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PROTOCOL TITLE:
Movement amplification to improve walking balance and physical activity post-stroke

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STUDY SUMMARY:

Investigational Agent(s) (Drugs or Devices)	Agility Trainer
IND / IDE / HDE #	NA
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	30
Funding Source	National Institute of Child Health & Human Development 1R21HD112813-01 American Heart Association Post-doctoral fellowship award: 24POST1195671
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	☐ Yes

Exposure	☒ No
DSMB / DMC / IDMC	☐Yes ☒No

OBJECTIVES:

People with chronic stroke demonstrate balance and gait dysfunctions and challenges in maintaining stability during walking. Thus, the main objective of this research is to develop new methods to improve stability during walking in people with chronic stroke. Our three session study involves application of forces to the pelvis during treadmill walking. Specifically, we are investigating how changes in the external environment through application of forces to the pelvis affect walking balance in people with chronic stroke.

Hypothesis:

a) After-effects of walking with lateral forces applied to the pelvis that amplify lateral motion will improve mediolateral walking stability.

b) After-effects of walking with lateral forces applied to the pelvis that resist lateral motion will decrease mediolateral walking stability and walking symmetry both spatially (between left and right joint angles, step and stride lengths) and temporally (between right and left swing, stance, step and stride times).

c) Locomotor adaptations for walking balance control will be proportional to the forces used to either resist or amplify lateral motion.

BACKGROUND:

Stroke induced sensorimotor deficits and changes in the lower-body mechanical properties negatively affect the ability to recover balance, resulting in gait dysfunction. While more than 80% of people with stroke recover their walking abilities post-gait rehabilitation, gait dysfunctions continue to persist (1,2). These gait dysfunctions lead to difficulties in performing activities of daily living and reduced mobility. Gait impairments are found to be more pronounced especially during the chronic stages of stroke recovery when individuals begin community ambulation (3). Nearly half of the individuals with recovered ability to walk demonstrate gait asymmetry, as compared to healthy people (4,5). Gait asymmetry is characterized by temporal asymmetry, quantified by the relation between step length of the paretic leg and the nonparetic leg and spatial asymmetry, quantified by the relation of single-limb-support time between legs (5,6). Literature suggests that such gait asymmetry is associated with slower walking speed (7) and shown to have a higher metabolic cost compared to that of unimpaired gait (8,9).

Post-stroke individuals exhibit shorter stride length (10), wider steps, variable step length and reduced gait stability (11) making them vulnerable to falls during walking (3,12,13). Furthermore, people with chronic stroke demonstrate variable mediolateral margin of stability (14,15). It has been reported that 31-38% of total falls occur side-ways towards the paretic limb as weight is shifted laterally (3,15). With lateral perturbations of the pelvis during standing, people with stroke demonstrated greater sway when pushed to their weak side (16) and exhibite abnormal activation (reduced amplitude and delayed onset latencies) of hemiplegic hip muscles (17). Such impaired mediolateral balance control is further reinforced by weight bearing asymmetry on the non-paretic side (18, 19) and reduced biomechanical limits of stability on the paretic side (20). Given the limited knowledge about mediolateral balance control and its potential impact on post-perturbation lateral protective stepping response, it is imperative to better understand the deficits in mediolateral balance control post-stroke.

Although several task-specific interventions have been implemented to facilitate locomotor recovery (21, 22), there is lack of protocols designed to explicitly enhance gait stability and remediate gait asymmetry. Recently, novel interventions have been designed based on error driven motor learning, wherein the motor error or asymmetry during walking is exaggerated (error augmentation) in order to facilitate the central nervous system to make movement corrections. For example, motor adaptation employing a split-belt treadmill walking paradigm that exacerbates asymmetry have shown promising improvements in walking symmetry in people with stroke (23). However, there is lack of studies providing balance training during walking to improve gait stability in this population. Moreover, it remains to be determined whether walking in an unstable environment (such as a treadmill mounted on a moving platform, or when subjected to lateral perturbations) can induce modulation in gait kinematics to enhance gait stability post-stroke. It can be hypothesized that repeated exposure to such a variable environment with both destabilizing (movement amplification) forces might significantly challenge lateral center of mass motion. Our previous study in people with incomplete spinal cord injury demonstrated adaptation by increasing step width and lateral margins of stability when placed in a movement amplification force field. Therefore, the use of robotic force fields to induce instability may provide a novel method for encouraging active learning of balance control strategies for improved gait stability and symmetry in people with chronic stroke.

