.009). The post-hoc analyses revealed faster treadmill speeds between adaptation vs. pre-adaptation (0.062±0.059 m/s, CV: 95%; Z=2.667, p =0.008), as well as between post-adaptation vs. pre-adaptation (0.072±0.083 m/s, CV: 115%; Z=2.276, p=0.023). Large effect sizes with r values ranging from 0.66 to 0.88 were observed with all the statistically significant results.

4.5.3 Responders vs non-responders of step length ratio to the side view

As illustrated in Figure 4.3, three out of four participants who initially had a larger paretic step length improved their step length ratio during the adaptation phase, and one participant did not change. In contrast, all participants with a larger non-paretic step length saw a deterioration in step length symmetry. When comparing the group mean values (those with larger paretic vs. non-paretic step length), the differences in step length ratio between adaptation and pre-adaptation were respectively -0.06 ±0.05 vs. 0.04±0.02, and this was found to be significant (Z=-2.46, p =0.014) (Figure 4.4). Furthermore, when comparing post-adaptation to pre-adaptation, three out of four participants who had a larger paretic step length improved their step length ratio (same participants who also improved during adaptation) while one deteriorated. Two out of five participants who had a larger non-paretic step length improved their step length ratio while three deteriorated. The group mean values, were respectively -0.05 ±0.06 vs. 0.02±0.03 for those with a larger paretic and non-paretic step length, but it was found to be non-significant (Z=-1.85, p=0.063). Responders, i.e. those who improved their step length symmetry in response to the side view during adaptation, also had significantly larger CMSA foot score compared to non-responders (4±0.58 vs 3±0.89, Z=-2.04, p =0.041). They presented, however, similar overground comfortable walking speed (Z=-0.78, p =0.439), CMSA leg scores (Z=-0.28, p =0.783) and initial step length ratio (Z=-1.58, p =0.115).

4.6 Discussion

This study examined for the first time the effects of visual feedback in the form of virtual avatars displaying locomotor movements in real time on gait symmetry and other parameters of gait among people with stroke. This study was also the first to compare the effects of back, front and side views of avatar on gait symmetry. Although no significant changes were seen in the primary outcomes (swing time ratio and step length ratio) in any view condition, the side view provided the most interesting changes on secondary outcomes across participants. These changes and possible mechanisms are discussed below.

4.6.1 A feasible modality with benefits on self-efficacy

It was shown in this study that real-time visual feedback in the form of virtual avatars was well tolerated by all participants and did not cause any discomfort. Furthermore, the results of acceptability showed that most participants felt more confident during the exposure of avatars compared to their everyday walking and were able to enjoy walking more with the training. In fact, people with stroke are often associated with low self-efficacy and perceived disability in physical activities [49, 50]. It is stated in the literature that self-efficacy on performing a motor task is largely influenced by the knowledge of performance and results [51, 52], and feedback on concurrent performance can be used to improve self-confidence in performance and quality of performance [51].

4.6.2 Effects of side view

Results revealed secondary gait changes that are specific to the side view of the real-time avatar, which included larger paretic and non-paretic step length, faster walking speed and, in the majority of participants displaying a larger paretic step length to start with, improvements in step length symmetry. A possible reason for participants performing better in the side view condition vs. back and frontal view could be that the side view offered optimal visual feedback on step length as well as lower limb sagittal joint amplitude compared to the other two views. Similarly, healthy participants in another recent study [38] recognized tasks such as punching and kicking faster in a profile (side) view compared to frontal view, suggesting that that the profile view (side view) provided more motion information for discernment [38]. The positive changes in gait that were observed for the side view in the present study were also consistent with the fact that this view was the most subjectively preferred view by participants. Interestingly, three out of five participants who reported of preferring the side view were also the responders of step length ratio improvement during the adaptation and post-adaptation phases in the side view.

4.6.3 Spatial vs. temporal changes

Positive changes in the spatial domain induced by the side view feedback were not necessarily consistent with changes in the temporal domain. For example, the bilateral increase in step length that was observed with the side view led to faster walking speed, despite an increase in swing time on the paretic side. Furthermore, improvements in symmetry, when present, were observed for step length but not for swing time. The increase in bilateral step length is possibly due to the attempt of participants to correct their spatial asymmetry, and we suggest that the increase in walking speed can also be seen as a result of such attempt. Such changes may have taken place at the expense of temporal parameters because in order to take a longer step, people with stroke may require a longer swing time.

The mechanisms in which spatial and temporal changes occur are also different. Vision is the sensory modality that is the most relied upon among humans to perceive spatial information, and it is essential for people to master the spatial aspects of a movement [53]. On the other hand, sounds and auditory feedback provide more information about the temporal aspect of a movement [54]. This is evidenced by healthy participants learning a rowing task, where auditory feedback could provide information about the temporal aspect of a movement and help performers in the advanced stages of learning to fine-tune their movement execution [54]. The same study also concluded that the groups receiving visual feedback had the least spatial error compared to haptic and auditory feedback after three training sessions [54]. Since only visual feedback was used in the avatar-based modality in this study, this could explain why the temporal asymmetry was not significantly changed in any view condition. Therefore, to improve the temporal aspect of gait asymmetry, only visual feedback might not be enough, and the auditory feedback would be a necessary addition to the avatar-based intervention.

4.6.4 Responders vs. non-responders in spatial symmetry

There were noticeable differences between the responders and non-responders of spatial symmetry improvement in the adaptation phase of the side view. First, the responders all had a larger paretic step length while the non-responders had a larger non-paretic step length, in agreement with a previous study [55]. There are possible reasons that could explain why this happened. As demonstrated from the results, the step length on the non-paretic side was increased to a significantly larger extent than the paretic side during adaptation for all participants. As mentioned previously, in an attempt to improve their spatial symmetry, the participants always tried to take larger steps, but since their paretic side was less functional than the non-paretic side, their paretic step length was increased to a lesser extent than the non-paretic step length. As a result, if the initial shorter step is on the non-paretic side, the spatial symmetry is improved, otherwise it is worsened. In addition, a previous study on gait analysis of people with chronic stroke reported that people with a longer paretic step length generated the least amount of propulsive force with the paretic leg compared to people with either symmetrical step length or longer non-paretic step length, and that asymmetry in step lengths is strongly related to asymmetry in propulsive forces [12]. Therefore, the responders of this study might have generated greater propulsive force with their paretic leg to improve the spatial symmetry, but additional research would be needed to confirm this. Another explanation could be the fact that the side view was always portrayed on the paretic side in this experiment. It is possible that people with a larger non-paretic step length would respond better to a non-paretic side view, so for these participants the paretic side view might not provide the necessary information for them to improve their spatial asymmetry.

The responders and non-responder might also have different preferences for biofeedback. In a study of gait training with avatar among children with cerebral palsy, it was stated that although the majority of children preferred biofeedback in the form of avatar, some considered feedback shown in bar style easier to understand [56]. It was possible that self-perception of walking, cognitive ability and previous experience with biofeedback were the factors that influenced the children's preference [56]. Similarly, these factors could also explain why some of the participants with stroke benefited from the biofeedback in the form of avatar while others did not in our study.

The responders had a significantly higher average CMSA foot score compared to the non-responders. This could suggest that a higher functional level makes correcting spatial asymmetry easier as the participants would have stronger control on their paretic step length. On the other hand, no significant difference was noted between responders and non-responders in terms of their initial step length ratio. In a previous study of Patterson and colleagues (2015), it was found that the participants who improved their spatial symmetry had worse initial step length ratio than those who did not change or deteriorated, but the authors did not report if this difference of initial step length ratio was statistically significant [18]. Further research would be needed to examine the relationship between the initial level of asymmetry and the likelihood to improve gait symmetry. It should also be noted that all responders in the adaptation phase maintained their improvement once the stimulus was removed (post-adaptation phase).

4.6.5 Increase in treadmill walking speed and its benefits

Another interesting finding is the increase in walking speed during the avatar exposure, which took place despite of the fact that participants were not instructed to walk faster during the experiment. Increasing walking speed through an increase in step length itself can be clinically beneficial for people with stroke. It has been shown that compared to healthy people, people with stroke tend to have a much smaller step length [57]. Although it is still not fully understood why people with stroke usually have shorter step length, it is possibly caused by fear of falls because taking small 'shuffle' steps can be interpreted as being cautious. In addition, the outcomes 'walking speed' and 'paretic step length' also showed significant retention effects in the post-adaptation phase, and this further demonstrated the fact that even with a very short duration of training, the avatar-based intervention can be an effective tool to improve the spatial aspect of the gait of the people with stroke.

4.6.6 Limitations

A primary limitation of this study is the short duration of the trials where the exposure was limited to 1 min. This time period was chosen considering the number of walking trials needed and limited endurance of the participants., However even with a short exposure duration, we were able to demonstrate statistically significant changes in treadmill walking speed, bilateral step length and paretic swing time in the adaptation phase. Possibly larger changes would be observed with longer as well as repeated exposures to avatar-based feedback. Another limitation is the small sample size in relation to the different types of asymmetries present in our sample. In a study of prevalence of gait asymmetry among people with chronic stroke, it was shown that 55.5% participants exhibited temporal asymmetry, and only 33.3% had spatial asymmetry [58]. Therefore, it is difficult to recruit a large number of participants from both categories of asymmetry due to the low prevalence. The information provided through this study, however, provides important indications as to who may best benefit from avatar-based feedback as a potential intervention for gait asymmetries following stroke.

4.7 Conclusion

In conclusion, the following statements can be made based on the results and analyses: (1) Real-time visual feedback provided by an avatar in the paretic side view is a feasible and acceptable intervention to elicit immediate positive changes in walking speed, and spatial asymmetry for people with a chronic stroke; (2) The side view is the only condition that demonstrated significant increase in walking speed, paretic and non-paretic step length; (3) There is also a retention effect of improvement in walking speed, paretic step length and responders of step length ratio in the side view during the post-adaptation phase where the feedback is removed; (4) Having a larger paretic step length and a greater CMSA foot score (better motor recovery) lead to a larger improvement in spatial symmetry. Overall, the real-time avatar-based feedback can provide many advantages as a gait training intervention: it is versatile because avatars and the scenes can be modified according the need of different participants; it received overwhelming positive feedback from the participants as it is engaging and intuitive; and most importantly, it provides unique concurrent information on walking performance that would otherwise be very difficult or even impossible for clinicians to deliver. In the future, clinical trials with longer and multiple training sessions are needed to test the applicability of avatar-based feedback in the clinical setting. Auditory feedback such as footstep sounds could also be incorporated to examine its effectiveness on temporal symmetry.

4.8 References

1. Bohannon R, Andrews A, Smith M: **Rehabilitation goals of patients with hemiplegia**. *Int J Rehabil Res* 1988, **11**:181-183.
2. Jorgensen HS, Nakayama H, Raaschou HO, Olsen TS: **Recovery of walking function in stroke patients: the Copenhagen Stroke Study**. *Arch Phys Med Rehabil* 1995, **76**(1):27-32.
3. Perry J, Garrett M, Gronley JK, Mulroy SJ: **Classification of walking handicap in the stroke population**. *Stroke* 1995, **26**(6):982-989.
4. Jonsdottir J, Recalcati M, Rabuffetti M, Casiraghi A, Boccardi S, Ferrarin M: **Functional resources to increase gait speed in people with stroke: strategies adopted compared to healthy controls**. *Gait Posture* 2009, **29**(3):355-359.
5. Nadeau S, Arsenault AB, Gravel D, Bourbonnais D: **Analysis of the clinical factors determining natural and maximal gait speeds in adults with a stroke**. *Am J Phys Med Rehabil* 1999, **78**(2):123-130.
6. De Quervain IA, Simon SR, Leurgans S, Pease WS, McAllister D: **Gait pattern in the early recovery period after stroke**. *J Bone Joint Surg Am* 1996, **78**(10):1506-1514.
7. Kerrigan DC, Frates EP, Rogan S, Riley PO: **Spastic paretic stiff-legged gait: biomechanics of the unaffected limb**. *Am J Phys Med Rehabil* 1999, **78**(4):354-360.
8. Kim CM, Eng JJ: **Magnitude and pattern of 3D kinematic and kinetic gait profiles in persons with stroke: relationship to walking speed**. *Gait Posture* 2004, **20**(2):140-146.
9. Brandstater ME, de Bruin H, Gowland C, Clark BM: **Hemiplegic gait: analysis of temporal variables**. *Arch Phys Med Rehabil* 1983, **64**(12):583-587.
10. Chen G, Patten C, Kothari DH, Zajac FE: **Gait differences between individuals with post-stroke hemiparesis and non-disabled controls at matched speeds**. *Gait Posture* 2005, **22**(1):51-56.
11. Titianova EB, Pitkanen K, Paakkonen A, Sivenius J, Tarkka IM: **Gait characteristics and functional ambulation profile in patients with chronic unilateral stroke**. *Am J Phys Med Rehabil* 2003, **82**(10):778-786; quiz 787-779, 823.
12. Balasubramanian CK, Bowden MG, Neptune RR, Kautz SA: **Relationship between step length asymmetry and walking performance in subjects with chronic hemiparesis**. *Arch Phys Med Rehabil* 2007, **88**(1):43-49.
13. Hsu AL, Tang PF, Jan MH: **Analysis of impairments influencing gait velocity and asymmetry of hemiplegic patients after mild to moderate stroke**. *Arch Phys Med Rehabil* 2003, **84**(8):1185-1193.
14. Weerdesteyn V, de Niet M, van Duijnhoven HJ, Geurts AC: **Falls in individuals with stroke**. *J Rehabil Res Dev* 2008, **45**(8):1195-1213.
15. Stoquart G, Detrembleur C, Lejeune TM: **The reasons why stroke patients expend so much energy to walk slowly**. *Gait Posture* 2012, **36**(3):409-413.
16. Patterson KK: **Gait asymmetry post-stroke: thesis for PhD degree**. University of Toronto 2010.
17. Michael KM, Allen JK, Macko RF: **Reduced ambulatory activity after stroke: the role of balance, gait, and cardiovascular fitness**. *Arch Phys Med Rehabil* 2005, **86**(8):1552-1556.
18. Patterson KK, Mansfield A, Biasin L, Brunton K, Inness EL, McIlroy WE: **Longitudinal changes in poststroke spatiotemporal gait asymmetry over inpatient rehabilitation**. *Neurorehabil Neural Repair* 2015, **29**(2):153-162.
19. Richards CL, Malouin F, Nadeau S: **Chapter 13 - Stroke rehabilitation: clinical picture, assessment, and therapeutic challenge**. In: *Prog Brain Res. Volume 218*, edn. Edited by Dancause N, Nadeau S, Rossignol S: Elsevier; 2015: 253-280.

20. Schmidt R: **Motor Control and Learning: A Behavioral Emphasis**, 2nd edn: Champaign, Ill: Human Kinetics Publishers; 1988.
21. Cech DJ, Martin ST: **Chapter 4 - Motor Control and Motor Learning**. In: *Functional Movement Development Across the Life Span (Third Edition).* edn. Saint Louis: W.B. Saunders; 2012: 68-87.
22. Barrios JA, Crossley KM, Davis IS: **Gait retraining to reduce the knee adduction moment through real-time visual feedback of dynamic knee alignment**. *J Biomech* 2010, **43**(11):2208-2213.
23. Darter BJ, Wilken JM: **Gait training with virtual reality-based real-time feedback: improving gait performance following transfemoral amputation**. *Phys Ther* 2011, **91**(9):1385-1394.
24. Tate JJ, Milner CE: **Real-Time Kinematic, Temporospatial, and Kinetic Biofeedback During Gait Retraining in Patients: A Systematic Review**. *Phys Ther* 2010, **90**(8):1123-1134.
25. Grosbras MH, Beaton S, Eickhoff SB: **Brain regions involved in human movement perception: a quantitative voxel-based meta-analysis**. *Hum Brain Mapp* 2012, **33**(2):431-454.
26. Grossman E, Donnelly M, Price R, Pickens D, Morgan V, Neighbor G, Blake R: **Brain areas involved in perception of biological motion**. *J Cogn Neurosci* 2000, **12**(5):711-720.
27. Johannson G: **Visual perception of biological motion and a model for its analysis**. *Percept Psychophys* 1973, **14**:201-211.
28. Ball K, Sekuler R: **A specific and enduring improvement in visual motion discrimination**. *Science* 1982, **218**(4573):697-698.
29. De Bruyn B, Orban GA: **Human velocity and direction discrimination measured with random dot patterns**. *Vision Res* 1988, **28**(12):1323-1335.
30. Gros BL, Blake R, Hiris E: **Anisotropies in visual motion perception: a fresh look**. *J Opt Soc Am A Opt Image Sci Vis* 1998, **15**(8):2003-2011.
31. Pasternak T, Merigan WH: **Effects of stimulus speed on direction discriminations**. *Vision Res* 1984, **24**(10):1349-1355.
32. Kannape OA, Blanke O: **Self in motion: Sensorimotor and cognitive mechanisms in gait agency**. *Journal of neurophysiology* 2013.
33. Koritnik T, Koenig A, Bajd T, Riener R, Munih M: **Comparison of visual and haptic feedback during training of lower extremities**. *Gait Posture* 2010, **32**(4):540-546.
34. Nessler JA, Gilliland SJ: **Interpersonal synchronization during side by side treadmill walking is influenced by leg length differential and altered sensory feedback**. *Human movement science* 2009, **28**(6):772-785.
35. Zivotofsky AZ, Gruendlinger L, Hausdorff JM: **Modality-specific communication enabling gait synchronization during over-ground side-by-side walking**. *Human movement science* 2012, **31**(5):1268-1285.
36. Zivotofsky AZ, Hausdorff JM: **The sensory feedback mechanisms enabling couples to walk synchronously: an initial investigation**. *Journal of neuroengineering and rehabilitation* 2007, **4**:28.
37. Nessler JA, Gilliland SJ: **Kinematic analysis of side-by-side stepping with intentional and unintentional synchronization**. *Gait & posture* 2010, **31**(4):527-529.
38. Fademrecht L, Bulthoff I, de la Rosa S: **Action recognition is viewpoint-dependent in the visual periphery**. *Vision Res* 2017, **135**:10-15.
39. Gianella MG, Gath CF, Bonamico L, Olmos LE, Russo MJ: **Prediction of Gait without Physical Assistance after Inpatient Rehabilitation in Severe Subacute Stroke Subjects**. *J Stroke Cerebrovasc Dis* 2019, **28**(11):104367.
40. Patterson KK, Gage WH, Brooks D, Black SE, McIlroy WE: **Evaluation of gait symmetry after stroke: a comparison of current methods and recommendations for standardization**. *Gait Posture* 2010, **31**(2):241-246.

41. Lin JH, Hsu MJ, Hsu HW, Wu HC, Hsieh CL: **Psychometric comparisons of 3 functional ambulation measures for patients with stroke**. *Stroke* 2010, **41**(9):2021-2025.
42. Gowland C, Stratford P, Ward M, Moreland J, Torresin W, Van Hullenaar S, Sanford J, Barreca S, Vanspall B, Plews N: **Measuring physical impairment and disability with the Chedoke-McMaster Stroke Assessment**. *Stroke* 1993, **24**(1):58-63.
43. Toglia J, Fitzgerald KA, O'Dell MW, Mastrogiovanni AR, Lin CD: **The Mini-Mental State Examination and Montreal Cognitive Assessment in persons with mild subacute stroke: relationship to functional outcome**. *Arch Phys Med Rehabil* 2011, **92**(5):792-798.
44. Whitney SL, Hudak MT, Marchetti GF: **The activities-specific balance confidence scale and the dizziness handicap inventory: a comparison**. *J Vestib Res* 1999, **9**(4):253-259.
45. Fung J, Richards CL, Malouin F, McFadyen BJ, Lamontagne A: **A treadmill and motion coupled virtual reality system for gait training post-stroke**. *Cyberpsychol Behav* 2006, **9**(2):157-162.
46. Kao PC, Srivastava S, Agrawal SK, Scholz JP: **Effect of robotic performance-based error-augmentation versus error-reduction training on the gait of healthy individuals**. *Gait Posture* 2013, **37**(1):113-120.
47. Rosenthal R: **Parametric measures of effect size**. In: *The handbook of research synthesis.* edn. New York, NY, US: Russell Sage Foundation; 1994: 231-244.
48. Cohen J: **Statistical Power Analysis for the Behavioral Sciences**, 2nd edn: Routledge; 1988.
49. Mayo NE, Wood-Dauphinee S, Ahmed S, Gordon C, Higgins J, McEwen S, Salbach N: **Disablement following stroke**. *Disabil Rehabil* 1999, **21**(5-6):258-268.
50. Vahlberg B, Cederholm T, Lindmark B, Zetterberg L, Hellstrom K: **Factors related to performance-based mobility and self-reported physical activity in individuals 1-3 years after stroke: a cross-sectional cohort study**. *J Stroke Cerebrovasc Dis* 2013, **22**(8):e426-434.
51. Escarti A, Guzman JF: **Effects of feedback on self-efficacy, performance, and choice in an athletic task**. *J Appl Sport Psychol* 1999, **11**(1):83-96.
52. Saemi E, Porter JM, Ghotbi-Varzaneh A, Zarghami M, Maleki F: **Knowledge of results after relatively good trials enhances self-efficacy and motor learning**. *Psychol Sport Exerc* 2012, **13**(4):378-382.
53. Freides D: **Human information processing and sensory modality: cross-modal functions, information complexity, memory, and deficit**. *Psychol Bull* 1974, **81**(5):284-310.
54. Sigrist R, Rauter G, Riener R, Wolf P: **Terminal feedback outperforms concurrent visual, auditory, and haptic feedback in learning a complex rowing-type task**. *J Mot Behav* 2013, **45**(6):455-472.
55. Tyrell CM, Roos MA, Rudolph KS, Reisman DS: **Influence of systematic increases in treadmill walking speed on gait kinematics after stroke**. *Phys Ther* 2011, **91**(3):392-403.
56. Booth AT, Buizer AI, Harlaar J, Steenbrink F, van der Krogt MM: **Immediate Effects of Immersive Biofeedback on Gait in Children With Cerebral Palsy**. *Arch Phys Med Rehabil* 2019, **100**(4):598-605.
57. Suzuki K, Yamada Y, Handa T, Imada G, Iwaya T, Nakamura R: **Relationship between stride length and walking rate in gait training for hemiparetic stroke patients**. *Am J Phys Med Rehabil* 1999, **78**(2):147-152.
58. Patterson KK, Parafianowicz I, Danells CJ, Closson V, Verrier MC, Staines WR, Black SE, McIlroy WE: **Gait asymmetry in community-ambulating stroke survivors**. *Arch Phys Med Rehabil* 2008, **89**(2):304-310.

Table 4.1 Summary of the demographic and clinical results of the participants

Subjects	Gender (Male/ Female)	Age (years)	Stroke Chronicity (months)	Type of stroke (Ischemic/ Hemorrhagic)	Stroke Location	Orthotics	Types of Asymmetry (Temporal: T/Nt; Spatial: Snp/Sp/Ns)	Comfortable Overground Walking Speed (m/s)	CMSA Score		Initial step length ratio	Initial swing time ratio
									Leg	Foot		
S1	Female	51	324	Ischemic	L MCA+ frontal	None	T, Snp	0.79	5	2	1.08	1.23
S2	Male	67	12	Ischemic	L Ic	R AFO	T, Sp	0.80	5	3	1.12	1.07
S3	Male	66	25	Hemorrhagic	R Ic	None	T, Ns	1.02	5	5	1.03*	1.16
S4	Male	66	22	Ischemic	R lacunar Ic	None	T, Snp	0.34	6	2	1.20	1.27
S5	Male	57	6	Ischemic	R Ic+Bg	None	Nt, Snp	1.10	5	4	1.14	1.02*
S6	Female	56	12	Ischemic	R MCA	None	T, Snp	0.89	4	4	1.08	1.12
S7	Male	77	40	Hemorrhagic	L thalamus	None	T, Sp	0.29	4	5	1.26	1.22
S8	Male	58	33	Ischemic	R MCA	None	Nt, Sp	1.06	6	5	1.09	1.03*
S9	Male	49	52	Ischemic	R Sylvian	L AFO	T, Ns	0.74	5	4	1.77	1.10
S10	Male	65	165	Ischemic	R Sylvian	None	T, Sp	0.35	3	2	1.04*	1.24
S11	Female	58	26	Ischemic	R thalamus	None	T, Snp	0.86	4	4	1.08	1.08
S12	Male	56	72	Ischemic	R Bg	L AFO	T, Ns	0.96	4	3	1.02*	1.09
Mean±SD, CV Ratio (:)	9:3	60.5 ±7.9, 13%	65.8±92.1, 139%	10:2	—	9:3	Temporal: 10:2 Spatial: 5:4:3	0.74±0.26, 35%	4.7 ±0.319 %	3.7 ±1.437 %	1.21±0. 22 18%	1.14±0.08, 7%

SD: standard deviation; CV: coefficient of variation; L: left; R: right; MCA: middle cerebral artery; Ic: internal capsule; Bg: basal ganglia; AFO: ankle-foot orthosis; T: temporal asymmetry; Nt: no temporal asymmetry; Snp: spatial asymmetry with non-paretic side larger; Sp: spatial asymmetry with paretic side larger; Ns: no spatial asymmetry; CMSA: Chedoke-McMaster Stroke Assessment; MoCA: Montreal Cognitive Assessment; DHI: Dizziness Handicap Inventory. *These values were not considered to be asymmetrical.

Figure 4.1 Different views of the avatar

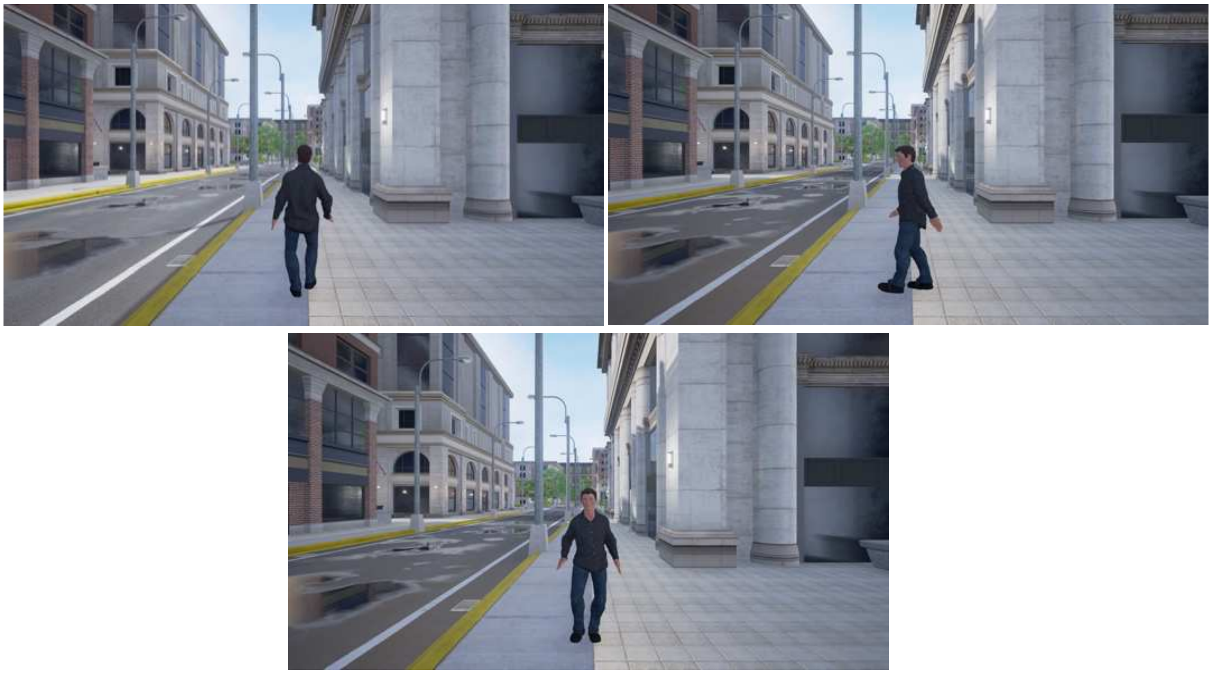

Figure 4.1 Different views of the avatar (top left: back; top right: paretic side; bottom: front).

Figure 4.2 Spatiotemporal parameters

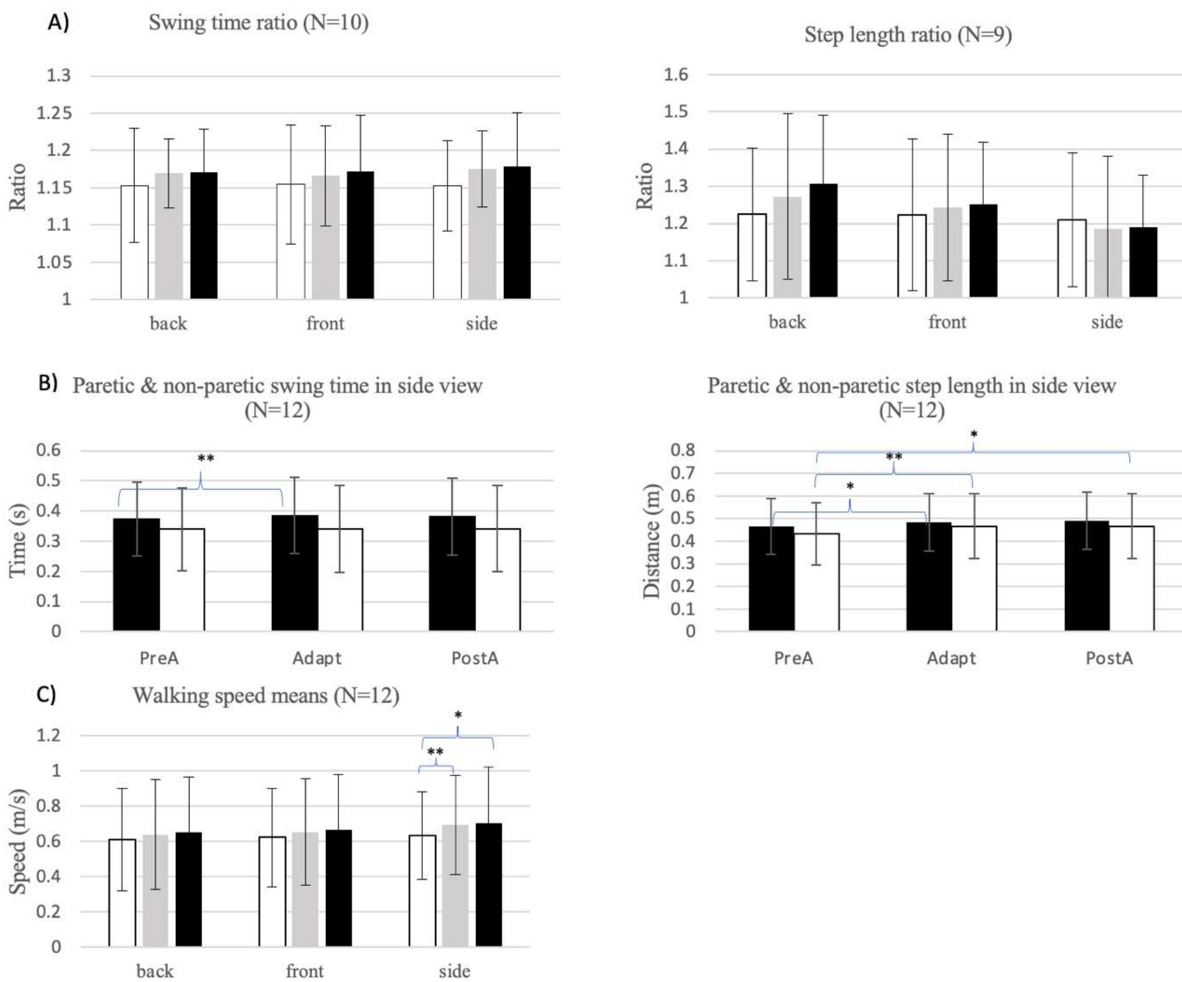

Figure 4.2 A) Spatiotemporal ratios across 3 phases of the 3 view conditions. The color indicates the 3 phases (white: pre-adaptation phase, grey: adaptation phase, black: post-adaptation phase). B) Paretic and non-paretic step length and swing time across three phases in the side view. Black and white represent the paretic side and non-paretic side respectively. C) Walking speed across 3 phases of the 3 view conditions. The color indicates the 3 phases (white: pre-adaptation phase, grey: adaptation phase, black: post-adaptation phase). Sample sizes in A) are different because only 10 and 9 participants presented asymmetry in swing time ratio and step length ratio respectively. For B) and C), all 12 participants were included for the analysis. Means and standard deviations are shown by the bars and whiskers. Statistically significant differences are indicated by * ($p \leq 0.05$) and ** ($p \leq 0.01$).

Figure 4.3 Step length ratio of each participant in side view

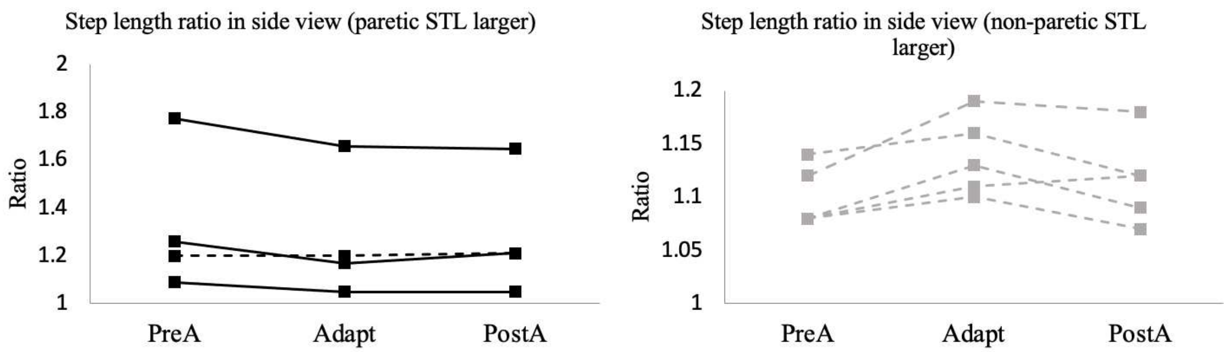

Figure 4.3 Step length (STL) ratios of each participant across 3 phases in the side view condition. Black represents a larger non-paretic step length while grey a larger paretic step length. The solid lines indicate responders and the dash lines non-responders.

Figure 4.4 Differences in step length ratio between larger paretic vs larger non-paretic step

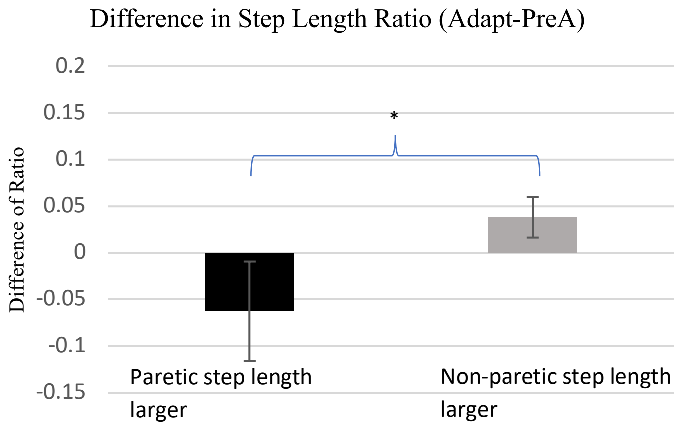

Figure 4.4 Difference of step length ratio between the adaptation phase (Adapt) and pre-adaptation (PreA) phase for participants with a larger paretic and non-paretic sides. A negative value of the difference in step length ratio is improvement while a positive value is deterioration. Means and standard deviations are shown by the bars and whiskers. Statistically significant differences are indicated by * ($p \leq 0.05$).

Chapter 5

5.1 Preface

In Manuscript 1, we examined the feasibility of a VR-based paradigm that involved real-time avatar-based feedback on locomotion among individuals with stroke, as well as the immediate effects of different view angles of avatar on gait symmetry. Based on the results of manuscript 1, the real-time feedback in the form of avatars is well tolerated and accepted by individuals with stroke. The paretic side view was also considered the most effective view in terms of spatial symmetry improvements. However, the effects of this feedback paradigm on other parameters of post-stroke gait such as inter-limb coordination and joint angle excursion remained unexplored.

In manuscript 2, further analyses were thus conducted using the same sample of participants as in manuscript 1 to examine the effects of the avatar feedback, presented in the paretic side view, on interlimb coordination of the lower extremities, as well as the relationship between gait symmetry and interlimb coordination.

Manuscript 2: Instantaneous effects of real-time avatar visual feedback on interlimb coordination during walking post-stroke

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5.2 Abstract

Background: Gait asymmetry, which is common after stroke, is typically characterized using spatiotemporal parameters of gait that do not consider the aspect of movement coordination. In this manuscript, we examined whether avatar-based feedback provided as a single-session intervention to improve gait symmetry also improved interlimb coordination among people with stroke and we examined the relationship between changes in coordination and step length symmetry.

Methods: Twelve stroke participants walked on a self-paced treadmill with and without a self-avatar that replicated their locomotor movements in real time. Continuous relative phase and angular coefficient of correspondence calculated using bilateral sagittal hip movements were used to quantify temporal and spatial interlimb coordination, respectively. Spatial gait symmetry, previously shown to improve with the avatar feedback, was quantified using step length ratio between both limbs, with the largest value as numerator.

