STU#: **STU00219151**

PROTOCOL TITLE: Movement Amplification Training to Enhance Walking Balance Post-Stroke

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VERSION DATE:
April 29, 2024

STUDY SUMMARY:

Investigational Agent(s) (Drugs or Devices)	Agility Trainer
IND / IDE / HDE #	Abbreviated IDE
Indicate Special Population(s)	☐ Children ☐ Children who are wards of the state ☐ Adults Unable to Consent ☐ Cognitively Impaired Adults ☐ Neonates of Uncertain Viability ☐ Pregnant Women ☐ Prisoners (or other detained/paroled individuals) ☐ Students/Employees
Sample Size	10
Funding Source	National Institute of Child Health & Human Development 1R21HD112813-01
Indicate the type of consent to be obtained	☒ Written ☐ Verbal/Waiver of Documentation of Informed Consent ☐ Waiver of HIPAA Authorization ☐ Waiver/Alteration of Consent Process
Site	☐ Lead Site (For A Multiple Site Research Study) ☐ Data Coordinating Center (DCC)
Research Related Radiation Exposure	☐ Yes ☒ No
DSMB / DMC / IDMC	☐ Yes ☒ No

STU#: **STU00219151**

FEDERAL FUNDING:

Funding Agency:	National Institute of Child Health & Human Development	
Sponsored Research ID#:	1R21HD112813-01	
Does the grant indicate that covered activities will include Human Research? (Yes / No / Unknown)	Yes	
	Institution Name: Northwestern University	Human Research Assessment *** (e.g., Non-Exempt Human Research, Exempt Human Research, Not Human Research, etc.) Non-Exempt Human Research
Prime Award Recipient*	Northwestern University (single site)	
Sub-Award Recipients**	None	

OBJECTIVES:

Balance is a strong, modifiable predictor of physical activity level among people with chronic stroke (PwCS)[1, 2]. Most PwCS exhibit significant balance deficits that contribute to a multitude of gait impairments[3, 4] and alarmingly low levels of physical activity including walking[5-9]. Given the strong association between balance and functional independence[10, 11], there is broad recognition that rehabilitation interventions should directly target walking balance[5, 12]. Current clinical practice guidelines for PwCS recommend high-intensity gait training to improve walking ability[13]. While this form of training has been shown to improve balance in PwCS[14, 15], the clinical significance of these improvements have been small[16-18]. We believe that improvements in walking balance with high-intensity gait training can be substantially enhanced by including supplemental training elements that directly challenge walking balance, augment balance-related feedback, and encourage exploration of new movement strategies. **To address the urgent need to improve walking balance in PwCS, we have developed a simple robotic tool to create and incorporate balance-challenging training elements into high-intensity gait training interventions.**

Our goal is to develop more effective interventions to help PwCS improve walking balance. We will evaluate if high-intensity gait training performed in a novel, balance-challenging environment can **encourage PwCS to practice walking patterns that enhance walking balance**. Specifically, we will use a custom-built, cable-driven robot to apply forces to the pelvis during treadmill walking. These forces will amplify the lateral velocity of a person's own movements[19, 20], increasing the difficulty to maintain lateral balance and a straight walking trajectory. This task-specific ***Movement Amplification Environment (MAE)*** may accelerate learning by augmenting sensorimotor feedback[21, 22], and encouraging motor exploration[22]. Preliminary outcomes from our ongoing clinical trial suggest that people with incomplete spinal cord injury (iSCI) make substantial improvements in walking balance following gait training performed in a MAE. We believe that this intervention will also be effective for improving walking balance in PwCS. Our

central hypothesis is that **gait training in a MAE will induce locomotor adaptations that enhance walking balance in PwCS.** Our purpose is to evaluate if PwCS improve walking balance following a high-intensity gait training intervention performed in a MAE.

Gait Training in a MAE. *To evaluate pre- to post- changes in walking balance in PwCS following high-intensity gait training performed in a MAE.*
Hypothesis: *PwCS will exhibit significant improvements in walking balance following gait training in a MAE.*

PwCS will participate in a 10-session gait training intervention performed in a MAE. We will evaluate changes in gait kinematics, clinical outcome measures, and daily walking activity (steps/day). Outcomes from this Aim are necessary to understand if PwCS make long-term adaptations in walking balance in response to gait training in a MAE.

This project will explore if and how PwCS adapt to gait training in a MAE and evaluate changes in walking balance. Promising findings will motivate a future randomized controlled trial assessing the efficacy of MAE training to enhance walking balance in PwCS.

BACKGROUND:

Stroke is the second leading cause of long-term disability worldwide[23]. For PwCS, physical inactivity is the strongest independent predictor of recurrent stroke and cardiovascular disease[24, 25]. Of great concern, ambulatory people with chronic stroke (PwCS) are more sedentary than adults without stroke [26, 27] and do not meet the American Heart Association (AHA) recommendations for daily steps or time engaged in moderate to vigorous physical activity[6, 28]. Despite known benefits of physical activity on cardiovascular disease risk factors[29-32], recurrent stroke and cardiovascular disease remain the leading causes of mortality among people with stroke[33]. Thus, reducing sedentary behavior and increasing physical activity are critical for management of cardio-cerebral and cardiovascular disease risk in PwCS[34].

The majority of PwCS have balance and gait dysfunctions, which are barriers for engaging in physical activity[3, 4, 35, 36]. There is a strong association between balance and physical activity in PwCS (people with the worst balance are the least active)[5]. To this end, the AHA recommends PwCS actively engage in balance and coordination training 2-3 times/week to improve functional mobility[36]. However, current recommended gait training interventions for PwCS have resulted in only limited improvement in walking balance [16, 37, 38]. With 80% of community dwelling PwCS experiencing gait and balance deficits[3, 4], there is a pressing need to improve walking balance in this population. Thus, our long-term goal is to develop effective interventions to improve walking balance in PwCS that will facilitate physical activity.

Innovation

Our innovative approach to training walking balance is built on a motor learning framework that has been shown to accelerate skill acquisition in PwCS[39]. The framework suggests that interventions that amplify self-generated movements (e.g., error augmentation or movement amplification) will enhance sensorimotor feedback[40] and facilitate motor exploration[41], which will ultimately accelerate motor learning[21, 22]. While movement amplification approaches have shown promise for retraining control of reaching movements in impaired populations[22, 39], the use of this approach to improve walking balance in PwCS has not been examined. Our central hypothesis is that gait training performed in a Movement Amplification Environment (MAE) will be beneficial for retraining walking balance in PwCS. To test this hypothesis, we will use a cable-driven robot to apply smooth continuous forces to a participant's pelvis during walking (Figure 1). These variable forces are dependent on a user's own movements and are proportional in magnitude and direction as their real-time lateral velocity[19, 20]. Since the applied forces are dependent on a person's motion, the nervous system can build a predictive model to plan walking movements in a manner that anticipates the applied forces[42]. This method of applying forces to improve balance is very different than popular forms of "perturbation" training that use unpredictable forces to disrupt balance with the goal to improve reactive balance control[43, 44]. In contrast, balance training in a MAE will target anticipatory balance control, an area of balance training that is less frequently addressed using robotic interventions.



Figure 1. The Agility Trainer, a state-of-the-art cable-driven robot designed to apply lateral forces (cables highlighted in red) to the pelvis that challenge walking balance.