References:

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STUDY ENDPOINTS:

- The primary study endpoint will be the successful recruitment of 30 participants with chronic stroke.
- The safety endpoints are established by individual participants. 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.

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 producing small forces that amplify lateral movements (like a small dog pulling on a leash).

PROCEDURES INVOLVED:
This study includes 2 sessions that are one week apart and involve a group of 30 people with chronic stroke.

Research Procedures: Potential participants interested in the study will be telephone screened to determine eligibility for the study, followed by in-person screening to determine if participant fulfills the inclusion criteria. Included participants with chronic stroke will undergo a clinical assessment prior to testing.

Visit 1: In-person screening: A licensed physical therapist will consent and screen participants. Participants demographic information, medical history, stroke specific history, current medications, information about ambulatory status, use of assistive devices and self-reported falls will be collected. To assess the functional recovery post-stroke, Chedoke-McMaster Stroke Assessment for leg and foot will be performed. During this assessment, participant will be asked to perform movement tasks to objectively measure physical impairment and stages of recovery. This will be followed by clinical assessment which includes:

1) Balance and functional mobility tests:
    a. Berg Balance test: A widely used test which objectively measures participant's ability to safely balance during a series of predetermined tasks. It is a 14-item list with each item consisting of a five-point ordinal scale ranging from 0 to 4 with a total score of 56.
    b. Timed up and go test: A widely used test for functional mobility assessment. Participant is asked to get up from the chair, walk 3 meters, walk back, and sit down. The time from getting off the chair to sitting back is recorded.
    c. Dynamic gait index: Tests the ability of the participant to maintain walking balance while responding to different task demands, through various dynamic conditions.
2) Gait speed assessment: 10-meter walk test is used to assess walking speed in meters per second over a short distance.
3) Balance confidence: Activities-specific Balance Confidence scale is a self-reported measure of balance confidence in performing various activities without losing balance.

This will be followed by the experimental setup.

Experimental set-up: First, participants heart rate and blood pressure will be assessed. We will then place reflective markers on participants' feet, legs, and trunk. We may also place several small plastic recording electrodes on their legs. These electrodes will monitor muscle activity. Participants will wear a safety harness attached to an overhead support during treadmill walking to prevent the possibility of falls and ensure participant safety. Participants will be asked to walk on our custom built extra-wide treadmill for a series of short walking sessions each lasting for 2 minutes. Participants comfortable and fast walking speed on the treadmill will be first determined. Participants will then be given 2-min to acclimate to treadmill walking at each speed.

A belt will be attached to the participant's waist to provide applied forces that pulls the participant right or left challenging their walking balance. Cables attached to the left and right side of this belt will be used to apply small forces to participant's hips that either make it more difficult to walk straight or make it easier to walk straight. Attachment to the robotic cable will create a destabilizing (movement amplification) force field. Participants will be warned before any force is applied to the belt. Each participant will then perform eight 2-min trials of treadmill walking. These trials will

consist of four different gain or magnitude of the applied forces in the Movement Amplification Environment (MAE) (1) Null Environment: no applied forces, (2) MAE Low Gain: 25 Nsm-1, (3) MAE Medium Gain: 35 Nsm-1, (4) MAE High Gain: 45 Nsm-1, that will be repeated at both the Preferred and Fast treadmill walking speeds. The trial order will be randomized. Participants will be given rest between trials. We will qualitatively assess when the magnitude of the applied forces makes it difficult for the participant to maintain straight-ahead walking. If a participant requires assistance to walk at a given gain, we will decrease the MAE Gain by 5 Nsm-1 until the participant can walk without assistance.

Participants will be given opportunity to rest as needed between sessions. Heart rate and blood pressure will be assessed at the end of the session. Participants will be asked to rate their perceived exertion to determine the severity of fatigue. This visit will take 2 hours and the participant will be asked to visit the laboratory again after a week.