Findings: Participants who improved their spatial symmetry during avatar exposure also improved their temporal coordination, while spatial coordination remained unchanged. Overall, improvements in spatial symmetry correlated positively with improvements in temporal coordination. The non-paretic hip and paretic ankle angle excursion in the sagittal plane also significantly increased during avatar exposure.

Interpretation: Improvements in gait symmetry may be explained by changes in interlimb coordination. Current data and existing literature further suggest that such improvements are largely driven by adaptations in non-paretic leg movements, notably at the hip. By providing real-time information on walking movements not affordable in other ways, avatar-based feedback shows great potential to improve gait symmetry and interlimb coordination post-stroke.

5.3 Introduction

Walking dysfunction is one of the most prevalent disabilities among people who had a stroke [1]. It is reported that immediately after a stroke, more than 50% of the people are not able to walk at all, and only 23% are able to regain independent walking after rehabilitation [2]. Amongst those who can walk, the gait pattern differs from that observed in healthy individuals. Post-stroke gait typically involves reduced walking speed [3-5], and various spatiotemporal differences including prolonged swing phase on the paretic side and longer step length on either the paretic side or the non-paretic side, which is commonly referred to as gait asymmetry [6]. Gait asymmetry could lead to many additional impairments and disabilities, namely poor balance [7], poor gait efficiency [8], musculoskeletal injuries [9] and reduced level of physical activity [10]. Unfortunately, despite clinicians being aware of the presence and impact of gait asymmetry among people with stroke, gait asymmetry itself does not significantly improve with rehabilitation [11].

In a recent article on post-stroke upper-extremity recovery, Levin and colleagues (2019) emphasized the need to characterize motor behavior at two levels, namely the movement performance level and the movement quality level [12]. In walking, literature has also suggested that quantifying and measuring the quality of movement is necessary to identify neurological pathology and assess the treatment efficacy [13]. However, it has been argued that the conventional spatiotemporal outcomes used to measure gait symmetry are limited and may not reveal the full picture when used to assess the quality of movement during gait [14]. An essential component of the quality of movement could be inter-joint coordination [15], and although it is different than symmetry, the two are considered to be closely related [14]. Studies have also shown that people with stroke often have intra or interlimb coordination deficits [16, 17]. As most of the research and literature on post-stroke gait asymmetry focus primarily on spatiotemporal outcomes (e.g. step length, swing time) [18-20], very little is known regarding possible underlying movement coordination deficits between paretic and non-paretic side explaining gait asymmetry. Interlimb coordination impairment was believed to be an important factor that causes asymmetrical propulsion during walking among people with stroke [21]. Furthermore, since a direct comparison between paretic and non-paretic side is desired to understand gait asymmetry, and that the interlimb coordination is an important clinical measure of the ability of maintaining spatial and temporal synchrony between paretic and non-paretic limbs [22], the focus of this study will be on interlimb coordination of lower extremities.

Interlimb coordination pertaining to locomotion can be defined as "the ability to maintain a context-dependent and phase-dependent cyclical relationship between different body segments or joints in both spatial and temporal domains [14]." The spatial component of interlimb coordination in walking can be defined as the relationship between the position of the segments and joints of both sides which can be measured using consistency across gait cycles, while the temporal component refers to the relative timing of movement of these different joints and segment throughout the gait cycle [14]. In post-stroke locomotion, the temporal aspect of interlimb coordination was shown to be altered, as reflected by an impaired relative timing between lower limb movements [23] that contrasts with the symmetrical, out-of-phase movement pattern observed in healthy individuals [24]. The spatial aspect of interlimb coordination has also been shown to have greater variability in post-stroke gait [23]. However, the extent to which altered interlimb coordination relates to the extent gait asymmetry post-stroke remains unclear.

Feedback, which can be either in the form of knowledge of results (KR) or knowledge of performance (KP) [25], plays a crucial role in motor skill reacquisition in rehabilitation [26, 27].

In terms of the timing of feedback, real-time feedback has been recently explored in gait training studies. Instantaneous, real-time biofeedback on kinematic, spatio-temporal, and kinetic variables [28, 29] can lead to narrower base of support and faster walking speed than conventional exercises and gait training among stroke survivors [30]. However, there is still a lack of knowledge regarding the effects of real-time feedback on movement coordination and other kinematic outcomes of post-stroke gait. Real-time feedback can be provided in the form of self-avatars to improve or modify different aspects of gait [31-33]. Given the remarkable ability of the brain to differentiate the kinematic patterns of human movements [34, 35], this type of feedback could have the advantage of providing more easily decipherable information about the movement quality compared to conventional forms of feedback such as numbers or scores. In a recent study on the effects of real-time avatar-based feedback on post-stroke gait symmetry, we have shown that such feedback, especially when presented in the paretic side view, can increase walking speed and spatial (i.e. step length) symmetry [33]. Whether such changes in spatial symmetry are explained by an improved interlimb movement coordination, however, remains unclear.

Specific objectives of this study were thus: (1) to explore whether avatar-based feedback provided as a single-session intervention to improve gait symmetry also improves interlimb coordination among people with stroke and; (2) to examine the relationship between the changes in coordination and step length symmetry, as well as between the changes in coordination and walking speed. We hypothesized that: (1) exposure to the avatar-based feedback improves interlimb coordination of lower extremities; (2) the improvement in interlimb coordination is correlated with the improvement in gait symmetry and; (3) the improvement of the interlimb coordination is also correlated with the improvement in walking speed.

5.4 Methods

5.4.1 Participants

Twelve participants with chronic stroke presenting with post-stroke gait asymmetry in either or both the spatial (step length ratio >1.08) and temporal (swing time ratio >1.06) domains were recruited (see Table 5.1 for demographic and clinical characteristics). These threshold values were determined from the upper confidence interval boundary for symmetry values of healthy adults in the study of Patterson and colleagues (2010) [18]. All participants used handrails for balance purpose during the experiment, and the use of handrails was kept constant throughout the experiment. These participants were the same as those included in a previous proof-of-concept study from our research group in which the impact of avatar-based feedback on gait symmetry was examined [33]. This study was approved by the Research Ethics Board of CRIR, and all participants provided informed consent prior to entering the study.

5.4.2 Experimental setup and procedure

Participants were assessed while walking on a 0.6 m x 1.5 m custom-built self-paced treadmill that allows individuals to modify their walking speed at will [36]. An overhead harness system and sliding handrails were used to prevent falling and to assist with balance. Participants who needed the handrails were instructed to use them for balance only and not to weight-bear on them during the experiment. The need of handrails was determined during the habituation stage and was kept constant throughout the experiment. The habituation stage involved participants walking on the treadmill until they felt comfortable and reached their overground comfortable walking speed tested a priori using the 10m walk test.

The virtual environment representing a long street with an avatar located 3.5 m ahead of the participants (Figure 5.1, bottom) was rear projected on a screen (2.44 m × 3.05 m) mounted in front of the treadmill. Kinematic data were acquired to animate the real-time avatars and for the purpose of off-line data analysis. Fifteen cluster of reflective markers were placed on specific body landmarks specified in Vicon Tracker™, and which were located on the upper (upper arms, lower arms, and hands) and lower (thighs, shins, and dorsum of feet) extremities, as well as on the head, chest, and pelvis (Figure 5.1, top left). To assist with the calculation of body segment length and localization of joints' axis of rotation needed for offline calculation of joint kinematics, 14 additional single reflective markers were positioned on other body landmarks (bilateral shoulders, elbows wrists, hips, knees, heels and first toes), as per Plug-in-Gait marker placement. Those additional markers were removed prior to the start of walking trials.

During the experiment, real-time tracking of the limb movement was provided by Vicon Tracker™ software (Vicon, UK) based on the displacement of the rigid body markers which were captured by the 6-camera Vicon™ (Vicon, UK) motion capture system (Figure 5.1, top middle). Pegasus Advanced™ (Vicon, UK) was used to retarget the limb positions onto an avatar which was created using Maya LT™ 2016 (Autodesk, USA), and was designed to have similar appearance and anthropometric characteristics to that of the participants (Figure 5.1, top right). The avatar was then displayed on the screen and controlled using Unreal Engine 4 (Epic Games, USA). Kinematic data of participants were collected at 120 Hz in Vicon Tracker.

The experiment consisted of 3 viewing conditions which were presented in a random order: (1) avatar seen from the back; (2) avatar seen from the paretic side and; (3) avatar seen from the front. This protocol was designed primarily to address the aim of the previous study which was comparing the effects of different views of avatar on gait symmetry. As previous analyses presented elsewhere revealed that only the paretic side view yielded improvements in step length symmetry [33], the present study is only focusing on data from the side view.

The participants walked two trials for the side view. Each walking trial was divided into three consecutive phases: a 30-s pre-adaptation phase which consisted of walking without the avatar; followed by a 1-min adaptation phase during which participants walked while visualizing a self-avatar replicating their walking pattern in real time; and finally, a 1-min post-adaptation phase that involved walking without the avatar. Prior to the start of each trial, the following instructions were given to participants: "*Please wait for the "Go" sign on the screen before starting walking. When the trial starts, always walk with your comfortable speed, and keep looking at the screen. For the first 30 secs, you will be looking at an empty street, then an avatar will appear. He (she) will mimic your way of walking in real-time, so please look at his (her) legs and feet for feedback and pay attention to your walking symmetry at the same time. The avatar will disappear after 1 min, and you will be looking at the empty street again. Keep walking until you see the "Stop" sign*." Rest was provided between the walking trials as needed.

5.4.3 Data analysis

Kinematic data were processed and exported using Vicon Nexus™ 1.8.5, before being analyzed in Matlab R2017b. To exclude the acceleration deceleration phases, data in the first and last 10 seconds of each trial were not included in the analysis. Data were filtered with a 10Hz, 4^{th} order Butterworth low-pass filter and normalized to 100% of the gait cycle.

Primary outcomes of this study included continuous relative phase (CRP) and angular coefficient of correspondence (ACC), which were used to characterize the temporal and spatial aspects of interlimb coordination, respectively. This analysis of coordination outcomes focused on the bilateral hip joints, given that CRP analysis itself can only be applied to sinusoidal signals [37], and provided that CRP and ACC outcomes were meant in the present context to be analysed in complementarity. In order to calculate CRP, phase diagrams which describe the joints' dynamics with a angular velocity-position plot were first computed (see Supplementary materials). The angular position (θ) and velocity (ω) were normalized (to a value between -1 to +1) using the following equations [38]:

$$\text{normalized } \theta_t = 2*(\theta_t - \min(\theta_t)) / (\max(\theta_t) - \min(\theta_t)) - 1$$

$$\text{normalized } \omega_t = \omega_t / \max(|\omega_t|)$$

where t represents each time point of the trial, $\min(\theta_t)$ and $\max(\theta_t)$ refers to the minimal and maximal points in angular position, respectively, and $\max(|\omega_t|)$ refers to the maximal value in the absolute angular velocity. Then based on the normalized phase diagrams, phase angles (φ) were calculated using the following equation [38]:

$$\varphi_t = \arctan[\text{normalized } (\omega_t) / \text{normalized } (\theta_t)]$$

Finally, the interlimb CRP was obtained by subtracting the phase angles of the bilateral joints at every time point throughout each phase of the walking trial [39], and the mean of all CRP values of the phase was calculated to obtained the outcome of 'CRP magnitude'. A CRP magnitude of 180° represents a perfect antiphase relationship between the bilateral joints (e.g. between the left vs. right hip joint angle). Beside CRP magnitude, the standard deviation (SD) of CRP across a time segment was also calculated to quantify 'CRP variability'. To account for the discontinuity of CRP measures, all values below 180° were converted to their corresponding above-180° values to facilitate data analysis (e.g.: 160° would be converted to 200°). As for ACC, it is a coefficient value which uses the vector coding technique to measure variability of cyclograms across gait cycles in a time segment [40]. In this study, cyclograms were computed by plotting the bilateral sagittal angle of the same joint type one on top of the other. A value of '1' in ACC would indicate that all cyclograms across gait cycles have absolutely the same form and size.

Secondary outcomes included sagittal joint angle excursion of bilateral hip, knee, and ankle joints. In addition, changes in step length ratio (SLR) and walking speed from pre-adaptation phase to adaptation phase were used in this study to address objective 2 of the present study. For SLR, step length was first calculated as the anteroposterior distance between markers placed on the ipsilateral heel and the contralateral big toe at the heel strike. SLR was then obtained by using the values of left and right side with the larger value in the numerator regardless of which side was the paretic. Participants were further identified as SLR responders vs. non-responders depending on whether their SLR improved from the pre-adaptation to the adaptation phase.

5.4.4 Statistical analysis

Coordination and kinematic outcomes were averaged for each of the three phases (pre-adaptation, adaptation, post-adaptation) across two trials. Since the Shapiro-Wilk test for normality indicated that the data did not follow a normal distribution, Friedman tests were used to assess differences in interlimb coordination and other outcomes across the phases. Wilcoxon signed-rank tests were then used to conduct post-hoc pairwise comparisons between phases. Differences between SLR responders and non-responders to the avatar-based feedback during the adaptation phase were analysed using Mann-Whitney U tests with Bonferroni-Holm correction adjustments. The significance level needed to reject the null hypothesis was set at $p \leq 0.05$.

Spearman's rank correlation coefficients were used to analyze the correlation between the changes in the coordination and the changes in SLR and walking speed. For those correlation analyses specifically, a 1-tail probability level of 0.05 was set given that only positive correlations were expected based on the hypotheses (2) and (3). According to the formula proposed by Rosenthal (1994) '$r=z/\sqrt{N}$' [41], values between 0.1 and <0.3, 0.3 and 0.5, and >0.5 were considered to reflect small, medium and large effect sizes respectively [42]. The same interpretation of the effect size also applied to other tests mentioned previously. The statistical analyses were performed in SPSS v.24 (IBM Inc, USA).

5.5 Results

5.5.1 Interlimb coordination

Figure 5.2 shows group average results for the interlimb coordination outcomes during the pre-adaptation, adaptation, and post-adaptation phases. No significant differences were observed in either CRP magnitude (χ^2=1.167, df=2, p=0.558), CRP variability (χ^2=1.167, df=2, p=0.558) or ACC (χ^2=0.5, df=2, p=0.779) across the different phases. Large standard deviation values, however, were observed for CRP magnitude and CRP variability, suggesting the presence of a large variability in interlimb temporal coordination across participants. Our previous findings have also shown that while SLR can improve due to the exposure to a self-avatar in the side view [33], not all participants responded to the exposure. For these reasons, an analysis of individual data was performed for the different coordination outcomes based on the responsiveness of their SLR to the intervention (Figure 5.3). Five participants were considered to be SLR responders (improvement from pre-adaptation to adaptation phase) while seven others were SLR non-responders (lack of change or deterioration from pre-adaptation to adaptation phase). Results indicate that all the SLR responders showed an improvement in CRP during the adaptation phase (Figure 5.3A), inferred by a reduction in CRP values (i.e. CRP values getting closer to 180°). Furthermore, three of the five SLR responders maintained or further improved their CRP magnitude in the post-adaptation phase while the other two returned to their pre-adaptation CRP values. Among the seven participants who were considered SLR non-responders, six deteriorated in their CRP magnitude during the adaptation phase, while all but one further deteriorated in the post-adaptation phase. At variance with the CRP magnitude outcome, neither CRP variability (Figure 5.3B) nor ACC (Figure 5.3 C) changed differently between the SLR responders and non-responders, as around half of the participants in each group showed improvement while the other half showed deterioration during the adaptation phase.

When comparing the group results for SLR responders vs. non-responders (Figure 5.4), significant differences in CRP magnitude change between the pre-adaptation and adaptation phases were observed (Z=-2.84, $p<0.01$) for non-responders (Δ=0.83±1.16 ° (mean±1SD)) and responders (Δ= -2.17±0.99 °). As expected, neither the changes in CRP variability (Z=-0.73, $p=0.46$) nor those in ACC (Z=-0.89, $p=0.37$) significantly differed between responders and non-responders.

5.5.2 Relationship between CRP, SLR and walking speed

Changes in CRP magnitude were positively correlated with changes in walking speed from pre-adaptation to adaptation phase ($\rho=0.596$, $p<0.05$) with a large effect size. Similarly, the relationship between the changes of CRP magnitude and changes in SLR from pre-adaptation to adaptation phase showed a statistically significant, positive correlation ($\rho=0.547$, $p<0.05$) with a large effect size. Changes in SLR, however, were not significantly correlated to changes in walking speed ($\rho=0.428$, $p=0.165$), neither are the changes in CRP with the stroke chronicity ($\rho=0.140$, $p=0.664$).

5.5.3 Joint excursions

Group analysis of lower limb joint excursion for the hip and ankle joints in the sagittal plane revealed significant main effects of the locomotor phase only for the non-paretic hip (χ^2=12.67, df=2, p<0.01) and paretic ankle joint excursions (χ^2=10.17, p<0.01). No significant effect locomotor phase was observed for knee joint excursion on both sides (Figure 5.5). Post-hoc analyses revealed a small but significant increase in non-paretic hip excursion in the adaptation (1.91±1.42 °, Z=3.06, p<0.01, effect size: 0.88), as well as in the post-adaptation phase (2.53±2.53 °, Z=2.74, p<0.01, effect size: 0.74) in comparison to the pre-adaptation phase, but values were similar between the post-adaptation phase and adaptation phase (0.61±1.76 °, Z=1.10, p=0.27). Similarly, ankle joint angle excursion on the paretic side was significantly larger for the adaptation (2.43±2.32 °, Z=2.74, p<0.01, effect size: 0.74) and post-adaptation phases (2.24±3.18 °, Z=2.28, p<0.05, effect size: 0.61) compared to the pre-adaptation phase but remained similar between the post-adaptation and adaptation phases (-0.20±2.44 °, Z=0.07, p=0.93). All the significant results showed large effect size.

5.6 Discussion

This study, which was part of a larger project designed to investigate the impact of real-time visual feedback in the form of avatars on gait symmetry among individuals with chronic stroke, examined whether this type of real-time feedback could also improve interlimb coordination while walking. The relationships between changes in interlimb coordination and changes in spatiotemporal symmetry outcomes were also examined. While coordination outcomes (ACC, and CRP magnitude and variability) on average did not show significant improvement with avatar-based feedback exposure, individual participants who improved spatial symmetry of gait due to the feedback also improved their interlimb temporal coordination (CRP magnitude). A positive correlation was also observed between the changes in interlimb temporal coordination and variables such as spatial gait symmetry and walking speed. Potential explanations and implications of finding are discussed below.

5.6.1 Contribution of non-paretic side to gait symmetry and coordination

Participants' responses in hip CRP magnitude to the real-time avatar feedback differed depending on their response in step length symmetry, as only those who improved their step length symmetry (SLR responders) also improved their hip CRP magnitude. In another study where acoustically-paced treadmill was used to improve gait coordination after stroke, the improvement in CRP was also observed alongside with the improvement in SLR [43]. Although the exact mechanisms behind this improvement in coordination in SLR responders is unclear, the results from a previous study of our research group [33] and this one suggests that these changes are mediated through non-paretic movement adaptations. Indeed, and as highlighted Liu et al. (2020), participants increase their non-paretic step length to a larger extent than that on their paretic side when exposed to the avatar-based feedback [33]. Similarly, in the present study, an increase in the sagittal hip joint angle excursion due to the avatar exposure was observed only on the non-paretic side. Although the paretic side experienced a significant increase on the sagittal ankle joint angle excursion, it has been shown in the literature that step length in stroke survivors is mostly influenced by hip joint angle excursion [44, 45], such that changes in ankle angle excursion may have not significantly impacted spatiotemporal outcomes nor interlimb coordination. Moreover, and as highlighted in our previous study, SLR responders were those who had initial larger paretic step length [33] and they achieved better gait spatial symmetry by increasing their non-paretic step length, as opposed to modifying their paretic step length. Thus, it appears that participants' response in CRP magnitude may depend on the direction of the spatial asymmetry, with those showing an initially larger paretic step length and increasing their non-paretic step in response to the intervention displaying improved CRP values.

Results of the present study also revealed a positive correlation between changes in SLR and changes in CRP magnitude. While this adds further support to the idea that improvement in symmetry and coordination are related, one may wonder why a measure of spatial symmetry (SLR) would be related to a measure typically associated with temporal coordination (CRP) [14]. We speculate that participants who improved their SLR and thus had an initially larger paretic step length at baseline also had an initially larger hip phase angle on the paretic side. Following the avatar exposure, since step length and hip joint angle excursion were increased to a larger extent on the non-paretic side and since a larger joint angle excursion may lead to a larger value of joint position, a smaller phase angle for the non-paretic hip joint was likely generated based on the formula: phase angle= arctan (joint velocity/joint position). Therefore, since CRP is calculated as the difference between the phase angles of paretic and non-paretic side, a smaller non-paretic phase angle could bring the CRP value closer to 180°, hence reflecting a better anti-phase coordination pattern.

5.6.2 Influence of walking speed on coordination through non-paretic side

Another factor that might have contributed to the enhanced interlimb temporal coordination is walking speed. Indeed, a positive correlation was found between the changes in walking speed and changes in interlimb CRP magnitude in the present study. Existing literature has shown that varying walking speed results in changes in phase relations of leg movements [46]. For instance, Kwakkel and Wagennar (2002) demonstrated that instructing participants with stroke to increase their walking speed causes them to display larger CRP values (closer to 180° or out of phase) characterizing arm-leg interlimb coordination on the non-paretic side [23]. Similarly, in the study of Sakuma and colleagues (2019), walking speed among people with stroke was influenced by the intra-limb (between thigh and shank) CRP value of the non-paretic side during the propulsive phase [47]. Once again, these changes on walking speed seem to be mediated through non-paretic movement adaptation [23, 47]. Thus, the improved temporal aspect of coordination observed in the present study, as evidenced by more anti-phase interlimb coupling, appears to result from an adaptation on the non-paretic side, which also leads to faster walking speed and better spatial symmetry.

5.6.3 Lack of relationship between spatial symmetry and walking speed

While changes in CRP in this study were found to be positively correlated to changes in both SLR and walking speed, changes in SLR did not significantly correlate to changes in walking speed. This lack of relationship contrasts with the results of an earlier longitudinal study about the effects of rehabilitation on post-stroke gait by Patterson and colleagues (2015), which showed a positive correlation between the changes in walking speed and SLR [11]. However, and as pointed out by the authors of this longitudinal study, the observed positive correlation might have been influenced by two outliers and participants generally did not improve their step length symmetry as a result of rehabilitation, despite showing an improvement in walking speed. In addition, Balasubramanian and colleagues (2007) reported a rather weak ($r=-.35$, $p<0.05$) correlation between SLR and self-selected walking speed in chronic stroke survivors, which is in the same order as that observed for changes in SLR vs. changes in walking speed in the present study ($\rho=0.428$) [48]. Therefore, it could be that step length symmetry and walking speed are separated determinants of temporal coordination.

5.6.4 Lack of changes in the variability of spatial coordination

Results of this study also did not reveal any changes in spatial coordination, as measured by ACC, due to the avatar-based feedback exposure. This could be due to the fact that ACC is a measure of variability of spatial coordination, rather than a direct measure of spatial coordination [40]. Similarly, CRP variability in the present study did not vary due to the avatar exposure. On one hand, better motor performance is often associated with less movement variability [49], and enhanced movement variability is typically observed in individuals with sensorimotor impairments subsequent to stroke [50]. On the other hand, learning a new task as experienced in the present study is also associated with greater movement variability [49]. As those two observations predict opposite responses in terms of changes in variability, it is unclear which direction of change in interlimb coordination variability was to be expected in the present study. In the study of Hammerbeck and colleagues (2017) on reaching accuracy, it was shown that the trial-to-trial movement variability of participants with chronic stroke was reduced after training [51]. However, the training program consisted of 420 repetitions per day for 4 days, therefore it is possible that in this study the short exposure to the avatar feedback (1 min) might have been insufficient to cause detectable changes in movement variability. In the future, other spatial measure such as planar covariance between lower limb segments (pelvis, thigh, shank and foot) [52], could be explored to further understand the impact of interventions such as avatar-based feedback on spatial coordination.

5.6.5 Limitations

One potential limitation is that the participants recruited in this experiment had a large variability of stroke chronicity. However, based on the correlation analysis, the stroke chronicity did not explain the change of CRP. The order of the view conditions could also cause a learning effect bias, but since the order of presenting the view conditions is randomized, the impact of learning effect is minimalized. Finally, since this study only has one session, conclusions about the clinical suitability of the avatar feedback as a gait intervention cannot be drawn until a study with repeated training sessions is conducted.

5.7 Conclusion

The present study demonstrated that avatar-based feedback presenting a paretic side view of individuals with stroke improves interlimb temporal coordination in those who also improve their spatial gait symmetry. Results further showed that improvements in the temporal aspect of interlimb coordination are associated with improvements in spatial gait symmetry and in walking speed. The observed changes in symmetry, coordination and speed appear to be mediated by adaptations taking place primarily on the non-paretic side. Post-stroke interlimb coordination can be regarded as a measure of movement quality and is often a difficult target for clinicians to measure and intervene on [12]. Real-time avatar-based feedback shows potential to improve movement coordination by providing unique, real-time information on walking movements not affordable in other ways. Future studies should focus on examining the effects of longer and multiple training sessions in sub-acute stroke survivors in order to determine whether avatar-based feedback is an effective rehabilitation strategy to improved gait symmetry and coordination.

5.8 References

1. Bohannon R, Andrews A, Smith M: **Rehabilitation goals of patients with hemiplegia**. *Int J Rehabil Res* 1988, **11**:181-183.
2. Jorgensen HS, Nakayama H, Raaschou HO, Olsen TS: **Recovery of walking function in stroke patients: the Copenhagen Stroke Study**. *Arch Phys Med Rehabil* 1995, **76**(1):27-32.
3. Perry J, Garrett M, Gronley JK, Mulroy SJ: **Classification of walking handicap in the stroke population**. *Stroke* 1995, **26**(6):982-989.
4. Jonsdottir J, Recalcati M, Rabuffetti M, Casiraghi A, Boccardi S, Ferrarin M: **Functional resources to increase gait speed in people with stroke: strategies adopted compared to healthy controls**. *Gait Posture* 2009, **29**(3):355-359.
5. Nadeau S, Arsenault AB, Gravel D, Bourbonnais D: **Analysis of the clinical factors determining natural and maximal gait speeds in adults with a stroke**. *Am J Phys Med Rehabil* 1999, **78**(2):123-130.
6. Titianova EB, Pitkanen K, Paakkonen A, Sivenius J, Tarkka IM: **Gait characteristics and functional ambulation profile in patients with chronic unilateral stroke**. *Am J Phys Med Rehabil* 2003, **82**(10):778-786; quiz 787-779, 823.
7. Weerdesteyn V, de Niet M, van Duijnhoven HJ, Geurts AC: **Falls in individuals with stroke**. *J Rehabil Res Dev* 2008, **45**(8):1195-1213.
8. Stoquart G, Detrembleur C, Lejeune TM: **The reasons why stroke patients expend so much energy to walk slowly**. *Gait Posture* 2012, **36**(3):409-413.
9. Patterson KK: **Gait asymmetry post-stroke: thesis for PhD degree**. University of Toronto 2010.
10. Michael KM, Allen JK, Macko RF: **Reduced ambulatory activity after stroke: the role of balance, gait, and cardiovascular fitness**. *Arch Phys Med Rehabil* 2005, **86**(8):1552-1556.
11. Patterson KK, Mansfield A, Biasin L, Brunton K, Inness EL, McIlroy WE: **Longitudinal changes in poststroke spatiotemporal gait asymmetry over inpatient rehabilitation**. *Neurorehabil Neural Repair* 2015, **29**(2):153-162.
12. Levin MF, Hiengkaew V, Nilanont Y, Cheung D, Dai D, Shaw J, Bayley M, Saposnik G: **Relationship Between Clinical Measures of Upper Limb Movement Quality and Activity Poststroke**. *Neurorehabil Neural Repair* 2019, **33**(6):432-441.
13. König N, Taylor WR, Baumann CR, Wenderoth N, Singh NB: **Revealing the quality of movement: A meta-analysis review to quantify the thresholds to pathological variability during standing and walking**. *Neurosci Biobehav Rev* 2016, **68**:111-119.
14. Krasovsky T, Levin MF: **Review: toward a better understanding of coordination in healthy and poststroke gait**. *Neurorehabil Neural Repair* 2010, **24**(3):213-224.
15. Levin MF, Kleim JA, Wolf SL: **What do motor "recovery" and "compensation" mean in patients following stroke?** *Neurorehabil Neural Repair* 2009, **23**(4):313-319.
16. Giannini RC, Perell KL: **Lower limb coordination during walking in subjects with post stroke hemiplegia vs. healthy control**. *Clinical Kinesiology: Journal of the American Kinesiotherapy Association* 2005, **59**:10.
17. Kwan MS, Hassett LM, Ada L, Canning CG: **Relationship between lower limb coordination and walking speed after stroke: an observational study**. *Braz J Phys Ther* 2019, **23**(6):527-531.
18. Patterson KK, Gage WH, Brooks D, Black SE, McIlroy WE: **Evaluation of gait symmetry after stroke: a comparison of current methods and recommendations for standardization**. *Gait Posture* 2010, **31**(2):241-246.

19. Reisman DS, McLean H, Keller J, Danks KA, Bastian AJ: **Repeated split-belt treadmill training improves poststroke step length asymmetry**. *Neurorehabil Neural Repair* 2013, **27**(5):460-468.
20. Lewek MD, Randall EP: **Reliability of spatiotemporal asymmetry during overground walking for individuals following chronic stroke**. *J Neurol Phys Ther* 2011, **35**(3):116-121.
21. Cleland BT, Gelting T, Arand B, Struhar J, Schindler-Ivens S: **Impaired interlimb coordination is related to asymmetries during pedaling after stroke**. *Clin Neurophysiol* 2019, **130**(9):1474-1487.
22. Garry MI, van Steenis RE, Summers JJ: **Interlimb coordination following stroke**. *Hum Mov Sci* 2005, **24**(5-6):849-864.
23. Kwakkel G, Wagenaar RC: **Effect of Duration of Upper- and Lower-Extremity Rehabilitation Sessions and Walking Speed on Recovery of Interlimb Coordination in Hemiplegic Gait**. *Phys Ther* 2002, **82**(5):432-448.
24. Haddad JM, van Emmerik RE, Whittlesey SN, Hamill J: **Adaptations in interlimb and intralimb coordination to asymmetrical loading in human walking**. *Gait Posture* 2006, **23**(4):429-434.
25. Schmidt R: **Motor Control and Learning: A Behavioral Emphasis**, 2nd edn: Champaign, Ill: Human Kinetics Publishers; 1988.
26. Richards CL, Malouin F, Nadeau S: **Chapter 13 - Stroke rehabilitation: clinical picture, assessment, and therapeutic challenge**. In: *Prog Brain Res. Volume 218*, edn. Edited by Dancause N, Nadeau S, Rossignol S: Elsevier; 2015: 253-280.
27. Winstein CJ: **Knowledge of results and motor learning--implications for physical therapy**. *Phys Ther* 1991, **71**(2):140-149.
28. Barrios JA, Crossley KM, Davis IS: **Gait retraining to reduce the knee adduction moment through real-time visual feedback of dynamic knee alignment**. *J Biomech* 2010, **43**(11):2208-2213.
29. Darter BJ, Wilken JM: **Gait training with virtual reality-based real-time feedback: improving gait performance following transfemoral amputation**. *Phys Ther* 2011, **91**(9):1385-1394.
30. Tate JJ, Milner CE: **Real-Time Kinematic, Temporospatial, and Kinetic Biofeedback During Gait Retraining in Patients: A Systematic Review**. *Phys Ther* 2010, **90**(8):1123-1134.
31. Kannape OA, Blanke O: **Self in motion: Sensorimotor and cognitive mechanisms in gait agency**. *Journal of neurophysiology* 2013.
32. Koritnik T, Koenig A, Bajd T, Riener R, Munih M: **Comparison of visual and haptic feedback during training of lower extremities**. *Gait Posture* 2010, **32**(4):540-546.
33. Liu LY, Sangani S, Patterson KK, Fung J, Lamontagne A: **Real-Time Avatar-Based Feedback to Enhance the Symmetry of Spatiotemporal Parameters After Stroke: Instantaneous Effects of Different Avatar Views**. *IEEE Trans Neural Syst Rehabil Eng* 2020, **28**(4):878-887.
34. Grossman E, Donnelly M, Price R, Pickens D, Morgan V, Neighbor G, Blake R: **Brain areas involved in perception of biological motion**. *J Cogn Neurosci* 2000, **12**(5):711-720.
35. Johannson G: **Visual perception of biological motion and a model for its analysis**. *Percept Psychophys* 1973, **14**:201-211.
36. Fung J, Richards CL, Malouin F, McFadyen BJ, Lamontagne A: **A treadmill and motion coupled virtual reality system for gait training post-stroke**. *Cyberpsychol Behav* 2006, **9**(2):157-162.
37. Peters BT, Haddad JM, Heiderscheit BC, Van Emmerik REA, Hamill J: **Limitations in the use and interpretation of continuous relative phase**. *J Biomech* 2003, **36**(2):271-274.
38. Galgon AK, Shewokis PA: **Using Mean Absolute Relative Phase, Deviation Phase and Point-Estimation Relative Phase to Measure Postural Coordination in a Serial Reaching Task**. *J Sports Sci Med* 2016, **15**(1):131-141.
39. van Emmerik RE, Wagenaar RC: **Effects of walking velocity on relative phase dynamics in the trunk in human walking**. *J Biomech* 1996, **29**(9):1175-1184.

40. Field-Fote EC, Tepavac D: **Improved Intralimb Coordination in People With Incomplete Spinal Cord Injury Following Training With Body Weight Support and Electrical Stimulation**. *Phys Ther* 2002, **82**(7):707-715.
41. Rosenthal R: **Parametric measures of effect size**. In: *The handbook of research synthesis.* edn. New York, NY, US: Russell Sage Foundation; 1994: 231-244.
42. Cohen J: **Statistical Power Analysis for the Behavioral Sciences**, 2nd edn: Routledge; 1988.
43. Roerdink M, Lamoth CJC, Kwakkel G, van Wieringen PCW, Beek PJ: **Gait Coordination After Stroke: Benefits of Acoustically Paced Treadmill Walking**. *Phys Ther* 2007, **87**(8):1009-1022.
44. Olney SJ, Richards C: **Hemiparetic gait following stroke. Part I: Characteristics**. *Gait Posture* 1996, **4**(2):136-148.
45. Schulz BW, Ashton-Miller JA, Alexander NB: **The effects of age and step length on joint kinematics and kinetics of large out-and-back steps**. *Clin Biomech (Bristol, Avon)* 2008, **23**(5):609-618.
46. Wagenaar RC, van Emmerik REA: **Dynamics of pathological gait**. *Human Movement Science* 1994, **13**(3):441-471.
47. Sakuma K, Tateuchi H, Nishishita S, Okita Y, Kitatani R, Koyama Y, Ibuki S, Ichihashi N: **Gait kinematics and physical function that most affect intralimb coordination in patients with stroke**. *NeuroRehabilitation* 2019, **45**(4):493-499.
48. Balasubramanian CK, Bowden MG, Neptune RR, Kautz SA: **Relationship between step length asymmetry and walking performance in subjects with chronic hemiparesis**. *Arch Phys Med Rehabil* 2007, **88**(1):43-49.
49. Dhawale AK, Smith MA, Ölveczky BP: **The Role of Variability in Motor Learning**. *Annu Rev Neurosci* 2017, **40**:479-498.
50. Thies SB, Tresadern PA, Kenney LP, Smith J, Howard D, Goulermas JY, Smith C, Rigby J: **Movement variability in stroke patients and controls performing two upper limb functional tasks: a new assessment methodology**. *J Neuroeng Rehabil* 2009, **6**:2.
51. Hammerbeck U, Yousif N, Hoad D, Greenwood R, Diedrichsen J, Rothwell JC: **Chronic Stroke Survivors Improve Reaching Accuracy by Reducing Movement Variability at the Trained Movement Speed**. *Neurorehabil Neural Repair* 2017, **31**(6):499-508.
52. Borghese NA, Bianchi L, Lacquaniti F: **Kinematic determinants of human locomotion**. *J Physiol* 1996, **494 (Pt 3)**(Pt 3):863-879.

Table 5.1 Characteristics of participants

Participant	Gender (Male/ Female)	Age (years)	Stroke Chronicity (months)	Comfortable Overground Walking Speed (m/s)	Temporal gait asymmetry[1] (Yes/No)	Spatial gait asymmetry[2] (Yes/No)
P1	Female	51	324	0.79	Yes	Yes
P2	Male	67	12	0.80	Yes	Yes
P3	Male	66	25	1.02	Yes	No
P4	Male	66	22	0.34	Yes	Yes
P5	Male	57	6	1.10	No	Yes
P6	Female	56	12	0.89	Yes	Yes
P7	Male	77	40	0.29	Yes	Yes
P8	Male	58	33	1.06	No	Yes
P9	Male	49	52	0.74	Yes	Yes
P10	Male	65	165	0.35	Yes	No
P11	Female	58	26	0.86	Yes	Yes
P12	Male	56	72	0.96	Yes	No
Mean±SD Ratio (:)	9:3	60.5 ±7.9	65.8±92.1	0.74±0.26	10:2	9:3

1: Temporal gait is considered asymmetrical if swing time ratio is equal or greater than 1.06.
2: Spatial gait is considered asymmetrical if step length ratio is equal or greater than 1.08.