The resulting effect of the MAE is to increase the real-time velocity of a person's own lateral (side-to-side) movements[19]. This lateral velocity amplification has an inherent benefit for training walking balance: the MAE increases the difficulty of maintaining a straight walking path which creates a task-specific balance-challenging training paradigm. We focus on medio-lateral motion because the requirements of the nervous system to successfully control lateral balance during walking are believed to be considerable in comparison to sagittal plane balance, which benefit from stabilizing body segment mechanics[45-47]. The challenges of controlling lateral walking balance are particularly relevant to PwCS. PwCS have significant deficits in lateral walking balance due to altered pelvic alignment[48], poor trunk control[49] and asymmetric mediolateral foot placement[50, 51]. In PwCS, lateral balance deficits increase fall risk when weight is shifted laterally onto the paretic limb[52-54]. Thus, we directly challenge lateral balance to maximize nervous system engagement and to provide task specific training. In addition, we will also evaluate improvements in walking balance by quantifying the ability of PwCS to control lateral motion during walking.

The MAE is similar in principle to error augmentation methods that have been shown to enhance experience-based learning of reaching[41], leg swing trajectories[39], and walking symmetry[55]. The consistent amplification of movement may accelerate motor learning by augmenting sensorimotor feedback making it easier for the nervous system to detect small movement errors and to learn the mapping between a given motor command and the resulting motion[56]. In addition, movement amplification may aid in the acquisition of new motor patterns by encouraging movement exploration and providing experience with a greater range of movement velocities than during movement in a natural environment[22]. **Training walking balance of PwCS by amplifying a person's self-generated movements is a radical departure from current practice and could create effective new clinical interventions.** This project will expand our knowledge of how PwCS adapt to movement amplification training. Successful outcomes will motivate a future randomized controlled trial, the next step to understanding efficacy of movement amplification training to improve walking balance in PwCS.

Preliminary Data

Our purpose is to explore if gait training performed in a MAE can improve walking balance in PwCS. Our preliminary data demonstrate that: 1) we can successfully create a MAE, 2) we can quantify walking balance, 3) people with and without neurologic injury adapt their gait in response to a MAE, and 4) gait training in a MAE could improve walking balance of people with neurologic injury.

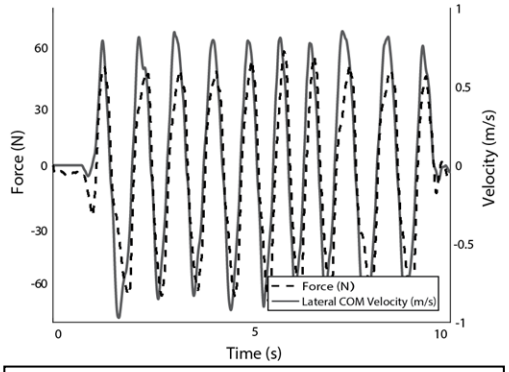


Figure 2. Movement Amplification Validation. Solid line: simulated lateral COM velocity (m/s) produced by a servo motor to simulate walking (frequency: 1 Hz, amplitude: 10 cm). Dashed line: Net force (N) created by the Agility Trainer. The MAE gain was 55 Nsm^{-1}, the peak gain in the proposed study. The Agility Trainer can successfully create continuous forces proportional to real-time lateral velocity.

Validation of Agility Trainer to Produce a Movement Amplification Environment. To assess the Agility Trainer's (Figure 1) performance capabilities and quantify its ability to create a MAE, we conducted a system identification test and an experimental simulation of human walking[19]. For these tests, the Agility Trainer was connected to an external servomotor (Kollmorgen, USA) used to simulate the lateral motion of a person's center of mass (COM) during walking. The force bandwidth of our system was ~4 Hz. Since human walking occurs almost entirely within this bandwidth, this performance exceeds the requirements for our purpose. In addition, the MAE forces produced by the Agility Trainer were qualitatively similar to the simulated COM movement velocity (Figure 2) demonstrating that the **Agility Trainer can produce the desired MAE during walking**.

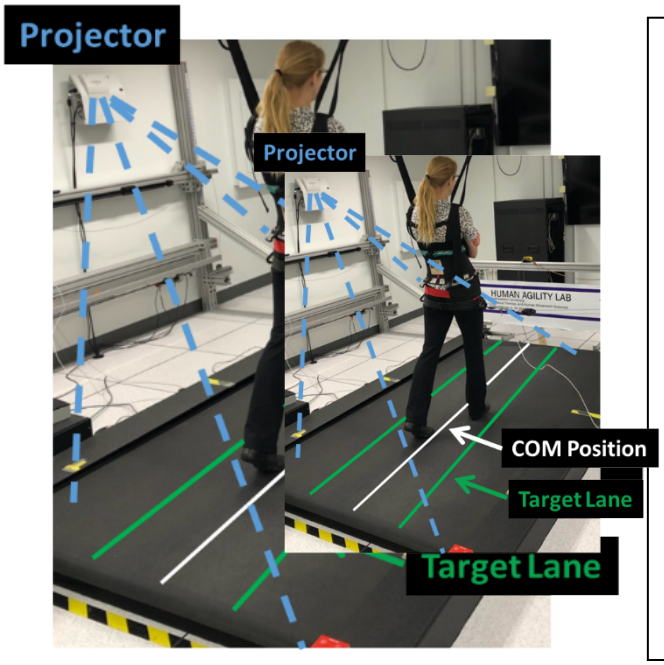


Figure 3. Assessment of COM Control. Real-time lateral COM position is projected on the treadmill. The participant is instructed to maintain their COM within a target lane. If successful, the target lane width is progressively decreased.

Method to Assess Control of Lateral COM Motion during Walking. There is no current standard for quantitatively assessing walking balance in PwCS. As discussed in the Innovation Section, the ability to control lateral COM motion during walking is fundamental for walking balance in PwCS. As such, we have developed a method to quantify the capacity to control lateral COM motion during treadmill walking. Specifically, participants will perform three 21-meter walking trials at their preferred speed without external assistance. During walking, real-time lateral COM position and a target lane are projected on the treadmill surface (Figure 3). Participants are instructed to keep their COM projection within the lane. If successful, an automated control algorithm progressively reduces (or increases if unsuccessful) the lane width. The visual feedback challenges each participant's maximum capacity to control their lateral COM motion. To quantify control of lateral COM motion, we use motion capture data to calculate lateral COM excursion and then identify the minimum average lateral COM excursion occurring during five consecutive gait cycles.

To evaluate if the ability to control lateral COM motion during gait is predictive of balance in a population with neurologic injury, we collected data from 18 ambulatory people with iSCI. Results from a correlation analysis (Pearson or Spearman depending on data normality) found that the minimum lateral COM excursion was significantly ($p<0.05$) and strongly correlated with clinical balance measures: Berg Balance Scale ($r=-0.75$), Timed Up and Go ($r=0.65$), 10 Meter Walk ($r=-0.73$), and Functional Gait Assessment ($r=-0.66$). **We therefore have a quantitative method to assess control of lateral COM motion during walking that has concurrent validity with clinical balance measures.**

Gait Adaptation in a MAE. Quantification of walking in the MAE was initially assessed in people with no known neurologic impairment, where the effects of the MAE could be isolated from impairment[20]. Fifteen people with no known neurologic impairment walked for 10-min at their preferred speed in three different external environments (Baseline: no applied force, Moderate MAE gain: 45 Nsm^{-1}, or High MAE gain: 55 Nsm^{-1}). Following 10-min of practice, participants adapted their steady-state walking patterns in response to the challenge of controlling their lateral COM motion in the MAE. We found that as the challenge of the external environment increased from Baseline to High MAE gain, participants were significantly less stable (short-term local divergence exponent calculated from lateral COM velocity), reduced their peak lateral COM velocity (least in the High MAE gain), increased their step width and step width variability, and increased their metabolic cost of transport (greatest in the High MAE gain). We replicated these major findings in a follow up study of twelve people with no known neurologic impairment and twelve people with iSCI[57]. During straight treadmill walking, at varying speeds, we found that both populations were significantly less stable, had a smaller lateral COM excursion, and took wider, more variable steps when walking in the MAE then Baseline walking. These findings suggest that people with neurologic injury adapt to control lateral COM motion when walking in a MAE.