We will attempt to collect all data during a single session, but if participants become fatigued during the data collection – as indicated by perceived exertion or elevated heart rate or blood pressure levels that do not return to baseline with rest – testing will be extended to a second or third day as needed. Based on past experience, we feel it is unlikely that we will need to extend testing across multiple sessions.

Visit 2: Experimental set-up: Similar to the set-up in visit 1, participants heart rate and blood pressure will be assessed followed by placing reflective markers on their legs. Participants will wear a safety harness and a belt will be attached to the participant's waist to provide applied forces. Participants will be given 2-min to acclimate to treadmill walking at their preferred treadmill speed. Next, we will assess participant's maximal control of their lateral COM motion during walking by performing three 21-meter walking trials on the treadmill. During this assessment, participants will receive visual feedback on the treadmill and will be instructed to maintain their center of mass within the projected lane. If participant successfully maintains their center of mass within the lane, this lane width will progressively narrow, making the task more challenging. If not, the projected lane width will increase. Next, participants will perform five 2-min trials of treadmill walking in either a Null environment (no applied forces that pulls the participant right or left and challenges their walking balance), or MAE (using the highest gain or intensity of the applied force that participants used in visit 1). The order of the external environments will be randomized across participants. Rest breaks will be given between each 2-min trial. Finally, we will repeat the COM control assessment with no forces applied to their body. Participants heart rate, blood pressure and the rate their perceived exertion will be assessed at the end of the session. This visit will take 2 hours.

Visit 3: Experimental Session: The set-up and procedure will be similar to visit 2. After assessment of participants heart rate and blood pressure and placement of reflective markers and safety harness, participants will be given 2-min to acclimate to treadmill walking at their preferred treadmill speed. Next, three trials of 21 meters each will be performed to assess their walking balance similar to visit 2. Next, we will ask the participant to walk for five 2-minute trials with the condition other than the one performed at visit 2. For example, if no forces were applied in visit 2, participant will be walking with applied forces that pulls the participant right or left and challenges their walking balance for visit 3. Rest breaks will be given between each 2-min trial. Finally, we will repeat the COM control assessment with no forces applied to their body. Participants heart rate, blood pressure and the rate their perceived exertion will be assessed at the end of the session. Participant may also choose to stop participating in testing at any time. This visit will take 2 hours.

For all the visits, motion tracking data will be collected via reflective markers placed on landmarks on the trunk, hips, and bilaterally on the upper and lower limbs of the participants and recorded using a 10-camera motion capture system (Qualisys, Gotheburg, Sweden). Surface electrodes (Delsys Inc, Matick, MA) will be used to record muscle activation patterns of major muscles groups of the lower limb and trunk. Additionally, footswitch sensors (Delsys Inc, Matick, MA) will be used to evaluate timing of specific gait events. Participant's video and photographs will be collected which will be later used for research presentations and publications.

DATA AND SPECIMEN BANKING

No specimens will be collected. 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. Data will be securely stored for a 10-year period following the conclusion of the study.

Data will not be available to outside entities except with the explicit written consent of the participant whose data is in question. The data released will not be identifiable to others.

SHARING RESULTS WITH PARTICIPANTS

Results of this study will not be shared with participants or others without the explicit written consent of the participant.

STUDY TIMELINES

People with chronic stroke will be tested during three visits of which the first two visits will be one week apart. On the first visit, consenting, in-person screening, clinical assessment and testing will be performed. On the second visit after a week and third visit, only testing will be performed. Total testing time is expected to be two hours during each visit.

INCLUSION AND EXCLUSION CRITERIA

A total of 30 participants with chronic stroke will be recruited. Potential participants interested in the study will be telephone screened to determine eligibility for the study, followed by in-person screening to determine if participant fulfills the inclusion criteria.

Inclusion Criteria

- Age 18 to 85 years
- History of chronic stroke (more than 6 months post-stroke) with weakness confined to one side
- Ability to ambulate over ground 10 m with or without a single cane), and/or braces that do not cross the knee joint (e.g., ankle-foot orthosis) are permitted.
- Passive range of motion of the legs within functional limits of ambulation (i.e., ankle dorsiflexion to neutral position, knee flexion from 0 to 120 degrees, and hip flexion to 90 degrees and extension to 10 degrees.)