Figure 5.1 Creation of visual feedback

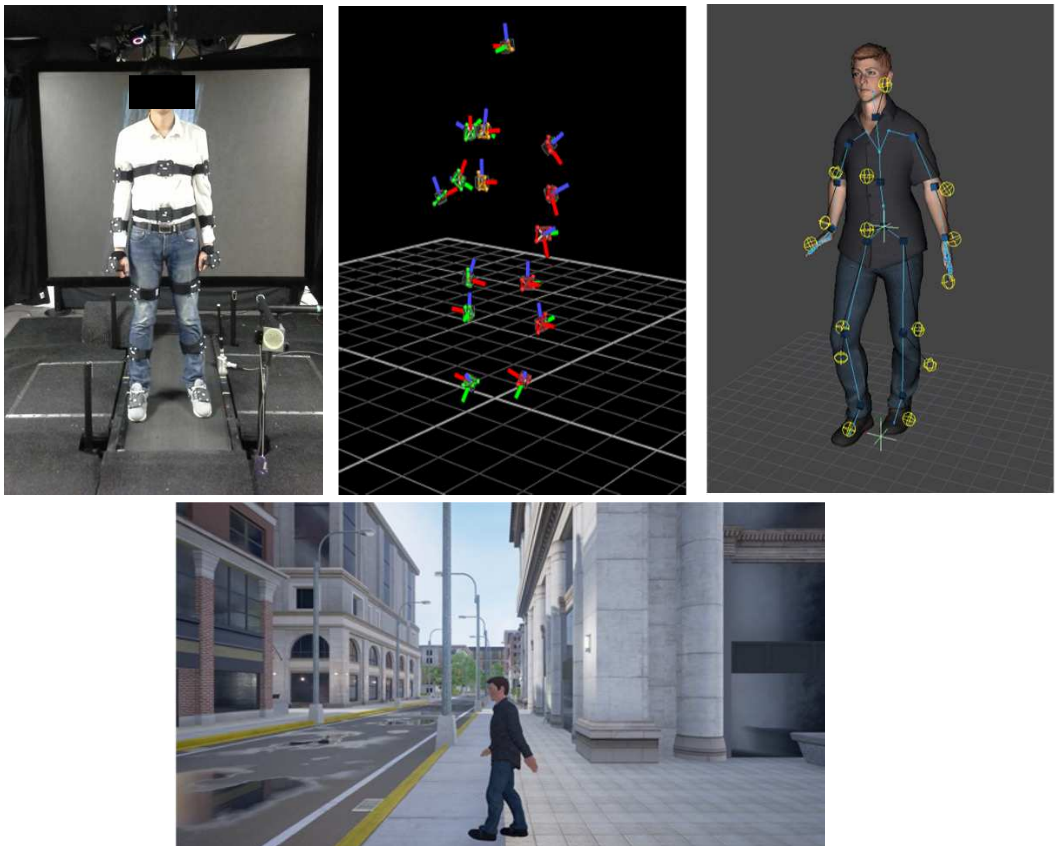


Figure 5.1 Creation of visual feedback. Top left: a participant standing on self-paced treadmill with rigid body markers strapped on his body; Top middle: kinematic data shown in Vicon Tracker™ based on rigid body markers; Top right: avatar created in Pegasus Advanced™ based on the kinematic data; Bottom: avatar being integrated (shown in the paretic side view) in the virtual scene generated by Unreal Engine 4.

Figure 5.2 Inter-hip coordination

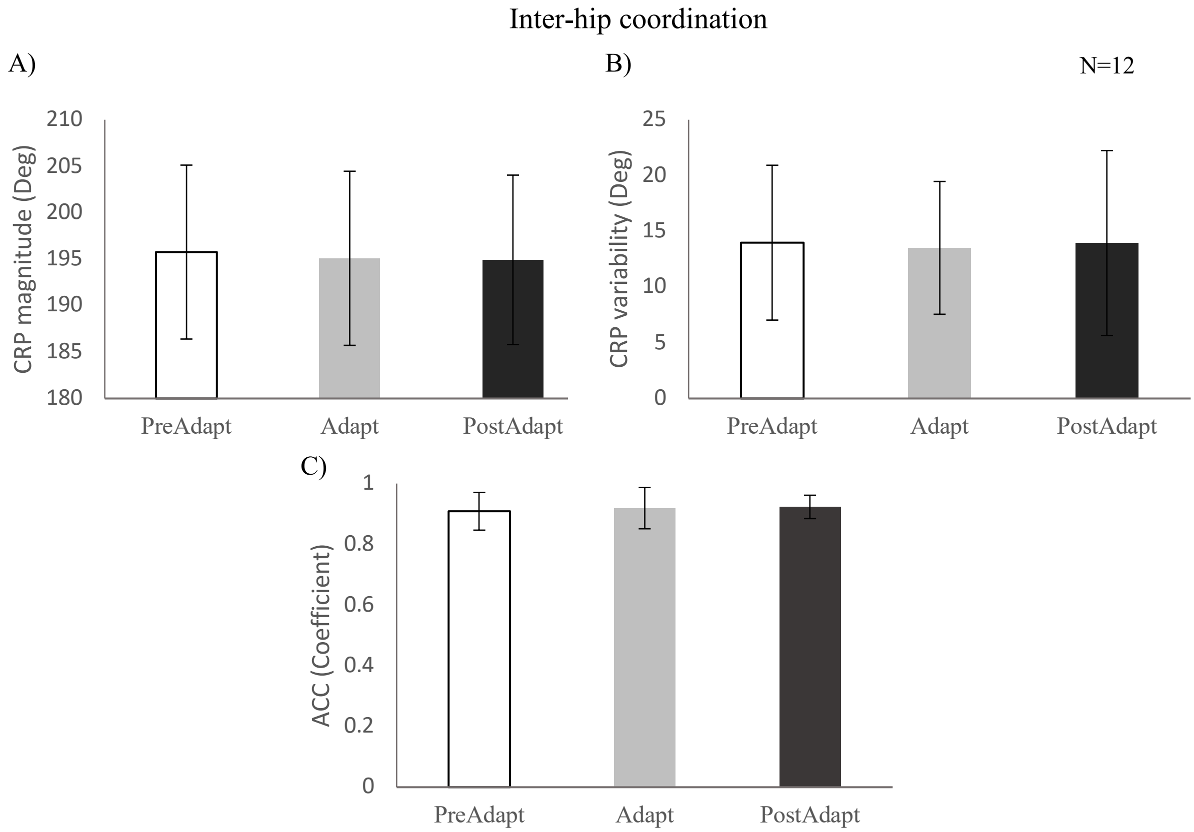


Figure 5.2 Coordination outcomes for the pre-adaptation (PreAdapt), adaptation (Adapt) and post-adaptation phases (PostAdapt). The graphs display mean values (± SD) for the magnitude of CRP A), the variability of CRP B) and the ACC calculated using bilateral hip angular displacement in the sagittal plane C).

Figure 5.3 Individual data of coordination across phases

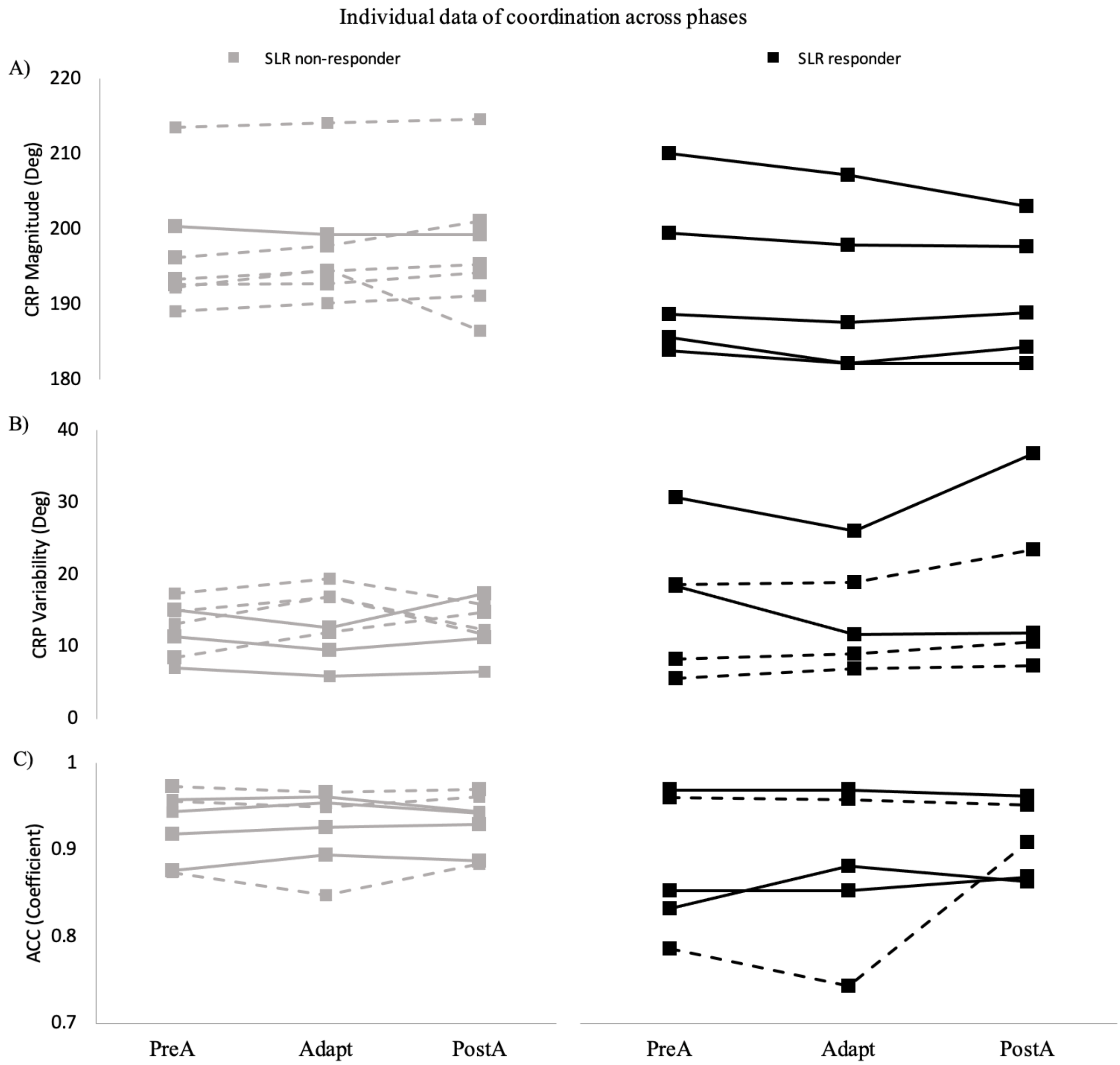


Figure 5.3 A) CRP magnitude; B) CRP variability; C) ACC of each participant across 3 phases (pre-adaptation, adaptation, and post-adaptation). Black represent SLR responders (left, N=5) and grey represent SLR non-responders (right, N=7). The solid lines indicate improvement and the dash lines deterioration.

Figure 5.4 Differences of coordination measures between pre-adaptation and adaptation

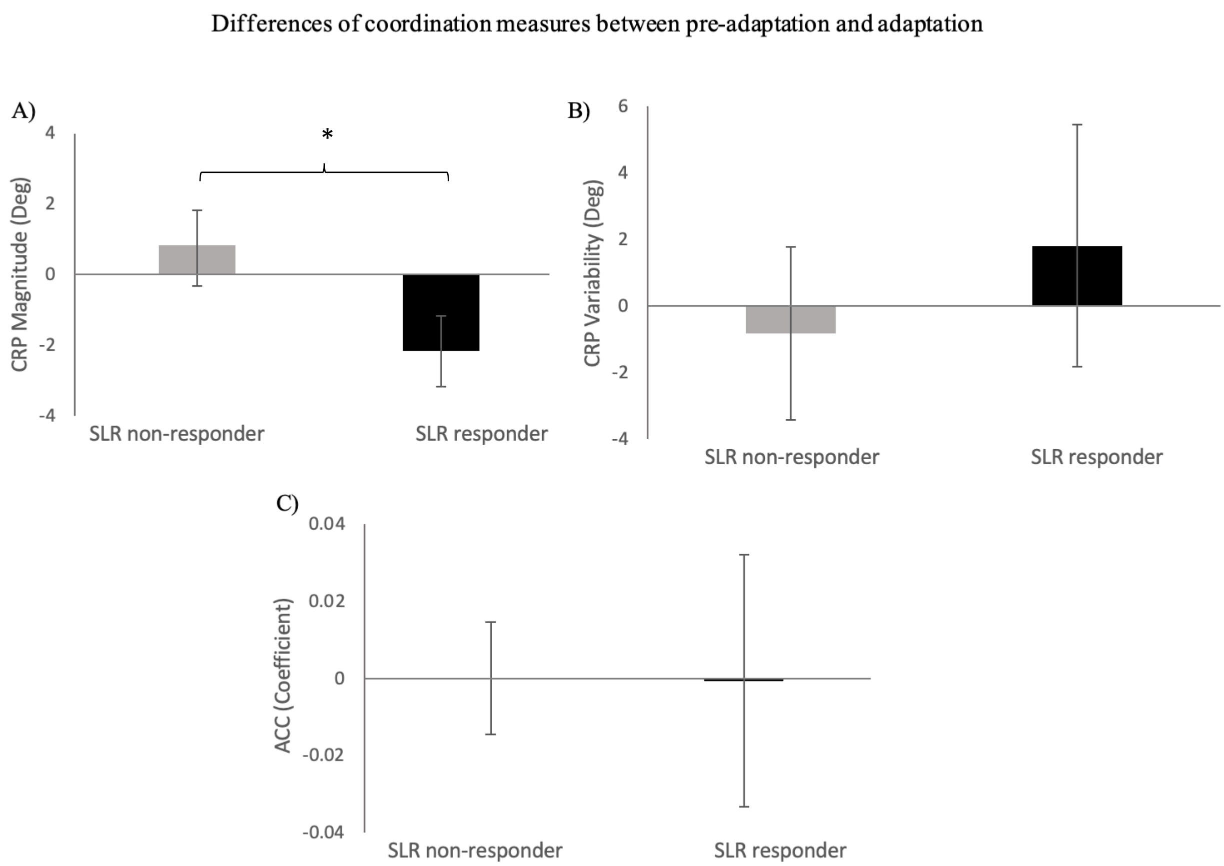


Figure 5.4 Mean difference (± SD) for A) CRP magnitude; B) CRP variability; C) ACC calculated between the adaptation phase and pre-adaptation phase for SLR responders (n=5, light grey) and non-responders (n=7, black). For CRP magnitude and variability, a negative angle value indicates an improvement while for ACC a positive value signifies an improvement. Statistically significant difference is indicated by * (p <0.05).

Figure 5.5 Lower limb joint excursions

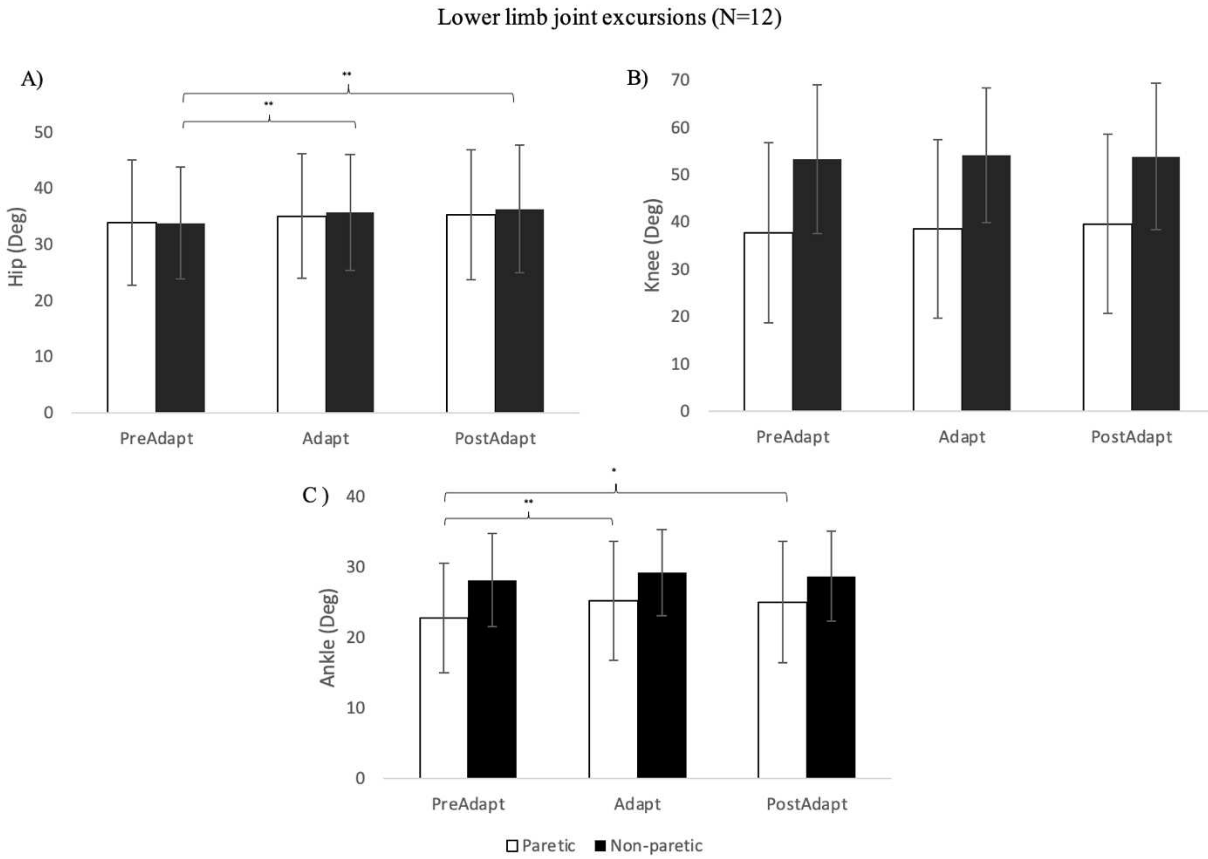
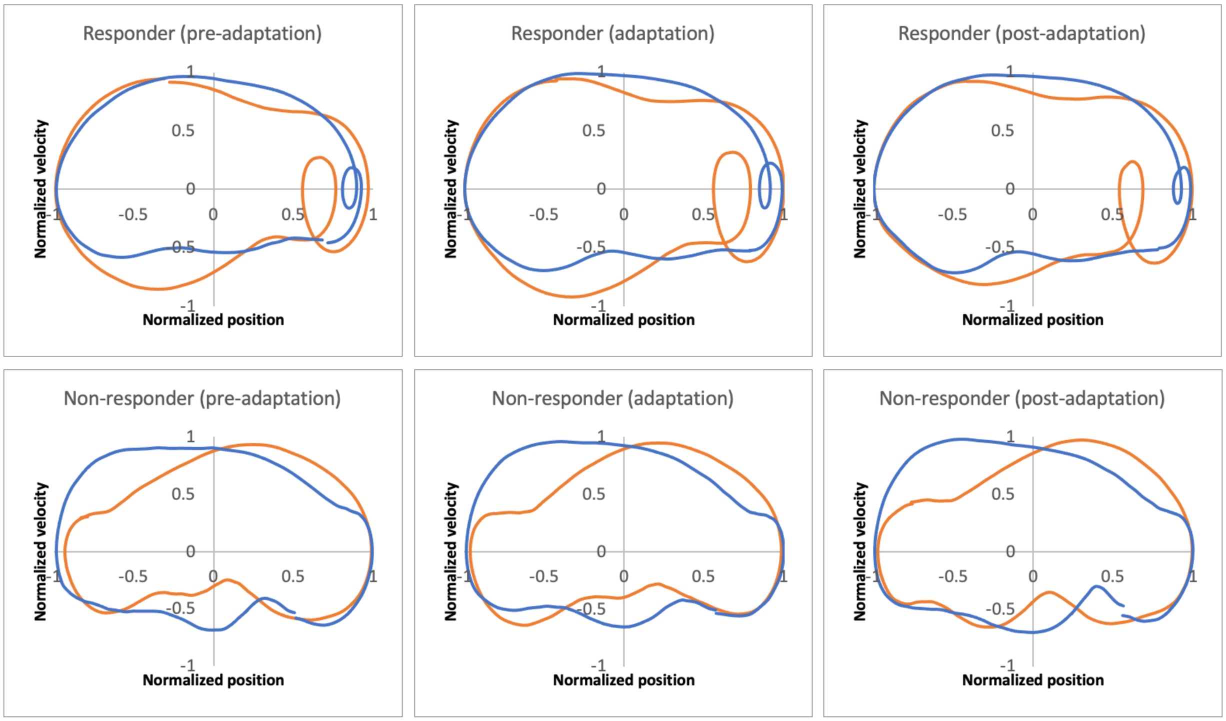


Figure 5.5 Mean (± SD) values for lower limb joint excursions of the hip (A), knee (B) and ankle (C) on the paretic (open bars) and non-paretic side (filled bars). Statistically significant differences are indicated as applicable with the following symbols: * (*p* <0.05) and ** (*p* <0.01).

Figure 5.6 Phase diagrams of responders and non-responders



Supplementary material. Top: phase diagrams of a responder (a person who improved in CRP during adaptation phase) in three phases (pre-adaptation, adaptation, and post-adaptation); Bottom: phase diagrams of a non-responder in three phases; Orange line: paretic hip, blue line: non-paretic hip.

Chapter 6

6.1 Preface

The purpose of Manuscript 1 and 2 was to study the effects of real-time feedback in the form of avatars on post-stroke gait symmetry and inter-limb coordination. While the results revealed that the avatar feedback could lead to changes in the spatial aspect of gait symmetry and that the improvement in CRP is correlated with the improvement in SLR, the temporal aspect of gait symmetry remained unchanged. A study has shown that visual feedback facilitates learning of spatial aspects of movement whereas auditory feedback facilitates learning of temporal aspects [174]. Therefore, it would be relevant to explore the use of auditory feedback in order to elicit changes in the temporal aspect of gait symmetry.

Manuscript 3 thus involved the use of different sensory modalities as sources of feedback to improve gait symmetry. More specifically, the effects of i) visual feedback provided in the form of a self-avatar replicating locomotor movements in real-time; ii) auditory feedback delivered in the form of footstep sound that signal foot strike events and iii) combined visual-auditory feedback (avatar walking plus footstep sounds) were examined and compared.

Manuscript 3: Immediate effects of visual avatar, auditory foot strike and combined feedback on gait symmetry post stroke

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Keywords: Cerebrovascular accident, gait asymmetry, spatiotemporal factors, virtual reality, biological feedback

6.2 Abstract

Background: Feedback plays an important role in motor rehabilitation post-stroke, but conventional feedback in the form of verbal cues is not sufficient to correct gait asymmetry. Biological feedback (arising from a living being in motion) has the advantage of being easily decipherable. Virtual reality (VR) also represents the ideal platform for applying such feedback in different sensory modalities. However, as most VR interventions rely on visual feedback alone, the use of auditory feedback and combined visual-auditory feedback remain unexplored.

Methods: Twelve participants with stroke walked on a self-paced treadmill while exposed to short bouts (one-minute) of three feedback modalities (visual avatar alone, auditory foot strikes alone or combination of a visual avatar and auditory foot strikes) presented in real time, in a random order. Gait symmetry was measured as ratios of left-right step length (SLR) and left-right swing time (SWR). Perceived usefulness ratings for each feedback were also examined.

Results: For SLR, more responders (participants who improved) were observed in the combined modality of feedback condition (4/12) vs. the single visual (3/12) or auditory (3/12) feedback, but the magnitude of changes was the same for all conditions. Changes in SLR for the combined modality of feedback correlated positively with the initial SLR of participants (r_s=0.693, p=0.026) and negatively with their perceived usefulness ratings (r_s=-0.667, p=0.036). Most responders utilized a strategy that involved increasing step length on both sides but to a larger extent on the shorter side. SWR remained largely unaltered in response to feedback conditions.

Discussion: Exposure to short bouts of combined visual-auditory feedback did not show superiority over single visual or auditory feedback in improving post-stroke gait asymmetry, but it was perceived as the most useful modality of feedback by participants. A smaller initial SLR and possibly an enhanced asymmetry awareness could lead to a better responsiveness to the

combined visual-auditory feedback. SWR may have been more resistant to change due to an altered rhythm perception following stroke. Future research could focus on investigating the effects of repeated and prolonged exposures to real-time biological feedback on gait asymmetry following stroke.

6.3 Introduction

Feedback is regarded as one of the most important factors in motor learning and recovery [1]. Among neurotypical individuals, motor learning can be achieved using intrinsic feedback, i.e., visual or proprioceptive inputs, allowing accurate perception of their motor performance and detection of performance error [2, 3]. However, for people with a neurological insult such as stroke, the perception of performance error could be altered and inaccurate [4]. Therefore, the feedback from external sources or extrinsic feedback (e.g., verbal guidance) plays a much more crucial role in their motor recovery and motor skills reacquisition [2, 3].

Conventional extrinsic feedback provided by therapists in stroke rehabilitation usually consists of verbal explanations, numbers from test results, etc. Such conventional feedback could be effective in training simple motor skills, but with only mitigated results to improve movement quality in the context of gait symmetry [5]. In fact, people with post-stroke locomotor disorders often present with a number of kinematic and spatiotemporal deviations which affect both the paretic and non-paretic limbs [6-8], making it difficult to provide precise, specific and comprehensible feedback to target the asymmetry problem [5].

The use of biological feedback has recently been investigated. Biological feedback are sensory cues that arise from live beings or animate objects. They have the advantage of being easily decipherable as they are used on a daily basis for social cognition and interaction [9]. In rehabilitation, the most common sensory modality used for biological feedback is vision because it is the modality most relied upon to perceive spatial information and to learn the spatial aspects of a movement [10]. Most applications of virtual reality (VR) for rehabilitation are based on the manipulation of visual information. A recent approach to apply visual feedback in gait training is using virtual self-avatars [11, 12], which allows individuals to obtain visual information about their own movements in real time. When the movement of the avatar is synchronized with the user's movement, a feeling of agency can be created over the avatar [13] and it can lead to a sense of embodiment [14]. The sense of embodiment can facilitate the user's perception of the cues on his/her body location provided via the avatar [15]. Feedback in the form of a visual avatar showed that it was possible to improve the spatial parameters of gait symmetry and increasing the bilateral step length in stroke participants [12]. Furthermore, our recent research has also shown that such feedback has the potential to improve interlimb coordination of lower extremities during walking post stroke [16]. The temporal aspect of gait symmetry, however, has so far not been shown to be responsive to avatar-based visual feedback [12].

Auditory feedback has also been shown to be an effective modality for motor learning in stroke rehabilitation [17]. Auditory feedback could provide information about the temporal aspect of a movement and help performers in the advanced stages of learning to fine-tune their movement execution [18]. The same research also suggested that auditory feedback is most successfully utilized in fast repetitive tasks, including walking [18]. Past studies have primarily focused on rhythmic auditory cueing as an intervention to improve gait symmetry, with mitigated results [19, 20]. One study which used footstep sound as auditory feedback showed that amplifying the footstep sounds led to a reduction in stance time asymmetry among people with stroke [21]. Furthermore, some studies utilized auditory feedback to improve weight bearing symmetry through the lower extremities [22, 23], and one study showed superiority of auditory feedback over conventional gait training to improve the symmetry of spatiotemporal features such as step time, single stance time and step length in individuals with stroke [24].

Combining different sensory modalities may offer additional benefits for motor learning as humans are adept in processing stimuli of different modalities simultaneously. Multimodal compared to unimodal stimuli are more frequently encountered in daily life and perceived more precisely and faster [25, 26], a phenomenon described as intersensory facilitation [27]. For instance, an auditory stimulus, which originates at approximately the same time and place as a visual stimulus, can amplify the overall neuronal processing of the construct [28]. The mechanism of intersensory facilitation is believed to be a product of a distribution of information processing to different modalities as opposed to a single modality [29]. Moreover, Doyle and Snowden (2001) hypothesized that having a visual signal accompanied by an auditory signal promotes an attentional 'disengagement' from irrelevant elements of the environment, thus allowing the processing of the visual target sooner [25]. Interestingly, it has been shown that the positive effect of combining visual-auditory feedback only occurs when the visual and auditory feedback are congruent [30]. In contrast, incongruent multimodal stimuli can lead to reduced perception of each of the modalities [31].

To date, feedback intervention on motor learning has focused mainly on the visual modality [18], while the application of auditory feedback and especially the use of combined visual and auditory feedback targeting gait asymmetry remains to be explored. We aim to investigate the instantaneous effects of the following modalities of feedback on the symmetry of spatiotemporal parameters of gait among people with stroke: i) visual feedback provided in the form of a self-avatar replicating locomotor movements in real-time; ii) auditory feedback delivered in the form of footstep sound that signal foot strike events and iii) combined visual-auditory feedback (avatar walking plus footstep sounds). Specific objectives were to: (1) compare the effects of visual only, auditory only, and combined visual-auditory feedback on post-stroke gait symmetry; (2) investigate the motor strategies leading to improvements in gait symmetry; and (3) examine the relationship between the improvements in gait symmetry and the individual characteristics of stroke participants. We hypothesized that (1) the combined visual-auditory feedback would provide the largest improvements in post-stroke gait symmetry; (2) individuals would improve their symmetry by adapting their spatiotemporal factors primarily on the non-paretic side, as seen previously with a single-modality visual avatar [12] and; (3) individuals with a smaller initial gait asymmetry, due to better sensorimotor functions, would show larger improvements in gait symmetry.

6.4 Methods

6.4.1 Participants

Twelve participants were recruited from the Jewish Rehabilitation Hospital, a McGill University-affiliated teaching hospital and a research site of the Montreal Centre for Interdisciplinary Research in Rehabilitation (CRIR) located in Laval, Quebec, Canada. This study received ethics approval from the Research Ethics Board of CRIR and all participants understood and signed the consent form prior to entering the study.

The inclusion criteria were: (1) having a first-time sub-acute or chronic (>6 months) supratentorial stroke; (2) age between 45 to 79 years; (3) being able to walk for 2 minutes independently while supervised, with or without a walking aid; (4) having a deficit in motor recovery of the lower limb, as indicated by stage scores ranging from 2 to 6 (more to less severe) on the leg and foot components of the Chedoke-McMaster Stroke Assessment (CMSA); Participants were excluded if they had (1) a stroke affecting brainstem or cerebellum; (2) co-morbid conditions such as cardiovascular, respiratory, musculoskeletal or other neurological conditions affecting locomotion; (3) dementia or cognitive deficits as indicated by scores < 24 on the Montreal Cognitive Assessment (MoCA); (4) severe aphasia or apraxia based on medical charts and initial screening; (5) impaired visual acuity (> 0.1 logMAR on Early Treatment Diabetic Retinopathy Study Letters (ETDRS) chart), hemispatial neglect (< 44 points on Star Cancellation Test) or self-reported auditory deficits; (6) a history of motion sickness or perceived handicap caused by dizziness, as indicated by a score > 16 on the Dizziness Handicap Inventory (DHI).

6.4.2 Experimental setup

The data collection consisted of two sessions. The first session included habituating participants to a self-paced treadmill (described below), and the habituation lasted about 5 minutes or until they feel comfortable, and neither visual nor auditory feedback was provided during familiarization. The participants were also evaluated with the 10-Meter Walk Test, CMSA, MoCA and DHI to determine their overground comfortable speed, stroke severity, presence of cognitive deficits and history of motion sickness, respectively. These tests have demonstrated excellent psychometric properties [32-35].

In the second session, the participants performed the walking task on a custom-built self-paced treadmill (0.6 m x 1.5 m). The motor of the treadmill is driven by PID servo-control based on the real-time distance and velocity feedback obtained with a potentiometer tethered to the participant [36]. A safety harness system suspended overhead was used to prevent the participants from falling. The treadmill is fitted with sliding handrails to assist with balance. The use of handrails was determined during habituation and was kept constant throughout the experiment. In the present study, all participants opted to use the handrails. They were instructed to only use it for balance, and not to put body weight on it during the habituation and the experiment. A screen (2.44 m × 3.05 m) was mounted in front of the treadmill for rear-projection of the virtual environment.

6.4.3 Visual feedback

Maya LT™ 2016 (Autodesk, USA) was used to design avatars of similar appearance and anthropometric characteristics to those of the participants. During the experiment, real-time tracking of the limb movement was provided by Tracker™ (Vicon, UK) based on the displacement of the 15 rigid bodies markers placed on the participant's specific body landmarks specified in Vicon Tracker™, which were tracked by a 6-camera Vicon™ (Vicon, UK) (Figure 6.1 top left and middle) motion capture system. Pegasus Advanced™ (Vicon, UK) was used to retarget the limb positions onto a virtual avatar (Figure 6.1 top right) which would then be displayed in a virtual scene representing a park created by Unity™ engine (Unity Technologies, USA) (Figure 6.1 bottom right). Kinematic data of participants were collected at 120 Hz in Vicon Tracker and Unity Engine.

6.4.4 Auditory feedback

The footstep sound file was created from a sound effect library (www.fesliyanstudios.com), and the same sound file was used for the footsteps on both sides. A pair of VIVE tracker™ devices (HTC corporation, Taiwan) (Figure 6.1 bottom left) were strapped around each of the participants' ankle as the sensors, and a 2-camera VIVE motion capture system (HTC corporation, Taiwan) was used to capture the movement of the sensors. The positions of the sensors were then tracked by Unity Engine (Unity Technologies, USA), and the baseline position of sensors was established in a static pose. The sound was played based on vertical threshold (+11 mm) detection, i.e. when a foot was descending and reaching the 11 mm above the baseline position of the sensor, a trigger was then activated to play the footstep sound. This threshold value was determined prior to conducting this experiment, to obtain a sound consistently with each foot strike.

6.4.5 Experimental procedure

The participants performed two walking trials for each of the following conditions in a random order determined by a random sequence generator: (1) avatar viewed from the paretic side view only; (2) footstep sound only; (3) avatar viewed from the paretic side view combined with footstep sound. The paretic side view was chosen because it provided the best results on gait symmetry from a previous study [12]. Each trial had three phases which included 30s of comfortable walking without any feedback modality (pre-adaptation phase), followed by 1 min of walking while visualizing the avatar replicating the exact walking pattern of the participant in real time and/or listening to the footstep sound that occur at the same time as their feet land (adaptation phase), and finally 1 min of walking without feedback (post-adaptation phase). The duration of trials was determined based on the protocol of a previous study which investigated the effects of different views of avatar on post-stroke gait asymmetry [12]. Prior to the start of each trial, participants were instructed to look at the avatar's legs and feet and/or listen to the rhythm of bilateral footstep sound while walking, depending on the modality feedback. They were also instructed to walk at comfortable speed and to correct their gait asymmetry based on the visual and/or auditory feedback provided. Participants were allowed to rest by sitting between the walking trials for 5 minutes or more if needed.

6.4.6 Data analysis

The raw kinematic data were exported from Unity™ 5, before being analyzed in Matlab™ R2020b. To avoid the effects of acceleration and deceleration, data in the first and last 10 seconds of each trial were excluded. The raw data were dual-pass filtered with a 2nd order Butterworth filter at a cut-off frequency of 8 Hz, then normalized to 100% of the gait cycle.

The primary outcomes were step length ratio (SLR) and swing time ratio (SWR). According to Patterson et al. (2010), the swing time ratio and step length ratio are the most appropriate outcomes to measure spatiotemporal characteristics of gait symmetry [37]. Furthermore, it was also recommended in the work of Brandstater and colleagues (1983) to use swing time ratio as a measure for post-stroke motor recovery [38]. The step length was calculated by measuring the distance between toes of avatars in Unity™. The swing time was calculated based on the time between the foot-off and foot-strike events of each gait cycle. The positions of toes were directly exported from Unity™, while the positions of heels were extrapolated in Matlab™ based on the positions of ankles and toes measured during a static pose. The ratios were calculated using the values of left and right side with the larger value in the numerator regardless of the paretic side [37]. A resulting value of '1.0' indicated perfect symmetry.

Secondary outcomes included paretic and non-paretic step length and swing time, treadmill walking speed and perceived usefulness of the intervention. The latter was assessed following the completion of all walking trials by asking participants to rate, on a scale ranging from 0-10, the usefulness of each modality on gait improvement. The questions were: 1- On a scale from 0 to 10, how do you rate the usefulness of the visual avatar at improving your walking? 2- On a scale from 0 to 10, how do you rate the usefulness of the footstep sound at improving your walking? 3- On a scale from 0 to 10, how do you rate the usefulness of combining the avatar with footstep sound at improving your walking?

6.4.7 Statistical analysis

The initial SLR and SWR (baseline values) of participants were used to determine if they were considered asymmetric in terms of their step length or swing time while walking. Based on the classification of Patterson and colleagues (2010) [37], a SLR value ≥ 1.08 and SWR value ≥ 1.06 are considered asymmetric. The primary outcomes, SLR and SWR, were examined exclusively among participants presenting an asymmetry in the respective outcome. After conducting the Shapiro-Wilk normality test, the data were found to deviate from a normal distribution, therefore non-parametric tests were chosen. To address hypothesis 1, NparLD statistical tests from the R Statistical Package were used to compare the mean SLR and SWR values between the conditions (visual, auditory, combined) and across different phases (pre-adaptation, adaptation, post-adaptation). The mean SLR and SWR were obtained by averaging values across gait cycles. To address hypothesis 2, bilateral patterns of change in step length and swing time were analyzed as responders and non-responders. Responders were defined as participants showing an improvement in symmetry (ratio change > 0), and non-responders were those who did not improve. To address the third hypothesis, correlation analyses using Spearman's rank correlation tests with Bonferroni-Holm correction adjustments were performed between changes in gait symmetry outcomes occurring between the pre-adaptation and the adaptation phase, and explanatory variables that included the initial magnitude of asymmetry, overground walking speed, and Chedoke McMaster Stroke Assessment Scale (CMSA) scores for the leg and foot. Additionally, Spearman's rank correlation tests were used to explore the relationship between actual changes in symmetry and perceived usefulness ratings. The significance level needed to reject the null hypothesis was set at $p<0.05$ for a 2-tail probability level. The coefficient values r_s between 0.1 and <0.3, 0.3 and 0.5, and >0.5 were considered to reflect small, medium and large effect sizes respectively [39].

