Protocol Title

Post stroke walking kinematics using the Honda Walking Assist (HWA) robotic exoskeleton

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Study Device: Honda Walking Assist designed and developed by Honda R & D Americas, Inc.

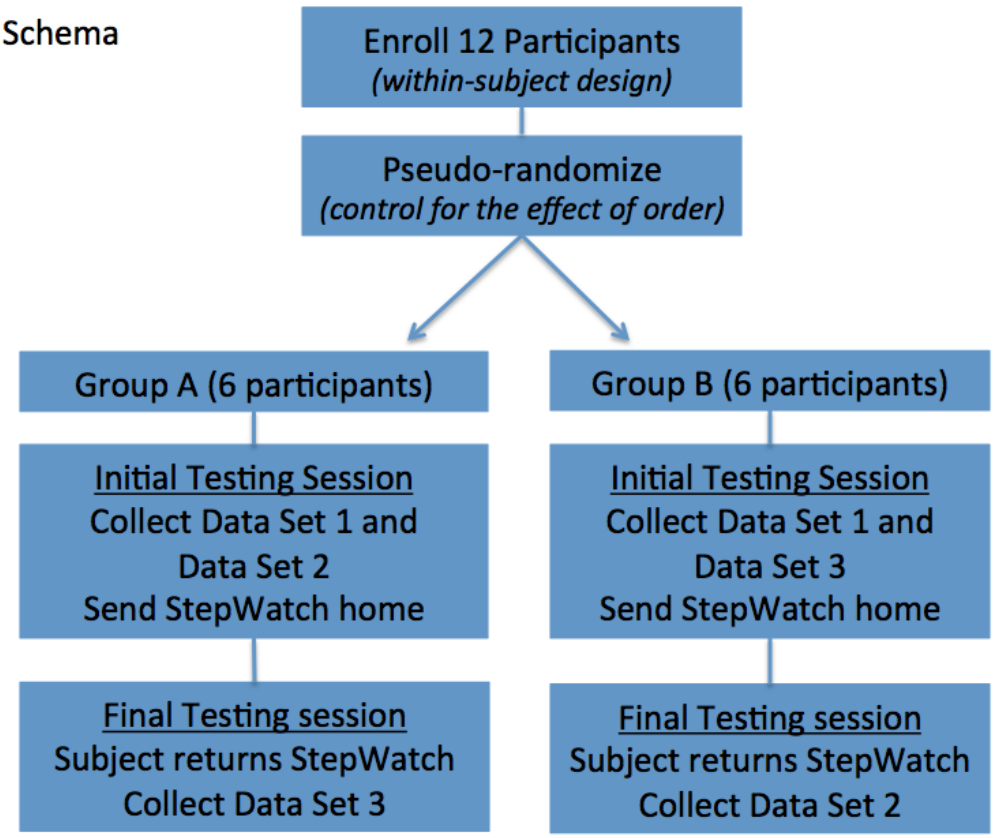
Funding Source: Honda R & D Americas, Inc.

Initial Version: 10-2-2018
10-8-2018 Revised by AB

Study Summary:

Title	Post stroke walking kinematics using the Honda Walking Assist (HWA) robotic exoskeleton
Short Title	Post stroke walking kinematics using the HWA robotic exoskeleton
Protocol Number	TBD
Methodology	Within-subjects design
Study Duration	10 months
Study Center(s)	College of St. Scholastica, maurices Community Clinic
Main Objective	Determine the effectiveness of the HWA to alter joint kinematic and EMG magnitudes in individuals post-stroke
Number of subjects	12
Diagnosis and main criteria	Cerebrovascular accident (CVA), ≥12 weeks but <1 year post, Age: 18-85 years, Walk 10 meters with stand by assistance with or without orthosis or cane
Study Product (s)	Honda Walking Assist (HWA) robotic exoskeleton
Duration of administration	2 Testing sessions (~5-6 hours total across the 2 sessions)
Reference condition	Walking without HWA
Statistical Methodology	Paired t-tests, Multiple ANOVAs

Study Schema



Background and rationale:

Background of the question and study rationale:

Walking dysfunction following stroke is prevalent. Traditional rehabilitation methods fall short of achieving desirable outcomes for most people who experience stroke. Robotic methods to assist or resist hip movements, such as the Honda Walking Assist Device (HWA) Robot from Honda R & D Americas Inc., are being explored as a means of improving the recovery of walking in people with poststroke hemiparesis. A previous study of HWA benefit in persons with stroke found an effect after use (aftereffect) of increased peak hip extension angle in terminal stance phase which correlated with increased hip extension internal moment (during loading response and midstance) on the paretic lower extremity (LE). (Ohata, 2018) A computational model of sensorimotor recovery proposed by Reinkensmeyer et al., 2012 may explain the aftereffect of HWA use.

Reinkensmeyer's model proposes that "Disrupting corticospinal (CS) cells (both sensory and motor) that are already optimized to a joint (e.g. hip) may allow non-optimized cells (e.g. knee and ankle) to become optimized." (Reinkensmeyer, Guigon, & Maier, 2012) Stated another way, changing somatosensory input to the cortex during walking may enable a reappropriation of cortical resources to activate latent residual capacity of the motor system in segments that are underperforming. Based on this model, we hypothesize the assist mode of the HWA, which facilitates hip flexion/extension during walking, disrupts currently optimized hip CS cells biased toward flexion/extension through reduced sensory input. This reduced input to the optimized CS cells allows more latent CS cells to become facilitated through practice. If accurate, we would expect to see evidence of heightened activity during walking at regions remote from the hip.

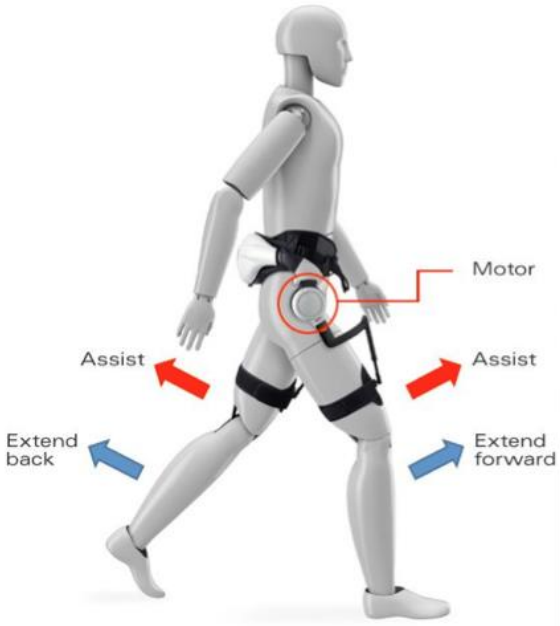
Here we propose to quantify the effect of the HWA on walking at the knee, ankle, trunk and arm segments during phases of the gait cycle (GC) as described by Perry. (Perry & Davids, 1992) Additionally, we will quantify the aftereffect of HWA use in these joints and segments. Quantification will include measurement of walking kinematics (joint angles), muscle activity (EMG output), ground reaction forces and Spatiotemporal gait characteristics measured in three conditions: 1) Walking at self-selected pace (control), 2) walking with the HWA (4Nm assist), 3) and immediately following HWA walking (aftereffect). Our overall hypothesis is that walking with the HWA in the (hip flexion and extension) assist mode results in reallocation of cortical motor resources to the knee, ankle, trunk and arm. We also propose that normalizing walking through optimization (activation of latent residual capacity) of previously non-optimized corticospinal motor units with the HWA will produce a short-term (or within-session) aftereffect. We hypothesize that aftereffect will be greater in individuals with less lower extremity use since their stroke. Therefore we will characterize lower extremity use by quantifying the average number of steps each participant takes using an activity monitor.

Background of the device:

The Honda Walking Assist (HWA) System (pictured below) is a robotic device developed by Honda R&D Corporation ®, Japan (https://world.honda.com/Walking-Assist/). It is controlled through software run on a tablet. The device weights 2.7 kgs and has two brushless motors that run on a lithium ion battery with an approximate running time of 60 minutes. It comes in 2 sizes with adjustable frames making it possible to fit a variety of body types/sizes.