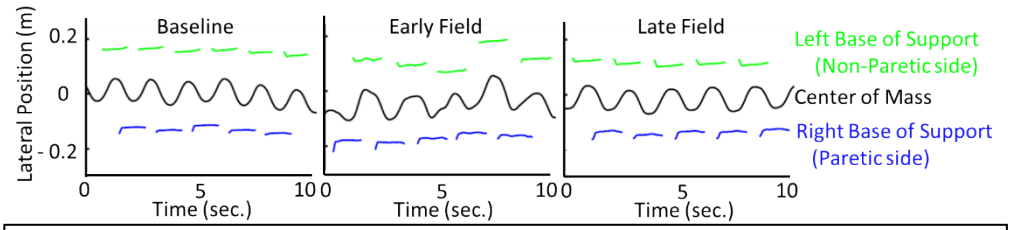


Figure 4. Representative participant with chronic stroke walking in the MAE. Lateral COM motion and base of support (5th metatarsal) during stance phase are shown for walking during Baseline (no applied forces), Early Field (minute 1) and Late Field (minute 10) in the MAE. The MAE disturbed lateral motion in the Early Field. With practice PwCS adapted to control their walking motion in the Late Field.

To examine if PwCS similarly adapt their gait to control lateral COM motion when walking in a MAE, we collected data from three PwCS (60.7 ± 11.3 years of age). Participants walked for 10-min in a MAE that was preceded and followed by 2-min of walking with no forces applied. Although challenged initially, all participants were able to successfully walk in the MAE. During the first 2-min of walking in the MAE (Early Field) participants' lateral COM excursion was 9% greater than Baseline and participants were observably challenged to control their walking direction. During the last 2-min of walking in the MAE (Late Field) participants' lateral COM excursion was 9% smaller than Baseline (Figure 4) and participants demonstrated an ability to control their walking in the MAE.

Collectively, these findings indicate that a MAE challenges walking balance, and that the challenge increases with MAE gain. Of importance, when walking in the MAE people with and without neurologic injury select gait patterns that stressed control of lateral motion as indicated by decreases in lateral COM velocity and excursion. Control of lateral COM was likely achieved by modifying step-to-step foot placement. The effort required to maintain lateral COM control also scales with MAE gain. Our preliminary data suggest that **PwCS will adapt their gait to control their lateral COM motion in a MAE**.

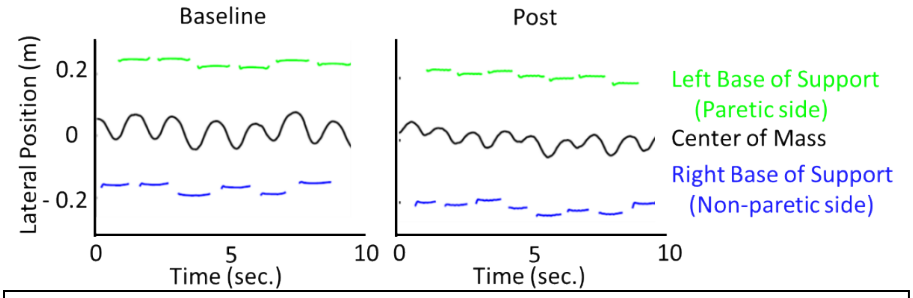


Figure 5. Representative participant with chronic stroke before and after walking in the MAE. Lateral COM motion and base of support (5th metatarsal) during stance phase are shown for walking with no external forces applied before (Baseline), and after (Post) 10 minutes of walking in the MAE. Lateral COM excursion decreased after the MAE was removed.

Short- and Long-Term Improvements in Walking Balance following MAE Training: To evaluate if walking behaviors practiced in a MAE persist when the MAE is removed, we evaluated lateral COM excursion in PwCS during treadmill walking with no external forces applied before (Baseline) and after (Post) 10-min of walking in a MAE. When the MAE was removed, we observed a substantial and significant 28% decrease in lateral COM excursion compared to baseline ($p<0.05$) (Figure 5). This rapid adaptation suggests **PwCS changed their walking patterns in response to the MAE in a manner that improved control of lateral COM motion**.

To evaluate long-term adaptations to MAE training, eight ambulatory people with iSCI received 20 high-intensity gait training sessions performed in a MAE. Comparison of pre- and post-training clinical outcome measures found significant improvements in balance (Timed Up and Go was 5.2±6.1 seconds faster, Berg Balance Scale score increased by 2.4±1.5). In addition, participants significantly reduced their lateral COM excursion by 23% during unassisted walking ($p<0.05$). Our findings indicate that people with iSCI significantly improved walking balance after gait training performed in a MAE. This data suggests that **gait training in a MAE is feasible for populations with neurologic injury** and strongly motivates the current proposal to explore the effects of gait training in a MAE on walking balance in PwCS**.**

STUDY ENDPOINTS:

The primary study endpoint will be when 10 participants have completed training intervention and post-training testing. The primary outcome measures will be changes in walking balance assessed using gait kinematics and changes in daily stepping measures by number of steps per day. Secondary outcome measures will include clinical outcome measures to assess changes in walking function, balance, balance confidence and walking endurance.

Participants can stop testing and study involvement at any time during either session. Any adverse events will be monitored and appropriately reported. Medical attention will be sought immediately for any injuries. Safety endpoints will include cardiovascular dysfunction (e.g., heart attack, severe or unusual shortness of breath, serious arrhythmias) and musculoskeletal injury that will limit the ability to continue participation in walking activities (e.g., bony fracture).

STUDY INTERVENTION(S) / INVESTIGATIONAL AGENT(S):
The Agility Trainer is powered by a set of moving coil brushless linear servomotors (Baldor, DC brushless linear motor: NB0124A01 controlled by a Baldor Linear Drive: FDH1A02TB-EN20) that travel along a linear magnetic rail positioned at the front of the treadmill. Each linear motor has a mass is 0.32 kg and has a peak and continuous force capability of 173 and 58 N respectively. The position of the moving coils will be measured using a linear optical encoder with one read head (Renishaw, RGH41) per coil at a resolution of 20 nanometer. The encoder read heads are capable of measurements up to 12 m/s. A steel cable attached to each motor is routed through a series of cables that connect a low friction trolley (able to move forward and backward along each side rail) to a pulley mounted on that lateral aspect of a pelvic harness worn by the participant. Any slack in the cable is removed by a winch prior to use. Thus, each individual motor can only apply a laterally directed force to the participant during walking. By coordinating the movements of the two motors the participant can be made to experience forces applied to their pelvis that pull them either to the right or left. Modulation of these forces based on the participants' movement can replicate virtual environments that feel like a set of springs that resist lateral motion (movement dampening) or small forces that amplify lateral movements (like a small dog pulling on a leash).

Our custom designed cable driven robotic device, Agility Trainer is developed in-house to apply highly controlled, lateral forces to people during walking. The Agility Trainer is composed of two independent series elastic actuators (SEAs) that apply forces bilaterally to a harness, donned by the participant, via a cable transmission system. The Trainer is anchored around an oversized treadmill (Tuff Tread, USA, belt width 1.39 m x length 2.65 m) that allows participants space to safely perform lateral and fore-aft maneuvers. The cables of the robotic Trainer are externally applied to participants pelvic harness to challenge participants walking balance. Thus, this device poses no threat or risk to the participant and does not help in sustaining life or used for diagnosing or curing a disease.