Friedman tests were used to assess the differences in perceived usefulness ratings between the three conditions, as well as in walking speed across phases (pre-adaptation, adaptation, post-adaptation) for each of the three conditions separately. Wilcoxon signed-rank test was then used to conduct post-hoc pairwise analysis between phases, with Bonferroni-Holm correction adjustments. To examine any possible confounding effect due to the feedback presentation order or training effect, Wilcoxon signed-rank tests were also used to assess differences in pre-adaptation values for SLR and SWR between the first vs. the last walking trial performed by participants. The formula '$r=z/\sqrt{N}$' proposed by Rosenthal (1994) was used for calculation of effect size of Wilcoxon signed-rank test [40]. The statistical analyses were performed in SPSS v.24 (IBM Inc, USA), except for the NparLD tests which were conducted in R v.4.2.1.

G*Power 3.1 (Heinrich Heine University Düsseldorf, Germany) was used a priori to calculate the sample size. A large effect size (>1) was obtained in previous studies examining the effects of split-belt treadmill walking on step length symmetry [41, 42], but since the present study focused on the immediate effects of the exposure, a more conservative effect size of 0.5 was postulated. In the absence of the NparLD option in G*Power, sample size estimation was based on a repeated-measure, within-subject analysis of variance. Considering a α-level of 0.05 and a power of 0.8, a sample size of twelve participants (n=12) was targeted for recruitment.

6.5 Results

The demographic and clinical information of the 12 participants is presented in Table 6.1. Most participants were males (10/12), affected on the right hemisphere, and had an ischemic stroke. All participants used handrails for balance purpose during the experiment. One participant had an overground comfortable speed that was considered below 'most-limited community ambulation level' (<0.4m/s), 5/12 participants were considered 'full community ambulation level' (>0.8m/s), and the rest (6/12) were at 'limited community ambulation level' (between 0.4 and 0.8m/s) [43]. Moreover, 11 out of 12 participants presented SWR asymmetry while 10 presented SLR asymmetry. No significant differences were found between the first and the last walking trial in terms of pre-adaptation values for SLR (Z=-1.20, p=0.230) and SWR (Z=-0.45, p=0.656).

6.5.1 Effects of sensory modalities of feedback on gait symmetry

When examining the group results, SLR (N=10) remained unaffected by the different sensory modalities of feedback (χ^2=5.84, df=2, p=0.054) and across phases (χ^2=0.94, df=2, p=0.624). Similarly, for SWR (N=11), neither the modality of feedback (χ^2=1.20, df=2, p=0.548) nor the phase (χ^2=2.12, df=2, p=0.347) led to significant changes. When examining the individual data (Figure 6.2), however, it was observed that for each of the three sensory modality conditions, there were participants who improved (solid lines) their SLR or SWR while others did not (dotted lines). Given these mixed results, an analysis of individual response to the intervention was performed.

Table 6.2 lists the individual responses in SLR, as well as changes in paretic and non-paretic step length in the combined modality condition. As indicated by the direction in SLR in that table, most (8/10) participants had a larger non-paretic step length while few (2/10) had a larger paretic step length to start with. In the combined modalities condition, 4/10 improved their SLR during the adaptation phase in the combined sensory modality condition (S1, S3, S4, S10, Table 6.2), while 3/10 improved in the visual condition (S2, S3, S7, Appendix 1) and 3/10 in the auditory condition (S2, S3, S11, Appendix 2). Furthermore, 3/4, 2/3 and 2/3 responders continued to be responders in the post-adaptation for the combined, visual, and auditory conditions respectively. As for the perceived usefulness rating, there was a significant main effect (χ^2=9.45, df=2, $p<0.01$) due to the feedback modality. Combined feedback was perceived to be most useful (9.1±2.0) compared to visual-only (8.5±1.7) or auditory-only (7.5±3.0) conditions. Post-hoc analyses indicated that the perceived usefulness rating was significantly higher in the combined modalities condition vs. the auditory condition (Z=-2.80, $p<0.01$, effect size: 0.81), but was not significantly different between the combined vs. visual (Z=-0.88, p=0.378) or between the visual vs. auditory condition (Z=-1.51, p=0.131). The mean ratings (± SD) of the responders in each of the three conditions were 10.0±0, 9.3±0.6 and 9.0±1.0 respectively.

A closer analysis of step length changes revealed that most of the responders utilized a strategy that consisted of increasing both their paretic and non-paretic step lengths, but to a larger extent on the side that initially displayed a smaller step, leading to an improvement in SLR. Only a few responders decreased their step length of the longer side while increasing it on the shorter side. As a concrete example, all 4 SLR responders to the combined sensory modality condition shown in Table 6.2 (S1, S3, S4, S10) presented a nonparetic larger step to start with. Three increased their step length on both sides during the adaptation phase, but to a larger extent on the paretic vs. non-paretic side, and only one increased step length on the paretic side while reducing it on the non-paretic side. Similar strategies were observed when exposed to the visual or auditory only modalities (Appendices 1 and 2). Examination of non-responders in SLR to the feedback modalities, especially those who deteriorated, revealed that they either increased their step length on both sides but more so on the side that already displayed a larger step to start with, or they changed their step length in the wrong direction (e.g., increasing it when it should be reduced, and vice versa).

As for the individual data on SWR, there were only 2 responders out of 11 participants for each of the sensory modality of feedback, and the responders were different in each condition (combined: S1 and S8; visual: S4 and S12; auditory: S3 and S7). When present, improvements in SWR were in the magnitude of 0.04 to 0.09. Individual SWR changes in the combined condition are shown in Appendix 3.

6.5.2 Relationship between the change in SLR and the characteristics of participants

An analysis of relationships between the SLR improvements and participant characteristics was performed for the combined sensory modality of feedback, which showed the most improvements among all three feedback conditions. The initial SLR was positively correlated with the change in SLR between the adaptation and pre-adaptation phases (r_s=0.693, p=0.026) (Figure 6.3A). In other words, those with a small initial SLR (less asymmetry) experienced a reduction in SLR (improvement) during the adaptation phase, while those who had a larger initial SLR (more asymmetry) showed an increase in SLR (deterioration). Additionally, a significant negative relationship was observed between the perceived usefulness of the combined condition and extent of SLR changes in the adaptation phase (r_s=-0.667, p=0.036) (Figure 6.3B). Thus, participants who rated the usefulness of the feedback as higher experienced improvements in SLR while those who rated usefulness as lower experienced a deterioration. Change in SLR was not found to be significantly correlated with the level of motor recovery (CMSA scores) of the leg (r_s=-0.258, p=0.472) and foot (r_s=-0.101, p=0.781), or to overground comfortable walking speed (r_s=-0.372, p=0.290).

6.5.3 Changes in walking speed

Walking speed while walking on the treadmill was found to be significantly increased in the visual condition (χ^2=12.16, df=2, p<0.01) (Figure 6.4), but no significant changes were found in the auditory (χ^2=1.50, df=2, p=0.47) and combined (χ^2=5.17, df=2, p=0.08) feedback conditions. Post-hoc analyses revealed that for the visual condition, walking speed was significantly larger in the adaptation vs. pre-adaptation phase (Δ= 0.63±0.87m/s, Z=-2.48, p=0.013, effect size: 0.72) and in the post-adaptation vs. pre-adaptation phases (Δ=0.81±0.75m/s, Z=-2.82, p<0.01, effect size: 0.81), but was not significantly different between the post-adaptation and adaptation phases (Z=-1.33, p=0.18).

6.6 Discussion

This study investigated, for the first time, instantaneous changes in spatiotemporal parameters of gait symmetry among individuals with stroke exposed to short bouts of real-time feedback provided as a visual avatar, auditory foot strike, and combined visual-auditory modalities. The analysis of group results revealed no significant differences in SWR or SLR when exposed to the feedback for any of the sensory modalities. The analysis of individual responses revealed individual differences, with the presence of responders vs. non-responders due to different modalities of feedback, but with no clear advantage of any one of the three conditions being superior. Further analyses of changes in step length showed that the responders achieved improved SLR primarily through a bilateral but differential increase in step length. Moreover, correlation analyses carried out for the combined sensory modality of avatar feedback revealed that smaller step length asymmetry at baseline and higher perception of usefulness about the intervention were associated with a larger SLR improvement, while a larger initial step length asymmetry and lower perception of usefulness were rather associated with SLR deterioration.

6.6.1 Effects of feedback modality

The combined modality condition yielded more SLR responders (4 out of 10) than the visual and auditory conditions (3 out of 10 for each), but the magnitude of change in SLR appeared similar in all conditions. The lack of difference between the visual, auditory, and audiovisual modalities was also reported in a study that examined the effects of different biofeedback on anterior ground reaction force generation of the paretic side among people with stroke [44]. However, the combined condition had the highest average of perceived usefulness rating reported by the participants, suggesting that the combined condition could be more easily decipherable or could potentially improve other parameters of gait that were not measured by the spatiotemporal outcomes analyzed in this study. In a previous study that aimed at modifying the foot-strike pattern and at reducing plantar loads among runners, the combined visual-auditory condition also showed the most improvements compared to the single visual and auditory conditions [45]. Moreover, a randomized controlled trial conducted in stroke survivors showed that a real-time combined visual and auditory feedback induced larger improvements in paretic arm movement accuracy compared to no feedback [46], adding further support to the use of combined sensory feedback in post-stroke rehabilitation. In the latter study, the authors suggested that the real-time feedback induced improvements by allowing participants to focus on movement quality, a mechanism we hypothesize applies as well for the effects of avatar-feedback on post-stroke gait symmetry [16].

The present results also indicate that neither the combined feedback nor the auditory or visual feedback alone induced changes in the SWR. This lack of SWR changes contrasts with our initial hypothesis that footstep sounds would primarily affect temporal aspect of gait symmetry, and with earlier work suggesting that auditory feedback would support the learning of the temporal aspect of movement post-stroke [18]. Patterson and colleagues (2018), however, demonstrated that individuals with stroke have altered rhythm perception compared to healthy controls [47]. As a result, the auditory feedback delivered in the form of footstep sounds in the present study may have been less effective than anticipated in providing information on footstep rhythm, resulting in a lack SWR improvement. It has also been shown that the severity of temporal asymmetry is correlated positively with time post-stroke [47]. In other words, temporal gait symmetry deteriorates as time goes on and individuals may perceive their temporal asymmetry as the "new normal." As participants in this present study had a chronic stroke with an average duration of 63.5 months, they possibly became habituated with their swing time asymmetry and may thus have difficulty making the necessary adaptations to reduce it.

6.6.2 Strategies of responders and non-responders

As part of this study, we also explored the strategies employed to improve gait symmetry. While we initially hypothesized that responders would primarily adapt their spatiotemporal parameters on the non-paretic side, we instead observed that most of them used a strategy where they increased both the paretic and non-paretic step lengths, but where the shorter side (in most instances the paretic step) would show the largest increase. First and foremost, these results apparently contrast with our earlier work where we showed that responders to real-time feedback in the form of a visual avatar primarily increased their step length on the non-paretic side [12]. It should be noted, however, that responders in this earlier study had a larger paretic step initially, while most participants in the present study (8/10), including the responders, instead had an initially larger non-paretic step. Balasubramanian and colleagues (2007) argued that the direction of the post-stroke step length asymmetry depends on the capacity to develop propulsive forces on either side [6]. Those with a longer paretic step, for instance, would show more propulsive forces on the non-paretic, and vice versa. Taken together, the present results and those from our previous study [12] suggest that the side that generates higher propulsive force is likely to exert the most adaptation when attempting to correct the asymmetry, resulting in a strategy that depends on the direction of the asymmetry. Thus, the direction of the asymmetry would predict the strategies employed to correct the asymmetry, as opposed to predicting whether an individual will respond or not to the intervention.

Another interesting observation that arises from the analysis of strategies in SLR responders is the fact that increasing step length bilaterally, although to a larger extent on the side that shows the smaller step to start with, does not appear as an optimal strategy. Indeed, one could have instead reduced step length on the side that showed larger steps and/or increased step length on the side displaying shorter steps. We speculate that increasing step length bilaterally, that is applying a change in the same direction (yet to a different extent), might have been easier to perform by the stroke participants than selectively adjusting one side or performing adjustments in opposite direction for the two lower limbs. In addition, as responders increased their bilateral step length, they also increased walking speed as a result. Given that adopting faster walking speeds normalizes spatiotemporal parameters and improves gait symmetry post-stroke [48], it is possible that the improvements in symmetry might have been mediated, at least in part, through a faster walking speed and the ensuing interlimb coordination that generally becomes enhanced [49].

As for the non-responders in SLR, they generally chose the wrong strategy (e.g. increasing step length on the longer side or to a larger extent on that side) as they attempted to correct their asymmetry. For SWR, the observed changes in bilateral swing time were limited, leading to insignificant changes globally. Such a failure to adopt successful strategies, which was observed for most participants in this study, could be related to i) an incorrect perception of gait asymmetry (perception deficit) and to ii) difficulties in implementing an adapted corrective strategy (execution deficit). In support of the former, it has been reported that half of individuals with stroke incorrectly perceive the presence and/or direction of gait asymmetry [50]. As a result of this impaired perception which prevents error detection, improving gait symmetry via practice remains very difficult [4]. The possible contribution of an executive function deficit is supported by the observation that the larger the initial asymmetry, the smaller the improvements in SLR in response to the avatar feedback. Given that individuals with a larger gait asymmetry are generally those with more pronounced motor control deficits [51], they are at a disadvantage to implement the proper strategies to improve their gait symmetry. In addition, experimenting and identifying the right strategy to improve gait symmetry likely requires high executive functioning while operating under dual-task conditions, i.e. walking with a cognitive load. Considering that dual-task walking can be altered post-stroke [52], and although participants in this study were screened for cognitive deficits, selecting the proper strategy to improve gait symmetry is cognitively challenging and may have been more difficult for some participants than others, especially considering that they only had a brief exposure to the avatar feedback.

Participants perceiving the intervention as most useful were those who experienced improvements in SLR. Beyond corroborating the objective SLR changes, this positive subjective perception experienced by the responders suggests that these individuals may have had an enhanced awareness of their gait symmetry and its online modulation during the avatar exposure, pointing towards better sensorimotor integration and cognitive processes overall. Thus, those with a smaller initial SLR to start with and possibly those with an enhanced awareness about their gait asymmetry appear more likely to respond to the avatar-based feedback provided in the combined visual and auditory modality.

6.6.3 Limitations

The duration of exposure to the feedback in this study was brief and delivered in a single session, which likely minimized the effects of the intervention while preventing us from examining the effect of repeated exposure. Furthermore, changes on the level of neural plasticity were unlikely to occur given the short duration of trials. It is reasonable to speculate that even larger changes would have been observed with longer and repeated exposures to the avatar feedback. Nevertheless, it has been shown in a study applying short training sessions of three motor tasks (different weight transfer or hip flexion movements) performed 5 times [53] that immediate changes to spatiotemporal parameters of gait could be elicited after a short practice. The small sample size of this study is another limitation which, while addressed with non-parametric statistics, may limit the generalization of findings to the general population with stroke that present with a great variety in terms of direction and severity of gait asymmetry. Lastly, this study focused on the spatiotemporal parameters of gait, but variables such ground reaction forces, and kinetic variables could provide additional information on the symmetry of weight bearing and propulsive forces during walking. Despite these limitations, however, strategies employed by participants to improve their SLR were identified, and moderate significant relationships between SLR changes and characteristics of participants (e.g., extent of initial asymmetry and perceived usefulness) could be established.

6.7 Conclusion

Contrary to our initial hypothesis, the combined visual and auditory modalities of avatar feedback did not show advantage over the single-modality feedback at improving the gait symmetry after stroke. The combined feedback, however, was perceived to be the most useful among all participants. The improvements in step length symmetry, when present, were achieved primarily through a bilateral increase in step length, with a larger increase on the side that shows a shorter step. Results also show that the smaller the initial step length asymmetry and the larger the perception of usefulness, the better the improvement in SLR in response to the combined modality condition. Future studies could focus on further characterizing individual factors explaining the response of individuals to the intervention and investigating the effects of a repeated exposure to the avatar-based feedback in individuals with sub-acute stroke.

6.8 References

1. Schmidt R: **Motor Control and Learning: A Behavioral Emphasis**, 2nd edn: Champaign, Ill: Human Kinetics Publishers; 1988.
2. Young D.E, Schmidt R.A, Lee T.D: **Human Motor Learning & Human Learning**, 1st edn: International Encyclopedia of Ergonomics and Human Factors; 2001.
3. Gilmore PE, Spaulding SJ: **Motor control and motor learning: implications for treatment of individuals post stroke**. *Phys Occup Ther Geriatr* 2001, **20**(1):1-15.
4. Crosby LD, Chen JL, Grahn JA, Patterson KK: **Perceptions of an over-ground induced temporal gait asymmetry by healthy young adults**. *Hum Mov Sci* 2021, **78**:102806.
5. Patterson KK, Mansfield A, Biasin L, Brunton K, Inness EL, McIlroy WE: **Longitudinal changes in poststroke spatiotemporal gait asymmetry over inpatient rehabilitation**. *Neurorehabil Neural Repair* 2015, **29**(2):153-162.
6. Balasubramanian CK, Bowden MG, Neptune RR, Kautz SA: **Relationship between step length asymmetry and walking performance in subjects with chronic hemiparesis**. *Arch Phys Med Rehabil* 2007, **88**(1):43-49.
7. Hsu AL, Tang PF, Jan MH: **Analysis of impairments influencing gait velocity and asymmetry of hemiplegic patients after mild to moderate stroke**. *Arch Phys Med Rehabil* 2003, **84**(8):1185-1193.
8. Titianova EB, Pitkanen K, Paakkonen A, Sivenius J, Tarkka IM: **Gait characteristics and functional ambulation profile in patients with chronic unilateral stroke**. *Am J Phys Med Rehabil* 2003, **82**(10):778-786; quiz 787-779, 823.
9. Brothers L: **The neural basis of primate social communication**. *Motivation and Emotion* 1990, **14**(2):81-91.
10. Freides D: **Human information processing and sensory modality: cross-modal functions, information complexity, memory, and deficit**. *Psychol Bull* 1974, **81**(5):284-310.
11. Kannape OA, Blanke O: **Self in motion: sensorimotor and cognitive mechanisms in gait agency**. *J Neurophysiol* 2013, **110**(8):1837-1847.
12. Liu LY, Sangani S, Patterson KK, Fung J, Lamontagne A: **Real-Time Avatar-Based Feedback to Enhance the Symmetry of Spatiotemporal Parameters After Stroke: Instantaneous Effects of Different Avatar Views**. *IEEE Trans Neural Syst Rehabil Eng* 2020, **28**(4):878-887.
13. Willaert I, Aissaoui R, Nadeau S, Duclos C, Labbe DR: **Modulating The Gait Of A Real-Time Self-Avatar To Induce Changes In Stride Length During Treadmill Walking**. In: *2020 IEEE Conference on Virtual Reality and 3D User Interfaces Abstracts and Workshops (VRW): 22-26 March 2020 2020*; 2020: 718-719.
14. Kilteni K, Groten R, Slater M: **The Sense of Embodiment in Virtual Reality**. *Presence: Teleoperators and Virtual Environments* 2012, **21**(4):373-387.
15. Steed A, Pan Y, Zisch F, Steptoe W: **The impact of a self-avatar on cognitive load in immersive virtual reality**. In: *2016 IEEE Virtual Reality (VR): 19-23 March 2016 2016*; 2016: 67-76.
16. Liu LY, Sangani S, Patterson KK, Fung J, Lamontagne A: **Instantaneous effect of real-time avatar visual feedback on interlimb coordination during walking post-stroke**. *Clinical Biomechanics* 2022, **100**:105821.
17. Secoli R, Milot MH, Rosati G, Reinkensmeyer DJ: **Effect of visual distraction and auditory feedback on patient effort during robot-assisted movement training after stroke**. *J Neuroeng Rehabil* 2011, **8**:21.

18. Sigrist R, Rauter G, Riener R, Wolf P: **Augmented visual, auditory, haptic, and multimodal feedback in motor learning: a review**. *Psychon Bull Rev* 2013, **20**(1):21-53.
19. Roerdink M, Lamoth CJC, Kwakkel G, van Wieringen PCW, Beek PJ: **Gait Coordination After Stroke: Benefits of Acoustically Paced Treadmill Walking**. *Phys Ther* 2007, **87**(8):1009-1022.
20. Thaut MH, Leins AK, Rice RR, Argstatter H, Kenyon GP, McIntosh GC, Bolay HV, Fetter M: **Rhythmic auditory stimulation improves gait more than NDT/Bobath training in near-ambulatory patients early poststroke: a single-blind, randomized trial**. *Neurorehabil Neural Repair* 2007, **21**(5):455-459.
21. Gomez-Andres A, Grau-Sánchez J, Duarte E, Rodriguez-Fornells A, Tajadura-Jiménez A: **Enriching footsteps sounds in gait rehabilitation in chronic stroke patients: a pilot study**. *Ann N Y Acad Sci* 2020, **1467**(1):48-59.
22. Cha Y-J, Kim J-D, Choi Y-R, Kim N-H, Son S-M: **Effects of gait training with auditory feedback on walking and balancing ability in adults after hemiplegic stroke: a preliminary, randomized, controlled study**. *Int J Rehabil Res* 2018, **41**(3):239-243.
23. Ki KI, Kim MS, Moon Y, Choi JD: **Effects of auditory feedback during gait training on hemiplegic patients' weight bearing and dynamic balance ability**. *J Phys Ther Sci* 2015, **27**(4):1267-1269.
24. Kim J, Jung S, Song C: **The Effects of Auditory Feedback Gait Training Using Smart Insole on Stroke Patients**. *Brain Sciences* 2021, **11**(11):1377.
25. Doyle MC, Snowden RJ: **Identification of visual stimuli is improved by accompanying auditory stimuli: the role of eye movements and sound location**. *Perception* 2001, **30**(7):795-810.
26. Fort A, Delpuech C, Pernier J, Giard MH: **Dynamics of cortico-subcortical cross-modal operations involved in audio-visual object detection in humans**. *Cereb Cortex* 2002, **12**(10):1031-1039.
27. Carson RG, Kelso JA: **Governing coordination: behavioural principles and neural correlates**. *Exp Brain Res* 2004, **154**(3):267-274.
28. Sigrist R, Rauter G, Riener R, Wolf P: **Terminal feedback outperforms concurrent visual, auditory, and haptic feedback in learning a complex rowing-type task**. *J Mot Behav* 2013, **45**(6):455-472.
29. Wickens CD: **Multiple resources and performance prediction**. *Theoretical Issues in Ergonomics Science* 2002, **3**(2):159-177.
30. Kim RS, Seitz AR, Shams L: **Benefits of stimulus congruency for multisensory facilitation of visual learning**. *PLoS One* 2008, **3**(1):e1532-e1532.
31. Calvert GA, Campbell R, Brammer MJ: **Evidence from functional magnetic resonance imaging of crossmodal binding in the human heteromodal cortex**. *Curr Biol* 2000, **10**(11):649-657.
32. Lin JH, Hsu MJ, Hsu HW, Wu HC, Hsieh CL: **Psychometric comparisons of 3 functional ambulation measures for patients with stroke**. *Stroke* 2010, **41**(9):2021-2025.
33. Gowland C, Stratford P, Ward M, Moreland J, Torresin W, Van Hullenaar S, Sanford J, Barreca S, Vanspall B, Plews N: **Measuring physical impairment and disability with the Chedoke-McMaster Stroke Assessment**. *Stroke* 1993, **24**(1):58-63.
34. Toglia J, Fitzgerald KA, O'Dell MW, Mastrogiovanni AR, Lin CD: **The Mini-Mental State Examination and Montreal Cognitive Assessment in persons with mild subacute stroke: relationship to functional outcome**. *Arch Phys Med Rehabil* 2011, **92**(5):792-798.
35. Whitney SL, Hudak MT, Marchetti GF: **The activities-specific balance confidence scale and the dizziness handicap inventory: a comparison**. *J Vestib Res* 1999, **9**(4):253-259.
36. Fung J, Richards CL, Malouin F, McFadyen BJ, Lamontagne A: **A treadmill and motion coupled virtual reality system for gait training post-stroke**. *Cyberpsychol Behav* 2006, **9**(2):157-162.

37. Patterson KK, Gage WH, Brooks D, Black SE, McIlroy WE: **Evaluation of gait symmetry after stroke: a comparison of current methods and recommendations for standardization**. *Gait Posture* 2010, **31**(2):241-246.
38. Brandstater ME, de Bruin H, Gowland C, Clark BM: **Hemiplegic gait: analysis of temporal variables**. *Arch Phys Med Rehabil* 1983, **64**(12):583-587.
39. Cohen J: **Statistical Power Analysis for the Behavioral Sciences**, 2nd edn: Routledge; 1988.
40. Rosenthal R: **Parametric measures of effect size**. In: *The handbook of research synthesis.* edn. New York, NY, US: Russell Sage Foundation; 1994: 231-244.
41. Reisman DS, McLean H, Keller J, Danks KA, Bastian AJ: **Repeated split-belt treadmill training improves poststroke step length asymmetry**. *Neurorehabil Neural Repair* 2013, **27**(5):460-468.
42. Reisman DS, Wityk R, Silver K, Bastian AJ: **Split-belt treadmill adaptation transfers to overground walking in persons poststroke**. *Neurorehabil Neural Repair* 2009, **23**(7):735-744.
43. Schmid A, Duncan PW, Studenski S, Lai SM, Richards L, Perera S, Wu SS: **Improvements in speed-based gait classifications are meaningful**. *Stroke* 2007, **38**(7):2096-2100.
44. Liu J, Kim HB, Wolf SL, Kesar TM: **Comparison of the Immediate Effects of Audio, Visual, or Audiovisual Gait Biofeedback on Propulsive Force Generation in Able-Bodied and Post-stroke Individuals**. *Appl Psychophysiol Biofeedback* 2020, **45**(3):211-220.
45. Phanpho C, Rao S, Moffat M: **Immediate effect of visual, auditory and combined feedback on foot strike pattern**. *Gait Posture* 2019, **74**:212-217.
46. Correia FD, Santos F, Branquinho A, Nogueira A, Candeias C, Quintaneiro P, Almeida A, Bento V: **Motor Task Performance under Visual and Auditory Feedback Post Stroke: A Randomised Crossover Trial**. *International journal of neurorehabilitation* 2017(4):5.
47. Patterson KK, Wong JS, Knorr S, Grahn JA: **Rhythm Perception and Production Abilities and Their Relationship to Gait After Stroke**. *Arch Phys Med Rehabil* 2018, **99**(5):945-951.
48. Lamontagne A, Fung J: **Faster Is Better**. *Stroke* 2004, **35**(11):2543.
49. Kwakkel G, Wagenaar RC: **Effect of Duration of Upper- and Lower-Extremity Rehabilitation Sessions and Walking Speed on Recovery of Interlimb Coordination in Hemiplegic Gait**. *Phys Ther* 2002, **82**(5):432-448.
50. DePaul V, Chow F, Thomas K, Azuma L, Chan W, Poon V, Patterson K: **Self-assessment of gait symmetry in individuals with unilateral stroke: A pilot study**. In: *International Society for Posture and Gait Research World Congress: 2015*; 2015.
51. Alexander LD, Black SE, Patterson KK, Gao F, Danells CJ, McIlroy WE: **Association between gait asymmetry and brain lesion location in stroke patients**. *Stroke* 2009, **40**(2):537-544.
52. Deblock-Bellamy A, Lamontagne A, McFadyen BJ, Ouellet MC, Blanchette AK: **Dual-Task Abilities During Activities Representative of Daily Life in Community-Dwelling Stroke Survivors: A Pilot Study**. *Front Neurol* 2022, **13**:855226.
53. Sakuma K, Tateuchi H, Nishishita S, Okita Y, Kitatani R, Koyama Y, Ibuki S, Ichihashi N: **Immediate effects of stance and swing phase training on gait in patients with stroke**. *Int J Rehabil Res* 2021, **44**(2):152-158.

Table 6.1 Summary of the demographic information of the participants

Participant	Gender (Male/ Female)	Age (years)	Stroke Chronicity (months)	Type of stroke (Ischemic/ Hemorrhagic)	Stroke Location	Comfortable Overground Walking Speed (m/s)	CMSA Score		Initial step length ratio	Initial swing time ratio
							Leg	Foot		
S1	Male	68	49	Ischemic	R Ic	1.35	5	5	1.08	1.07
S2	Male	58	96	Ischemic	R Bg	1.09	4	3	1.40	1.03*
S3	Male	68	46	Ischemic	R lacunar Ic	0.43	6	2	1.12	1.07
S4	Male	59	30	Ischemic	R Ic+Bg	1.10	5	4	1.14	1.08
S5	Male	67	189	Ischemic	R Sylvian	1.07	4	3	1.02*	1.14
S6	Male	69	36	Ischemic	L Ic	0.80	5	3	1.04*	1.20
S7	Male	60	57	Ischemic	R MCA	1.04	6	5	1.09	1.07
S8	Female	60	50	Ischemic	R thalamus	0.74	4	4	1.14	1.10
S9	Male	78	53	Ischemic	R MCA	0.64	6	4	1.24	1.21
S10	Male	71	28	Hemorrhagic	R Sylvian	0.51	4	3	1.18	1.43
S11	Female	72	52	Ischemic	R MCA	0.26	3	2	1.36	1.07
S12	Male	51	76	Ischemic	R Sylvian	0.49	5	4	1.49	1.55
Mean±SD Ratio (:)	10:2	65.1 ±7.5	63.5±45.8	11:1	—	0.79±0.34	4.8 ±1.0	3.5 ±1.0	1.19±0.12	1.18±0.16

Abbreviations: SD: standard deviation; L: left; R: right; MCA: middle cerebral artery; Ic: internal capsule; Bg: basal ganglia; CMSA: Chedoke-McMaster Stroke Assessment; *these ratio did not meet the threshold of asymmetry.

Table 6.2 Individual data of SLR in the combined modality condition

ID	Initial SLR (ratio)	Direction of SLR	Pre-Adaptation to Adaptation			Pre-Adaptation to Post-Adaptation		
			∆SLR (ratio)	∆Paretic (mm)	∆Non-paretic (mm)	∆SLR (ratio)	∆Paretic (mm)	∆Non-paretic (mm)
1	**1.08**	**Np**	**-0.05**	**↑↑ 55.61**	**↑ 38,3**	0	↑ 89.98	↑ 94.85
2	1.4	Np	0.13	↑ 8.65	↑↑ 33.53	0.26	↓ -19.81	↑ 38.97
3	**1.12**	**Np**	**-0.06**	**↑↑ 44.75**	**↑ 33.85**	-0.09	↑↑ 47.84	↑ 26.07
4	**1.14**	**Np**	**-0.23**	**↑↑ 69.35**	**↑ 49.74**	-0.1	↑↑ 56.57	↑ 47.56
5	1.02*	-	-	-	-	-	-	-
6	1.04*	-	-	-	-	-	-	-
7	1.09	Np	0	↑ 23.09	↑ 22.52	0.01	↑ 33.12	↑ 38.92
8	1.14	Np	0.04	↑ 2.7	↑↑ 19.79	0.05	↓↓ -36.56	↓ -22.17
9	1.24	Np	0.06	↓↓ -34.53	↓ -28.51	0.08	↓ -6.14	↑ 12.01
10	**1.18**	**Np**	**-0.15**	**↑ 22.66**	**↓ -6.38**	-0.2	↑ 6.29	↓ -31.63
11	1.36	P	0.08	↑ 26.99	↓ -13.45	0.18	↑ 47.29	↓ -26.13
12	1.49	P	0.22	↑ 6.85	↓ -20.83	0.04	↓ -33.5	↓↓-38.89

Abbreviations: SLR: step length ratio; Np: non-paretic side being larger; P: paretic side being larger
*: participant is not considered to be asymmetric in SLR; ∆: change; paretic: paretic step length; non-paretic: non-paretic step length ↑: increase; ↑↑: larger increase (>10) compared to the opposite side; ↓: decrease; ↓↓: larger decrease (>10) compared to the opposite side; **Bold**: participants identified as responders (improvement in ∆SLR).

Table 6.3 Appendix 1. Individual data of SLR in the visual modality condition

ID	Initial SLR (ratio)	Direction of SLR	Pre-Adaptation to Adaptation			Adaptation to Post-Adaptation		
			∆SLR (ratio)	∆Paretic (mm)	∆Non-paretic (mm)	∆SLR (ratio)	∆Paretic (mm)	∆Non-paretic (mm)
1	1.08	Np	0	↑ 23.09	↑ 22.52	0.01	↑ 33.12	↑ 38.92
2	**1.4**	**Np**	**-0.2**	**↑↑ 62.4**	**↑ 14.95**	**-0.09**	**↑↑ 89**	**↑ 67.02**
3	**1.12**	**Np**	**-0.04**	**↑↑ 34.31**	**↑ 26.18**	**0.03**	**↑ 78.41**	**↑↑ 92.19**
4	1.14	Np	0.06	↑ 15.97	↑↑ 41.57	0.07	↑ 23.11	↑↑ 47.83
5	1.02*	-	-	-	-	-	-	-
6	1.04*	-	-	-	-	-	-	-
7	**1.09**	**Np**	**-0.06**	**↑↑ 103.51**	**↑ 71.09**	**-0.07**	**↑↑ 80.5**	**↑ 45.69**
8	1.14	Np	0.01	↑ 23.87	↑ 30.36	0.03	↑15.23	↑↑ 29.98
9	1.24	Np	0	↓ -4.26	↓ -3.25	0.03	↓ -1.53	↑ 6.89
10	1.18	Np	0	↓ -36.5	↓ -41.93	0.16	↓ -16.61	↑ 11.41
11	1.36	P	0.14	↑ 8.15	↓ -1.61	0.19	↑ 26.12	↓ -3.14
12	1.49	P	0.29	↑ 33.21	↓ -32.02	0.03	↓ -15.16	↓↓ -19.59

Abbreviations: SLR: step length ratio; Np: non-paretic side being larger; P: paretic side being larger
*: participant is not considered to be asymmetric in SLR; ∆: change; paretic: paretic step length; non-paretic: non-paretic step length ↑: increase; ↑↑: larger increase (>10 mm) compared to the opposite side; ↓: decrease; ↓↓: larger decrease (>10 mm) compared to the opposite side; **Bold**: participants identified as responders (improvement in ∆SLR).

Table 6.4 Appendix 2. Individual data of SLR in the auditory modality condition

ID	Initial SLR (ratio)	Direction of SLR	Pre-Adaptation to Adaptation			Adaptation to Post-Adaptation		
			∆SLR (ratio)	∆Paretic (mm)	∆Non-paretic (mm)	∆SLR (ratio)	∆Paretic (mm)	∆Non-paretic (mm)
1	1.08	Np	0	↑ 15.84	↑ 20.86	0.01	↑ 57.23	↑ 64.43
2	**1.4**	**Np**	**-0.22**	**↑ 33.48**	**↓ -15.12**	**-0.11**	**↑ 19.56**	**↓ -16.9**
3	**1.12**	**Np**	**-0.05**	**↑↑ 66.63**	**↑ 31.89**	**-0.09**	**↑↑ 101.74**	**↑ 57.08**
4	1.14	Np	0.07	↓↓ -35.22	↓ -3	0.07	↓ -27.29	↑ 5.77
5	1.02*	-	-	-	-	-	-	-
6	1.04*	-	-	-	-	-	-	-
7	1.09	Np	0.03	↑ 6.63	↑↑ 26.68	0	↑ 21.36	↑ 22.43
8	1.14	Np	0.02	↓↓ -43	↓ -31.07	0.04	↓↓ -68.61	↓ -49.48
9	1.24	Np	0.19	↓ -11.17	↑ 34.48	0.19	↑ 13.85	↑↑ 63.39
10	1.18	Np	0.04	↓↓ -80.47	↓ -61.81	0.01	↓ -21.4	↓-10.6
11	**1.36**	**P**	**-0.29**	**↓ -21.02**	**↑ 55.63**	**-0.33**	**↓ -20.01**	**↑ 66.18**
12	1.49	P	0.13	↑ 44	↓ -23.25	0.09	↑ 43.68	↓ -18.79

Abbreviations: SLR: step length ratio; Np: non-paretic side being larger; P: paretic side being larger
*: participant is not considered to be asymmetric in SLR; ∆: change; paretic: paretic step length; non-paretic: non-paretic step length ↑: increase; ↑↑: larger increase (>10 mm) compared to the opposite side; ↓: decrease; ↓↓: larger decrease (>10 mm) compared to the opposite side; **Bold**: participants identified as responders (improvement in ∆SLR).