It takes approximately 5 minutes to fit the HWA on to the user. It's computer-activated motors use hip angle information to guide assistance delivered through the thigh straps to the legs in time with the walking cycle. The maximum torque delivered is 4 Nm. Wearers have described this level of assistance as "mild" to "moderate". The goal of device use is to promote walking ease by increasing stride length and improving the step symmetry.

Honda began leasing the HWA in Japan in 2015, in January of 2018 they obtained medical device approval in the European Union. Food and Drug administration approval of the HWA in the United States is in process at this time.



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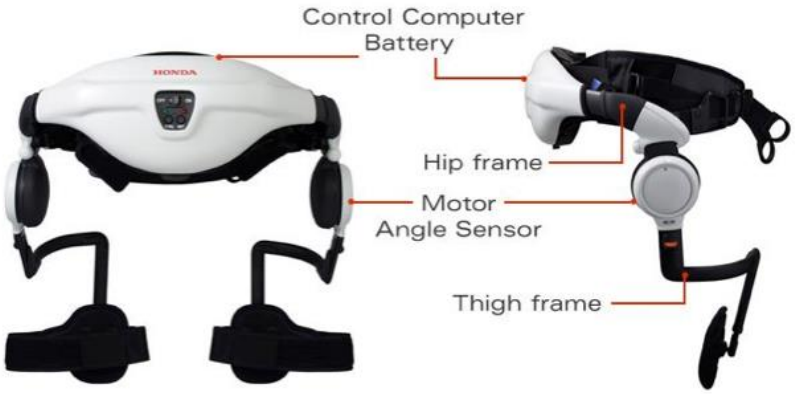
https://global.honda/innovation/robotics/WalkingAssist.html *(accessed 9-28-2018)*



Key Specifications

Overall width	Approx. 430mm - 495mm
Weight	Approx. 2.7kg (including battery)
Operating time per charge	Approximately 60 minutes
Battery	Lithium-ion battery, 22.2V-1Ah
Motor output	Maximum torque: 4N · m
Use environment	Indoor or outdoor (except when raining) on flat floor/ground
Appropriate temperature range for storage	Between -20°C and 55°C
Appropriate temperature range for use	Between 10°C and 30°C
Appropriate humidity range for use	Between 30% and 85%

Study Objectives:

Specific Aim I: Determine the effectiveness of the HWA to alter joint **kinematic** and **EMG** magnitudes at the knees and ankles in individuals post-stroke.

Sub Aim I- Determine the effect of HWA on paretic limb weight acceptance patterns. Specifically, knee flexion angle achieved at initial swing (62-75% GC) and EMG output at terminal swing and initial contact.

Hypothesis: In the HWA walking and after-assist condition, knee flexion angle will be increased at initial swing and will positively correlate with the magnitude and/or timing of EMG output of the hamstring at terminal swing and quadriceps at initial contact compared to the control (no SMA) condition.

Sub Aim II- Determine the effect of HWA on walking propulsion. For example: ankle plantar flexion angle and EMG output achieved at terminal stance to preswing phase (~50% GC) of the gait cycle.

Hypothesis: In the HWA walking and after-assist condition, peak plantarflexion angle will increase at terminal stance and will positively correlate with the magnitude and/or timing of EMG output of the medial gastrocnemius compared to the control condition.

Sub Aim III- Determine the effect of HWA on ankle dorsiflexion angle at midswing.

Hypothesis: In the HWA walking and after-assist condition, peak ankle dorsiflexion angle at midswing will increase and will positively correlate with the magnitude and/or timing of EMG output of the tibialis anterior compared to the control condition.
Note: Our ability to answer this sub aim will be dependent on the number of participants enrolled who are able to ambulate safely without ankle foot orthoses (AFO).

Sub Aim IV- Determine the effect of HWA on EMG magnitudes in the non-paretic hip, knee and ankle musculature.

Hypothesis: EMG magnitudes will be lower in the non-paretic limb muscles in the HWA walking condition compared to the same muscles in the control condition.

Specific Aim II: Determine the effectiveness of the HWA to improve arm and trunk **kinematics** in individuals post-stroke.