Exclusion Criteria

- Brainstem and/or cerebellar lesion
- Perinatal stroke

- Presence of cognitive impairment (score of ≤22/30 on the Montreal Cognitive Assessment scale (MoCA))
- Presence of aphasia (score of ≥71/100 on the Mississippi Aphasia Screening Test (MAST))
- Excessive spasticity in the lower limbs as measured by a score of > 3 on the Modified Ashworth Scale
- Inability to tolerate 10 minutes of standing
- Severe cardiovascular and pulmonary disease affecting gait and balance
- History of recurrent fractures or known orthopedic problems in the lower extremities (i.e. heterotopic ossification) affecting gait and balance
- Concomitant central or peripheral neurological injury (i.e. traumatic head injury or peripheral nerve damage in lower limbs) affecting gait and balance
- Presence of unhealed decubiti or other skin compromise
- Enrollment in research involving locomotor balance training
- Use of braces/orthotics crossing the knee joint
- Known pregnancy

The following groups will be excluded from the study:
- Adults unable to consent
- Individuals who are not yet adults (infants, children, teenagers)
- Pregnant women
- Prisoners

VULNERABLE POPULATIONS
NA

PARTICIPANT POPULATION(S)

Accrual Number:	Category/Group: (Adults/Children Special/Vulnerable Populations)	Consented: Maximum Number to be Consented or Reviewed/Collected/Screened	Enrolled: Number to Complete the Study or Needed to Address the Research Question
Local	Adults	30	30
Study-wide	Adults	30	30
Total:	Adults	30	30

RECRUITMENT METHODS
A total of 30 people with chronic stroke will be recruited for this study over the period of next 24 months beginning from February 2021 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 Northwestern University and the Shirley Ryan AbilityLab (CRR Stroke) 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.

Interested participants will undergo telephone screening to determine their eligibility. Potential participants will then be scheduled for an in-person screening to be ensure they fulfill the inclusion criteria and then enrolled in the study.

This small sample study will recruit participants from the CRR Stroke database. We will recruit individuals meeting our study inclusion/exclusion criteria. The CRR Stroke database is populated from individual post-stroke who are involved in a wide range of clinical and community groups. We anticipate that the use of the database to recruit participants will result in a study sample representative of the stroke-community in the Chicago-land area. Our study is open to individuals of all races, ethnicity, gender, sexual orientation.

COMPENSATION FOR PARTICIPATION IN RESEARCH ACTIVITIES

Participants with chronic stroke will be paid $150 ($50 per session) for their involvement in this study on the same day at the end of the session. Participants will be paid with a $50 VISA gift card immediately after the first two study visits and will be issued a $50 check for the third visit. Participants are provided both gift card and check in accordance with the Northwestern University policy that recommends this arrangement for a total participant stipend that exceeds $100.

WITHDRAWAL OF PARTICIPANTS

- Participants may be withdrawn from this study for safety reasons if they exhibit significant adverse effects that do not go away with rest.
- Participants will be brought to a comfortable seated or lying down position and medical attention will be provided if necessary. Emergency medical service is routinely available at the adjacent Northwestern Memorial Hospital emergency room.
- Data from participants who withdraw from the study will not be used for analysis and will be safely stored with other study data. The conditions of the withdrawal will be recorded. The participant will not be contacted any further with regards to the study

RISKS TO PARTICIPANTS

Following are the risks to participants and precautions taken to lessen the probability or magnitude of risks:

- Procedures performed to lessen the probability or magnitude of risks:
- Risk/fear of falling: Participants will wear a safety harness attached to an overhead support during all treadmill walking to prevent the possibility of falls and ensure participant safety.
- Dizziness/cardiovascular discomfort: If participants are unaccustomed to moderate durations of standing and/or walking, as a result of participation in this experiment, they may experience dizziness and cardiovascular discomfort. Every effort will be made to prevent occurrence of these symptoms by providing scheduled and "as needed" rest breaks.
- Musculoskeletal injury: Participants might sprain their ankle or suffer other musculoskeletal injury when walking.