Table 6.5 Appendix 3. Individual data of SWR in the combined modality condition

ID	Initial SWR (ratio)	Direction of SWR	Pre-Adaptation to Adaptation			Pre-Adaptation to Post-Adaptation		
			ΔSWR (ratio)	ΔParetic (s)	ΔNon-paretic (s)	ΔSWR (ratio)	ΔParetic (s)	ΔNon-paretic (s)
1	**1.07**	**Np**	**-0.03**	**↓ -0.006**	**↓↓ -0.019**	**-0.02**	**↑ 0.001**	**↓ -0.005**
2	1.03*	-	-	-	-	-	-	-
3	1.07	P	0	↑ 0.005	↑ 0.009	0	↑ 0.003	↑ 0.019
4	1.08	P	0.04	↑ 0.014	↓ -0.002	0.04	↑ 0.013	↓ -0.001
5	1.14	P	0	↓ -0.003	↓ -0.006	0	↑ 0.003	-0.001
6	1.2	P	0	↑ 0.055	↑ 0.053	-0.14	↓ -0.022	↑ 0.038
7	1.07	P	0	↑ 0.001	↑ 0.003	-0.03	↓↓ -0.029	↓ -0.007
8	**1.1**	**P**	**-0.09**	**↓↓ -0.096**	**↓ -0.031**	**-0.05**	**↓↓ -0.077**	**↓ -0.043**
9	1.21	P	0	↓ -0.015	↓ -0.018	0	↑ 0.005	↑ 0.005
10	1.43	P	0.04	↑ 0.002	↓ -0.008	0	↓ -0.011	↓ -0.017
11	1.07	P	0.15	↑ 0.039	↓ -0.005	0.12	↑ 0.024	↓ -0.005
12	1.55	P	0.02	↑ 0.004	↓ -0.014	0.04	↑↑ 0.036	↑ 0.007

Abbreviations: SLR: step length ratio; Np: non-paretic side being larger; P: paretic side being larger
*: participant is not considered to be asymmetric in SLR; Δ: change; paretic: paretic step length; non-paretic: non-paretic step length ↑: increase; ↑↑: larger increase (>10 mm) compared to the opposite side; ↓: decrease; ↓↓: larger decrease (>10 mm) compared to the opposite side; **Bold**: participants identified as responders (improvement in ΔSLR).

Figure 6.1 Creation of visual and auditory feedback

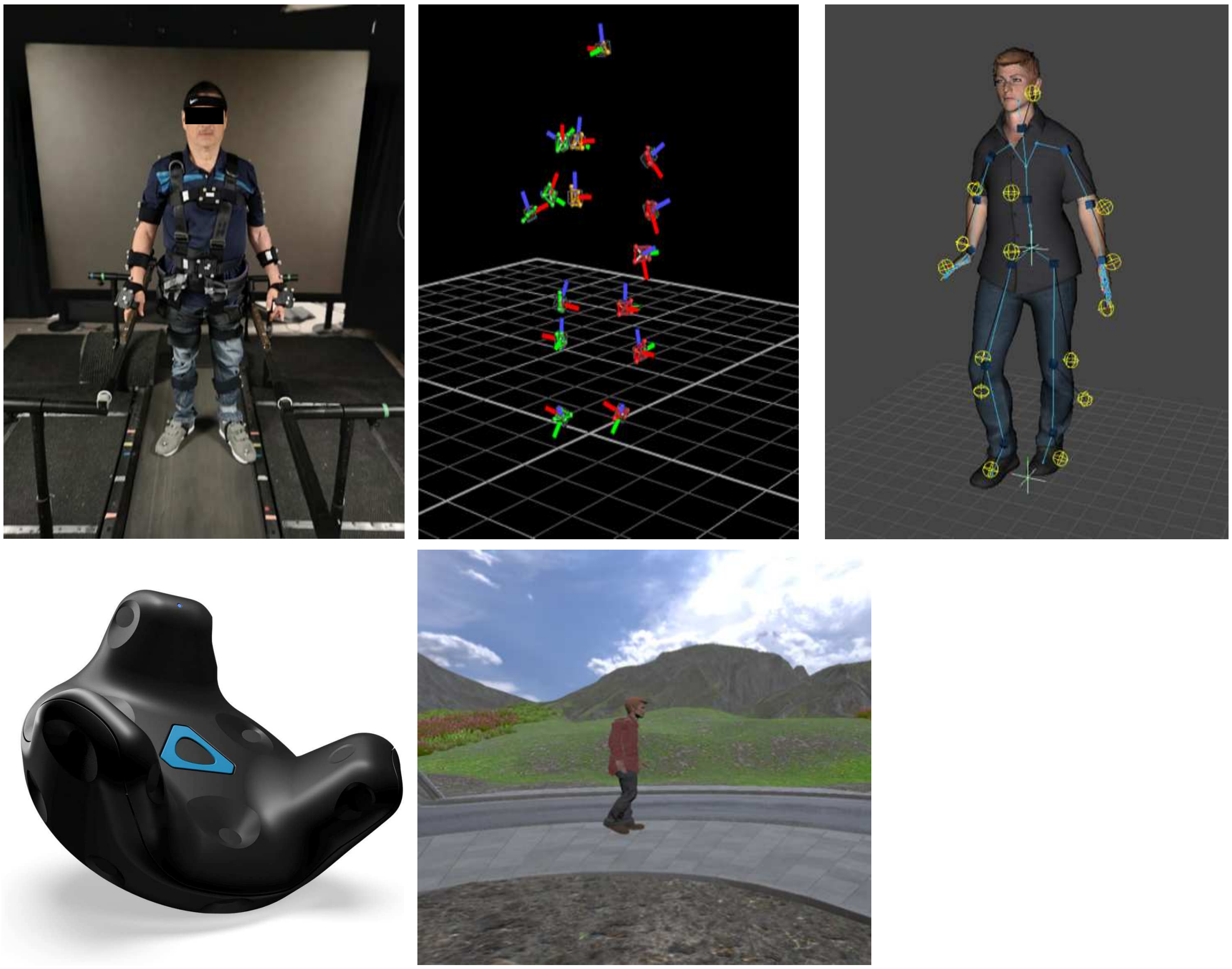


Figure 6.1 Top left: a participant with rigid body markers standing on the self-paced treadmill; Top middle: mapping of markers on Vicon Tracker; Top right: avatar created by Vicon Pegasus based on the mapping of Vicon Tracker. Bottom left: VIVE tracker which is wrapped around each of participants' ankles; Bottom right: the virtual scene with self-avatar in the paretic side view.

Figure 6.2 Step length ratio and swing time ratio of all participants

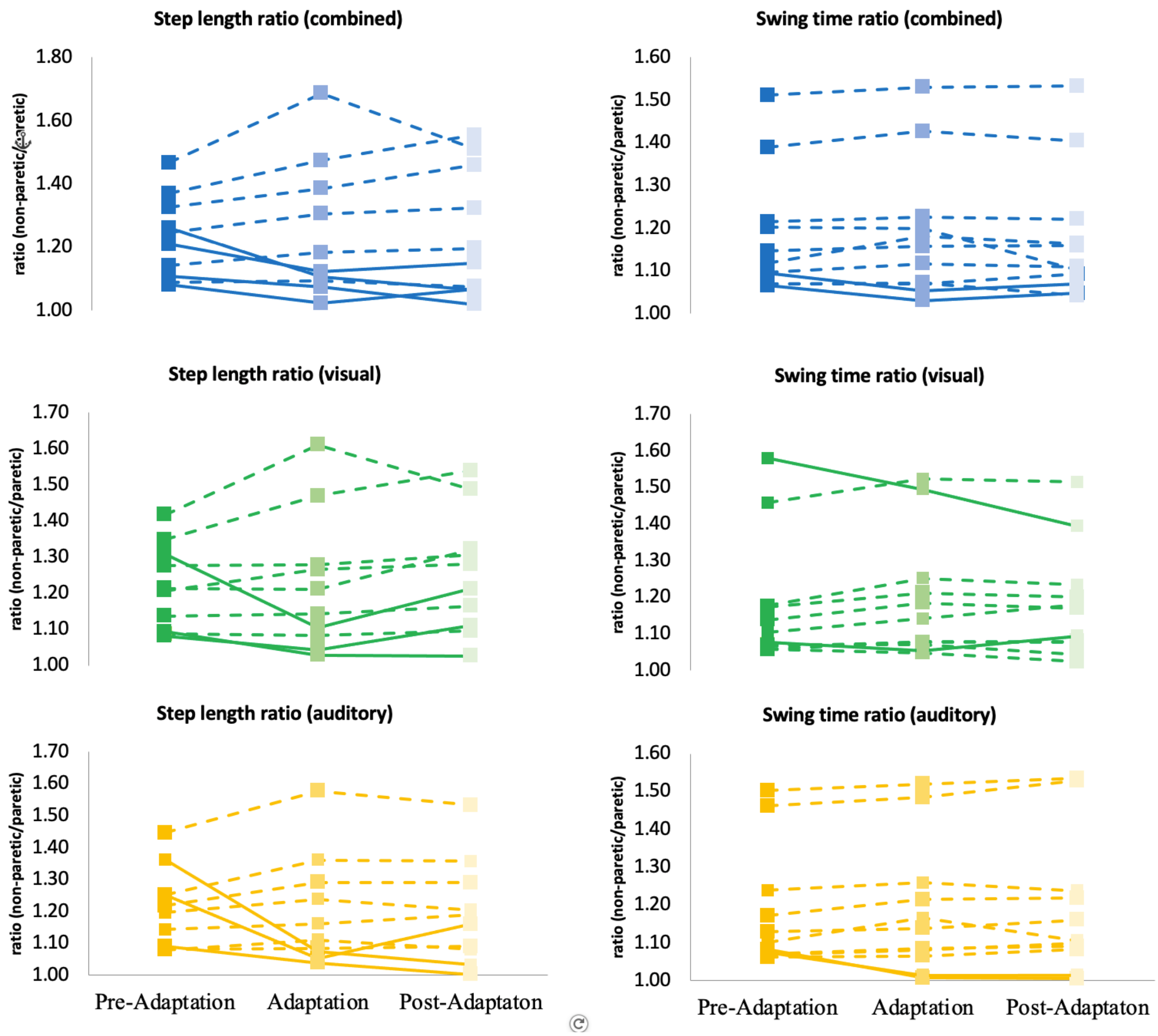
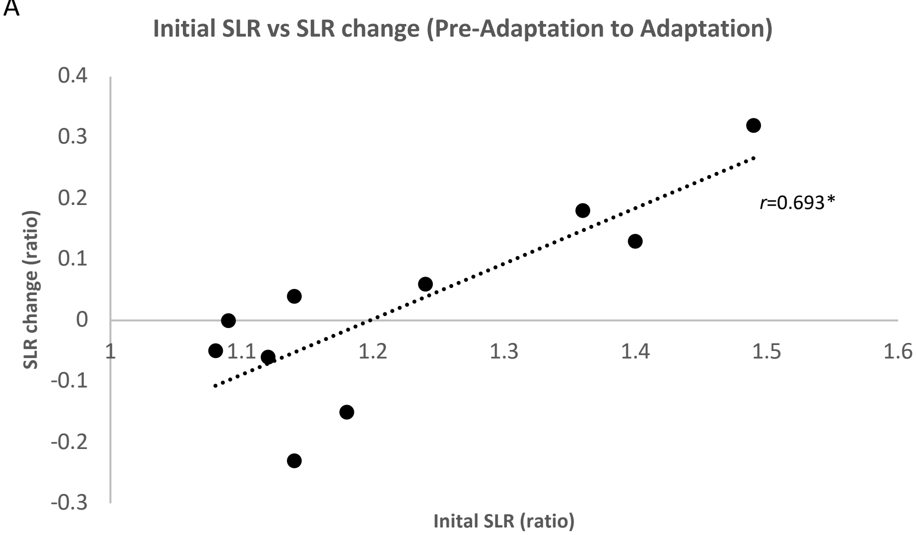


Figure 6.2 Step length ratios (left) and swing time ratio (right) of each participant across 3 phases (most opaque: pre-adaptation; medium opaque: adaptation; least opaque: post-adaptation) in the combined modality (top, blue), visual modality (middle, green) and auditory modality (bottom, orange) conditions. The solid lines indicate responders (improvement in adaptation) and the dash lines non-responders.

Figure 6.3 Scatterplot of correlations

A



B

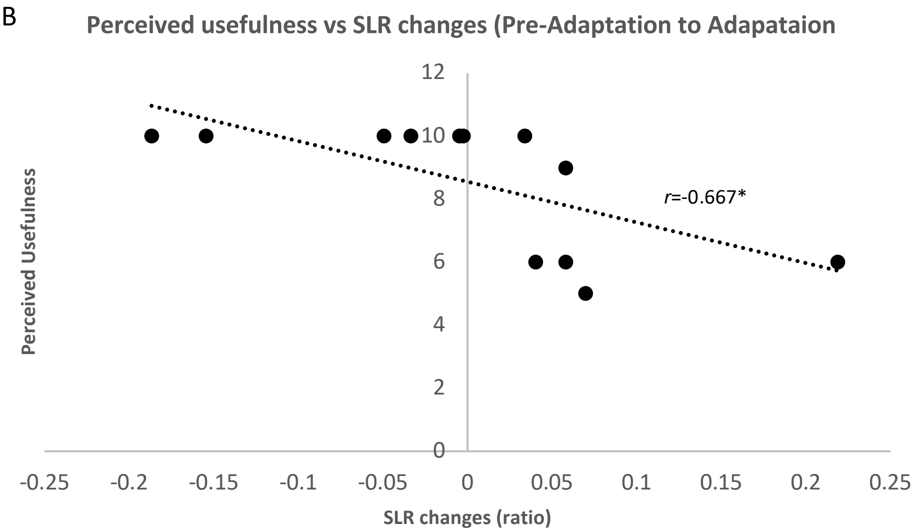


Figure 6.3 Scatter plot illustrating the relationship between initial SLR and the changes in SLR (top), and between perceived usefulness and the changes in SLR (bottom) between pre-adaptation and post-adaptation phases in the combined modality condition. *: p value <0.05

Figure 6.4 Walking speed

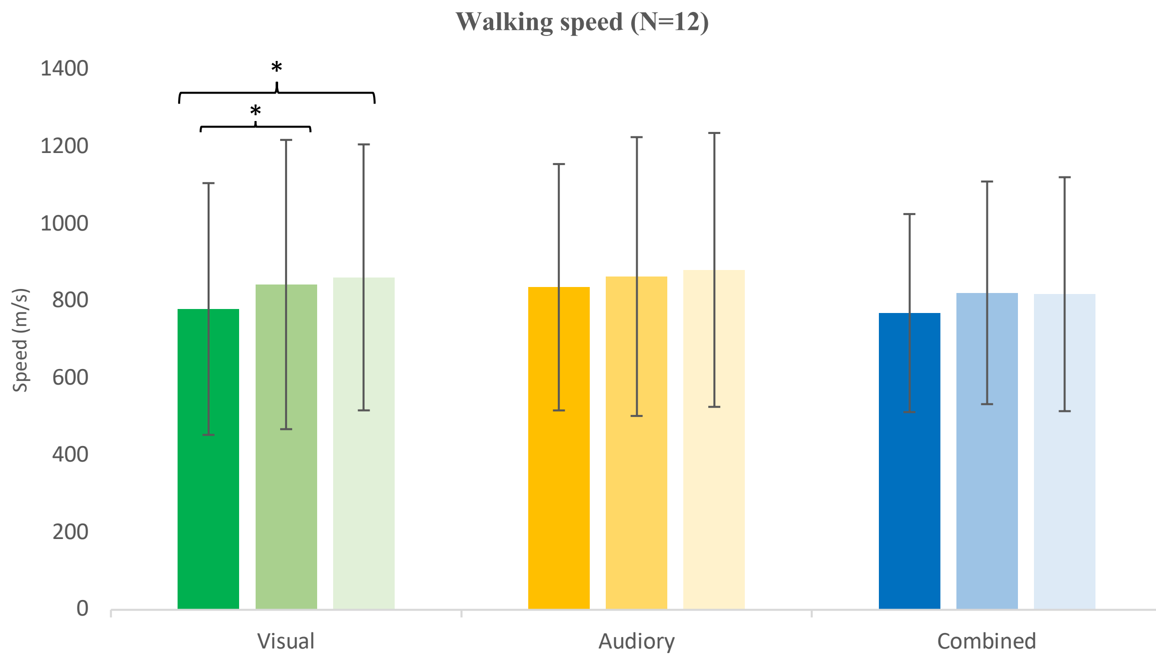


Figure 6.4 Walking speed across three phases of the three conditions. The color indicates three conditions (visual: green, auditory: orange, combined: blue). The first bar (most opaque) of each cluster represents pre-adaptation phase, the middle (medium opaque) represents adaptation, and the last (least opaque) post-adaptation *: *p* value <0.05. **: *p* value <0.01

Chapter 7

7.1 Preface

In Manuscript 3, we compared the effects of the visual feedback, auditory feedback and combined visual and auditory feedback on gait symmetry of participants with stroke. The results showed that the temporal aspect of gait symmetry remained unchanged, even in the auditory and combined visual auditory conditions. This lack of change in temporal gait symmetry among the stroke participants could be due to their altered perception of symmetry, as previous studies showed that perceiving gait asymmetry could be a challenging task [69] and that rhythm perception could be impaired by stroke [123].

Augmenting the extent of asymmetry (i.e., the ‘error’) via distorted feedback could improve the perception of gait asymmetry and the resulting correction in terms of gait temporal distance factors. In this last manuscript (Manuscript 4), we thus explored the impact of different types (delayed or advanced) and magnitudes (small or large) of distortion of auditory feedback provided in the form of footstep sounds on gait symmetry, as well as temporal-distance factors and kinematic adaptations. The study was carried out in healthy young adults, as a first step, in order to understand the bilateral adaptations in temporal distance factors caused by the distorted feedback, before it is applied to the stroke population.

In conclusion, all manuscripts (1-4) presented in this thesis contributed to the knowledge of application of feedback in the form biological cues in post-stroke gait asymmetry.

Manuscript 4: Application of an auditory-based error-augmentation paradigm to modify gait symmetry in healthy individuals

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Keywords: gait asymmetry, auditory feedback, footstep sound, error-augmentation, augmented feedback

7.2 Abstract

Background: Auditory feedback has shown promising effects on post-stroke gait asymmetry but applying auditory feedback with error-augmentation paradigm among people with stroke has not been examined yet. As people with stroke have an impaired perception of their gait asymmetry, augmented feedback like error-augmentation paradigm could facilitate the detection of asymmetry. Thus, in this study we are proposing the use of distorted auditory feedback on footstep sounds in healthy young participants and examine the effects of the feedback on alterations of gait symmetry.

Methods: Twelve healthy participants walked on a self-paced treadmill while listening to short bouts (75 sec in the adaptation period) of their footstep sound, and the footstep sound were modified differently in five conditions as follows: (1) small delay; (2) small advance; (3) large delay; (4) large advance; (5) unmodified (control condition). The distortion was only applied on one side. Gait symmetry was measured as ratios of left-right step length (SLR) and left-right swing time (SWR). Bilateral step length and swing time, as well as kinematic outcomes such as walking speed, maximum toe height, hip/knee/ankle joint excursions were also analyzed.

Results: During the adaptation period, SWR ($p<0.001$) were increased in all four distortion conditions while SLR were unchanged. Increased swing times on the perturbed side ($p<0.001$) were observed in the advanced conditions, while swing time increased bilaterally ($p<0.001$) in the delayed conditions but to a larger extent on the unperturbed vs. perturbed side. In addition, similar increase was also observed in the maximum toe height, hip, and knee joint excursions (between $p<0.05$ to $p<0.001$). Bilateral step length, ankle excursions, and walking speed were not changed significantly.

Discussion: Participant used the same strategies as expected in the delayed (adaptation on the unperturbed side) and advanced (adaptation on the perturbed side) conditions, although a small increase also occurred on the perturbed side in the delayed conditions was possibly due to their intuitive strategy to adapt on the perturbed side. The lack of change in the spatial aspect of gait symmetry could be explained by the fact that audition primarily conveys temporal information where vision conveys spatial information. The magnitude difference between the small and large distortion was not easily detected by the participants, therefore there was a lack of difference between small and large magnitude of distortion on changes in gait symmetry. For future application of the auditory feedback with error-augmentation paradigm in people with stroke, it would be necessary to tailor the magnitude of distortion according to the perception impairment of participants.

7.3 Introduction

Motor learning is an important component of motor recovery following stroke [1] and it is believed that both learning and recovery processes lead to brain reorganization and cortical changes [2]. Amongst various factors that modulate motor learning, feedback is considered to be paramount [3]. Feedback can be classified as intrinsic provided by the internal sensory information that a person feels about his/her own movement; or extrinsic provided by an external source, via a therapist or a device [4]. Extrinsic feedback would be crucial in stroke rehabilitation when the intrinsic feedback system which can be impaired due to the brain lesion [5]. Conventional means to provide extrinsic feedback in the clinical setting, such as verbal guidance during movement, can be effective in improving performance on simple motor tasks. However, gait symmetry, achieved through coordinated movements between limbs and across multiple joints [6, 7], cannot be simply accomplished with conventional rehabilitation. A longitudinal study on changes in gait from pre- to post- conventional inpatient rehabilitation did not find changes in gait symmetry [8].

Rhythmic auditory cueing is an intervention that has been studied extensively in gait training in people with neurological impairments [9, 10]. Unlike feedback that provides information on a person's gait performance, the rhythmic auditory cueing uses an external auditory cue to align the footstrike of participants to the auditory stimuli, and the phenomenon of synchronization between footstrike and external cueing is referred as 'entrainment.' [11] Compared to the visual and tactile modalities, auditory cueing has the largest influence on gait parameters such as gait speed, stride time, stride time variability, etc. [12]. Auditory cueing can also be used to attenuate post-stroke asymmetry for short-term effects [13-15], but its application in the motor learning which would require longer period of training is still unknown. Besides auditory rhythmic cueing, another way to apply the auditory modality to improve spatiotemporal gait parameters is via the use of auditory feedback as a source of real-time extrinsic feedback. Gait training incorporating auditory feedback on foot strike gait events in different patient populations such cerebral palsy, Parkinson's disease, and stroke, was shown to not significant alter stride length [16-18]. However, swing time and other temporal measures of gait symmetry were not examined in those studies. For people with stroke, Kim and colleagues (2021) used auditory feedback on weight bearing during walking and showed that the intervention, compared to conventional gait training, led to larger improvements in various spatiotemporal parameters such as paretic step time and non-paretic step length, as well as gait symmetry outcomes such as step length ratio, step time ratio and single stance time ratio [19]. Auditory feedback thus shows a potential to improve gait symmetry in neurological populations, but direct feedback on spatiotemporal aspects of gait has not been utilized and examined.

Feedback can be modified and distorted to enhance its effectiveness. The error-augmentation (EA) paradigm, which has mainly been studied in robotics, can be used to facilitate sensory-motor learning. Feedback is an essential basis for motor learning, and it is believed that artificially increasing the movement error would lead to faster learning [20]. A systematic review on the use of distorted haptic feedback to improve reaching function after stroke revealed that the EA paradigm was more effective than conventional feedback at improving the upper extremity motor recovery and performance, and more effective than the error-reduction (ER) paradigm at improving movement trajectory [21]. Studies comparing an EA paradigm vs. ER paradigm applied via a robotic device while walking in healthy individuals [22] and individuals with stroke [23] concluded that the EA was more effective to modify gait parameters such as step height, joints kinematics and ankle trajectories [22, 23], making such paradigm an interesting avenue to explore to alleviate gait asymmetry.

To our knowledge, the application of EA paradigm with auditory feedback on gait symmetry is yet to be explored. A possible explanation of the mixed results observed regarding the effectiveness of auditory feedback on post-stroke gait symmetry is that people with stroke often have difficulty perceiving the presence and direction of their gait asymmetry [24]. The EA paradigm could potentially make the asymmetry more apparent and decipherable to the participants by increasing the extent of their asymmetry conveyed by the auditory feedback. It is important to recognize that post-stroke gait asymmetry varies in type (spatial, temporal or both), direction (larger swing time on paretic side vs. non-paretic side) and magnitude [25, 26]. Any application of an EA paradigm in this population would thus need to be personalized.

As a first step, we explored in the present study the use of distorted auditory feedback on footstep sounds in healthy young participants and examined the impact of such feedback on alterations of gait symmetry. To do so, we delayed or advanced the footstep sounds on either the left or right lower limb while walking and varied the magnitude of these temporal perturbations. More specifically, the primary objective of this study was to determine changes in step length and swing time ratios in response to distorted footstep sound feedback of different directions (delay vs. advance) and magnitudes (small vs. large) applied to either the right or left lower limb. The secondary objective was to examine changes in sagittal plane joint kinematics of the lower limbs associated with the different variations in auditory feedback. We hypothesized that (1) participants would modify their gait pattern by increasing their *swing time and step length* on the *perturbed side in the advanced feedback conditions*, and on the *unperturbed side in the delayed feedback conditions*, leading in both instances to altered swing time and step length symmetry;

(2) a large feedback distortion would lead to larger alterations in temporal-distances factors and gait symmetry in comparison to a small distortion and; (3) changes in swing time and step length symmetry would be accompanied by changes in sagittal joint excursion at multiple joints (hip, knee and ankle), and possibly changes in maximum toe height during swing.

7.4 Methods

7.4.1 Participants

Twelve (n=12) healthy young adults (5 males; 7 females) aged 26.4 ± 4.7 years (mean ± SD) participated in this study. Based on the assessment of Edinburgh Handedness Inventory (EHI), 11 participants were right-handed and only 1 was considered left-handed. The mean height, weight and overground comfortable walking speed were 171.1 ± 10.3 cm, 66.8 ± 18.4 kg, and 1.52 ± 0.20 m/s respectively. Participants were recruited based on the following criteria: (1) age between 18 to 35 years old, which corresponds to the young adulthood [27]; (2) having no self-reported auditory deficits; (3) having no conditions such as cardiovascular, respiratory, musculoskeletal or other neurological conditions that could affect locomotion; (4) having no cognitive deficits indicated by a score < 25 on the Montreal Cognitive Assessment (MoCA). This study received ethics approval from the Research Ethics board of the Montreal Centre for Interdisciplinary Research in Rehabilitation (CRIR). All participants understood and signed the consent form before entering the study.

7.4.2 Experimental setup

The walking task was performed on a custom-built self-paced treadmill (dimensions: 0.6 m x 1.5 m). The motor of the treadmill is driven by PID servo-control based on the real-time distance and velocity feedback obtained with a potentiometer tethered to the participant [28], thus the speed of the treadmill was constantly adjusted by the participant's acceleration and deceleration.

The footstep sound file used for the auditory feedback was created from a sound effect library (www.fesliyanstudios.com), and the same sound file was used for the footsteps on both sides. A pair of VIVE tracker™ devices (HTC corporation, Taiwan) (Figure 7.1 top left) were strapped around each of the participants' ankle as the sensors (Figure 7.1 top right), and a 2-camera VIVE motion capture system (HTC corporation, Taiwan) was used to capture the position of the sensors in real time in the Unity Engine (Unity Technologies, USA). First, a baseline position of the sensors was established in a static pose. The footstep sounds would be later played based on vertical threshold detection, i.e., when a foot would descend and the tracker would reach the pre-established threshold value, a trigger would be activated to play the footstep sound. The threshold value was determined for each participant prior to conducting this experiment.

During the experiment, full body movements were recorded at 120Hz in Vicon Tracker™ (Vicon, UK) using a 6-camera system and 36 reflective markers (14 mm) placed on the participant's specific body landmarks according to the Plug-in Gait model (Figure 7.1 bottom left and right).

7.4.3 Experimental procedure

Prior to the start of the walking trials, the participants were habituated to the self-paced treadmill. The habituation lasted about 5 minutes or until the participants felt comfortable walking on the treadmill. The undistorted auditory feedback was also played during the habituation to provide the participants a sense of their symmetrical footstep sound. This symmetrical sound would serve as a reference for the participants when they were later exposed to distorted feedback.

There were five conditions of feedback which the participants were exposed to, including 4 distorted feedback conditions and one control condition. The distorted feedback conditions were as follows: (1) a small magnitude of delay (sDelay) where a delay of 15% of the normal stride time was added to the footstep sound; (2) a large magnitude of delay (lDelay) where the delay was 30% of the stride time; (3) a small magnitude of advance (sAdvance) where the threshold value of sound detection was raised to a higher value (further from the floor) simulate an advance of footstep sound by 15% of stride time; (4) a large magnitude of advance (lAdvance) where the threshold was raised further to simulate an advance of 30% of stride time. The control condition consisted of walking with undistorted sound feedback. The participants performed, in a random order, four walking trials for each condition, with two trials for the distorted feedback applied on the left side and two trials on the right side, as well as two trials of the control condition, for a total of 18 walking trials.

Each walking trial consisted of three phases, which included 30 s of comfortable walking without the footstep sound presented (pre-adaptation phase), followed by 75 s of walking while listening to the distorted footstep sound (adaptation phase), and finally 45 s of walking without the sound (post-adaptation phase). Before starting the trials, the participants were instructed to listen to the rhythm of bilateral footstep sound and, if made asymmetrical by the distortion, to modify their gait pattern to make it sound symmetrical. However, if they perceived the sound to be symmetrical as in the control condition, then they were not to make any gait change. Sitting and resting for 5 minutes or more was allowed between the walking trials, although none of the participants needed resting. The diagram illustrating the experiment procedure along with the expected gait pattern change according to the type of feedback distortion can be found in Figure 7.2

7.4.4 Data analysis

The kinematic data were processed and exported from Vicon Nexus™ 1.8.5, before being analyzed in Matlab™ R2020b. To avoid the effects of acceleration of speed, data in the first 10 seconds of each trial were excluded. The data were dual-pass filtered with a 2nd order Butterworth filter at a cut-off frequency of 8 Hz, then normalized to 100% of the gait cycle.

The primary outcomes were swing time ratio (SWR) and step length ratio (SLR), which were used to measure the temporal and spatial aspects of gait symmetry, respectively [29]. The swing time was calculated as the time between the foot-off and foot-strike events of the same foot for each gait cycle, while step length was calculated by measuring the anteroposterior distance between toes at the foot strike of the same leg. Ratios were calculated using the values of left and right leg with the larger value as the numerator [29]. A resulting value of '1.0' indicated perfect symmetry. The secondary outcomes included walking speed on the treadmill, bilateral swing time, step length, maximum toe height, as well as sagittal hip, knee, and ankle angle excursions. For the purpose of analysis, the 'left' and 'right' sides were referred to as the 'perturbed' and 'unperturbed' sides based on the side the distortion was applied to. The means of all the outcome measures were obtained by averaging the values across gait cycles in each of the three phases.

7.4.5 Statistical analysis

The data were found to deviate from a normal distribution, as revealed by the Shapiro-Wilk normality test; therefore, non-parametric tests were used to carry out the analysis. Generalized estimating equations (GEE) were used to compare SWR and SWR between the conditions (sDelay, lDelay, sAdvance, lAdvance) and across walking phases (pre-adaptation, adaptation, and post-adaptation). Outcomes of swing time, step length, maximum toe height, as well as hip, knee and ankle angle excursion were also analyzed using a GEE model separately for the perturbed and the unperturbed side. When the GEE model revealed a significant effect, pairwise post-hoc comparisons were conducted with Bonferroni-Holm correction adjustments. The statistical analyses were performed in SPSS v.24 (IBM Inc, USA), and the p-level was set at <0.05 as significant.

7.5 Results

Figure 7.3 illustrates traces of bilateral swing time and step length of a representative participant. In both the sDelay (Figure 7.3A, left) and lDelay (Figure 7.3B, left) conditions, the participant showed a bilateral increase in swing time but to a greater extent on the unperturbed vs. perturbed side during the adaptation phase. In the sAdvance (Figure 7.3C, left) and lAdvance (Figure 7.3D, left) conditions, only the swing time on the perturbed side showed an observable increase during the adaptation phase. As for the step length (Figure 7.3A-D, right), neither of the four distorted feedback conditions showed a noticeable increase or decrease on either side. In the control condition (Figure 7.3E), the participant maintained the same swing time and step length on both sides throughout the entire trial.

7.5.1 Changes in spatiotemporal parameters

When examining the group results (Figure 7.4, left), the SWR showed significant differences between the phases (χ^2=63.56, df=2, p<0.001) but not between the conditions (χ^2=1.26, df=3, p=0.738). The interaction between the conditions and phases was not found to be significant (χ^2=2.82, df=6, p=0.830). In the post-hoc pairwise analysis, the SWR in the adaptation phases of all four conditions involving distorted feedback was significantly increased compared to the pre-adaptation (mean of difference: 0.08±0.01, p<0.001) and post-adaptation phases (mean of difference: 0.07±0.01, p<0.001), while there were no significant differences between the pre- and post-adaptation phases (0.00±0.01 p=0.195). The SLR, however, (Figure 7.4, right) was not found to be significantly modified by the feedback perturbation conditions (χ^2=0.62, df=3, p=0.891) and the phases (χ^2=5.16, df=2, p=0.081), and no significant interaction between conditions and phases was observed (χ^2=5.09, df=6, p=0.532). Of note, this lack of significant effects subsisted despite one participant (shown as a single dot in Figure 7.4, right) showing high values of SLR compared to the rest of the group during the adaptation phase for the sDelay, sAdvance and lAdvance conditions.

Similar to the SWR, the swing time of the perturbed side (Figure 7.5A left) was also modulated across phases (χ^2=50.20, df=2, p<0.001), but it did not differ between perturbed feedback conditions (χ^2=1.18, df=3, p=0.758) and showed no condition X phase interaction (χ^2=1.28, df=6, p=0.973). Furthermore, the post-hoc analysis showed that the swing time of the perturbed side was significantly increased in the adaptation phases of all perturbed feedback conditions compared to the pre-adaptation and post-adaptation phases (p<0.001), but no difference was found between the pre-adaptation and post-adaptation phases (p=0.263). The swing time of the unperturbed side (Figure 7.5A right), contrary to the perturbed side, was significantly altered by the conditions (χ^2=29.48, df=3, p<0.001) and phases (χ^2=61.27, df=2, p<0.001), with also a significant condition X phase interaction (χ^2=34.28, df=6, p<0.001). In the post-hoc analysis, only the delay conditions (sDelay and lDelay) induced larger swing time on the unperturbed side in the adaptation vs. the pre-adaptation and post-adaptation phases (p <0.001). Moreover, in the adaptation phase, the swing time of the unperturbed side for the delayed feedback conditions (sDelay and lDelay) were significantly larger (p<0.001) than that of the advanced feedback conditions (sAdvance and lAdvance), and swing time was similar between the sDelay and lDelay conditions (p=0.523).

The step length on both the perturbed side and unperturbed side remained unaffected by the feedback perturbation conditions (perturbed: χ^2=4.34, df=3, *p*=0.227; unperturbed: χ^2=5.81, df=3, *p*=0.121) and the phases (perturbed: χ^2=3.88, df=2, *p*=0.144; unperturbed: χ^2=4.41, df=2, *p*=0.110), with no significant condition X phase interactions (perturbed: χ^2=0.48, df=6, *p*=0.998; unperturbed: χ^2=3.31, df=6, *p*=0.769). Similarly, the walking speed (not shown on the graphs) was also not changed significantly by the conditions (χ^2=3.35, df=3, *p*=0.340), the phases (χ^2=5.83, df=2, *p*=0.054), and showed no significant condition X phase interaction (χ^2=0.28, df=6, *p*=0.999).

7.5.2 Changes in kinematic outcomes

7.5.2.1 Maximum toe height

The maximum toe height on the perturbed side (Figure 7.6A, left) was significantly altered by the feedback perturbation conditions (χ^2=10.16, df=3, *p*=0.017) and the phases (χ^2=27.71, df=2, *p*<0.001), with no significant condition X phase interactions (χ^2=4.34, df=3, *p*=0.227). Specifically, an increase in toe height from pre-adaptation to adaptation was observed for all distorted feedback conditions except sDelay (lDelay (*p*=0.014); sAdvance (*p*=0.018); lAdvance (*p*<0.001), with lAdvance further showing larger toe height during the adaptation vs. post-adaptation phase (*p*<0.01). In addition, maximum toe height in the adaptation phase for lAdvance was not significantly different from sAdvance (*p*=0.059), but larger than sDelay (*p*<0.01) and lDelay (*p*<0.01).

The maximum toe height on the unperturbed side (Figure 7.6A, right) followed a similar pattern as the swing time. i.e., it was influenced by the conditions (χ^2=36.58, df=3, *p*<0.001), phases (χ^2=33.22, df=2, *p*<0.001) with a significant interaction effect of condition X phase (χ^2=36.99, df=6, *p*<0.001). Like the swing time on the unperturbed side, only the delayed feedback conditions (sDelay and lDelay) showed a significant increase of maximum toe height in the adaptation compared to the pre-adaption and post-adaptation ($p<0.001$). Furthermore, toe height in the adaptation phase for the delayed conditions (sDelay and lDelay) were significantly larger than for advanced conditions (sAdvance and lAdvance) ($p<0.001$). Toe height did not differ between sDelay and lDelay ($p=0.226$).

7.5.2.2 Hip, knee, and ankle joint excursion

Overall, the changes in sagittal joint excursion on both the perturbed and unperturbed sides were only present at the hip and knee joints, while ankle joint excursion remained mostly unchanged. Changes in hip and knee joint excursions also followed a similar pattern in that they both increased on the perturbed side in the advanced feedback conditions, and on the unperturbed side in the delayed feedback conditions. More specifically, the hip joint excursion on the perturbed side (Figure 7.6B, left) differed across phases ($\chi^2=42.70$, df=2, $p<0.001$) in a similar way across feedback conditions ($\chi^2=3.87$, df=3, $p=0.275$) and showed no condition X phase interaction ($\chi^2=9.36$, df=6, $p=0.16$). The post-hoc analysis indicated that only the sAdvance and lAdvance conditions induced increase in hip excursion in the adaptation vs. pre-adaption and post adaptation phases ($p<0.001$), while the sDelay ($p=0.052$) and lDelay ($p=0.065$) showed a similar trend, although it did not reach statistical significance.