PROCEDURES INVOLVED:
Our objective is to evaluate if PwCS improve walking balance and increase walking in their home and community following high-intensity gait training performed in a MAE. We hypothesize that post-training, PwCS will improve clinical measures of gait and balance and increase participation in daily walking activities (steps/day). Our goal is to understand if and how PwCS adapt to a multi-session gait training intervention performed in a MAE. Participants will receive high intensity locomotor training performed on a treadmill in a movement amplification environment created by the Agility Trainer.

Participants will make 12 laboratory visits over 7 weeks period. Assessment will occur during visits #1 and #12. Gait training will occur during visits #2 through #11. A 1-week period will separate assessments from gait training visits.

Telephone screening: During the telephone screening, our researchers will provide participants all the details of our study and ask them specific questions about their health and functional status to determine their eligibility. Based on participants responses, if the participant qualifies for the study, then we will send out a medical clearance form to get their physicians approval. Obtaining medical clearance is necessary before beginning the training intervention to ensure participant safety.

Baseline in-person Screening and Assessment
A licensed physical therapist will consent participants followed by collecting their demographic information. This will be followed by in-person screening to ensure that the participant meets the

study inclusion/exclusion criteria. Participants will be asked questions about their age to ensure they are within 18-85 years and medical history to confirm incidence of stroke more than 6 months ago. Participants will be asked if they are currently participating in any other research studies or undergoing physical therapy for improving walking. Participants will then be screened for cognitive impairments using Montreal Cognitive Assessment (MoCA) which involves questions related to different aspects of memory, thinking and other cognitive functions. Participants will also be screened for speech deficits or aphasia using Mississippi Aphasia Screening Test (MAST) which involves questions related to different aspects of language skills. Muscle tone assessment will be performed to rule out excessive spasticity more than 3 on the Modified Ashworth Scale. If participants pass these screening tests and meet all inclusion criteria, then further information will be collected. These screening tests are performed only during visit 1 to determine and confirm participants eligibility for the study.

We will ask questions about participants' current medications, the use of assistive devices, and falls. We will also collect data using performance-based and self-report measures that span each level of the International Classification of Function, Disability, and Health (body structure and function, activity, and participation).

- **Clinical Outcome Measures**: We will administer a 10-meter walk test (10MWT)[58], Timed Up and Go (TUG)[59], Berg Balance Scale (BBS)[60], Activities-specific Balance Confidence (ABC) Scale[61], Dynamic Gait Index (DGI)[62] and 6-minute walk test[63]. Participants' level of stroke impairment in leg and foot (Chedoke-McMaster Stroke Assessment) will be collected to provide a baseline status.
- **Biomechanical Assessments**: We will collect kinematic data during 2-min of normal walking (no applied forces) at the participant's preferred treadmill walking speed. Next, we will assess participant's maximum ability to control their lateral COM motion during treadmill walking with no forces applied to their body. For the COM control assessments participants will perform three 21-meter walking trials on the treadmill (Figure 3). During the assessment, visual projections on the treadmill will provide feedback used to challenge each participant to maximally control their lateral COM motion. Thus, participants' ability to control their lateral COM motion during forward walking will be calculated.
- **Daily Stepping**: The average number of steps taken per day will be measured using a StepWatch4 (Modus, Edmonds, WA) activity monitor worn on the ankle. We will measure steps/day for two 1-week periods that occur between the pre-training assessment visit and the first gait training session, and between the last gait training session and the post-training assessment visit. During each assessment period, participants will be asked to wear the activity monitor during all waking hours (except bathing) for seven continuous days.

All the clinical outcome measures, biomechanical assessments and Chedoke-McMaster Stroke Assessment for leg and foot will be performed at visit 1 and visit 12. Participant will be given activity monitor on visit 1 and one week of daily stepping data will be downloaded at visit 2. Similarly, post-training the participant will be given activity monitor on visit 11 and one week of daily stepping data will be downloaded at visit 12. The table below lists the outcomes collected during visit 1 and visit 12 and provides information about when the step watch is given, and data is downloaded. The assessment performed before and after training at visit 1 and visit 12 will take about 2.5 hours.

Visit 1	Visit 2	Visit 11	Visit 12
Clinical Outcome Measures: -10-meter walk test (10MWT) -Timed Up and Go (TUG) -Berg Balance Scale (BBS) -Activities-specific Balance Confidence (ABC) Scale -Dynamic Gait Index (DGI) -6-minute walk test -Chedoke-McMaster Stroke Assessment			Clinical Outcome Measures: -10-meter walk test (10MWT) -Timed Up and Go (TUG) -Berg Balance Scale (BBS) -Activities-specific Balance Confidence (ABC) Scale -Dynamic Gait Index (DGI) -6-minute walk test -Chedoke-McMaster Stroke Assessment
Biomechanical Assessments			Biomechanical Assessments
Activity monitor is given to the participant for one week monitoring	Activity monitor data downloaded	Activity monitor is given to the participant for one week monitoring	Activity monitor data downloaded

Gait Training Intervention
Participants medical clearance will be obtained from their physician after the consent form has been signed and before beginning with gait training intervention to ensure participant safety.

Each participant will engage in ten 45-min high-intensity gait training sessions performed in a MAE. Training sessions will occur 2x/week. All training will be led by a licensed Physical Therapist. The goal of each training session is to achieve 40-min of stepping practice within a targeted range of heart rate (HR) and perceived excursion (RPE). Each session will begin and end with a 2.5-min warm-up and cool down, respectively. The remaining 40-min will include two 10-min Speed-training blocks (interval training designed to attain the highest possible speed while maintaining target HR and RPE), and two 10-min Balance-training blocks (variable training designed to maximize repetitions of forward walking while introducing balance challenges). Balance training activities will include lateral maneuvers, head turns, obstacle negotiation, and backward walking. All training will be performed in the MAE. The MAE gain, training speeds and balance activities will be progressively increased within and across sessions to challenge the participant. Participants' HR and RPE (6-20 Borg scale)[64] will be monitored to determine if exercise should be stopped to minimize cardiovascular risks. Intensity of training will be individually tailored to a target HR of 70 to 80% of estimated age-predicted HR max. HR max is calculated as (208 – (0.7 x age)). For participants on anti-hypertensive beta blocker medications, who demonstrate a blunted HR response to exercise and are not able to achieve the target HR, a target RPE of 15 "hard" to 17 "very hard" will be used as a secondary measure of intensity.

Each training session including the 45 minutes of training and 15 minutes of preparation time will take about one hour in total.

DATA AND SPECIMEN BANKING

De-identified data will be banked. No biological specimens will be collected or banked.

SHARING RESULTS WITH PARTICIPANTS

Results of this study will not be shared with participants or others without the explicit written consent of the participant. If requested, our research physical therapist can share clinical outcome measures with the participant after their session.

STUDY TIMELINES

The proposed project will take one year to complete. We will begin recruiting and enroll participants. We will have 2-3 participants involved in the training interventions at a time. We will time study enrollments to limit disruptions during high travel/vacation periods (winter holidays). We will stagger start times in the intervention, so data collection periods and step tracking periods are spread out.

Individual participation

Each participant's timeline will vary slightly depending on their training session schedule, but in total, will last approximately 7-8 weeks.

INCLUSION AND EXCLUSION CRITERIA

The research physical therapist will perform an initial phone screen for inclusion and exclusion criteria. The phone screen will be followed up with an in-person screening performed by the research physical therapist during the study participant's first visit to the laboratory. The inclusion and exclusion criteria are as follows:

Inclusion criteria: a) age 18 to 85 years; b) medically stable with medical clearance from physician to participate; c) diagnosis of hemiparetic stroke; d) more than 6 months post-stroke; e) ability to ambulatory 10 m with no physical assistance, use of assistive devices, such as a single cane, rolling walker and use of braces that do not cross the knee joint, such as an ankle-foot orthosis, are permitted.