Sub Aim I- Determine the effect of the HWA on the Arm posture score for each limb.(Riad, Coleman, Lundh, & Broström, 2011)

Hypothesis: In the HWA walking and after-assist condition, an arm posture score that falls within normal parameters will be present in contrast to the control condition.

Sub Aim II- Determine the kinematic dissociation between trunk and pelvis during the gait cycle. Determine the change in trunk to pelvis angle (uprightness).

Hypothesis: In the SMA walking and after-assist condition, the peak angle of dissociation between trunk and pelvis will demonstrate evidence of increased stability relative to the control condition.

Specific Aim III: Determine the effectiveness of the HWA to alter **STAIR** ascend/descend test (Flansbjer, Holmbäck, Downham, Patten, & Lexell, 2005) scores in individuals post-stroke. Determine the changes in paretic and non-paretic limb EMG magnitudes at critical stair climbing timepoints.

Hypothesis: In the HWA walking condition, stair ascent and descent times will be reduced compared to the control condition.

Specific Aim IV: Determine the effect of the HWA on the magnitude of **ground reaction forces** (vertical load, horizontal shear, vector patterns, and center of pressure) for both lower extremities in individuals post-stroke.

Specific Aim V: Determine the effect of the HWA on **Spatial and Temporal gait variables** (Gait speed, step length, stride length, stride symmetry, step width, cadence) in individuals post-stroke.

Exploratory Aim VI: (Exploratory ONLY- not a study outcome) Appling inverse dynamic mathematics, we will develop our methods for internal joint moment measurement and analysis using hip joint data.

Participant Eligibility:

Potential participants will be recruited through networking with local care providers (letter attached) fliers (flier attached) and word of mouth. Those who express interest in study participation will be screened over the phone or in person to determine if they meet study criteria (below) before beginning the process of obtaining written informed consent (consent form is also attached).

Inclusion criteria

1. ≥12 weeks but <1 year post stroke at time of study participation
2. Age: 18-85 years
3. Ability to walk a minimum of 10 meters with standby assistance with or without orthosis or assistive device (Functional Ambulation categories 3, 4 or 5)
4. Able to follow three step commands
5. Express the ability to understand study tasks and purpose
6. Able and willing to provide written informed consent
7. Living in the community with the ability to travel to maurices Community Clinic for testing
8. Willingness to wear the StepWatch pedometer for a period of 3 days in their home
9. (If applicable) ≥ 90 days post major orthopedic surgery (such as a joint replacement)
10. (If applicable) ≥ 6 months post cardiac surgery