As for the hip angle excursion on the unperturbed side (Figure 7.6B, right), it followed a similar pattern as for the perturbed side, showing a main effect of phase ($\chi^2=52.20$, df=2, $p<0.001$) and no effect of condition ($\chi^2=7.22$, df=3, $p=0.065$), but it also showed a significant interaction of phase and condition ($\chi^2=24.09$, df=6, $p<0.01$). Post-hoc analyses revealed that contrary to findings for the perturbed side, however, it was the sDelay and lDelay conditions that induced a significant increase in hip excursion angle during the adaptation vs. pre-adaption and post adaptation phases (p<0.001).

The knee angle excursion on the perturbed side (Figure 7.6C left) was modulated by the conditions (χ^2=62.47, df=3, p<0.001), phases (χ^2=76.16, df=2, p<0.001) and showed an interaction effect of condition X phase (χ^2=47.47, df=6, p<0.001). The post-hoc analysis revealed that only sAdvance and lAdvance induced an increase in the adaptation compared to the pre-adaptation and post-adaptation (p<0.001). In addition, both sAdvance and lAdvance were larger than sDelay and lDelay in the adaptation (p<0.001), but no significant difference was found between sAdvance and lAdvance (p=0.082). The knee angle excursion on the unperturbed side (Figure 7.6C right) was also influenced by the conditions (χ^2=68.22, df=3, p<0.001), phases (χ^2=75.24, df=2, p<0.001) with a significant phase X condition interaction (χ^2=56.49, df=6, p<0.001). It followed a similar pattern with the swing time and maximum toe height on the unperturbed side as only sDelay and lDelay induced a significant increase in knee angle excursion in the adaptation compared to the pre-adaption and post adaptation (p<0.001). Moreover, sDelay and lDelay induced significantly larger knee angle excursion than sAdvance and lAdvance (p<0.001) conditions in the adaptation phase. The difference between sDelay and lDelay was not significant (p=0.301).

The ankle angle excursion on both the perturbed side (Figure 7.6D left) and unperturbed side (Figure 7.6D right) was not found to be affected by the conditions (perturbed: χ^2=4.78, df=3, p=0.189; unperturbed: χ^2=3.46, df=3, p=0.326) or the phases (perturbed: χ^2=4.44, df=2, p=0.109; unperturbed: χ^2=2.62, df=2, p=0.270), and did not show significant interaction (perturbed: χ^2=0.72, df=6, p=0.994; unperturbed: χ^2=0.34, df=6, p=0.999).

7.6 Discussion

This study examined, for the first time, the effects of distorted auditory feedback in the form of delayed and advanced footstep sounds on the gait symmetry of healthy young participants. Overall, all distorted auditory feedback conditions successfully elicited changes in temporal gait symmetry, as reflected by changes in SWR. Changes in kinematic outcomes such as maximum toe height, as well as sagittal hip and knee joint angle excursion, were also observed. Once the distorted feedback was removed, the spatiotemporal and kinematic parameters of gait returned to the baseline values. Different magnitudes of distorted feedback were also tested and, in contrast to our hypothesis (2), no significant differences were observed between the small and large magnitudes of distortion.

7.6.1 Changes in spatiotemporal parameters

As hypothesized, in the advanced feedback conditions, participants modified their swing time ratio by increasing the swing time on the perturbed side. This strategy of prolonging the swing time on the perturbed side allowed participants to delay the foot strike on that side for the bilateral footstep sound rhythm to become symmetrical. For the delayed feedback conditions, we hypothesized that participants would increase the swing time on the unperturbed side for the footsteps to sound symmetrical, as opposed to decreasing the swing time on the perturbed side given that the latter always remained subjected to a perturbation (i.e., always delayed). However, results show that although participants indeed increased SWR primarily via an increase in the swing time of the unperturbed side, the swing time on the perturbed side also increased but to a lesser extent. A potential explanation for this bilateral increase in swing time could be that while increasing the swing time on the unperturbed side is an appropriate strategy, the intuitive strategy for the participants was to perform some degree of adaptation on the perturbed side, as done for the advanced feedback conditions.

We also found that the step length ratio and the bilateral step length remained unaffected by all feedback conditions, which did not correspond to our hypothesis (1). Studies that examined the use auditory feedback on footstrike have also shown a lack of effect on stride length which is another measure of the spatial aspect of gait, although they did not examine the temporal parameters of gait[16-18]. In fact, it has been suggested that visual feedback facilitates learning of spatial aspects of movement whereas auditory feedback facilitates learning of temporal aspects [30], because vision is precise in the perception of spatial information whereas hearing is precise in the perception of temporal information [31, 32]. Sejdic and colleagues (2012) showed that auditory rhythmic cues had the most effects on temporal dynamics of gait of healthy participants compared to visual and tactile cues, but spatial parameters of gait were not examined [12]. Therefore, providing exclusively auditory extrinsic feedback, as in this study, would lead to changes in the temporal domain while leaving the spatial aspect of gait unaltered.

Most of the kinematic outcomes (the maximum toe height, hip and knee joint angle excursions) in this study followed a roughly similar pattern as the swing time, which was an increase on the perturbed side in the advanced feedback conditions and an increase on the unperturbed side in the delayed conditions, which agrees with our hypothesis (3). In fact, an increased swing time is normally associated with an increased hip and knee flexion which would also contribute to elevating swing phase toe position. However, the ankle joint excursion remained unaltered by the provision of feedback. We believe that in the present case, changing ankle range of motion would not assist in prolonging swing time. Larger ankle plantarflexion, for instance, is associated with a greater push-off force in late stance, resulting in shorter swing time/increased cadence, longer step length, and faster walking speed [33]. The fact that ankle angle excursion remained unchanged in the present study is consistent with the lack of adaptation in walking speed or step length observed. Therefore, the observed kinematic changes were aimed at modifying the temporal aspect of gait and not the spatial aspect.

7.6.2 Magnitude of distortion does not matter

In contrast to our initial hypothesis, the spatiotemporal changes observed in the small and large magnitudes of feedback distortion were similar. A tentative explanation for this finding is that the magnitude difference between small and large perturbations might not have been large enough to be perceived by the participants and thus did not induce a significant disparity in the magnitude of the swing phase, which was the gait parameter that was found to be modified by the different feedback conditions. Crosby and colleagues (2021) conducted a study on creating a temporal gait asymmetry on healthy participants by putting a cuff weight on their non-dominant leg. Their results suggested that detecting the extent of asymmetry in gait was not an easy task as most participants incorrectly estimated the magnitude of temporal asymmetry [34]. Thus, perceiving changes in the extent of asymmetry, as in the present study, may have proved to be challenging for the participants. Our results, however, also show that kinematic outcomes such as maximum toe height, hip and knee angle excursions tended to be larger for the large vs. small magnitude perturbations (advanced condition on perturbed side and delayed condition on unperturbed side), although not significantly different and not to an extent that led to changes in swing time. Thus, it cannot be ruled out that participants did implicitly perceive, at least to a limited extent, the perturbation magnitude. It is possible that a larger difference between the small and large distortion conditions would have been easier for the participants to detect, thus would have led to more significant differences in lower limb kinematics and swing time adaptation, as well as resulting SWR.

7.6.3 Significance for future studies

This study has implications for the use of auditory feedback as part of an EA paradigm to improve gait symmetry among patient populations such as stroke. First, the distorted auditory feedback as applied in this study only had effect on the temporal aspect of gait (i.e., swing time and resulting SWR). Since individuals with stroke present with either or both swing time and step length asymmetry [8], the EA paradigm used in this study may only be applicable to improving swing time symmetry. Second, since people with stroke may have more difficulty perceiving the presence of asymmetry than neurotypical individuals [24], and their capacity to respond to distortion may be limited due to the sensorimotor impairment, their response to distorted feedback should also be investigated. It is possible that a larger magnitude of distortion of auditory feedback may be needed to induce swing time adaptations in people with stroke. Finally, as people with stroke generally present a larger swing time on the paretic side [35], we suggest applying the advanced feedback on the non-paretic side, and/or applying the delayed feedback on the paretic side, in order to enhance the perception of swing time asymmetry to induce the desired swing time adaptation. In both scenarios, potential gait adaptations in people with stroke would occur on the non-paretic side as it would be the unperturbed side in the delayed feedback condition and perturbed side in the advanced condition. While it is more desirable for changes to take place on the paretic side instead, a past study of our research group that examined different views of avatar feedback on post-stroke gait symmetry also showed that adaptation in step length, when present, took place on the non-paretic side [36].

7.6.4 Limitations

This study focussed on instantaneous adaptations to distorted auditory feedback in healthy young adults, as a first step towards understanding potential applications in gait rehabilitation in patient populations with gait asymmetry. Such duration of exposure was sufficient to elicit changes in swing time symmetry and to identify the nature of the adaptations taking place cross the different conditions, but it may also explain the lack of after-effect observed in the post-adaptation period once the feedback was removed. The impact of longer and repeated exposure of distorted auditory feedback on the extent of SWR changes should be explored in future studies. This study was also limited to a homogenous sample of healthy young adults, which limits the generalization of findings to other age groups and patient populations. Further research is thus needed before such paradigm can be applied to population such as stroke, who presents different patterns and extents of asymmetry as well as variable capabilities in terms of sensorimotor function and rhythm perception.

7.7 Conclusion

In conclusion, distorted auditory feedback in the form of footstep sounds modifies swing time symmetry in healthy young adults, leading to different patterns of gait adaptation, depending on whether the auditory feedback is delayed or advanced. Results also revealed similar extents of gait adaptation between small and larger magnitudes of distortion. Larger differences in perturbation magnitude may be needed to induce a scaling effect in gait adaptations. Overall, the distorted auditory feedback examined in this study shows potential to improve gait symmetry in patient populations, although further work would be needed to determine how to tailor the perturbations according to the asymmetry profile of the individual.

7.8 References

1. Krakauer JW: **Motor learning: its relevance to stroke recovery and neurorehabilitation**. *Curr Opin Neurol* 2006, **19**(1):84-90.
2. Kleim JA, Hogg TM, VandenBerg PM, Cooper NR, Bruneau R, Remple M: **Cortical synaptogenesis and motor map reorganization occur during late, but not early, phase of motor skill learning**. *J Neurosci* 2004, **24**(3):628-633.
3. Schmidt R: **Motor Control and Learning: A Behavioral Emphasis**, 2nd edn: Champaign, Ill: Human Kinetics Publishers; 1988.
4. Schmidt RA: **Motor learning & performance: From principles to practice**. Champaign, IL, US: Human Kinetics Books; 1991.
5. Gilmore PE, Spaulding SJ: **Motor control and motor learning: implications for treatment of individuals post stroke**. *Phys Occup Ther Geriatr* 2001, **20**(1):1-15.
6. Krasovsky T, Levin MF: **Review: toward a better understanding of coordination in healthy and poststroke gait**. *Neurorehabil Neural Repair* 2010, **24**(3):213-224.
7. Liu LY, Sangani S, Patterson KK, Fung J, Lamontagne A: **Instantaneous effect of real-time avatar visual feedback on interlimb coordination during walking post-stroke**. *Clinical Biomechanics* 2022, **100**:105821.
8. Patterson KK, Mansfield A, Biasin L, Brunton K, Inness EL, McIlroy WE: **Longitudinal changes in poststroke spatiotemporal gait asymmetry over inpatient rehabilitation**. *Neurorehabil Neural Repair* 2015, **29**(2):153-162.
9. Ghai S, Ghai I: **Effects of (music-based) rhythmic auditory cueing training on gait and posture post-stroke: A systematic review & dose-response meta-analysis**. *Sci Rep* 2019, **9**(1):2183.
10. Ghai S, Ghai I, Schmitz G, Effenberg AO: **Effect of rhythmic auditory cueing on parkinsonian gait: A systematic review and meta-analysis**. *Sci Rep* 2018, **8**(1):506.
11. Thaut MH: **The discovery of human auditory-motor entrainment and its role in the development of neurologic music therapy**. *Prog Brain Res* 2015, **217**:253-266.
12. Sejdić E, Fu Y, Pak A, Fairley JA, Chau T: **The effects of rhythmic sensory cues on the temporal dynamics of human gait**. *PLoS One* 2012, **7**(8):e43104.
13. Crosby LD, Wong JS, Chen JL, Grahn J, Patterson KK: **An Initial Investigation of the Responsiveness of Temporal Gait Asymmetry to Rhythmic Auditory Stimulation and the Relationship to Rhythm Ability Following Stroke**. *Front Neurol* 2020, **11**.
14. Roerdink M, Lamoth CJC, Kwakkel G, van Wieringen PCW, Beek PJ: **Gait Coordination After Stroke: Benefits of Acoustically Paced Treadmill Walking**. *Phys Ther* 2007, **87**(8):1009-1022.
15. Thaut MH, Leins AK, Rice RR, Argstatter H, Kenyon GP, McIntosh GC, Bolay HV, Fetter M: **Rhythmic auditory stimulation improves gait more than NDT/Bobath training in near-ambulatory patients early poststroke: a single-blind, randomized trial**. *Neurorehabil Neural Repair* 2007, **21**(5):455-459.
16. Baram Y, Lenger R: **Gait improvement in patients with cerebral palsy by visual and auditory feedback**. *Neuromodulation* 2012, **15**(1):48-52; discussion 52.
17. Brasileiro A, Gama G, Trigueiro L, Ribeiro T, Silva E, Galvão É, Lindquist A: **Influence of visual and auditory biofeedback on partial body weight support treadmill training of individuals with chronic hemiparesis: a randomized controlled clinical trial**. *Eur J Phys Rehabil Med* 2015, **51**(1):49-58.
18. Ginis P, Nieuwboer A, Dorfman M, Ferrari A, Gazit E, Canning CG, Rocchi L, Chiari L, Hausdorff JM, Mirelman A: **Feasibility and effects of home-based smartphone-delivered automated**

feedback training for gait in people with Parkinson's disease: A pilot randomized controlled trial. *Parkinsonism Relat Disord* 2016, **22**:28-34.
19. Kim J, Jung S, Song C: **The Effects of Auditory Feedback Gait Training Using Smart Insole on Stroke Patients**. *Brain Sciences* 2021, **11**(11):1377.
20. Milot MH, Marchal-Crespo L, Green CS, Cramer SC, Reinkensmeyer DJ: **Comparison of error-amplification and haptic-guidance training techniques for learning of a timing-based motor task by healthy individuals**. *Exp Brain Res* 2010, **201**(2):119-131.
21. Liu LY, Li Y, Lamontagne A: **The effects of error-augmentation versus error-reduction paradigms in robotic therapy to enhance upper extremity performance and recovery post-stroke: a systematic review**. *J Neuroeng Rehabil* 2018, **15**(1):65.
22. Kao PC, Srivastava S, Agrawal SK, Scholz JP: **Effect of robotic performance-based error-augmentation versus error-reduction training on the gait of healthy individuals**. *Gait Posture* 2013, **37**(1):113-120.
23. Kao PC, Srivastava S, Higginson JS, Agrawal SK, Scholz JP: **Short-term Performance-based Error-augmentation versus Error-reduction Robotic Gait Training for Individuals with Chronic Stroke: A Pilot Study**. *Phys Med Rehabil Int* 2015, **2**(9).
24. DePaul V, Chow F, Thomas K, Azuma L, Chan W, Poon V, Patterson K: **Self-assessment of gait symmetry in individuals with unilateral stroke: A pilot study**. In: *International Society for Posture and Gait Research World Congress: 2015*; 2015.
25. Dettmann MA, Linder MT, Sepic SB: **Relationships among walking performance, postural stability, and functional assessments of the hemiplegic patient**. *Am J Phys Med* 1987, **66**(2):77-90.
26. Kim CM, Eng JJ: **Symmetry in vertical ground reaction force is accompanied by symmetry in temporal but not distance variables of gait in persons with stroke**. *Gait Posture* 2003, **18**(1):23-28.
27. Petry NM: **A Comparison of Young, Middle-Aged, and Older Adult Treatment-Seeking Pathological Gamblers**. *The Gerontologist* 2002, **42**(1):92-99.
28. Fung J, Richards CL, Malouin F, McFadyen BJ, Lamontagne A: **A treadmill and motion coupled virtual reality system for gait training post-stroke**. *Cyberpsychol Behav* 2006, **9**(2):157-162.
29. Patterson KK, Gage WH, Brooks D, Black SE, McIlroy WE: **Evaluation of gait symmetry after stroke: a comparison of current methods and recommendations for standardization**. *Gait Posture* 2010, **31**(2):241-246.
30. Sigrist R, Rauter G, Riener R, Wolf P: **Augmented visual, auditory, haptic, and multimodal feedback in motor learning: a review**. *Psychon Bull Rev* 2013, **20**(1):21-53.
31. Welch RB, Warren DH: **Immediate perceptual response to intersensory discrepancy**. *Psychol Bull* 1980, **88**(3):638-667.
32. Freides D: **Human information processing and sensory modality: cross-modal functions, information complexity, memory, and deficit**. *Psychol Bull* 1974, **81**(5):284-310.
33. Winter DA: **Kinetics: Forces and Moments of Force**. In: *Biomechanics and Motor Control of Human Movement.* edn.; 2009: 107-138.
34. Crosby LD, Chen JL, Grahn JA, Patterson KK: **Perceptions of an over-ground induced temporal gait asymmetry by healthy young adults**. *Hum Mov Sci* 2021, **78**:102806.
35. Brandstater ME, de Bruin H, Gowland C, Clark BM: **Hemiplegic gait: analysis of temporal variables**. *Arch Phys Med Rehabil* 1983, **64**(12):583-587.
36. Liu LY, Sangani S, Patterson KK, Fung J, Lamontagne A: **Real-Time Avatar-Based Feedback to Enhance the Symmetry of Spatiotemporal Parameters After Stroke: Instantaneous Effects of Different Avatar Views**. *IEEE Trans Neural Syst Rehabil Eng* 2020, **28**(4):878-887.

Figure 7.1 Creation of auditory feedback and markers placement

Figure 7.1 Top left: a tracker device from VIVE^{TM} used for the foot strike detection. Top right: The placement of the tracker device (around the ankle) during the experiment. Bottom: The 14 mm pearl hard markers placed on a participant based on the plug-in gait model (left: back view; right: frontal view). The participant is standing on a self-paced treadmill.

Figure 7.2 Diagram illustrating expected gait pattern

Control	**No sound** Symmetrical gait pattern	**Unmodified footstep sound** Symmetrical gait pattern	**No sound** Symmetrical gait pattern
Delay	**No sound** Symmetrical gait pattern	**Unilateral footstep sound delayed** Larger step on the unperturbed side	**No sound** Symmetrical gait pattern
Advance	**No sound** Symmetrical gait pattern	**Unilateral footstep sound advanced** Larger step on the perturbed side	**No sound** Symmetrical gait pattern
	Pre-Adaptation 30 sec	**Adaptation** 75 sec	**Post-Adaptation** 45 sec

Figure 7.2 Expected gait pattern and how it would change. Top row: the control condition where the auditory feedback is unmodified; Second row: the delay condition where the auditory feedback on one side is delayed; Third row: the advanced condition where the auditory feedback on one side is advanced. Last row: different phases of a walking trial and their duration.

Figure 7.3 Traces of bilateral swing time and step length of a participant

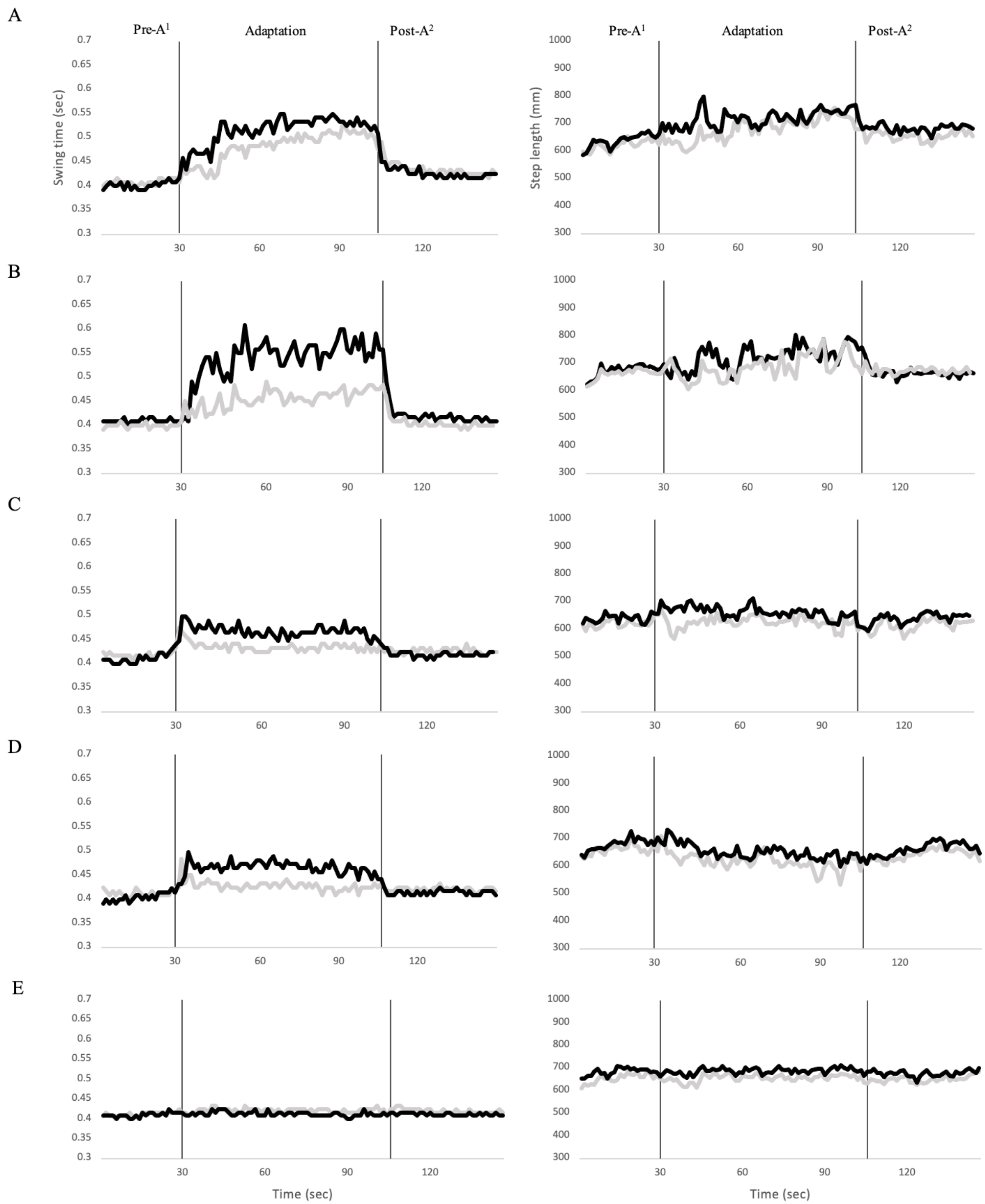

Figure 7.3 Traces of the bilateral swing time (left) and step length (right) of a participant over an entire walking trial in different conditions. Left and right sides are represented by the grey and black lines respectively. Conditions are indicated by the letters, A: small delay on the left side; B: large delay on the left side; C: small advance on the right side; D: large advance on the right side; E: control (unmodified footstep sound). [1]Pre-A: pre-adaptation, [2]Post-A: post-adaptation

Figure 7.4 Swing time ratio and step length ratio

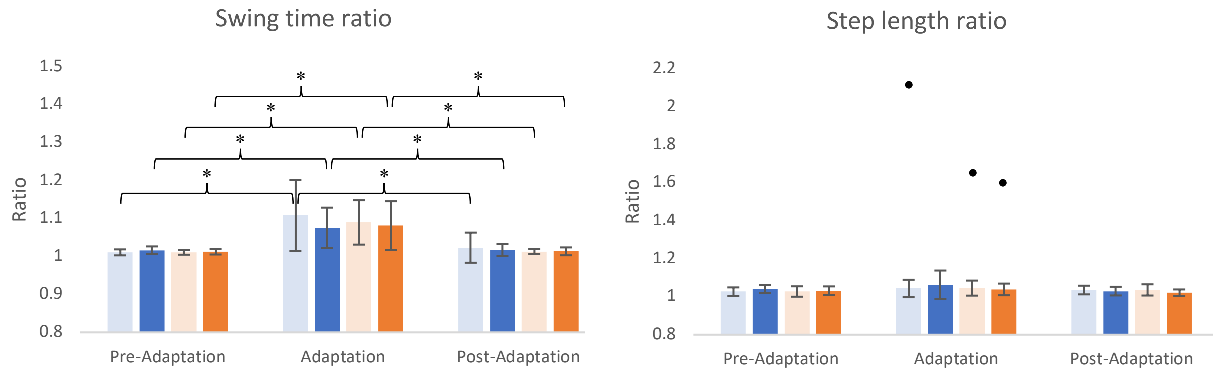

Figure 7.4 Spatiotemporal ratio of the four conditions across three phases, with swing time ratio on the left and step length ratio on the right. The conditions are indicated by different colors (light blue: small delay, blue: large delay, light orange: small advance, orange: large advance). Means and standard deviations are shown by the bars and whiskers. Circles above the bars represent the outliers. Statistically significant differences are indicated by * (p<0.001).

Figure 7.5 Bilateral swing time and step length

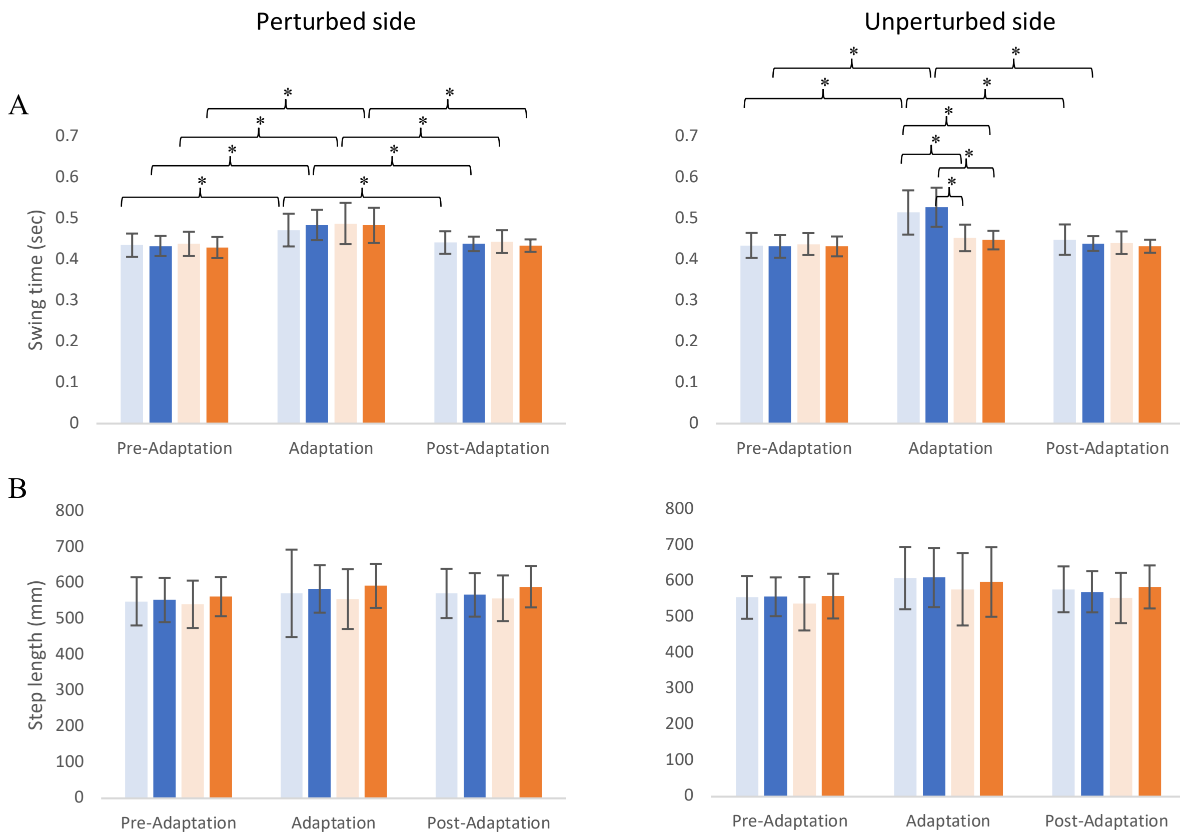

Figure 7.5 Bilateral swing time (A) and step length (B) of the four conditions across three phases, with the perturbed side shown on the left and the unperturbed side shown on the right. The conditions are indicated by different colors (light blue: small delay, blue: large delay, light orange: small advance, orange: large advance). Means and standard deviations are shown by the bars and whiskers. Statistically significant differences are indicated by * (p<0.001).

Figure 7.6 Bilateral kinematic results

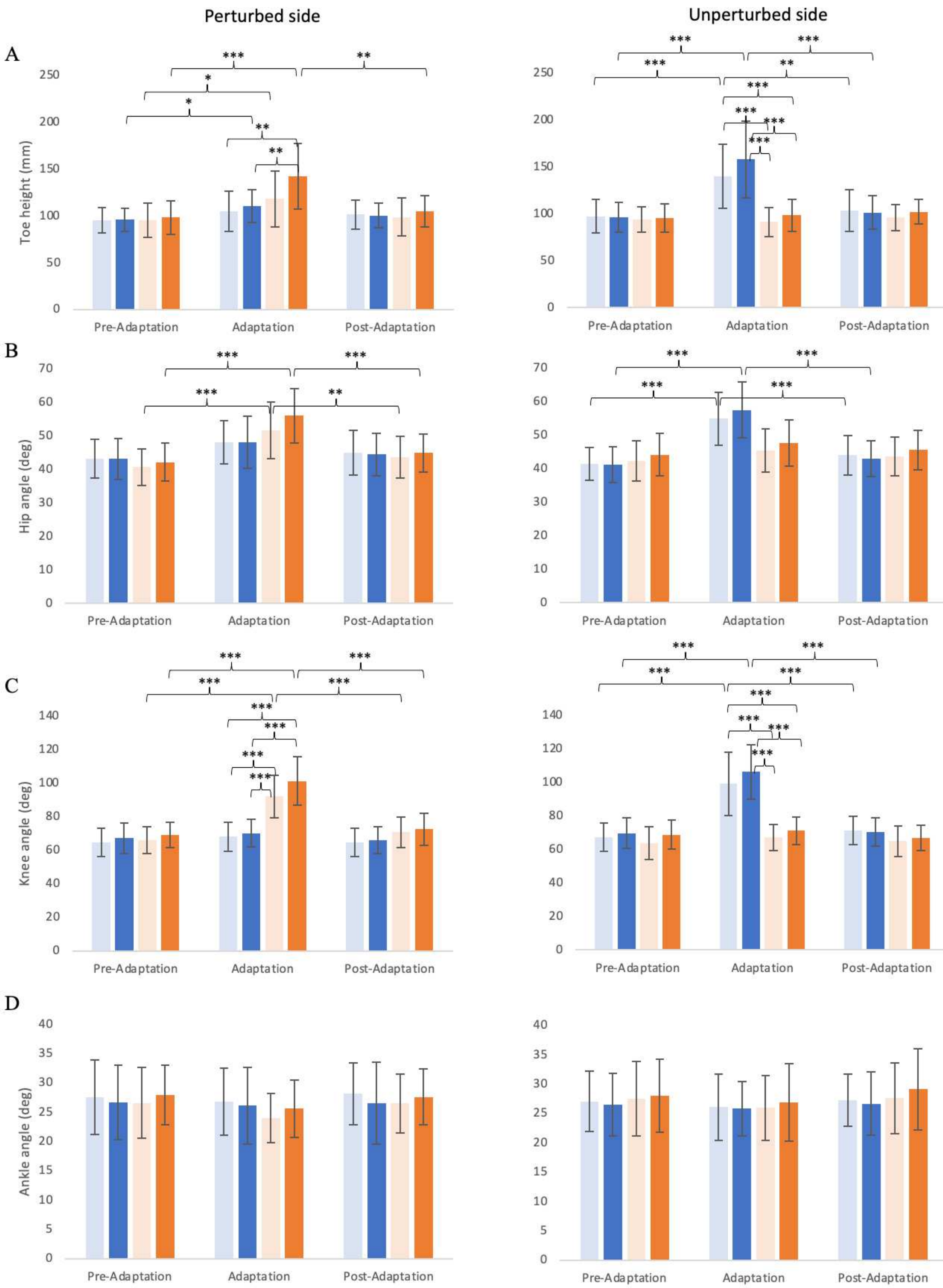

Figure 7.6 Bilateral maximum toe height (A), hip angle excursion (B), knee angle excursion (C) and ankle angle excursion (D) of the four conditions across three phases, with the perturbed side shown on the left and the unperturbed side shown on the right. The conditions are indicated by different colors (light blue: small delay, blue: large delay, light orange: small advance, orange: large advance). Means and standard deviations are shown by the bars and whiskers. Statistically significant differences are indicated by * (p<0.05) ** (p<0.01) *** (p<0.001).

Chapter 8. General discussion and conclusion

8.1 Summary of findings

This PhD dissertation investigated the effects of real-time feedback in the form of biological cues on post-stroke gait asymmetry, with the long-term goal of generating a VR-based intervention involving real-time avatar-based feedback that can be applied as part of post-stroke rehabilitation to improve gait symmetry. Specifically, this PhD dissertation examined the immediate effects of avatar feedback on post-stroke gait asymmetry and other parameters of gait, focusing on the effects of i) different avatar views and ii) different sensory modalities. It further examined the immediate effects of distorted auditory feedback on gait symmetry in healthy participants.

In manuscript 1 (Chapter 4), we examined for the first time the effects of visual feedback in the form of virtual avatars displaying locomotor movements in real time on gait symmetry among people with stroke, and we also compared the effects of back, front, and paretic side views of avatar on gait symmetry. It was hypothesized that the approach would be feasible (hypothesis 1), that the paretic side view would provide the largest improvement in gait symmetry compared to other views (hypothesis 2) and that participants with higher gait capacity and better motor recovery would be more likely to respond to the avatar-based feedback (hypothesis 3). Hypothesis 1 about feasibility was supported by the full adherence of participants to the whole protocol, the lack of adverse events, and the acceptability of the intervention to participants. As for hypothesis 2, it was partially supported, as that the paretic side view was the only condition where significant increases in walking speed and bilateral step length were observed, but group results failed to reveal symmetry improvements due the presence of both responders and non-responders. Furthermore, it was shown in this study that participants increased their step length to a larger extent on their non-paretic side during the avatar exposure, causing those with a larger paretic step length to start with to be the ‘responders’ to the avatar-based feedback. Once the feedback was removed, responders showed retention effects in terms of walking speed, paretic step length and SLR. In relation to hypothesis 3, it was shown that having a higher level of motor recovery, as reflected by greater CMSA foot score, lead to a larger improvement in SLR (i.e., spatial symmetry).

In manuscript 2 (Chapter 5), we extended our investigation on the effects of real-time visual feedback in the form of avatars on gait symmetry by examining whether this type of feedback could also improve interlimb coordination during walking. We also examined the correlations between the changes in interlimb coordination and the changes in gait symmetry ratio, as well as between the changes in interlimb coordination and the changes in walking speed. We posed the following two hypotheses: (1) the avatar-based feedback improves interlimb coordination of lower extremities and; (2) the improvement in interlimb coordination is correlated with the improvement in gait symmetry and in walking speed. While the coordination measures (ACC, CRP magnitude and variability) did not show significant differences due to the visual avatar-based feedback, it was observed that the participants who improved their step length symmetry also improved their CRP magnitude (temporal aspect of coordination). Moreover, the changes in CRP magnitude were positively correlated with the changes in step length symmetry and walking speed. In this manuscript, we reaffirmed the findings of manuscript 1, showing that the changes in gait symmetry, coordination and walking speed were mediated by adaptations on the non-paretic side.

Manuscript 3 (Chapter 6) investigated the instantaneous changes in gait symmetry among people with stroke exposed to short bouts of real-time feedback provided as a visual avatar, auditory foot strike, and combined visual-auditory modalities. It was hypothesized that: (1) the combined visual-auditory feedback would provide the largest improvements in post-stroke gait symmetry; (2) individuals would improve their symmetry by adapting their spatiotemporal factors primarily on the non-paretic side and; (3) individuals with a smaller initial gait asymmetry would show larger improvements in gait symmetry. Contrary to hypothesis 1, the combined modality feedback did not show advantage over the single-modality feedback at improving gait symmetry, although it was perceived to be the most useful condition by the participants. Moreover, as opposed to what was postulated under hypothesis 2, the responders used a strategy where they increased bilateral step lengths, but where the shorter side (in most instances the paretic step) would show the largest increase. Thus, the direction of the asymmetry would predict the strategies used to correct the asymmetry, as opposed to predicting whether an individual will respond or not to the intervention, as initially proposed in manuscripts 1 & 2. Hypothesis 3 was confirmed as participants with smaller initial step length asymmetry had larger improvements in SLR in response to the combined modality condition.