Exclusion criteria: a) Brainstem and/or cerebellar lesion; b) Perinatal stroke; c) Cognitive impairment (score of ≤22/30 on the Montreal Cognitive Assessment scale)[65]; d) aphasia (score of ≥71/100 on the Mississippi Aphasia Screening Test)[66]; e) excessive spasticity in lower limbs (score of > 3 on the Modified Ashworth Scale)[67]; f) unable to tolerate 10-min. of standing; g) enrollment in concurrent physical therapy; h) use of braces/orthotics crossing the knee joint; i) known pregnancy; j) severe cardiovascular, musculoskeletal, or concomitant central or peripheral neurological injury (i.e. traumatic head injury or peripheral nerve damage in lower limbs) affecting gait and balance and k) presence of unhealed decubiti or other skin compromise.

VULNERABLE POPULATIONS

This study will not include individuals under 18 years of age, prisoners, or vulnerable populations. Women of childbearing potential will not be excluded, although women who are pregnant will be excluded because of pregnancy-related body changes on balance.

PARTICIPANT POPULATION(S)

Accrual Number:	Category/Group:	Consented:	Enrolled: Number to Complete the Study or Needed

	(Adults/Children Special/Vulnerable Populations)	Maximum Number to be Consented or Reviewed/Collected/Screened	to Address the Research Question
Local	Adults	15 consented	10 to complete the study
Study-wide	Adults	15 consented	10 to complete the study
Total:	Adults	15 consented	10 to complete the study

RECRUITMENT METHODS

We will enroll up to 15 participants with stroke in the study. Potential participants will be recruited through local resources via phone, in person contact, flyers, email, word-of-mouth, and/or social media posts. Participants will be recruited through postings at clinics, stroke support groups, and other organizations and through referrals from outpatient physical therapy clinics in Chicagoland area. Stroke volunteers registered in the jointly maintained Northwestern University and Shirley Ryan AbilityLab Clinical Research Registry (CRR) will also be contacted. This registry provides a database of 680 individuals with stroke that have consented to be contacted for research studies. Our study team members have been granted access to the registry as necessary for purposes of recruiting study participants. Study information will be posted on http://www.clinicaltrials.gov/. Interested individuals will be directed to contact the study PI and research staff by phone or mail. Finally, a recruitment flyer will be posted on the PI's laboratory website and social media. Interested individuals will be directed to contact the study PI and research staff by phone or email.

Participation in this study will be open to all individuals who meet the inclusion/exclusion criteria for participation. Participation will be open to people of all racial and ethical backgrounds, gender, and sexual orientation. Minorities and female participants will be actively recruited. We anticipate that the recruitment resources available through the Northwestern University Feinberg School of Medicine should be more than sufficient to recruit our target population from a diverse and representative sample of the Chicago area.

An approved study team member will obtain written informed consent from all participants in the study. Potentially eligible participants will have the study described to them verbally, either in person or over the phone before they are scheduled for their assessment visit that will take place at the Northwestern University Feinberg School of Medicine. Upon arrival at the in-person consultation, potential participants will be provided with a detailed oral explanation of the study by an approved study-personnel. The oral explanation will use statements from the consent form and be performed in a private room with only the participant and investigators present. Participants will be asked;

"Do you understand what is being asked of you in this study?"
"Do you have any questions regarding this procedure or study?"

Participants will be given the opportunity to ask questions during the consent process. Participants will have the option to have a family member present during the consent process. Individuals who are not yet adults, cognitively impaired adults, and adults unable to consent will not be recruited for this study. All participants will receive a copy of the informed consent form.

COMPENSATION FOR PARTICIPATION IN RESEARCH ACTIVITIES

All participants will receive a stipend of $25 for visits including assessments and participation in the locomotor training intervention. Participant will be paid via two checks, one check of $150 will be provided after the first 6 sessions and another check of $150 will be provided after the final 6 sessions. If participant requires parking, the study team will provide a parking voucher for the parking garage at 222 E. Huron St., Chicago, IL at the conclusion of each visit.

If the conclusion of the in-person screening that will occur during visit 1 is that the participant does not meet all the study inclusion/exclusion criteria, the participant will then be informed that they are not eligible to continue in the study. The participant will receive a full $25 stipend for the visit.

If the assessment during visit 1 or visit 12 goes beyond the specified time frame of 2.5 hours, we will not be able to reimburse participants for any additional time required to complete the assessment during the same visit due to lack of external funding. In the event that all the assessment procedures during visit 1 or visit 12 does take more than 2.5 hours to complete, we will give the participant a choice of how to proceed. First, at the 2.5 hour time point, we will ask the participant if they would like to continue the assessment and complete all the remaining procedures during the same visit. We will give the participant an estimate of the time to complete the remaining procedures to assist them with your decision. If the participant does decide to continue the assessment that same day, they will not receive any additional stipend beyond the original $25. The participant's second option is to end the visit at the 2.5 hour time point and return for a follow up visit. During the follow up visit they will complete the remaining testing items. If the participant does return for a follow up visit they will receive $25 for that visit.

WITHDRAWAL OF PARTICIPANTS

It is unlikely that participants will be withdrawn from the study without their consent. However, there are circumstances that we would withdraw a participant. We will withdraw a participant from the study if:

We identify that their participation is putting their health at risk.

They miss scheduled study appointment visits without a valid excuse or fail to notify study team members of their absence. We will provide participants with a warning prior to withdrawal.

We learn that they were dishonest when answering our screening (inclusion/exclusion) questionnaire.

They arrive for study procedures while under the influence of illegal drugs or alcohol.

Participation in this study is voluntary. All participants have the option to choose not to participate in the study or to withdraw from the study at any time without penalty or consequences.

RISKS TO PARTICIPANTS

All participants will engage in a high intensity locomotor training intervention. The greatest risks participants will face are comparable to risks associated with other intense cardiovascular exercise and gait rehabilitation programs. Specifically, the potential risks to participation include:

- Fall and/or loss of balance and fear of falling while performing an activity that challenges balance and associated potential for a musculoskeletal injury.
- Breathlessness and/or fatigue while performing sustained walking or a muscular endurance task.
- Mental confusion during an activity that assesses cognition.
- Pain and/or physical discomfort due to physical activities during outcome measure testing.

- Cardiovascular risks during high intensity treadmill training
- Participants may experience emotional or psychological discomfort due to certain questions asked regarding their medical history.
- Discomfort from the pelvic harness which fits snuggly around the participants waist and is used to gently push participants waist with a cable-driven robotic device.
- Loss of participant confidentiality

Risks	**Due to**	**Probability**
Falling or fear of falling	Walking and balance activities	Low
Breathlessness, Fatigue (feeling tired)	Walking and balance activities	Moderate
Injury to joints, muscles, or bones	Walking and balance activities	Low
Mental confusion, frustration	Tests assessing for cognition and speech	Low
Pain or physical discomfort	Walking and balance activities	Moderate
Chest pain, heart attacks or irregular heart rhythms	Walking and balance activities	Moderate
Emotional distress or frustration with testing	Tests assessing for cognition, memory and speech	Low
Discomfort from the pelvic harness	Walking and balance activities during training	Low
Loss of confidentiality	Breach in data storage and accessibility	Low

Protection against risks

We will monitor participants for any evidence of adverse or unanticipated events during training and testing sessions. We will monitor heart rate, and blood pressure. Participants will also be allowed to stop and rest at any time. During all gait and balance related testing, the qualified study personnel administering the tests will guard the participant. In addition, participants will wear a gait belt that the study personnel will be able to use to provide support if the participant should stumble or lose their balance during gait and balance related tasks. We will also monitor participants for any loss of balance trips, slips, stumbles, or missteps. Should any occur, we will stop testing to examine the participant for orthopedic injury prior to resuming testing. The qualified study personnel administering outcome measure tests will continually interact with the participant to monitor for any evidence of adverse or unanticipated events during testing. Participants will be reminded that they have the contact information for the PI and research staff (included in their copy of the informed consent form), and they will be encouraged to contact us immediately should they experience any adverse or unanticipated events that may have been in any way related to their participation in the research study. We will also take these specific following steps to minimize risk to participants.