Exclusion criteria

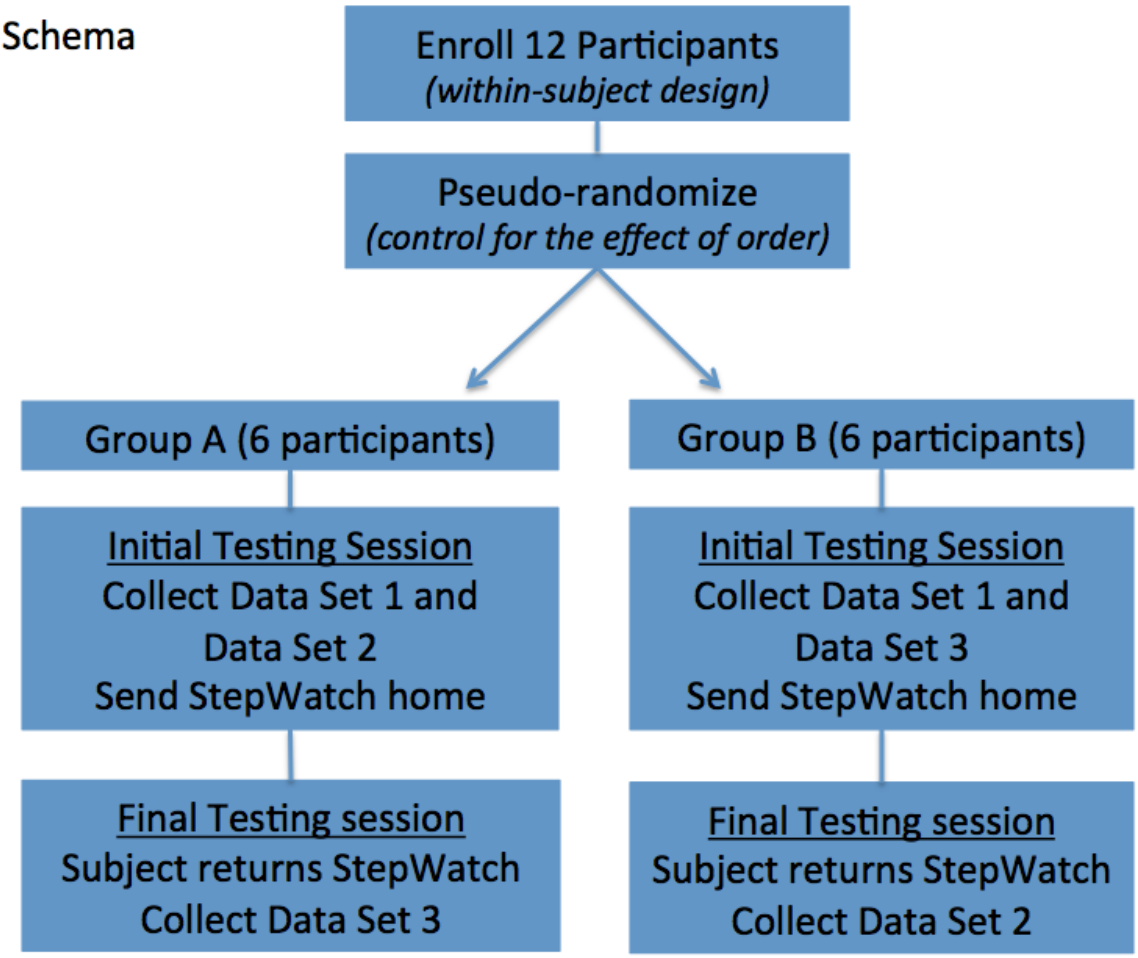
1. Serious cardiac conditions (hospitalized for myocardial infarction or heart surgery within 3 months, congestive heart failure, unstable cardiac arrhythmias, hypertrophic cardiomyopathy, severe aortic stenosis, angina or dyspnea at rest or during activities of daily living)
2. Severe arthritis or orthopedic conditions that limit lower extremity range of motion (> 10° or < 90° knee flexion, lacking > 25° hip extension, >15° from neutral plantar flexion.)
3. Preexisting neurologic disorders such as Dementia, Multiple Sclerosis, Amyotrophic Lateral Sclerosis, Parkinson's Disease or Ataxia.
4. History of lower limb amputation, non-healing ulcers, legal blindness or severe visual impairment

Testing Plan:

Enrolled participants will be pseudo-randomized by drawing from an envelope into either Group A or Group B and scheduled for two testing sessions 1-week ± 3 days apart. Demographic interview, MoCA, Biometrics and StepWatch activity monitor instruction will be conducted on the first testing day for participants in both groups. Group A participants will complete measures in Data Set 2 during the initial

testing session and Data Set 3 during the final testing session. Group B participants will complete measures in Data Set 3 during the initial testing session and Data Set 2 during the final testing session.