- Skin irritation: The adhesive used for the skin electrodes can cause minor irritation of the underlying skin. Skin areas will be wiped with alcohol prior to applying the electrodes. Skin irritation, if present, subsides within approximately 24 hours. Participants will be informed to keep the regions of the electrodes clean and dry following the experiment. There have been no reports of significant injury following adhesive use in our laboratory. The risks are negligible but worthy of mentioning in potential case of allergic reaction. Additionally, if participants are unaccustomed to moderate durations of standing and/or walking, they may experience compromised skin integrity. Every effort will be made to prevent occurrence of these symptoms by providing rest as needed and providing padding to specific skin locations if needed.
- Discomfort from the application of force fields: The application of force fields may be uncomfortable for participants. Participants will wear a padded harness that will distribute the applied forces across the participants' hips and pelvis. We will provide additional foam padding as needed.
- Emotional discomfort: 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.
- Fatigue: Walking on the treadmill is exercise and may cause individuals to become fatigued. Participants will be given regular scheduled rest periods throughout the experiment. However, they may request additional rest time at any point during the experiment.
- Muscle Soreness: Participants may experience muscle soreness following participation in the various walking exercises.
- Loss of confidentiality: This study involves the use of participants identifiable, personal information and there is a chance that a loss of confidentiality could occur.

POTENTIAL BENEFITS TO PARTICIPANTS

There are no potential benefits to participants who in this study. There is no direct benefit to the participant. However, possible benefits to others include facilitating our understanding of how changes in the environment affect walking in people with chronic stroke. This understanding may help us develop effective clinical rehabilitation programs for improving walking in people with chronic stroke.

DATA MANAGEMENT AND CONFIDENTIALITY

Data analysis plan

- Data will be pre-processed using a combination of Qualysis Track Manager (Qualysis, Gothenburg, Sweden), Visual 3D (C-Motion, Germantown, MD), and custom Matlab (Mathworks, Cambridge, MA) programs. Statistical analysis will be done using separate two-way repeated measures ANOVAs (step x leg side). All statistical analysis will be conducted in SPSS (IBM, Armonk, NY).
- To investigate the differences between the two speeds and four MAE gains, we will generate separate linear mixed-effects models for each gait-related metric. Fixed effects will include Speed (Preferred and Fast) and Field (Null, MAE Gain Low, Medium, and High), as well as the interactions between Speed and Field. Random intercepts will allow participants to deviate from the main intercept. If there is a significant main effect, a pairwise comparison will be made to determine the significant difference within the pair. If there was a significant interaction between Speed and Field, separate pairwise comparisons will be made to evaluate the significant pair (Preferred vs. Fast) within each Field. Significance will be set at $\alpha = 0.05$ for all tests.

- To evaluate changes in participants' ability to control their lateral COM excursion, we will perform a one-way repeated measures ANOVA to compare the minimum lateral COM excursion during the four assessment periods (before and after walking in the Null Environment or MAE). If sphericity is violated, we will use a Greenhouse–Geisser F-statistic and p-value to test the main effect of the field. If assumptions of the parametric repeated measures ANOVA model are violated, a Friedman's test will be used. When a significant main effect is found, Bonferroni-corrected pairwise comparisons will be made. Significance will be set at $p < 0.05$ for all tests and 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 30 participants was calculated based on our previous data from people with incomplete spinal cord injury.

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.

Certificate of confidentiality

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify participant in any action or suit unless the participant says it is okay. They also cannot provide them as evidence unless the participants have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that the participant need to know. The Certificate does not stop reporting that federal, state or local laws require. Some examples are laws that require reporting

of child or elder abuse, some communicable diseases, and threats to harm self or others. The Certificate cannot be used to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate does not stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also does not prevent participant information from being used for other research if allowed by federal regulations.

Researchers may release information about you when the participant says it is okay. For example, the participant may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop the participant from willingly releasing information about your involvement in this research. It also does not prevent the participant from having access to their own information.

The sponsor, monitors, auditors, the IRB, the Northwestern University Office for Research Integrity, the US Office of Research Integrity (ORI), the US Office for Human Research Protections (OHRP), and the US Food and Drug Administration (FDA) may be granted direct access to participants medical records to conduct and oversee the research. By signing the informed consent document, participants are authorizing this access. We may publish the results of this research. However, we will keep participants name and other identifying information confidential.

PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF PARTICIPANTS
NA, this study involves only minimal risk.