In the fourth and last manuscript (Chapter 7), we examined the effects of distorted auditory feedback in the form of delayed and advanced footstep sounds of different magnitudes on the gait symmetry of healthy young participants. Initially, we hypothesized that: (1) participants would modify their gait pattern by increasing their swing time and step length on the perturbed side in the advanced feedback conditions, but on the unperturbed side in the delayed feedback conditions; (2) the large feedback distortion would lead to larger changes in gait symmetry in comparison to the small distortion and; (3) changes in swing time and step length symmetry would be accompanied by changes in sagittal joint excursion at multiple lower limb joints (hip, knee and ankle), and in maximum toe height during the swing phase. While hypothesis 1 was partially confirmed as the participants increased their swing time on the perturbed side in the advanced conditions and on the unperturbed side to a greater extent in the delayed conditions, it was not expected that they would not change their step length nor that they would also increase their swing time to a less extent on the perturbed side in the delayed conditions. Hypothesis 2 was not confirmed by the results as there was not a significant difference between the small and large magnitude of distortion in eliciting changes in spatiotemporal parameters. For hypothesis 3, the kinematic measures, namely sagittal hip and knee joint excursions, as well as maximum toe height, were increased, but the ankle joint excursion remained unchanged due to feedback exposure.

8.2 General discussion

Overall, the manuscripts presented in this dissertation deepen the knowledge on gait symmetry adaptations and corresponding movement strategies of people with stroke and healthy individuals exposed to real-time biological motion feedback presented in the form of a visual avatar and/or footstep sounds. Not only did this dissertation explore, for the first time, the use of such feedback to improve walking and gait symmetry in stroke survivors, but it was also the first time that the effects of distorted auditory feedback on spatiotemporal parameters of gait were examined in healthy people. In the following section, additional discussion and interpretations of the findings are presented, based on two main themes that emerged from the different manuscripts included in this dissertation: (1) movement strategies involved in spatial symmetry adaptations and (2) lack of changes in temporal symmetry among people with stroke.

8.2.1 Movement strategies involved in spatial symmetry adaptations

As shown in the manuscript 1, participants with stroke used the strategy of increasing bilateral step length in an attempt to improve spatial symmetry, but as their paretic side was less functional than the non-paretic side, the non-paretic step length was increased to a larger extent than the paretic side. As a result, and although all participants increased their walking speed due to the increase of bilateral step length, only the participants who had a larger initial paretic step length were SLR responders. Those results were corroborated by findings of manuscript 2 where improvements in CRP magnitude were mediated by the non-paretic side, which showed an increase in hip angle excursion, as opposed to the paretic side which did not. Thus, it appears that the visual avatar-based feedback elicited changes primarily on the non-paretic side.

The findings of manuscript 3 differ, at least in part, with what was observed in the two previous manuscripts. Indeed, the responders in manuscript 3 had a larger initial step length on the non-paretic side, which contrasts with the responders in manuscript 1 & 2 who had a larger paretic step to start with. Similarly to responders in manuscript 1 & 2, however, responders in manuscript 3 predominantly used a strategy where they increased their bilateral step length to improve their step length symmetry, but step length was increased to a larger extent on the paretic (shorter side) vs. non-paretic side. Thus, a similar strategy that consists of increasing to a larger extent the step length on the 'shorter side' emerged for all responders in the different manuscripts. Such strategy aligns with the work of Balasubramanian and colleagues (2007), which showed that the side with a shorter step length produced larger amount of propulsive force [62], and a larger propulsive force can lead to larger increase in step length. It is unclear, however, why responders in manuscripts 1 & 2 vs. 3 had different profiles in terms of their direction of spatial asymmetry. Indeed, other than the stroke being slightly more chronic in manuscript 3 vs. the first two manuscripts, individuals showed similar levels of motor recovery, walking capacity and extent of asymmetry. Such conflicting results illustrate the complexity of post-stroke gait asymmetry, where each individual may present with a different type/combination of asymmetry (spatial, temporal or both) and direction of asymmetry (larger or small paretic step length) that may interact and influence the response to the intervention. As further outlined by Wutzke and colleagues (2015), people with stroke may have a 'recalibrated' perception of asymmetry and the spatiotemporal parameters of their current gait become their 'new symmetrical gait [11]. If the perception of asymmetry is altered to a different extent across individuals, this would also possibly impact differently on their ability to respond to the feedback intervention. Also, elements such as limb proprioception that affects the sense of limb position, dynamic balance, and spasticity that may affect the use of the real-time feedback while walking, could also influence the response to the feedback intervention. In fact, Subramanian and colleagues (2018) have pointed in their study that the presence of spasticity could impede motor execution, thus resulting in non-adaptation of the paretic side among stroke participants despite their motor planning ability was intact [209].

8.2.2 Lack of changes in temporal symmetry among stroke participants

There was a lack of changes in bilateral swing time and SWR among stroke participants in manuscript 1. Initially, it was postulated that this lack of change in temporal symmetry was due to participants only receiving visual feedback, and that temporal information of a movement would be better appraised through the auditory modality of feedback which provides precise perception of rhythm and temporal information in general [170, 174, 210]. However, in manuscript 3, neither the auditory feedback alone nor the combined visual and auditory feedback had any impact on temporal gait symmetry in stroke participants. This is in contrast with the findings of Gomez-Andres and colleagues (2020) where the authors stated that amplifying the footstep sound, thus creating enhanced auditory feedback, could improve stance time symmetry among stroke participants [211]. Therefore, the lack of auditory feedback alone cannot explain the lack of change in temporal symmetry in the different manuscripts. In manuscript 4, however, all distorted auditory feedback conditions successfully elicited a temporal gait asymmetry in the healthy participants, as reflected by changes in swing time and SWR. In addition, changes only occurred in the temporal aspect of gait and not in the spatial aspect, as no differences were found in step length, SLR or walking speed due to distorted feedback exposure. This support the idea that auditory feedback is effective at changing the temporal aspect of gait.

The reason why participants in the manuscript 3 did not show any change in the temporal parameters of gait when exposed to auditory feedback could be that the participants had difficulty perceiving their temporal asymmetry, as studies have demonstrated that individuals with stroke have altered auditory rhythm perception [123] and a pronounced difficulty to correctly perceive the presence and direction of their temporal asymmetry [69]. Furthermore, it has been shown that even healthy individuals have difficulty perceiving the direction and the magnitude of asymmetry [70]. In fact, the latter observation is also supported by findings of manuscript 4, where healthy participants did not respond differently to the large vs. small distortion of auditory feedback. The distorted auditory feedback approach developed and tested in manuscript 4, however, does show potential to improve post-stroke temporal asymmetry. Indeed, the auditory modality can be augmented via an EA paradigm to facilitate the perception of temporal asymmetry and result in subsequent temporal symmetry adaptation. However, providing auditory feedback augmented with an EA paradigm in stroke survivors presents significant challenges. It may be necessary to assess the level of perception toward feedback distortion in each individual with stroke before the intervention is used. In addition, it would be imperative to tailor the feedback to the asymmetry profile of the individual. Results of manuscript 4 provided insights in that regard, but further work is needed to test the feasibility and potential effectiveness of such approach for post-stroke gait asymmetry.

A last point to be noted before moving on to the limitations section is that although the paretic side view was the only visual modality condition where adaptations in spatial symmetry occurred in manuscript 1, and that for this reasons this view was selected for manuscripts 2 & 3, we cannot rule out the possibility that the back and frontal views might provide information on other aspects of gait, such as hip abduction angle (circumduction) and step width, which were not examined as part of this thesis. Although this would not be considered as a limitation per se, as the focus of this PhD work was on gait asymmetry, the impact of other views such as the back and frontal views could be further explored as they have the potential to be used to improve gait deviations other than asymmetry.

8.3 Limitations

The studies included in this dissertation have limitations, which are listed in greater detail in the respective manuscripts. A main limitation across studies is the choice of an instantaneous adaptation design which involves a short duration of feedback exposure, allowing a limited adaptation period lasting between 60s or 75s depending on the studies. While the common objective of these studies was to examine the instantaneous effects of the feedback conditions, the short duration of feedback could have contributed, to a certain extent, to the lack of group-level changes in terms of gait symmetry and interlimb coordination in manuscripts 1-3, as well as to the lack of retention effects in the post-adaptation period in manuscript 4. Moreover, another limitation for manuscripts 1-3 is the small sample size considering the large variability in the profiles of asymmetry of participants with stroke, with 10/12 (manuscript 1 & 2) and 11/12 (manuscript 3) participants showing temporal asymmetry, and 9/12 (manuscript 1 & 2) and 10/12 (manuscript 3) displaying spatial asymmetry. This small sample size might limit the generalization of findings to the general population with stroke that present with a great variety in terms of severity and type of gait asymmetry. Also, and as highlighted earlier, the presence of a combined temporal/spatial asymmetry may have impacted the response of individuals with stroke to the feedback exposure. While it would be interesting to look further into this question in the future, and while the proportion of individuals with stroke presenting spatial and temporal asymmetry is documented as 33.3% and 55.5% respectively in the literature [56], the proportion of individuals showing a co-occurrence of both types of symmetry is unclear. Findings from this PhD project, although drawn from a relatively small sample of individuals compared to epidemiological studies, suggest that a co-occurrence of temporal and spatial asymmetry could be the norm rather than the exception. Another potential limitation could be that based on the observed strategies from healthy participants in manuscript 4, the distorted auditory feedback would be applied in stroke survivors in a way that leads to adaptations on the non-paretic side. Such phenomenon, while not unexpected given the extensive body of literature showing the presence adaptations occurring on the non-paretic side during gait (see section 1.2) could potentially reinforce this development of compensation instead of motor recovery [212].

8.4 Conclusion and future directions

In conclusion, and based on the findings of the four manuscripts included in this dissertation, I wish to answer my initial research question (see section 1.8), which is: Among *people in the chronic phase of stro*ke performing a walking task, to what extent does avatar-based feedback on their gait pattern impact on gait asymmetry? The visual feedback in the form of avatars presented in the paretic side view has improved the spatial symmetry in selected individuals with stroke, while improving other parameters of gait such as walking speed when considering group results. The exact elements that make some people with stroke improve their spatial symmetry while others do not are still unclear and need further investigations. Findings also showed that combining footstep sounds to a visual avatar yields no advantage over a single modality feedback in terms of symmetry improvement, and that symmetry improvements observed in individual with stroke are limited to the spatial aspect, with no changes in temporal symmetry. To improve temporal asymmetry, auditory feedback in the form of footstep sound shows potential, but the impaired perception of people with stroke of their temporal asymmetry must first be addressed, possibly using an EA paradigm that can facilitate perception and ensuing movement adaptations.

In order for feedback in the form of biological cues to be implemented as part of stroke of a rehabilitation program to improve gait asymmetry, I suggest that future studies should first incorporate multiple sessions of training with longer durations of feedback exposure, as repetition of practice is also an important component of motor learning [130, 213], and to examine the long-term effects of such feedback intervention. To better understand how people with stroke adapt in their spatial symmetry with the real-time feedback, and to characterize responders vs non-responders, elements such as feedback perception, limb proprioception, balance and executive functions could be documented as part of the assessments. To ensure the effectiveness of the feedback on the temporal aspect of symmetry, it would also be important to first assess the perception of the gait asymmetry of the stroke participant as they might incorrectly perceive the presence and/or direction of their asymmetry [69]. For the implementation of auditory feedback with EA among people with stroke, it will also be necessary to tailor the magnitude of feedback distortion according to the magnitude and direction of their asymmetry, as well as their extent of their response to sensory distortion. Furthermore, future studies on the application of EA on gait symmetry could also explore the use of distorted kinematic feedback provided by a visual avatar to maximize the effects on spatial asymmetry. Moreover, coupling the feedback-based interventions with excitatory or inhibitory brain stimulation tools such as transcranial direct current stimulation or transcranial magnetic stimulation could potentially provide greater benefits in terms of gait symmetry improvements, by favoring motor adaptations on the paretic side.

As a closing remark, the feedback in the form of biological cues is a versatile approach for it can be modified according to the profile of individuals and has shown the potential to change spatiotemporal parameters of gait. In addition, it has also received overwhelming positive feedback from the stroke participants, as it is engaging and intuitive. More importantly, it provides unique real-time information on the 'quality' of walking that would otherwise be very challenging for clinicians to deliver. As post-stroke gait asymmetry remains difficult to improve, I would like to encourage future clinicians and researchers to continue the development of interventions which utilize feedback in the form of biological cues.

References for Chapter 1, 2, 3, and 8

1. Robinson CA, Shumway-Cook A, Ciol MA, Kartin D: **Participation in community walking following stroke: subjective versus objective measures and the impact of personal factors**. *Physical therapy* 2011, **91**(12):1865-1876.
2. Singam A, Ytterberg C, Tham K, von Koch L: **Participation in Complex and Social Everyday Activities Six Years after Stroke: Predictors for Return to Pre-Stroke Level**. *PloS one* 2015, **10**(12):e0144344.
3. Patterson KK, Mansfield A, Biasin L, Brunton K, Inness EL, McIlroy WE: **Longitudinal changes in poststroke spatiotemporal gait asymmetry over inpatient rehabilitation**. *Neurorehabil Neural Repair* 2015, **29**(2):153-162.
4. Ellis RG, Howard KC, Kram R: **The metabolic and mechanical costs of step time asymmetry in walking**. *Proc Biol Sci* 2013, **280**(1756):20122784.
5. Jorgensen L, Crabtree NJ, Reeve J, Jacobsen BK: **Ambulatory level and asymmetrical weight bearing after stroke affects bone loss in the upper and lower part of the femoral neck differently: bone adaptation after decreased mechanical loading**. *Bone* 2000, **27**(5):701-707.
6. Shumway-Cook A, Patla AE, Stewart A, Ferrucci L, Ciol MA, Guralnik JM: **Environmental demands associated with community mobility in older adults with and without mobility disabilities**. *Physical therapy* 2002, **82**(7):670-681.
7. Teasell RW, Bhogal SK, Foley NC, Speechley MR: **Gait retraining post stroke**. *Topics in stroke rehabilitation* 2003, **10**(2):34-65.
8. Thaut MH, Leins AK, Rice RR, Argstatter H, Kenyon GP, McIntosh GC, Bolay HV, Fetter M: **Rhythmic auditory stimulation improves gait more than NDT/Bobath training in near-ambulatory patients early poststroke: a single-blind, randomized trial**. *Neurorehabil Neural Repair* 2007, **21**(5):455-459.
9. Roerdink M, Lamoth CJ, Kwakkel G, van Wieringen PC, Beek PJ: **Gait coordination after stroke: benefits of acoustically paced treadmill walking**. *Physical therapy* 2007, **87**(8):1009-1022.
10. Reisman DS, McLean H, Keller J, Danks KA, Bastian AJ: **Repeated split-belt treadmill training improves poststroke step length asymmetry**. *Neurorehabil Neural Repair* 2013, **27**(5):460-468.
11. Wutzke CJ, Faldowski RA, Lewek MD: **Individuals Poststroke Do Not Perceive Their Spatiotemporal Gait Asymmetries as Abnormal**. *Phys Ther* 2015, **95**(9):1244-1253.
12. Thomas JP, Shiffrar M: **I can see you better if I can hear you coming: action-consistent sounds facilitate the visual detection of human gait**. *Journal of vision* 2010, **10**(12):14.
13. Wuerger SM, Crocker-Buque A, Meyer GF: **Evidence for auditory-visual processing specific to biological motion**. *Seeing and perceiving* 2012, **25**(1):15-28.
14. Wuerger SM, Parkes L, Lewis PA, Crocker-Buque A, Rutschmann R, Meyer GF: **Premotor cortex is sensitive to auditory-visual congruence for biological motion**. *Journal of cognitive neuroscience* 2012, **24**(3):575-587.
15. von Saldern S, Noppeney U: **Sensory and striatal areas integrate auditory and visual signals into behavioral benefits during motion discrimination**. *The Journal of neuroscience : the official journal of the Society for Neuroscience* 2013, **33**(20):8841-8849.
16. Bidet-Caulet A, Voisin J, Bertrand O, Fonlupt P: **Listening to a walking human activates the temporal biological motion area**. *NeuroImage* 2005, **28**(1):132-139.
17. Israely S, Carmeli E: **Error augmentation as a possible technique for improving upper extremity motor performance after a stroke - a systematic review**. *Top Stroke Rehabil* 2016, **23**(2):116-125.

18. Kao PC, Srivastava S, Agrawal SK, Scholz JP: **Effect of robotic performance-based error-augmentation versus error-reduction training on the gait of healthy individuals**. *Gait Posture* 2013, **37**(1):113-120.
19. Kao PC, Srivastava S, Higginson JS, Agrawal SK, Scholz JP: **Short-term Performance-based Error-augmentation versus Error-reduction Robotic Gait Training for Individuals with Chronic Stroke: A Pilot Study**. *Phys Med Rehabil Int* 2015, **2**(9).
20. Betschart M, Lauziere S, Mieville C, McFadyen BJ, Nadeau S: **Changes in lower limb muscle activity after walking on a split-belt treadmill in individuals post-stroke**. *J Electromyogr Kinesiol* 2017, **32**:93-100.
21. Dettmann MA, Linder MT, Sepic SB: **Relationships among walking performance, postural stability, and functional assessments of the hemiplegic patient**. *Am J Phys Med* 1987, **66**(2):77-90.
22. Kim CM, Eng JJ: **Symmetry in vertical ground reaction force is accompanied by symmetry in temporal but not distance variables of gait in persons with stroke**. *Gait Posture* 2003, **18**(1):23-28.
23. **Stroke, Cerebrovascular accident** [http://www.who.int/topics/cerebrovascular_accident/en/] Access date: 2023-06-06
24. **Leading causes of death** [http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/hlth36a-eng.htm] Acess date: 2023-06-06
25. Zorowitz RD, Gross E, Polinski DM: **The stroke survivor**. *Disabil Rehabil* 2002, **24**(13):666-679.
26. Hodgson C: **Prevalence and disabilities of community-living seniors who report**

the effects of stroke. *Can Med Assoc J* 1998, **6**:9-14.
27. Verbrugge LM, Lepkowski JM, Imanaka Y: **Comorbidity and its impact on disability**. *Milbank Q* 1989, **67**(3-4):450-484.
28. **Tracking Heart Disease and Stroke in Canada**. In.: Public Health Agency of Canada; 2009.
29. Mayo NE, Wood-Dauphinee S, Ahmed S, Gordon C, Higgins J, McEwen S, Salbach N: **Disablement following stroke**. *Disabil Rehabil* 1999, **21**(5-6):258-268.
30. **Age and Sex Highlight Tables, 2016 Census** [http://www12.statcan.gc.ca/census-recensement/2016/dp-pd/hlt-fst/as/Table.cfm?T=31] Access date: 2023-06-06
31. Patterson KK: **Gait asymmetry post-stroke: thesis for PhD degree**. University of Toronto 2010.
32. Bohannon R, Andrews A, Smith M: **Rehabilitation goals of patients with hemiplegia**. *Int J Rehabil Res* 1988, **11**:181-183.
33. Jorgensen HS, Nakayama H, Raaschou HO, Olsen TS: **Recovery of walking function in stroke patients: the Copenhagen Stroke Study**. *Arch Phys Med Rehabil* 1995, **76**(1):27-32.
34. Perry J, Garrett M, Gronley JK, Mulroy SJ: **Classification of walking handicap in the stroke population**. *Stroke* 1995, **26**(6):982-989.
35. Jonsdottir J, Recalcati M, Rabuffetti M, Casiraghi A, Boccardi S, Ferrarin M: **Functional resources to increase gait speed in people with stroke: strategies adopted compared to healthy controls**. *Gait Posture* 2009, **29**(3):355-359.
36. Nadeau S, Arsenault AB, Gravel D, Bourbonnais D: **Analysis of the clinical factors determining natural and maximal gait speeds in adults with a stroke**. *Am J Phys Med Rehabil* 1999, **78**(2):123-130.
37. Bohannon RW: **Comfortable and maximum walking speed of adults aged 20-79 years: reference values and determinants**. *Age Ageing* 1997, **26**(1):15-19.
38. De Quervain IA, Simon SR, Leurgans S, Pease WS, McAllister D: **Gait pattern in the early recovery period after stroke**. *J Bone Joint Surg Am* 1996, **78**(10):1506-1514.

39. Kerrigan DC, Frates EP, Rogan S, Riley PO: **Spastic paretic stiff-legged gait: biomechanics of the unaffected limb**. *Am J Phys Med Rehabil* 1999, **78**(4):354-360.
40. Kim CM, Eng JJ: **Magnitude and pattern of 3D kinematic and kinetic gait profiles in persons with stroke: relationship to walking speed**. *Gait Posture* 2004, **20**(2):140-146.
41. Daly JJ, Sng K, Roenigk K, Fredrickson E, Dohring M: **Intra-limb coordination deficit in stroke survivors and response to treatment**. *Gait Posture* 2007, **25**(3):412-418.
42. Stephenson JL, De Serres SJ, Lamontagne A: **The effect of arm movements on the lower limb during gait after a stroke**. *Gait Posture* 2010, **31**(1):109-115.
43. Lamontagne A, De Serres SJ, Fung J, Paquet N: **Stroke affects the coordination and stabilization of head, thorax and pelvis during voluntary horizontal head motions performed in walking**. *Clin Neurophysiol* 2005, **116**(1):101-111.
44. Knutsson E, Richards C: **Different types of disturbed motor control in gait of hemiparetic patients**. *Brain* 1979, **102**(2):405-430.
45. Raja B, Neptune RR, Kautz SA: **COORDINATION OF THE NON-PARETIC LEG DURING HEMIPARETIC GAIT: EXPECTED AND NOVEL COMPENSATORY PATTERNS**. *Clin Biomech (Bristol, Avon)* 2012, **27**(10):1023-1030.
46. Olney SJ, Richards C: **Hemiparetic gait following stroke. Part I: Characteristics**. *Gait Posture* 1996, **4**(2):136-148.
47. Olney SJ, Griffin MP, Monga TN, McBride ID: **Work and power in gait of stroke patients**. *Arch Phys Med Rehabil* 1991, **72**(5):309-314.
48. Lamontagne A, Stephenson JL, Fung J: **Physiological evaluation of gait disturbances post stroke**. *Clin Neurophysiol* 2007, **118**(4):717-729.
49. Brandstater ME, de Bruin H, Gowland C, Clark BM: **Hemiplegic gait: analysis of temporal variables**. *Arch Phys Med Rehabil* 1983, **64**(12):583-587.
50. Chen G, Patten C, Kothari DH, Zajac FE: **Gait differences between individuals with post-stroke hemiparesis and non-disabled controls at matched speeds**. *Gait Posture* 2005, **22**(1):51-56.
51. Titianova EB, Pitkanen K, Paakkonen A, Sivenius J, Tarkka IM: **Gait characteristics and functional ambulation profile in patients with chronic unilateral stroke**. *Am J Phys Med Rehabil* 2003, **82**(10):778-786; quiz 787-779, 823.
52. Weerdesteyn V, de Niet M, van Duijnhoven HJ, Geurts AC: **Falls in individuals with stroke**. *J Rehabil Res Dev* 2008, **45**(8):1195-1213.
53. Kramer S, Johnson L, Bernhardt J, Cumming T: **Energy Expenditure and Cost During Walking After Stroke: A Systematic Review**. *Arch Phys Med Rehabil* 2016, **97**(4):619-632.e611.
54. Stoquart G, Detrembleur C, Lejeune TM: **The reasons why stroke patients expend so much energy to walk slowly**. *Gait Posture* 2012, **36**(3):409-413.
55. Michael KM, Allen JK, Macko RF: **Reduced ambulatory activity after stroke: the role of balance, gait, and cardiovascular fitness**. *Arch Phys Med Rehabil* 2005, **86**(8):1552-1556.
56. Patterson KK, Parafianowicz I, Danells CJ, Closson V, Verrier MC, Staines WR, Black SE, McIlroy WE: **Gait asymmetry in community-ambulating stroke survivors**. *Arch Phys Med Rehabil* 2008, **89**(2):304-310.
57. Patterson KK, Gage WH, Brooks D, Black SE, McIlroy WE: **Evaluation of gait symmetry after stroke: a comparison of current methods and recommendations for standardization**. *Gait Posture* 2010, **31**(2):241-246.
58. Hodt-Billington C, Helbostad JL, Moe-Nilssen R: **Should trunk movement or footfall parameters quantify gait asymmetry in chronic stroke patients?** *Gait Posture* 2008, **27**(4):552-558.
59. Herzog W, Nigg BM, Read LJ, Olsson E: **Asymmetries in ground reaction force patterns in normal human gait**. *Med Sci Sports Exerc* 1989, **21**(1):110-114.

60. Lin PY, Yang YR, Cheng SJ, Wang RY: **The relation between ankle impairments and gait velocity and symmetry in people with stroke**. *Arch Phys Med Rehabil* 2006, **87**(4):562-568.
61. Titianova EB, Tarkka IM: **Asymmetry in walking performance and postural sway in patients with chronic unilateral cerebral infarction**. *J Rehabil Res Dev* 1995, **32**(3):236-244.
62. Balasubramanian CK, Bowden MG, Neptune RR, Kautz SA: **Relationship between step length asymmetry and walking performance in subjects with chronic hemiparesis**. *Arch Phys Med Rehabil* 2007, **88**(1):43-49.
63. Hsu AL, Tang PF, Jan MH: **Analysis of impairments influencing gait velocity and asymmetry of hemiplegic patients after mild to moderate stroke**. *Arch Phys Med Rehabil* 2003, **84**(8):1185-1193.
64. Patterson SL, Rodgers MM, Macko RF, Forrester LW: **Effect of treadmill exercise training on spatial and temporal gait parameters in subjects with chronic stroke: a preliminary report**. *J Rehabil Res Dev* 2008, **45**(2):221-228.
65. Vidoni ED, Boyd LA: **Preserved motor learning after stroke is related to the degree of proprioceptive deficit**. *Behavioral and Brain Functions* 2009, **5**(1):36.
66. Vidoni ED, Acerra NE, Dao E, Meehan SK, Boyd LA: **Role of the primary somatosensory cortex in motor learning: An rTMS study**. *Neurobiol Learn Mem* 2010, **93**(4):532-539.
67. Ostry DJ, Darainy M, Mattar AA, Wong J, Gribble PL: **Somatosensory plasticity and motor learning**. *J Neurosci* 2010, **30**(15):5384-5393.
68. Kessner SS, Bingel U, Thomalla G: **Somatosensory deficits after stroke: a scoping review**. *Top Stroke Rehabil* 2016, **23**(2):136-146.
69. DePaul V, Chow F, Thomas K, Azuma L, Chan W, Poon V, Patterson K: **Self-assessment of gait symmetry in individuals with unilateral stroke: A pilot study**. In: *International Society for Posture and Gait Research World Congress: 2015*; 2015.
70. Crosby LD, Chen JL, Grahn JA, Patterson KK: **Perceptions of an over-ground induced temporal gait asymmetry by healthy young adults**. *Hum Mov Sci* 2021, **78**:102806.
71. Hoogkamer W: **Perception of Gait Asymmetry During Split-Belt Walking**. *Exerc Sport Sci Rev* 2017, **45**(1):34-40.
72. Lauzière S, Miéville C, Duclos C, Aissaoui R, Nadeau S: **Perception threshold of locomotor symmetry while walking on a split-belt treadmill in healthy elderly individuals**. *Percept Mot Skills* 2014, **118**(2):475-490.
73. Hoogkamer W, Bruijn SM, Potocanac Z, Van Calenbergh F, Swinnen SP, Duysens J: **Gait asymmetry during early split-belt walking is related to perception of belt speed difference**. *J Neurophysiol* 2015, **114**(3):1705-1712.
74. König N, Taylor WR, Baumann CR, Wenderoth N, Singh NB: **Revealing the quality of movement: A meta-analysis review to quantify the thresholds to pathological variability during standing and walking**. *Neurosci Biobehav Rev* 2016, **68**:111-119.
75. Krasovsky T, Levin MF: **Review: toward a better understanding of coordination in healthy and poststroke gait**. *Neurorehabil Neural Repair* 2010, **24**(3):213-224.
76. Wang X, O'Dwyer N, Halaki M: **A review on the coordinative structure of human walking and the application of principal component analysis**. *Neural Regen Res* 2013, **8**(7):662-670.
77. Bianchi L, Angelini D, Orani GP, Lacquaniti F: **Kinematic Coordination in Human Gait: Relation to Mechanical Energy Cost**. *J Neurophysiol* 1998, **79**(4):2155-2170.
78. Matsuo Y, Asai Y, Nomura T, Sato S, Inoue S, Mizukura I, Yoneda T, Miki A, Sakoda S, Abe K: **Intralimb and Interlimb Incoordination: Comparative Study between Patients with Parkinsonism and with Cerebellar Ataxia**. *J Jpn Phys Ther Assoc* 2005, **8**(1):47-52.
79. Serrao M, Ranavolo A, Casali C: **Neurophysiology of gait**. *Handb Clin Neurol* 2018, **154**:299-303.
80. Grieve D: **Gait patterns and the speed of walking**. *Bio-Med Eng* 1968, **3**:119-112.

81. Goswami A: **A new gait parameterization technique by means of cyclogram moments: Application to human slope walking**. *Gait Posture* 1998, **8**(1):15-36.
82. Field-Fote EC, Tepavac D: **Improved Intralimb Coordination in People With Incomplete Spinal Cord Injury Following Training With Body Weight Support and Electrical Stimulation**. *Phys Ther* 2002, **82**(7):707-715.
83. Borghese NA, Bianchi L, Lacquaniti F: **Kinematic determinants of human locomotion**. *J Physiol* 1996, **494 (Pt 3)**(Pt 3):863-879.
84. van Emmerik RE, Wagenaar RC: **Effects of walking velocity on relative phase dynamics in the trunk in human walking**. *J Biomech* 1996, **29**(9):1175-1184.
85. Ford MP, Wagenaar RC, Newell KM: **Phase manipulation and walking in stroke**. *J Neurol Phys Ther* 2007, **31**(2):85-91.
86. Wagenaar RC, Beek WJ: **Hemiplegic gait: a kinematic analysis using walking speed as a basis**. *J Biomech* 1992, **25**(9):1007-1015.
87. Ford MP, Wagenaar RC, Newell KM: **The effects of auditory rhythms and instruction on walking patterns in individuals post stroke**. *Gait Posture* 2007, **26**(1):150-155.
88. Kwakkel G, Wagenaar RC: **Effect of Duration of Upper- and Lower-Extremity Rehabilitation Sessions and Walking Speed on Recovery of Interlimb Coordination in Hemiplegic Gait**. *Phys Ther* 2002, **82**(5):432-448.
89. Stephenson JL, Lamontagne A, De Serres SJ: **The coordination of upper and lower limb movements during gait in healthy and stroke individuals**. *Gait Posture* 2009, **29**(1):11-16.
90. Barela JA, Whitall J, Black P, Clark JE: **An examination of constraints affecting the intralimb coordination of hemiparetic gait**. *Human Movement Science* 2000, **19**(2):251-273.
91. Giannini RC, Perell KL: **Lower limb coordination during walking in subjects with post stroke hemiplegia vs. healthy control**. *Clinical Kinesiology: Journal of the American Kinesiotherapy Association* 2005, **59**:10.
92. Cleland BT, Schindler-Ivens S: **Symmetry Is Associated With Interlimb Coordination During Walking and Pedaling After Stroke**. *J Neurol Phys Ther* 2022, **46**(2):81-87.
93. Roerdink M, Lamoth CJC, Kwakkel G, van Wieringen PCW, Beek PJ: **Gait Coordination After Stroke: Benefits of Acoustically Paced Treadmill Walking**. *Phys Ther* 2007, **87**(8):1009-1022.
94. Haddad JM, van Emmerik RE, Wheat JS, Hamill J, Snapp-Childs W: **Relative phase coordination analysis in the assessment of dynamic gait symmetry**. *J Appl Biomech* 2010, **26**(1):109-113.
95. Latham NK, Jette DU, Slavin M, Richards LG, Procino A, Smout RJ, Horn SD: **Physical therapy during stroke rehabilitation for people with different walking abilities**. *Arch Phys Med Rehabil* 2005, **86**(12 Suppl 2):S41-s50.
96. Kuys SS, Brauer SG, Ada L, Russell TG: **Immediate effect of treadmill walking practice versus overground walking practice on overground walking pattern in ambulatory stroke patients: an experimental study**. *Clin Rehabil* 2008, **22**(10-11):931-939.
97. Hesse S, Konrad M, Uhlenbrock D: **Treadmill walking with partial body weight support versus floor walking in hemiparetic subjects**. *Arch Phys Med Rehabil* 1999, **80**(4):421-427.
98. Suputtitada A, Yooktanan P, Rarerng-Ying T: **Effect of partial body weight support treadmill training in chronic stroke patients**. *J Med Assoc Thai* 2004, **87 Suppl 2**:S107-111.
99. da Cunha IT, Jr., Lim PA, Qureshy H, Henson H, Monga T, Protas EJ: **Gait outcomes after acute stroke rehabilitation with supported treadmill ambulation training: a randomized controlled pilot study**. *Arch Phys Med Rehabil* 2002, **83**(9):1258-1265.
100. Nilsson L, Carlsson J, Danielsson A, Fugl-Meyer A, Hellström K, Kristensen L, Sjölund B, Sunnerhagen KS, Grimby G: **Walking training of patients with hemiparesis at an early stage after stroke: a comparison of walking training on a treadmill with body weight support and walking training on the ground**. *Clin Rehabil* 2001, **15**(5):515-527.

101. Bishnoi A, Lee R, Hu Y, Mahoney JR, Hernandez ME: **Effect of Treadmill Training Interventions on Spatiotemporal Gait Parameters in Older Adults with Neurological Disorders: Systematic Review and Meta-Analysis of Randomized Controlled Trials**. *Int J Environ Res Public Health* 2022, **19**(5).
102. Druzbicki M, Guzik A, Przysada G, Kwolek A, Brzozowska-Magon A, Sobolewski M: **Changes in Gait Symmetry After Training on a Treadmill with Biofeedback in Chronic Stroke Patients: A 6-Month Follow-Up From a Randomized Controlled Trial**. *Med Sci Monit* 2016, **22**:4859-4868.
103. Hase K, Suzuki E, Matsumoto M, Fujiwara T, Liu M: **Effects of therapeutic gait training using a prosthesis and a treadmill for ambulatory patients with hemiparesis**. *Arch Phys Med Rehabil* 2011, **92**(12):1961-1966.
104. Gama GL, de Lucena Trigueiro LC, Simao CR, de Sousa AV, de Souza ESEM, Galvao ER, Lindquist AR: **Effects of treadmill inclination on hemiparetic gait: controlled and randomized clinical trial**. *Am J Phys Med Rehabil* 2015, **94**(9):718-727.
105. Kahn JH, Hornby TG: **Rapid and long-term adaptations in gait symmetry following unilateral step training in people with hemiparesis**. *Phys Ther* 2009, **89**(5):474-483.
106. Gama GL, Celestino ML, Barela JA, Forrester L, Whitall J, Barela AM: **Effects of Gait Training With Body Weight Support on a Treadmill Versus Overground in Individuals With Stroke**. *Arch Phys Med Rehabil* 2017, **98**(4):738-745.
107. Miéville C, Lauzière S, Betschart M, Nadeau S, Duclos C: **More symmetrical gait after split-belt treadmill walking does not modify dynamic and postural balance in individuals post-stroke**. *J Electromyogr Kinesiol* 2018, **41**:41-49.
108. Lauzière S, Miéville C, Betschart M, Duclos C, Aissaoui R, Nadeau S: **A more symmetrical gait after split-belt treadmill walking increases the effort in paretic plantar flexors in people post-stroke**. *J Rehabil Med* 2016, **48**(7):576-582.
109. Malone LA, Bastian AJ: **Spatial and temporal asymmetries in gait predict split-belt adaptation behavior in stroke**. *Neurorehabil Neural Repair* 2014, **28**(3):230-240.
110. Alcântara CC, Charalambous CC, Morton SM, Russo TL, Reisman DS: **Different Error Size During Locomotor Adaptation Affects Transfer to Overground Walking Poststroke**. *Neurorehabil Neural Repair* 2018, **32**(12):1020-1030.
111. Lewek MD, Braun CH, Wutzke C, Giuliani C: **The role of movement errors in modifying spatiotemporal gait asymmetry post stroke: a randomized controlled trial**. *Clin Rehabil* 2018, **32**(2):161-172.
112. Cherry-Allen KM, Statton MA, Celnik PA, Bastian AJ: **A Dual-Learning Paradigm Simultaneously Improves Multiple Features of Gait Post-Stroke**. *Neurorehabil Neural Repair* 2018, **32**(9):810-820.
113. Hinton DC, Conradsson DM, Paquette C: **Understanding Human Neural Control of Short-term Gait Adaptation to the Split-belt Treadmill**. *Neuroscience* 2020, **451**:36-50.
114. Dzewaltowski AC, Hedrick EA, Leutzinger TJ, Remski LE, Rosen AB: **The Effect of Split-Belt Treadmill Interventions on Step Length Asymmetry in Individuals Poststroke: A Systematic Review With Meta-Analysis**. *Neurorehabil Neural Repair* 2021, **35**(7):563-575.
115. Tyrell CM, Roos MA, Rudolph KS, Reisman DS: **Influence of systematic increases in treadmill walking speed on gait kinematics after stroke**. *Phys Ther* 2011, **91**(3):392-403.
116. Chen IH, Yang YR, Chan RC, Wang RY: **Turning-based treadmill training improves turning performance and gait symmetry after stroke**. *Neurorehabil Neural Repair* 2014, **28**(1):45-55.
117. Thaut MH, McIntosh GC, Rice RR: **Rhythmic facilitation of gait training in hemiparetic stroke rehabilitation**. *J Neurol Sci* 1997, **151**(2):207-212.
118. Chen JL, Penhune VB, Zatorre RJ: **Listening to musical rhythms recruits motor regions of the brain**. *Cereb Cortex* 2008, **18**(12):2844-2854.