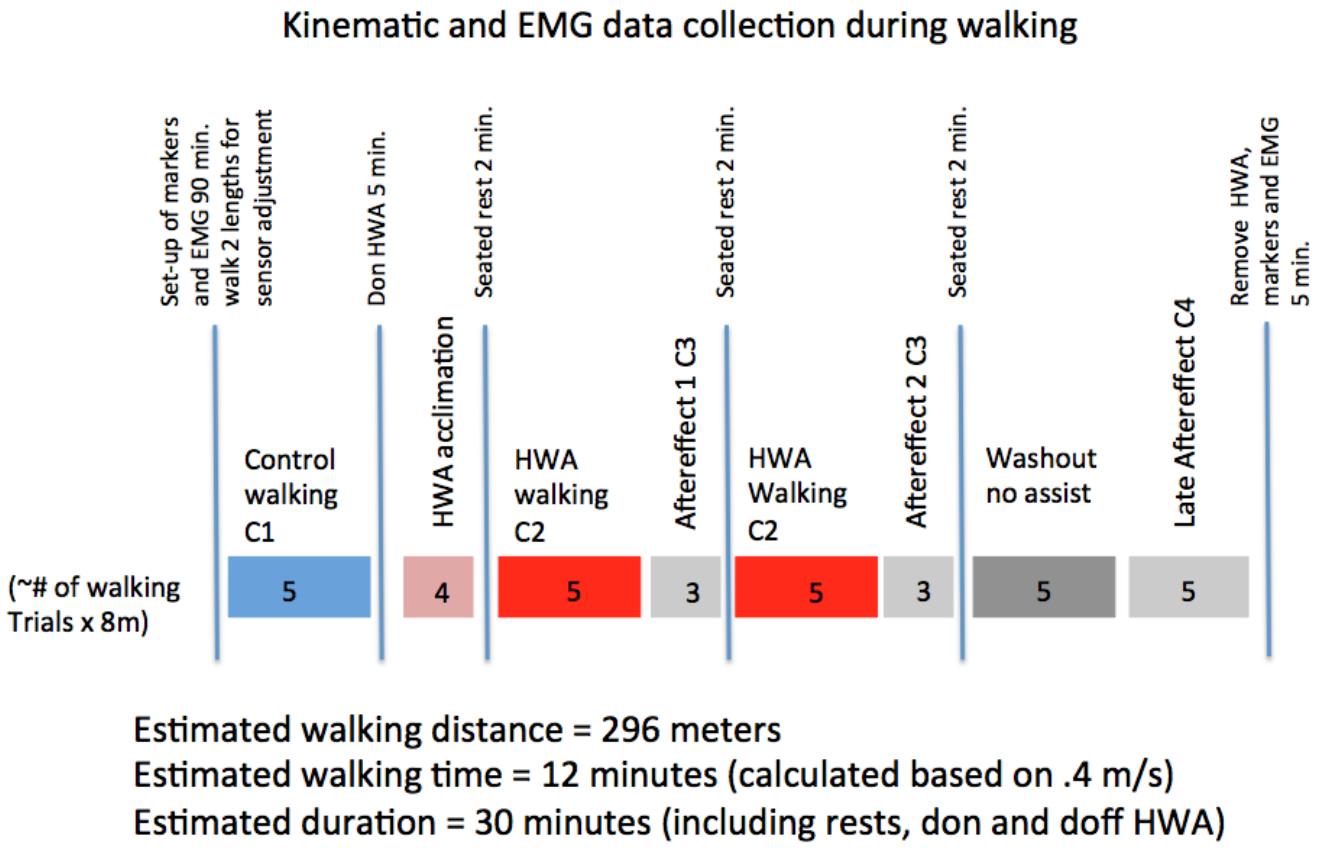
Study Schema



Each testing sessions will be approximately 2.5 to 3 hours in length. The estimated time for each measure or procedure is indicated in the table below. (data collection forms are attached)

	Measure or procedure	Time estimate (minutes)

Data Set #1	Demographic interview (DOB, sex, date of stroke, type of stroke, body side affected, assistive devices, Orthoses, handedness)	5
	Montreal Cognitive Assessment (MoCA)	8
	Biometrics (height, weight, leg length)	5
	Instruct participant on use of the StepWatch (send it with them for 3 days of use during their daily routine)	10
	Total time	**~28 min**
Data Set #2	Collect StepWatch from participants (Group B)	5
	Somatosensory testing	15
	Modified Tardieu Scale (muscle tone)	10
	Lower extremity Fugl-Meyer (motor recovery)	10
	Biometrics, EMG and HWA set-up for stairs	30
	Control Stair climbing Ascend/Descent test (1st for grp A)	15
	Activities-Specific Balance Confidence Scale	10
	HWA Stair climbing Ascend /Descend test (1st for grp B)	15
	Total time	**~1 hour 50 min**
Data Set #3	Collect StepWatch from participants (Group A)	5
	Set-up of 40 motion capture markers and 16 EMG electrodes on participants body	90
	Kinematic and EMG data collection during walking (see detailed schematic below)	30
	Total time	**~2 hours, 5 minutes**