Fall and/or loss of balance and fear of falling while performing an activity that challenges balance and associated potential for a musculoskeletal injury

Participants might stumble, lose their balance, or fall while performing activities that assess gait and balance. Such an event might result in musculoskeletal injury such as an ankle sprain. To

minimize this risk, participants will wear a gait belt and will be guarded by a physical therapist or clinician during outcome measure testing. Participants will wear a harness that will prevent them from falling more than several inches if they were to trip or stumble during treadmill walking. Participants will also be given time to acclimate to walking on a treadmill. The treadmill and Agility Trainer both have emergency shut-off “kill” switches to rapidly disengage the devices at any time. The emergency shut down switches will be easily accessible to both the physical therapist and the participant.

Breathlessness and/or fatigue while performing sustained walking or a muscular endurance task
Performing tasks intended to assess gait, balance, and walking on the treadmill may cause individuals to become breathless or fatigued. Participants will be asked to rate their fatigue from time to time using the 6–20-point rate of perceived exertion scale and will be given regular scheduled rest periods throughout the testing. However, participants may request additional rest at any point.

Mental confusion or frustration during assessment of cognition and speech
Participants will be given detailed instructions and sufficient time to respond to all the questions during assessment of cognition and speech to avoid mental confusion or frustration during screening.

Pain and/or physical discomfort due to physical activities during outcome measure testing
Participants will be repeatedly asked if they are experiencing any pain or physical discomfort during outcome measurement. They will be provided rest periods throughout the testing.

Cardiovascular risks during high intensity treadmill training
Participants might experience cardiovascular difficulties during the high-intensity treadmill training intervention. We will monitor heart rate (HR) and blood pressure (BP) along with an ensemble of information from all participants to minimize cardiovascular risk. We will monitor BP and HR and use this information in conjunction with other guidelines provided by the American College of Sports Medicine for indications to terminate exercise. Specifically, we will stop exercise if any of the following signs are observed:

- Suspicion of a myocardial infarction or acute myocardial infarction (heart attack)
- Onset of moderate-to-severe angina (chest pain)
- Drop in systolic blood pressure (SBP) below standing resting pressure or drop in SBP with increasing workload accompanied by signs or symptoms
- Signs of poor perfusion (circulation or blood flow), including pallor (pale appearance to the skin), cyanosis (bluish discoloration), or cold and clammy skin
- Severe or unusual shortness of breath
- CNS (central nervous system) symptoms (e.g., ataxia (failure of muscular coordination), vertigo (an illusion of dizzying movement), confusion)
- Serious arrhythmias (abnormal heart rhythms) (e.g., second / third degree AV block, atrial fibrillation with fast ventricular response, increasing premature ventricular contractions or sustained ventricular tachycardia)
- Participant's request to stop

After testing is complete, we will check heart rate and blood pressure of all participants to ensure that these measures have returned to baseline levels before participants leave the laboratory. We will continually interact with participants to monitor for any evidence of adverse or unanticipated events during this time.

Participants may experience emotional or psychological discomfort due to certain questions asked regarding their medical history.

Some of the questions we ask may be upsetting, or participants may feel uncomfortable answering them. If they do not wish to answer a question, they may skip it and go to the next question.

Discomfort from the pelvic harness which fits snuggly around the participants waist and is used to gently push participants waist with a cable-driven robotic device
We will use a well-padded pelvic harness (Barry USA Inc., Delaware) and will offer all participants additional padding as desired to minimize any discomfort. This harness is specifically designed to comfortably suspend circus trapeze performers. In addition, the Agility Trainer has several safety features that limit the magnitude of force that can be applied to participants, including mechanical stops to ensure the device does not move participants beyond their normal range of motion and emergency shut off switches that will be within research of both participants and researchers during testing. Also, we will gradually increase the magnitude of force the device applies to participants and continually monitor participants' responses so that the magnitude of the applied forces does not exceed the individual's ability.

Loss of participant confidentiality
All participants will be given a secret identification code. All experimental data collected from participants will be identified only with this identification code. Data that link the participant to the identification code will be kept in a locked file cabinet.

All hard copy data recorded from this study will be stored in a locked file cabinet. All electronic data from this study will be stored on secure server run by the Northwestern University Feinberg School of Medicine. Only approved study-team members will have access to hard copy data or digital data.

Participants' responses to questionnaires, and medical history questions and clinical testing will be documented in writing by authorized study personnel. These forms will be identified strictly by the participant's secret identification code. This data will be entered into Microsoft Excel Spreadsheets. This data too will only be identified using the participant's identification code. When not in use by authorized study personnel, all hardcopies of these forms collected at the Northwestern University Feinberg School of Medicine will be stored in a secure, locked file cabinet at the following address:

645 N Michigan Ave, Suite 1119, Chicago IL 60611.

The file cabinet will be accessible by approved study personnel. If authorized personnel leave the research team, their access to data will be terminated.

Electronic data will be de-identified. This data will be labeled with the participant's secret identification code. The data will be stored on hard drives and analyzed on secure encrypted computers located at Northwestern University Feinberg School of Medicine, 645 N Michigan Ave, Suite 1119, Chicago IL 60611.

The electronic data will be accessible only by approved study personnel.

Data will be stored for 10 years after completion of the study. Only approved study personnel will have access to the data during this time. The study team members who collect hard copy data during the experiment will be responsible for receipt and transmission of the data from the testing site to a locked filing cabinet. Digital data will be backed up on an encrypted, password-protected server.

Availability of Emergency Services
All assessments will be conducted at Northwestern University Feinberg School of Medicine. In the event of an emergency, this facility is equipped to provide immediate care to participants.

POTENTIAL BENEFITS TO PARTICIPANTS

The overarching goal of this project is to assess the effects of a novel intervention, gait training performed in a MAE, on walking balance and participation in mobility-related activities in PwCS. Recent scientific research[22, 41] has provided an evidence-based framework for motivating the development of tools which are able to create the movement amplification training environment examined in the proposed research. Gait training performed on a treadmill is frequently administered in clinical settings and is well-accepted because it provides a safe and straightforward method of thoroughly training many important components of walking while not requiring much space or complex equipment. However, treadmill training alone is limited because it lacks a balance-specific component. If outcomes from the proposed research are successful, the supplementation of treadmill-based gait training with a MAE could dramatically improve the capacity of treadmill training to enhance walking balance. The MAE has the potential to transform an ordinary treadmill into a dynamic environment where PwCS can receive safe, challenging, and customized locomotor balance training. Overall, this proposal has the potential to dramatically enhance how gait rehabilitation is delivered to significantly improve components of walking balance post-stroke.

Participants engaging in Aim 2 of the proposed study will undergo a 10-session high-intensity gait training in a MAE under the supervision of a licensed physical therapist. There is strong evidence that gait training can improve walking speed, and endurance[37, 68-70]. Our proposed intervention will explicitly train walking balance along with walking speed. As such, individuals enrolled in the proposed study may improve aspects of their health and functional walking ability. However, as this is an experimental study, it possible that participants may not improve their own walking ability by participating. The risk of participating is similar to that involved when participating in any physical therapy intervention aimed at improving gait.