119. Comstock DC, Hove MJ, Balasubramaniam R: **Sensorimotor Synchronization With Auditory and Visual Modalities: Behavioral and Neural Differences**. *Front Comput Neurosci* 2018, **12**.
120. Thaut MH: **The discovery of human auditory-motor entrainment and its role in the development of neurologic music therapy**. *Prog Brain Res* 2015, **217**:253-266.
121. Ghai S, Ghai I: **Effects of (music-based) rhythmic auditory cueing training on gait and posture post-stroke: A systematic review & dose-response meta-analysis**. *Sci Rep* 2019, **9**(1):2183.
122. Yoo GE, Kim SJ: **Rhythmic Auditory Cueing in Motor Rehabilitation for Stroke Patients: Systematic Review and Meta-Analysis**. *J Music Ther* 2016, **53**(2):149-177.
123. Patterson KK, Wong JS, Knorr S, Grahn JA: **Rhythm Perception and Production Abilities and Their Relationship to Gait After Stroke**. *Arch Phys Med Rehabil* 2018, **99**(5):945-951.
124. Kim J-s, Oh D-w: **Home-Based Auditory Stimulation Training for Gait Rehabilitation of Chronic Stroke Patients**. *Journal of Physical Therapy Science* 2012, **24**(8):775-777.
125. Cha Y, Kim Y, Hwang S, Chung Y: **Intensive gait training with rhythmic auditory stimulation in individuals with chronic hemiparetic stroke: a pilot randomized controlled study**. *NeuroRehabilitation* 2014, **35**(4):681-688.
126. Schauer M, Mauritz KH: **Musical motor feedback (MMF) in walking hemiparetic stroke patients: randomized trials of gait improvement**. *Clin Rehabil* 2003, **17**(7):713-722.
127. Suh JH, Han SJ, Jeon SY, Kim HJ, Lee JE, Yoon TS, Chong HJ: **Effect of rhythmic auditory stimulation on gait and balance in hemiplegic stroke patients**. *NeuroRehabilitation* 2014, **34**(1):193-199.
128. Richards CL, Malouin F, Nadeau S: **Chapter 13 - Stroke rehabilitation: clinical picture, assessment, and therapeutic challenge**. In: *Prog Brain Res. Volume 218*, edn. Edited by Dancause N, Nadeau S, Rossignol S: Elsevier; 2015: 253-280.
129. Schmidt R: **Motor Control and Learning: A Behavioral Emphasis**, 2nd edn: Champaign, Ill: Human Kinetics Publishers; 1988.
130. Kleim JA, Jones TA: **Principles of experience-dependent neural plasticity: implications for rehabilitation after brain damage**. *J Speech Lang Hear Res* 2008, **51**(1):S225-239.
131. Young D.E, Schmidt R.A, Lee T.D: **Human Motor Learning & Human Learning**, 1st edn: International Encyclopedia of Ergonomics and Human Factors; 2001.
132. Gilmore PE, Spaulding SJ: **Motor control and motor learning: implications for treatment of individuals post stroke**. *Phys Occup Ther Geriatr* 2001, **20**(1):1-15.
133. Cirstea C, Ptito A, Levin M: **Feedback and cognition in arm motor skill reacquisition after stroke**. *Stroke* 2006, **37**(5):1237-1242.
134. Milot MH, Marchal-Crespo L, Green CS, Cramer SC, Reinkensmeyer DJ: **Comparison of error-amplification and haptic-guidance training techniques for learning of a timing-based motor task by healthy individuals**. *Exp Brain Res* 2010, **201**(2):119-131.
135. Molenberghs P, Cunnington R, Mattingley JB: **Is the mirror neuron system involved in imitation? A short review and meta-analysis**. *Neurosci Biobehav Rev* 2009, **33**(7):975-980.
136. Rizzolatti G, Fabbri-Destro M, Cattaneo L: **Mirror neurons and their clinical relevance**. *Nat Clin Pract Neurol* 2009, **5**(1):24-34.
137. Latash ML: **The bliss (not the problem) of motor abundance (not redundancy)**. *Exp Brain Res* 2012, **217**(1):1-5.
138. Shadmehr R, Mussa-Ivaldi F: **Adaptive representation of dynamics during learning of a motor task**. *The Journal of Neuroscience* 1994, **14**(5):3208-3224.
139. Dancause N, Ptito A, Levin MF: **Error correction strategies for motor behavior after unilateral brain damage: short-term motor learning processes**. *Neuropsychologia* 2002, **40**(8):1313-1323.
140. Fine MS, Thoroughman KA: **Trial-by-trial transformation of error into sensorimotor adaptation changes with environmental dynamics**. *J Neurophysiol* 2007, **98**(3):1392-1404.

141. Franklin DW, Burdet E, Tee KP, Osu R, Chew CM, Milner TE, Kawato M: **CNS learns stable, accurate, and efficient movements using a simple algorithm**. *J Neurosci* 2008, **28**(44):11165-11173.
142. Halsband U, Lange RK: **Motor learning in man: a review of functional and clinical studies**. *J Physiol Paris* 2006, **99**(4-6):414-424.
143. Thoroughman KA, Shadmehr R: **Learning of action through adaptive combination of motor primitives**. *Nature* 2000, **407**(6805):742-747.
144. Weeks DL, Aubert MP, Feldman AG, Levin MF: **One-trial adaptation of movement to changes in load**. *J Neurophysiol* 1996, **75**(1):60-74.
145. Rumelhart DE, Hinton GE, Williams RJ: **Learning representations by back-propagating errors**. *Nature* 1986, **323**(6088):533-536.
146. Liu LY, Li Y, Lamontagne A: **The effects of error-augmentation versus error-reduction paradigms in robotic therapy to enhance upper extremity performance and recovery post-stroke: a systematic review**. *J Neuroeng Rehabil* 2018, **15**(1):65.
147. Israely S, Carmeli E: **Error augmentation as a possible technique for improving upper extremity motor performance after a stroke -- a systematic review**. *Topics in Stroke Rehabilitation 2016 Apr;23(2):116-125* 2016.
148. Patton JL, Stoykov ME, Kovic M, Mussa-Ivaldi FA: **Evaluation of robotic training forces that either enhance or reduce error in chronic hemiparetic stroke survivors**. *Exp Brain Res* 2006, **168**(3):368-383.
149. Tropea P, Cesqui B, Monaco V, Aliboni S, Posteraro F, Micera S: **Effects of the alternate combination of errorenhancing and active assistive robot-mediated treatments on stroke patients**. *IEEE Journal of Translational Engineering in Health and Medicine 2013 Aug 8;1(2100109):Epub* 2013.
150. Emken JL, Benitez R, Reinkensmeyer DJ: **Human-robot cooperative movement training: learning a novel sensory motor transformation during walking with robotic assistance-as-needed**. *J Neuroeng Rehabil* 2007, **4**:8.
151. Fortin K, Blanchette A, McFadyen BJ, Bouyer LJ: **Effects of walking in a force field for varying durations on aftereffects and on next day performance**. *Exp Brain Res* 2009, **199**(2):145-155.
152. Lam T, Pauhl K, Krassioukov A, Eng JJ: **Using robot-applied resistance to augment body-weight-supported treadmill training in an individual with incomplete spinal cord injury**. *Phys Ther* 2011, **91**(1):143-151.
153. Lam T, Wirz M, Lunenburger L, Dietz V: **Swing phase resistance enhances flexor muscle activity during treadmill locomotion in incomplete spinal cord injury**. *Neurorehabil Neural Repair* 2008, **22**(5):438-446.
154. Marchal-Crespo L, Reinkensmeyer DJ: **Review of control strategies for robotic movement training after neurologic injury**. *J Neuroeng Rehabil* 2009, **6**:20.
155. Reisman DS, Wityk R, Silver K, Bastian AJ: **Locomotor adaptation on a split-belt treadmill can improve walking symmetry post-stroke**. *Brain* 2007, **130**(Pt 7):1861-1872.
156. Reisman DS, Wityk R, Silver K, Bastian AJ: **Split-belt treadmill adaptation transfers to overground walking in persons poststroke**. *Neurorehabil Neural Repair* 2009, **23**(7):735-744.
157. Cech DJ, Martin ST: **Chapter 4 - Motor Control and Motor Learning**. In: *Functional Movement Development Across the Life Span (Third Edition).* edn. Saint Louis: W.B. Saunders; 2012: 68-87.
158. Yamamoto R, Ohashi Y: **The effects of inaccessible visual feedback used concurrently or terminally**. *Journal of Physical Therapy Science* 2014, **26**(5):731-735.
159. Powers J, Wallace A, Mansfield A, Mochizuki G, Patterson KK: **The effect of frequency of feedback on overground temporal gait asymmetry post stroke**. *Top Stroke Rehabil* 2022, **29**(6):401-410.

160. Subramanian SK, Chilingaryan G, Levin MF, Subramanian SK, Chilingaryan G, Levin MF, Sveistrup H: **Influence of training environment and cognitive deficits on use of feedback for motor learning in chronic stroke**. In: *2015 International Conference on Virtual Rehabilitation (ICVR): 9-12 June 2015 2015*; 2015: 38-43.
161. Subramanian SK, Lourenço CB, Chilingaryan G, Sveistrup H, Levin MF: **Arm Motor Recovery Using a Virtual Reality Intervention in Chronic Stroke:Randomized Control Trial**. *Neurorehabil Neural Repair* 2013, **27**(1):13-23.
162. Ronsse R, Puttemans V, Coxon JP, Goble DJ, Wagemans J, Wenderoth N, Swinnen SP: **Motor Learning with Augmented Feedback: Modality-Dependent Behavioral and Neural Consequences**. *Cereb Cortex* 2010, **21**(6):1283-1294.
163. Winstein CJ, Schmidt RA: **Reduced frequency of knowledge of results enhances motor skill learning**. *J Exp Psychol Learn Mem Cogn* 1990, **16**(4):677-691.
164. Barrios JA, Crossley KM, Davis IS: **Gait retraining to reduce the knee adduction moment through real-time visual feedback of dynamic knee alignment**. *J Biomech* 2010, **43**(11):2208-2213.
165. Darter BJ, Wilken JM: **Gait training with virtual reality-based real-time feedback: improving gait performance following transfemoral amputation**. *Phys Ther* 2011, **91**(9):1385-1394.
166. Tate JJ, Milner CE: **Real-Time Kinematic, Temporospatial, and Kinetic Biofeedback During Gait Retraining in Patients: A Systematic Review**. *Phys Ther* 2010, **90**(8):1123-1134.
167. Kim JS, Oh DW: **Use of real-time visual feedback during overground walking training on gait symmetry and velocity in patients with post-stroke hemiparesis: randomized controlled, single-blind study**. *Int J Rehabil Res* 2020, **43**(3):247-254.
168. Jung J, Choi W, Lee S: **Immediate augmented real-time forefoot weight bearing using visual feedback improves gait symmetry in chronic stroke**. *Technol Health Care* 2020, **28**(6):733-741.
169. Sigrist R, Rauter G, Riener R, Wolf P: **Terminal feedback outperforms concurrent visual, auditory, and haptic feedback in learning a complex rowing-type task**. *Journal of Motor Behavior* 2013, **45**(6):455-472.
170. Freides D: **Human information processing and sensory modality: cross-modal functions, information complexity, memory, and deficit**. *Psychol Bull* 1974, **81**(5):284-310.
171. Chunduru P, Kim S-J, Lee H: **Gait symmetric adaptation: Comparing effects of implicit visual distortion versus split-belt treadmill on aftereffects of adapted step length symmetry**. *Human Movement Science* 2019, **66**:186-197.
172. Kim SJ, Krebs HI: **Effects of implicit visual feedback distortion on human gait**. *Exp Brain Res* 2012, **218**(3):495-502.
173. Secoli R, Milot MH, Rosati G, Reinkensmeyer DJ: **Effect of visual distraction and auditory feedback on patient effort during robot-assisted movement training after stroke**. *J Neuroeng Rehabil* 2011, **8**:21.
174. Sigrist R, Rauter G, Riener R, Wolf P: **Augmented visual, auditory, haptic, and multimodal feedback in motor learning: a review**. *Psychon Bull Rev* 2013, **20**(1):21-53.
175. Cha Y-J, Kim J-D, Choi Y-R, Kim N-H, Son S-M: **Effects of gait training with auditory feedback on walking and balancing ability in adults after hemiplegic stroke: a preliminary, randomized, controlled study**. *Int J Rehabil Res* 2018, **41**(3):239-243.
176. Ki KI, Kim MS, Moon Y, Choi JD: **Effects of auditory feedback during gait training on hemiplegic patients' weight bearing and dynamic balance ability**. *J Phys Ther Sci* 2015, **27**(4):1267-1269.
177. Kim J, Jung S, Song C: **The Effects of Auditory Feedback Gait Training Using Smart Insole on Stroke Patients**. *Brain Sciences* 2021, **11**(11):1377.
178. Doyle MC, Snowden RJ: **Identification of visual stimuli is improved by accompanying auditory stimuli: the role of eye movements and sound location**. *Perception* 2001, **30**(7):795-810.

179. Fort A, Delpuech C, Pernier J, Giard MH: **Dynamics of cortico-subcortical cross-modal operations involved in audio-visual object detection in humans**. *Cereb Cortex* 2002, **12**(10):1031-1039.
180. Carson RG, Kelso JA: **Governing coordination: behavioural principles and neural correlates**. *Exp Brain Res* 2004, **154**(3):267-274.
181. Stein BE, London N, Wilkinson LK, Price DD: **Enhancement of perceived visual intensity by auditory stimuli: a psychophysical analysis**. *J Cogn Neurosci* 1996, **8**(6):497-506.
182. Calvert GA, Campbell R, Brammer MJ: **Evidence from functional magnetic resonance imaging of crossmodal binding in the human heteromodal cortex**. *Curr Biol* 2000, **10**(11):649-657.
183. Grosbras MH, Beaton S, Eickhoff SB: **Brain regions involved in human movement perception: a quantitative voxel-based meta-analysis**. *Hum Brain Mapp* 2012, **33**(2):431-454.
184. Grossman E, Donnelly M, Price R, Pickens D, Morgan V, Neighbor G, Blake R: **Brain areas involved in perception of biological motion**. *J Cogn Neurosci* 2000, **12**(5):711-720.
185. Johansson G: **Visual perception of biological motion and a model for its analysis**. *Percept Psychophys* 1973, **14**:201-211.
186. Ball K, Sekuler R: **A specific and enduring improvement in visual motion discrimination**. *Science* 1982, **218**(4573):697-698.
187. De Bruyn B, Orban GA: **Human velocity and direction discrimination measured with random dot patterns**. *Vision Res* 1988, **28**(12):1323-1335.
188. Gros BL, Blake R, Hiris E: **Anisotropies in visual motion perception: a fresh look**. *J Opt Soc Am A Opt Image Sci Vis* 1998, **15**(8):2003-2011.
189. Pasternak T, Merigan WH: **Effects of stimulus speed on direction discriminations**. *Vision Res* 1984, **24**(10):1349-1355.
190. Kannape OA, Blanke O: **Self in motion: sensorimotor and cognitive mechanisms in gait agency**. *J Neurophysiol* 2013, **110**(8):1837-1847.
191. Keshner EA, Lamontagne A: **The Untapped Potential of Virtual Reality in Rehabilitation of Balance and Gait in Neurological Disorders**. *Frontiers in Virtual Reality* 2021, **2**.
192. Willaert I, Aissaoui R, Nadeau S, Duclos C, Labbe DR: **Modulating The Gait Of A Real-Time Self-Avatar To Induce Changes In Stride Length During Treadmill Walking**. In: *2020 IEEE Conference on Virtual Reality and 3D User Interfaces Abstracts and Workshops (VRW): 22-26 March 2020 2020*; 2020: 718-719.
193. Kilteni K, Groten R, Slater M: **The Sense of Embodiment in Virtual Reality**. *Presence: Teleoperators and Virtual Environments* 2012, **21**(4):373-387.
194. Steed A, Pan Y, Zisch F, Steptoe W: **The impact of a self-avatar on cognitive load in immersive virtual reality**. In: *2016 IEEE Virtual Reality (VR): 19-23 March 2016 2016*; 2016: 67-76.
195. Labbe DR, Kouakoua K, Aissaoui R, Nadeau S, Duclos C: **Proprioceptive Stimulation Added to a Walking Self-Avatar Enhances the Illusory Perception of Walking in Static Participants**. *Frontiers in Virtual Reality* 2021, **2**.
196. Nessler JA, Gilliland SJ: **Interpersonal synchronization during side by side treadmill walking is influenced by leg length differential and altered sensory feedback**. *Human movement science* 2009, **28**(6):772-785.
197. Zivotofsky AZ, Gruendlinger L, Hausdorff JM: **Modality-specific communication enabling gait synchronization during over-ground side-by-side walking**. *Hum Mov Sci* 2012, **31**(5):1268-1285.
198. Zivotofsky AZ, Hausdorff JM: **The sensory feedback mechanisms enabling couples to walk synchronously: an initial investigation**. *J Neuroeng Rehabil* 2007, **4**:28.
199. van Ulzen NR, Lamoth CJ, Daffertshofer A, Semin GR, Beek PJ: **Characteristics of instructed and uninstructed interpersonal coordination while walking side-by-side**. *Neuroscience letters* 2008, **432**(2):88-93.

200. Nessler JA, Gilliland SJ: **Kinematic analysis of side-by-side stepping with intentional and unintentional synchronization**. *Gait & posture* 2010, **31**(4):527-529.
201. Koritnik T, Koenig A, Bajd T, Riener R, Munih M: **Comparison of visual and haptic feedback during training of lower extremities**. *Gait Posture* 2010, **32**(4):540-546.
202. Booth AT, Buizer AI, Harlaar J, Steenbrink F, van der Krogt MM: **Immediate Effects of Immersive Biofeedback on Gait in Children With Cerebral Palsy**. *Arch Phys Med Rehabil* 2019, **100**(4):598-605.
203. Saygin AP, Driver J, de Sa VR: **In the footsteps of biological motion and multisensory perception: judgments of audiovisual temporal relations are enhanced for upright walkers**. *Psychol Sci* 2008, **19**(5):469-475.
204. Thomas JP, Shiffrar M: **Meaningful sounds enhance visual sensitivity to human gait regardless of synchrony**. *J Vis* 2013, **13**(14).
205. Keshner EA, Fung J: **Editorial: Current State of Postural Research - Beyond Automatic Behavior**. *Front Neurol* 2019, **10**:1160.
206. Fademrecht L, Bulthoff I, de la Rosa S: **Action recognition is viewpoint-dependent in the visual periphery**. *Vision Res* 2017, **135**:10-15.
207. Gianella MG, Gath CF, Bonamico L, Olmos LE, Russo MJ: **Prediction of Gait without Physical Assistance after Inpatient Rehabilitation in Severe Subacute Stroke Subjects**. *J Stroke Cerebrovasc Dis* 2019, **28**(11):104367.
208. Liu LY, Sangani S, Patterson KK, Fung J, Lamontagne A: **Real-Time Avatar-Based Feedback to Enhance the Symmetry of Spatiotemporal Parameters After Stroke: Instantaneous Effects of Different Avatar Views**. *IEEE Trans Neural Syst Rehabil Eng* 2020, **28**(4):878-887.
209. Subramanian SK, Feldman AG, Levin MF: **Spasticity may obscure motor learning ability after stroke**. *J Neurophysiol* 2018, **119**(1):5-20.
210. Welch RB, Warren DH: **Immediate perceptual response to intersensory discrepancy**. *Psychol Bull* 1980, **88**(3):638-667.
211. Gomez-Andres A, Grau-Sánchez J, Duarte E, Rodriguez-Fornells A, Tajadura-Jiménez A: **Enriching footsteps sounds in gait rehabilitation in chronic stroke patients: a pilot study**. *Ann N Y Acad Sci* 2020, **1467**(1):48-59.
212. Ardestani MM, Kinnaird CR, Henderson CE, Hornby TG: **Compensation or Recovery? Altered Kinetics and Neuromuscular Synergies Following High-Intensity Stepping Training Poststroke**. *Neurorehabil Neural Repair* 2019, **33**(1):47-58.
213. Schmidt RA: **Motor learning & performance: From principles to practice**. Champaign, IL, US: Human Kinetics Books; 1991.

Appendix. Consent forms

INFORMED CONSENT FORM

Interaction of visual and auditory cues to enhance locomotion in stroke survivors: a pilot study

Investigators

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Preamble

We are inviting you to participate in a research study that is aimed to understand how visual and auditory (sound) information can be used to modify the gait pattern of persons who had a stroke. In the context of this study, participants will be evaluated while walking in a virtual environment that comprises of virtual avatars. Before agreeing to participate in this project, please take time to read and carefully consider the following information.

This consent form explains the aim of this study, the procedure, advantages, risks, and inconvenience as well as the persons to contact, if necessary.

This consent form may contain words that you do not understand. We invite you to ask any questions that you deem useful to the researcher and the other members of the staff assigned to the research project and ask them to explain any work or information which is not clear to you.

Introduction:

One of the most common complaints following stroke is a reduced ability to walk safely and efficiently in the community. Locomotion in persons with stroke is characterized by a reduced walking speed, poor endurance, and an asymmetrical pattern of gait which translates by unequal steps between the two lower limbs. As current rehabilitation approaches often lead to modest improvements in gait speed and gait symmetry, there is a need to explore new intervention strategies. In this project, we will evaluate the impact of changing sensory information (vision and sound) on the gait pattern of persons with stroke. The sensory information will be provided in the form of virtual avatar(s) synced to footstep sounds. As you will be walking on a treadmill and watching the avatars a virtual environment, we will examine the changes in your gait pattern. The data collected in this project will be later used as a basis to design a novel rehabilitation intervention.

Objectives:

1. To determine the effects of auditory, visual and combined cues, presented in the form of a virtual avatar(s), on the gait pattern of persons with stroke.
2. To compare the effects of individual and combined cues on the gait pattern of persons with stroke to that of healthy participants.

Nature of my participation: My participation will consist of 2 separate sessions of 1.5 to 2 hours each, including the preparation time. The evaluation will be conducted at Jewish Rehabilitation Hospital (Laval). Ideally, the 2 sessions will take place within the same week.

The **first session** (1.5 hours) will consist of clinical tests to assess my level of motor recovery using the Chedoke McMaster Stroke Assessment, my overground walking speed over 10m (comfortable and fast walking speed) and my walking function (Functional Gait Assessment). My vision (Snellen Chart, Bells' test and Goldmann's perimetry test), audition (Weber and Rinne test) and cognitive function (Montreal Cognitive Assessment test) will also be tested to ensure that I can properly see, hear and understand the visual and auditory information during the experiment. I can wear my glasses or auditory aid, if needed, for all the tests. Thereafter I will be asked to practice walking on the self-paced treadmill with the virtual environment until I am comfortable. My comfortable and fast walking speed on the treadmill will be measured.

The **second session** (2 hours) will consist of an evaluation of my gait pattern while exposed to the changing visual and auditory information. This session will require 30 min of preparation time, and approximately 1.5 hour of evaluation.

Preparation: In order to collect your movements while walking, small reflective markers will be placed on different body parts such as hands, legs, head and trunk using a small adhesive tape. In addition, small surface electrodes (EMG) will also be positioned on the skin over my leg muscles. These electrodes record the activity of the muscles and cannot deliver any electrical current.

Evaluation: I will be evaluated while walking and watching, on a large screen located in front of the treadmill, a virtual environment comprising of avatars walking at different speeds. I will be wearing specialised glasses that allow to see the 3-D virtual environment projected on the screen. The sound will be delivered through earphones or speakers. In order to ensure safety, a body harness will be worn and attached to the ceiling that can support full body weight in case of a fall. A therapist will also remain next to me throughout the experiment. Depending on my endurance, I will be invited to walk 3 to 5 trials that last 3 to 4 minutes each. You will be provided as much time to rest as needed between the trials. At the end of the session, you will fill in the Short Feedback Questionnaire (SFQ) to address your experience in the virtual environment.

Benefits: This study does not provide you any direct benefit. However, the results from this study will be later used to design an intervention that uses virtual reality to improve locomotion in stroke survivors.

Risks and inconveniences: Risks associated with your participation in this study are minimal. A therapist will always be present to provide any assistance, as needed. You may however feel tired following the evaluation and you may also experience slight nausea or dizziness due to the virtual environment. However, these are temporary feeling and will completely subside with rest. In addition, the habituation session will further minimise the possibility of it occurring during the actual evaluation. In rare circumstances of a mild skin reactions due to the adhesive tape used to fix the reflective markers or the electrodes, a calming solution will be applied to the skin.

Access to my medical chart: If I had a stroke, I understand that some relevant information concerning my medical history may need to be collected, and for that purpose, a member of the researcher team may need to consult my medical file. Only the sections pertaining to my stroke, however, will be consulted.

Confidentiality: Any personal information collected during this study will be codified to ensure confidentiality. Only members of the research team will have access to this information. For monitoring purposes, however, research documents could be accessed by a representative of the REB of CRIR or of the Ethics Unit of the Ministry of Health and Social Services of Quebec, which adhere to a strict privacy policy. Data will be kept locked up for a duration of 5 years following project termination, after which they will be destroyed. If research findings are presented in the form of scientific presentations or publications, nothing will identify you.

Voluntary participation: You can be assured that the information that you have received about this project is accurate and complete. Your participation in this project is entirely voluntary. Your refusal to participate would in no way affect the treatment you receive in this hospital, if applicable. In addition, you may withdraw from the study at any time. If you withdraw your participation from this project, all the research data collected will be destroyed.

Responsibility clause: In accepting to participate in this study, I shall not relinquish any of my rights and I shall not liberate the researchers or their sponsors or the institutions involved from any of their legal or professional obligations.

Financial compensation: Transportation and parking costs incurred through my participation in this project will be reimbursed, up to a maximum of $30.00 per visit, upon presentation of receipts.

Resource persons: Should you have any questions or require further information regarding the study, you can contact Anouk Lamontagne (phone number 450-688-9550 ext. 531; e-mail anouk.lamontagne@mcgill.ca). If I have any questions regarding your rights and recourse concerning your participation in this study, you can contact Ms. Anik Nolet, Research Ethics Co-ordinator of the CRIR establishments: 514-527-4527 ext 2643 or by e-mail at: anolet.crir@ssss.gouv.qc.ca. You can also contact the Commissioner of complaints of the Institution.

CONSENT:

My signature indicates that I have read this document, that I understand the purpose of the research, the nature of and extent of my participation as well as the benefits and risks/inconveniences to which I will exposed to as presented in this form. I have been given the opportunity to ask questions concerning any aspects of the study and have received answers to my satisfaction.

I, the undersigned, voluntary agree to take part in this study. I can withdraw from the study anytime without prejudice of any kind. I certify that I have had sufficient time to consider my decision to participate in this study.

A signed copy of this consent form will be given to me.

Participant:__________________________ Date: __________________________

(Participant)

__________________________ Contact No.____________________

(Name)

Responsibility of the principal investigator:

I, the undersigned, _________________________________ certify that I have explained to the participant their involvement in this project, I have responded to all the questions posed to me and I have clearly indicated that the participant is free to leave the study described above at any time and have provided a signed and dated copy of this consent document to the participant.

Name and Signature of the investigator: ______________________________________

Date: ___________________________ Contact No.:____________________________

FORMULAIRE D'INFORMATION ET DE CONSENTEMENT

Interaction des indicateurs visuels et auditifs pour rehausser la locomotion chez les survivants d'un accident vasculocérébral (AVC) : un projet pilote

Chercheurs au projet:

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Préambule

Nous sollicitons votre participation à un projet de recherche visant à mieux comprendre comment l'information visuelle et auditive (sons) peut être utilisée pour modifier la démarche d'une personne ayant subi un AVC. Dans le cadre de cette étude, les participants seront évalués pendant une marche dans un environnement virtuel comprenant des avatars virtuels. Avant d'accepter de participer à ce projet de recherche, veuillez prendre le temps de comprendre et de considérer attentivement les renseignements qui suivent.

Ce formulaire de consentement vous explique le but de cette étude, les procédures, les avantages, les risques et inconvénients, de même que les personnes avec qui communiquer au besoin.

Le présent formulaire de consentement peut contenir des mots que vous ne comprenez pas. Nous vous invitons à poser toutes les questions que vous jugerez utiles au chercheur et aux autres membres du personnel affecté au projet de recherche et à leur demander de vous expliquer tout mot ou renseignement qui n'est pas clair.

Introduction:

Une des plaintes les plus fréquentes suite à un AVC est la capacité réduite de marcher de façon sécuritaire et efficiente. Les déplacements chez une personne ayant eu un AVC sont souvent caractérisés par une réduction de la vitesse de marche, une résistance amoindrie ainsi qu'une démarche asymétrique se traduisant par des pas inégaux entre les deux membres inférieurs. Les approches en réadaptation actuelles apportent peu d'amélioration à la symétrie et à la vitesse de la démarche créant ainsi un besoin d'explorer de nouvelles stratégies d'intervention. Dans ce projet, nous évaluerons l'impact d'un changement de l'information sensorielle (vision et son) sur la démarche d'une personne ayant un traumatisme crânien. L'information sensorielle sera donnée sous forme d'avatar virtuel synchronisé au son des pas. Pendant que vous marcherez sur un tapis-roulant en surveillant des avatars dans un environnement virtuel, nous examinerons les changements dans votre démarche. Les données recueillies dans ce projet serviront de base pour le développement de nouvelles interventions en réadaptation.

Objectifs:

3. Déterminer les effets des indicateurs auditifs, visuels et combinés présentés sous forme d'avatars virtuels, sur la démarche d'une personne ayant eu un AVC.
4. Déterminer les effets des indicateurs auditifs modifiés (augmentation d'asymétrie) sur la démarche d'une personne avec AVC.

Nature et durée de ma participation: Votre participation à ce projet s'effectuera sur 2 sessions individuelles d'une durée d'une heure et demie à deux heures chacune, incluant le temps de préparation. Ces évaluations se tiendront à l'Hôpital juif de réadaptation à Laval et, idéalement, se feront au cours de la même semaine.

La première session (1h30m) consistera en des tests cliniques servant à évaluer le niveau de votre récupération motrice en utilisant l'échelle d'évaluation Chedoke-McMaster, votre vitesse de marche au sol sur 10 mètres (vitesse de marche confortable et rapide), votre équilibre (ABC scale) et vos fonctions de marche (Dynamic Gait Index, 6-minutes walk test). Votre vision (Snellen Chart, Bells' test and Star Cancellation Test), votre audition (Weber and Rinne test) et vos fonctions cognitives (Montreal Cogntive Assessment test) seront également testés pour s'assurer que vous pouvez voir, entendre et comprendre les informations visuelles et auditives pendant l'expérience. Au besoin, vous pourrez porter vos lunettes ou votre appareil auditif pendant tous les tests. Par la suite, on vous demandera de vous pratiquer à marcher sur un tapis-roulant auto-rythmé dans un environnement virtuel jusqu'à ce que vous soyez à l'aise. Le tapis-roulant mesurera votre marche à des vitesses confortables et rapides.

La deuxième session (2 heures) consistera en l'évaluation de votre démarche en étant exposé à des changements d'informations visuelles et auditives. Cette session demandera 30 minutes de préparation et environ une heure et demie d'évaluation.

Préparation: Afin de capter vos mouvements pendant la marche, des marqueurs réfléchissants seront placés, à l'aide de ruban adhésif médical, sur différentes parties de votre corps tels que vos mains, vos jambes, votre tête et votre tronc.

Évaluation: Vous serez évalué pendant que vous marchez tout en regardant, sur un grand écran placé devant le tapis-roulant, un environnement virtuel comportant des avatars marchant à différentes vitesses. Vous porterez des lunettes spécialisées vous permettant de voir l'environnement virtuel en 3-D projeté sur l'écran. Le son proviendra d'écouteurs ou de haut-parleurs. Pour assurer votre sécurité, vous porterez un harnais attaché au plafond et capable de supporter le poids du corps en cas de chute. Un(e) thérapeute sera à vos côtés pendant toute l'expérience. Selon votre endurance, vous ferez de 6 à 8 essais de marche d'une durée de 2 minutes et demie chacun. Vous aurez le temps requis de repos entre chaque essai. À la fin de la session, vous devrez compléter un court questionnaire (Short Feedback Questionnaire (SFQ) relatant votre expérience de l'environnement virtuel.

Bénéfices: Vous ne retirerez aucun bénéfice direct de votre participation à cette étude. Toutefois les résultats de cette étude donneront des informations pouvant aider au développement d'interventions se servant de la réalité virtuelle pour améliorer la locomotion des survivants d'AVC.

Risques et inconvénients: Les risques reliés à votre participation à cette étude sont minimes. Pendant l'évaluation, un(e) thérapeute sera toujours présent(e) pour vous assister au besoin. Vous pourriez cependant ressentir de la fatigue suite à l'évaluation et aussi avoir de légères nausées ou étourdissements causés par le visionnement des images. Ces sensations sont temporaires et se résorberont avec un peu de repos. De plus, la session d'adaptation minimisera la possibilité que cela se produise pendant l'évaluation. Dans de rares cas, une irritation de la peau peut se produire causée par le ruban adhésif utilisé pour fixer les marqueurs réfléchissants ou les électrodes. Une lotion calmante sera alors appliquée sur la peau.

Accès à mon dossier médical: Ayant été victime d'un AVC, je comprends que des informations sur mon état de santé devront être recueillies et que, à cette fin, un membre de l'équipe de recherche pourrait consulter mon dossier médical. Dans ce cas, seules les sections concernant mon AVC seront consultées.

Confidentialité: Les renseignements personnels recueillis au cours de cette étude, seront codifiés pour en assurer la confidentialité. Seul les membres de l'équipe de recherche auront accès à l'information. Cependant, à des fins de contrôle, les documents de recherche pourraient être consultés par une personne mandatée par le comité d'éthique de la recherche des établissements du CRIR (Centre de recherche interdisciplinaire en réadaptation du Montréal métropolitain) ou par l'Unité d'éthique du Ministère de la Santé et des services sociaux du Québec. Ces personnes adhèrent à des politiques strictes de confidentialité. Les données de recherche seront conservées sous clé au Centre de recherche de l'HJR pour une période de cinq (5) ans suivant la fin de l'étude après quoi elles seront détruites. Les données du projet ne seront dévoilées que sous forme de présentations scientifiques ou de publications, sans que votre nom ou toute autre information pouvant révéler votre identité n'y apparaisse.

Participation volontaire et retrait de l'étude: Nous vous assurons que l'information que vous avez reçu à propos de cette étude est exacte et complète. Votre participation à cette étude est volontaire. Votre refus de participer n'aura aucun effet sur les traitements que vous recevez dans cet hôpital. De plus, vous pouvez vous retirer en tout temps, sans avoir à donner de raisons, en faisant connaître votre décision à un membre de l'équipe de recherche. Advenant votre retrait de l'étude et si vous en faites la demande, toutes les données vous concernant seront détruites.

Clause de responsabilité: En acceptant de participer à cette étude, vous ne renoncez à aucun de vos droits ni ne libérez les chercheurs, le commanditaire ou les institutions impliquées de leurs obligations légales et professionnelles envers vous.

Indemnité compensatoire Aucune compensation financière ne vous sera offerte pour votre participation à cette étude. Des frais de déplacement encourus pour votre participation vous seront remboursés jusqu'à concurrence de $30.00 par visite, sur présentation de reçus.

Personnes ressources: Si vous avez des questions concernant le projet de recherche, si vous souhaitez vous retirer de l'étude ou si vous voulez faire part à l'équipe de recherche d'un incident, vous pouvez contacter Anouk Lamontagne (numéro de téléphone 450-688-9550 poste

531; courriel anouk.lamontagne@mcgill.ca). Si vous avez des questions sur vos droits et recours ou sur votre participation à ce projet de recherche, vous pouvez communiquer avec Mme. Mariama Touré, coordonnatrice à l'éthique de la recherche des établissements du CÉR au (514) 527-9565 poste 3789 ou par courriel à l'adresse suivante: mariama.toure.ccsmtl@ssss.gouv.qc.ca. Vous pouvez également contacter Mme. Hélène Bousquet, commissaire aux plaintes et à la qualité des services de l'HJR au (450) 668-1010 poste 23628.

CONSENTEMENT:

Je déclare avoir lu et compris le présent projet, la nature et l'ampleur de ma participation, ainsi que les risques auxquels je m'expose tels que présentés dans le présent formulaire. J'ai eu l'occasion de poser toutes les questions concernant les différents aspects de l'étude et de recevoir des réponses à ma satisfaction.

Je, soussigné(e), accepte volontairement de participer à cette étude. Je peux me retirer en tout temps sans préjudice d'aucune sorte. Je certifie qu'on m'a laissé le temps voulu pour prendre ma décision.

Une copie signée de ce formulaire d'information et de consentement doit m'être remise.

Participant: ______________________________ Date: _________________________

(Signature)

______________________________ Téléphone. ____________________

(Nom)

ENGAGEMENT DU CHERCHEUR:

Je, soussigné(e) ___________________________________, certifie :

a) avoir expliqué au signataire les termes du présent formulaire;

b) avoir répondu aux questions qu'il m'a posées à cet égard;

c) lui avoir clairement indiqué qu'il reste, à tout moment, libre de mettre un terme à sa participation au projet de recherche décrit ci-dessus; et

d) confirmé que je lui remettrai une copie signée et datée du présent formulaire.

Nom et signature du chercheur: ____

Date:____________________________Téléphone:_______________________