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
NA, this study involves only minimal risk.

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.

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, height, weight, sex, ethnicity, race, along with date and cause of stroke. We will also collect their telephone numbers.

QUALIFICATIONS TO CONDUCT RESEARCH AND RESOURCES AVAILABLE
A total of 30 people with chronic stroke will be recruited for this study over the period of next 24 months beginning from February 2022 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 by the Shirley Ryan AbilityLab 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 1) 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 1). 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.

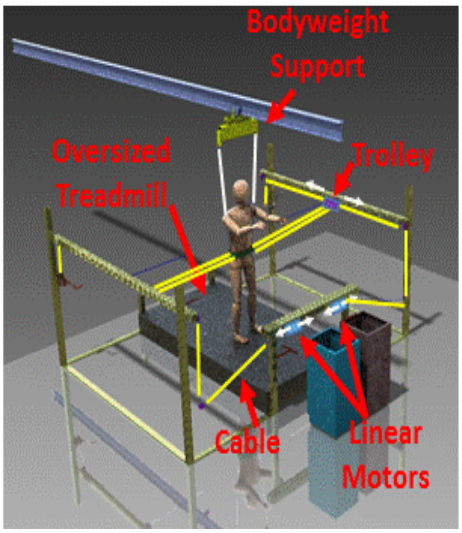


Figure 1: Balance Augmentation Trainer Overview: Participants walk on an oversized treadmill with bodyweight support for safety. Movement of linear motors positioned at the front of the treadmill impose laterally directed forces on a pelvic harness via a cable transmission system. The motors work independently. 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 2). A computer monitor or mirror positioned in front of the treadmill, as

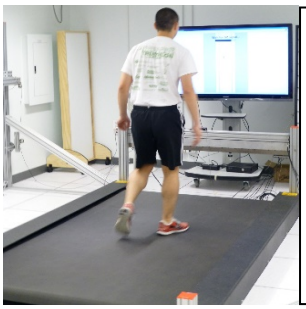


Figure 2: A healthy participant is shown walking on the oversized treadmill to illustrate the size of the walking surface. In this photo, a 60-inch monitor positioned in front of the treadmill is used to provide visual feedback to the participant about their location on the treadmill.

well as projection on the treadmill itself can be used to provide participants with visual feedback about their position 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 3).

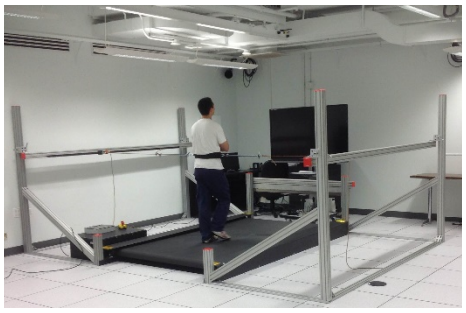


Figure 3: A 3"x3" aluminum strut frame has been constructed around the treadmill. The frame supports a magnetic rail that the linear motors run on at the front of the treadmill. The trolley system allowing fore-aft motion is mounted on the side rails. The height of the side rails are adjustable for participants 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 4).

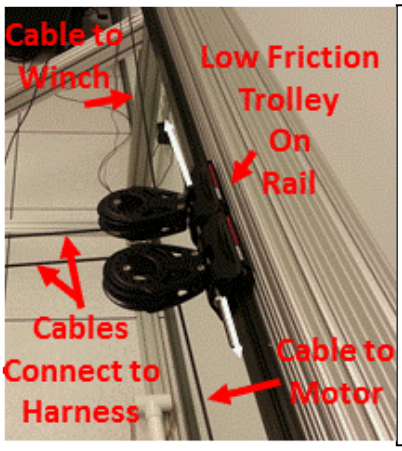


Figure 4: The cable transmission runs through a set of pulleys mounted on a low friction trolley. The cable running through these trolley pulleys loops around a third pulley attached to the lateral aspect of the participant's harness. The trolley can travel freely on a rail fixed to the side rail of 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.

- EMG Recording Electrodes: Up to 16 wireless surface electrodes (Delsys Inc, Matick, MA) will be used to record muscle activation patterns of major muscles groups of the lower limb and trunk.

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:

NA, this is not a multicenter study