DATA MANAGEMENT AND CONFIDENTIALITY

Data analysis plan

- Data will be pre-processed using a combination of Qualisys Track Manager (Qualisys, Gothenburg, Sweden), Visual 3D (C-Motion, Germantown, MD), and custom MATLAB (Mathworks, Cambridge, MA) programs. All statistical analysis will be conducted in SPSS (IBM, Armonk, NY).
- To compare differences between pre- and post- training, we will perform separate one-way repeated measures ANOVAs to evaluate changes in our clinical, biomechanical, and daily stepping measures. Significance will be set at the $p < 0.05$ level for the repeated measures ANOVAs and pairwise comparisons.
- Since this is a novel research question, we do not have preliminary data from people with chronic stroke. Thus, a sample of convenience of 10 participants was calculated based on our previous data from people with incomplete spinal cord injury. The findings from this study will provide foundation to design and power future clinical trial.

Steps to secure data and maintain confidentiality

- All participants will be identified by a code number that is unrelated to name, initials, or numbers used by other entities for the purpose of identification. This code number will be

used to report findings of this study to prevent direct or indirect identification. Data files will only be identified using this code number.
- All digital data will be kept on password protected computers. Hard copy data will be kept in a locked file cabinet in a locked office space. Only the research team will have access to this data.
- All data collected will be expressly for research purposes and will not be shared with outside entities except with the explicit written consent of the participant whose data is in question.

All de-identified data will be reviewed for quality to ensure appropriate recording of information by members of the research team.

Data Handling
- Recorded data will include the quantitative data described in section 9.4 as well as answers to the attached questionnaire.
- Digital data will be stored on a password-protected computer. Hard copy data will be kept in a locked file cabinet in a locked office space.
- Data will be stored for 10 years after completion of the study.
- Only the principal investigator and the sub-investigators will have access to the data.
- The sub-investigator (student researcher) who collects the data during the experiment will be responsible for receipt and transmission of the data.
- Hard copy data will be transported by hand by a member of the research team from the experiment room to the locked filing cabinet. Digital data will be backed up on a password-protected drive in the lab and accessed by password-protected computers within the laboratory.

PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF PARTICIPANTS

Dr. Gordon (PI) will be responsible for establishing and implementing the Data Safety Monitoring Plan. Dr. Gordon will work with his respective IRB Office at Northwestern University to gain study approval. Dr. Gordon will be responsible for all IRB related reporting (annual progress reports, adverse event reporting, etc.). Dr. Gordon will be responsible for ensuring that all study team members have completed all research and safety training mandated before engaging in any research related activities. Dr. Dusane and Dr. Martinez will be responsible for screening potential participants for inclusion/exclusion criteria and for obtaining written informed consent from study participants. Audits conducted by compliance officers at Northwestern University will be performed to ensure screening and consent procedures have been performed in accordance with the approved study protocol. Dr. Dusane and Dr. Martinez will be responsible for collecting outcome measure data from the study participants. After collecting data, Dr. Dusane will be responsible for transporting the hard copies of data to be stored in the locked file cabinet. Dr. Dusane will be responsible for transposing and entering the hard copy data into digital format. The research technician will double check data entry. Dr. Gordon will be responsible for checking the accuracy of the digital data.

In the event of any adverse health effects occurring because of participation in the study procedures, the PI will discuss the event with the clinical team members Drs. Dusane and Martinez to identify if changes in protocol should be initiated to minimize the potential for future occurrence.

PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS
- Participants' privacy will be protected. Screening phone calls will occur in a private office space. Consent and intake procedures will be performed in a laboratory space with only

the research team present. A privacy screen is provided if the participant must change clothing. The laboratory space will be closed throughout the experiment.

- Participants will be reminded that all responses to questions in the questionnaire will be de-identified and only be used in aggregate with all other participants' information. The P.I. will explain all palpation procedures (for motion capture marker) and ask the participants' consent before performing them.

- All participant-identifying data will be kept in a locked cabinet in a locked office space accessible only to the research team. Hard copies of de-identified data will be stored in a separate folder in the same locked storage cabinet. All electronic data will be de-identified and kept on a password protected and encrypted computer database and back up hard drive in the PI's laboratory. Only key study personnel will be given access to the database. This system is highly effective in reducing risks to privacy of all participant data.

COMPENSATION FOR RESEARCH-RELATED INJURY
Northwestern University will provide necessary medical treatment to the study participant if they are injured by participation in this research project. Emergency and ongoing medical treatment will be provided as needed. If someone should have a medical concern or get hurt or injured as a result of taking part in this study, they will be instructed to call the study PI.

If a study participant becomes ill or is injured as a result of this study (medications, devices or procedures), they will be advised to seek medical treatment through their doctor or treatment center of their choice. Northwestern University will not pay for medical care required because of a bad outcome resulting from your participation in this research study.

ECONOMIC BURDEN TO PARTICIPANTS
None

CONSENT PROCESS
Upon arrival at the Human Agility Lab for testing, a member of the research team will provide a detailed oral explanation of the study using statements from the consent form. This will be done either in the laboratory or in a private office space at which time participants will be asked to give written consent, with only the research team present.

Prior to each step of the experiment, participants will be asked, "Do you understand what is being asked of you in this task?" and "Do you have any questions regarding this task or study?". Participants will be asked to summarize the study details to ensure their understanding.

Consent procedures will follow SOP: Informed Consent Process for Research (HRP-090). Research persons authorized to obtain consent will be listed in the application. The research person will describe the procedure of the study, details about number of visits and time for each visit, along with potential benefits and risks involved in the study. Additionally, participants will be informed that they can withdraw from the study at any instance.

Consent process will be performed in English. Non-English speaking participants will not be recruited for this study. Consent process will take approximately 15 minutes.

During consenting, we will provide the participant a copy of the consent form to review and reiterate throughout their participation that participation is completely voluntary and that withdrawal from this study will not affect participation in our future studies. We will also give

participants several opportunities to ask questions to ensure their understanding about the study procedures.

NON-ENGLISH SPEAKING PARTICIPANTS
Non-English speaking participants will not be recruited since English will be used for consenting process and for providing instructions during the study procedures.

PROTECTED HEALTH INFORMATION (PHI AND HIPAA)
The study involves use of participant's self-reported medical history, details about the stroke (date, type of stroke (hemorrhagic vs ischemic)) and current medication. HIPAA Authorization will be obtained from all participants. We will collect participants' demographic information including address, date of birth, age, sex along with date of stroke. We will also collect their telephone numbers.

QUALIFICATIONS TO CONDUCT RESEARCH AND RESOURCES AVAILABLE
A total of 15 people with chronic stroke will be recruited for this study over the period of next 12 months beginning from May 2023 at the Department of Physical Therapy and Human Movement Sciences at Northwestern University. Participants will be recruited via phone, in person contact, flyer, or email.

Participants will be recruited from the database of stroke volunteers maintained jointly by the Northwestern university and Shirley Ryan AbilityLab registry through referrals from the associated inpatient and outpatient physical therapy clinics of AbilityLab and through postings at clinics, support groups and other organizations.

Additionally, recruitment flyers for individuals with chronic stroke will be posted on the PI's laboratory website and the Physical Therapy and Human Movement Sciences (PTHMS) department's website. We will utilize social media to direct potential participants to the department and laboratory website to view the study flyer.

For the participants involved, the study PI will devote 3 hours per week and research assistants/personnel will devote 5-10 hours per week for conducting and completing the research.

All research will be conducted in the Human Agility Laboratory at the Dept. of Physical Therapy and Human Movement Sciences at Northwestern University. The space is a 1000-square-foot biomechanics laboratory designed to study stability and maneuverability during human walking. It offers a large, unconstrained space for movement. The Human Agility Lab houses the following devices:

- Lateral force field device also known as the Agility Trainer: (Figure 6) The Agility Trainer is powered by a set of moving coil brushless linear servomotors (Baldor, DC brushless linear motor: NB0124A01 controlled by a Baldor Linear Drive: FDH1A02TB-EN20) that travel along a linear magnetic rail positioned at the front of the treadmill (Figure 6). Each linear motor has a mass is 0.32 kg and has a peak and continuous force capability of 173 and 58 N respectively. The position of the moving coils will be measured using a linear optical encoder with one read head (Renishaw, RGH41) per coil at a resolution of 20 nanometer. The encoder read heads are capable of measurements up to 12 m/s. A steel cable attached to each motor is routed through a series of cables that connect a low friction trolley (able to move forward and backward along each side rail) to a pulley mounted on that lateral aspect of a pelvic harness worn by the participant. Any slack in the cable is removed by a winch prior to use. Thus, each individual motor can only apply a laterally

directed force to the participant during walking. By coordinating the movements of the two motors the participant can be made to experience forces applied to their pelvis that pull them either to the right or left. Modulation of these forces based on the participants' movement can replicate virtual environments that feel like a set of springs of a small force like a small dog pulling on a leash.

The device is not banned by the USFDA. The investigator will label the device in accordance with USFDA regulations. (21 CFR §812.5). The IRB will approve the research under 21 CFR §50 and §56 and determine that the investigational device is Non-Significant Risk. The investigator will comply with USFDA requirements for monitoring investigations. (21 CFR §812.46). The investigator will comply with USFDA requirements for records and reports. (21 CFR §812.140, 21 CFR §812.150). The investigator will not market or promote the device (21 CFR §812.7).

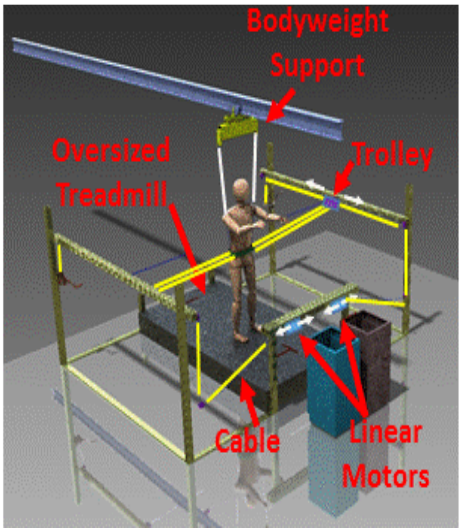


Figure 6: Balance Augmentation Trainer Overview: Participants walk on an oversized treadmill with bodyweight support for safety. Movement of linear motors positioned at the front of the treadmill impose laterally directed forces on a pelvic harness via a cable transmission system. The motors work independently. The left motor can only pull the participant to their left and vice-versa for the right motor. A steel cable runs from each motor through a low-friction trolley, to a pulley on the harness, back through the trolley and anchors on a winch toward the rear of the treadmill. The trolley system allows the application of lateral forces without constriction fore-aft motion on the treadmill.

- Participants will walk on a custom-built oversized treadmill (Tuff Tread) that has a treadmill belt-walking surface of 55 x 105 inches, approximately three times the size of a standard treadmill (Figure 7). A computer monitor or mirror positioned in front of the treadmill, as well as projection on the treadmill itself can be used to provide participants with visual feedback about their position on the treadmill.

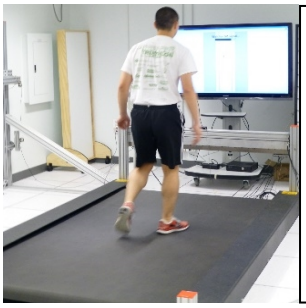


Figure 7: A healthy participant is shown walking on the oversized treadmill to illustrate the size of the walking surface. In this photo, a 60-inch monitor positioned in front of the treadmill is used to provide visual feedback to the participant about their location on the treadmill.

- For safety, participants will wear a harness around their trunk that is attached to a commercial overhead safety support (ZeroG, Aretech) that was installed by the manufacturer.
- For safety a cable will be attached to the front of the participant's trunk harness. The cable will run to a magnetic "kill switch" located at the front of the treadmill. If the magnet is pulled off of its mount (either voluntarily or in the event of a fall) power to the system will be shut off immediately.

- Participants will also wear a harness around their waist. Cables from will run from a pair of linear motors through a series of cables that connect to the waist harness.
- The robot itself is mounted on a high strength aluminum strut frame that has been constructed around the perimeter of the treadmill. The frame is used to route the cable transmission from the motors to the participant (Figure 8).

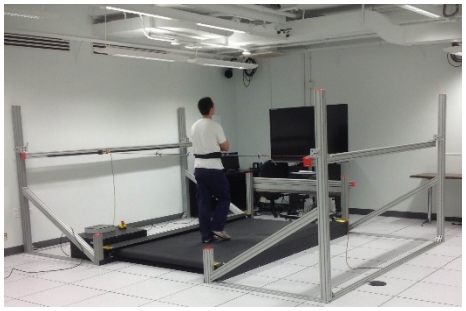


Figure 8: A 3"x3" aluminum strut frame has been constructed around the treadmill. The frame supports a magnetic rail that the linear motors run on at the front of the treadmill. The trolley system allowing fore-aft motion is mounted on the side rails. The height of the side rails are adjustable for participants of different height.

- Movement of the linear motors will produce laterally (side-to-side) directed forces that are transmitted to the participant through the cables. The cable system runs over a trolley that will allow the participant fore-aft movement on the treadmill (Figure 9).

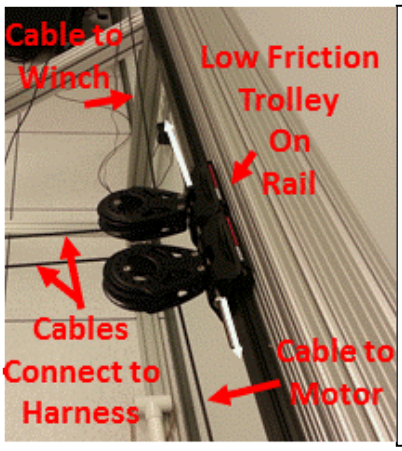


Figure 9: The cable transmission runs through a set of pulleys mounted on a low friction trolley. The cable running through these trolley pulleys loops around a third pulley attached to the lateral aspect of the participant's harness. The trolley can travel freely on a rail fixed to the side rail of the frame. With this setup, movement of the motors will produce a lateral force that is applied to the participant without inhibition fore-aft movement of the participant on the treadmill.

- Motion capture cameras: Ten optical motion capture cameras (Qualisys, Gotheburg, Sweden) will be used to monitor the position of reflective markers placed on the participant to determine kinematic, kinetic, and spatiotemporal characteristics during locomotion. This is a commercial, non-medical device.

If participant is injured as a result of this study, the participant will be informed to seek medical treatment through their doctor or treatment center of choice. Participant will be instructed to promptly inform the study doctor about any illness or injury.

All persons assisting with this research have extensive experience using the equipment and devices described in this protocol and have performed previous studies with a different population in the laboratory. All current authorized study personnel have up to date CITI Human Subject Research Training.

Since this is not a multicenter study, NU is the Lead Site.

MULTI-SITE OR COLLABORATIVE RESEARCH:
N/A; this is not a multi-site research study.

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