Description of Measures used to characterize participants

1. Montreal Cognitive Assessment (MoCA)-a 16-item rapid screen of cognitive abilities designed to detect mild cognitive dysfunction (Nasreddine et al., 2005), 30 points possible.
2. Activities-Specific Balance Confidence Scale (ABC)-a 16-item questionnaire with an ordinal scale designed to measure an individual's confidence in their ability to perform daily activities without falling. It has good to excellent reliability and adequate construct validity. (Botner, Miller, & Eng, 2005)
3. Fugl-Meyer Assessment of Motor Recovery after Stroke (FMA) The domain for lower extremity motor function will be used (Sections E and F). It has been found to be valid and reliable among individuals with stroke. (Fugl-Meyer, J‰‰skˆ, Leyman, Olsson, & Steglind, 1975) 34 points possible.
4. Modified Tardieu Scale- A measure of resistance to passive movement at different movement velocities used to quantify the dynamic component of the muscle spasticity. It has been found to be a valid and reliable method of quantifying these features of spasticity in adults with stroke. (Singh, Joshua, Ganeshan, & Suresh, 2011)
5. Somatosensation-Three methods of quantifying paretic lower limb somatosensation will be used. Great toe Sharp/dull (# correct/10 trials) assesses the integrity of the anterior Spinothalamic tract. (Kandel, Schwartz, Jessell, Siegelbaum, & Hudspeth, 2000) Great toe up/down testing (# correct/10 trials) assesses the integrity of the dorsal column medial lemniscal system and the higher-level task of discriminating the direction of movement (kinesthesia) (Goble, 2016), Vibration Detection Threshold is a quantitative psychophysical

measure of sensitivity thought to reflect Aα axon transmission. (Rolke et al., 2006) It will be quantified in seconds and scored using the average of three trials with a 128 Hz tuning fork placed on the skin at the base of the great toenail. (Janz, Bjorkland, Kramer, Oczak, & Borstad, 2018)

6. The StepWatch Activity Monitor will be used to characterize participants physical activity based on their daily step counts. Participants will wear StepWatch Activity Monitor on the less affected lower extremity during their daily routines for 8 hours per day for three days. Verbal and written instructions will be provided. The StepWatch is reliable and has been validated to provide the most accurate measurements of physical activity in persons with slow walking, such as may be caused by stroke. (Mudge, Stott, & Walt, 2007) (Mudge & Stott, 2008) Physical activity as measured by daily step count is a potentially large source of variability within the participants that will be important to characterize and understand. In Specific Aims 1 and 2 we will be attempting to quantify a differenced between the control condition and the aftereffect of walking with the HWA. Because we hypothesize that aftereffect will be greater in individuals with less lower extremity use (those who take fewer steps) since their stroke it is important to collect data on this variable.

Description of measures used to quantify effect of HWA on walking

7. Kinematic Analysis of Gait will be obtained using a Qualisys 8-camera motion capture system. Sample rate 120 Hz. A modified IOR gait marker set (~40 markers) applied bilaterally. (Cappozzo, Catani, Della Croce, & Leardini, 1995)
8. Analysis of muscle activation during gait using 16 Delsys Tringo EMG sensors applied over bilateral LE muscle groups including gluteus maximus (1), quadriceps (3), hamstrings (2), tibialis anterior (1), medial gastrocnemius (1), totaling 8 sensors per lower extremity. Sample rate 2000Hz.
9. 2 AMTI Force platforms will be used to quantify ground reaction forces (vertical load, horizontal shear, vector patterns, and center of pressure) for both lower limbs during gait. Sample rate 1200Hz.
10. Stair Climbing Ascent/Descent test- A timed test of the ability to ascend and descend stairs with our without a rail. For this study a flight of 7 stairs will be used. The means of two trials of ascending and descending will be recorded. (Flansbjer et al., 2005)

Withdrawal or removal of participants from the study

In the case that a participant, for any reason, does not complete the study the following categories will be used to record the occurrence:

1. Patient withdraws
2. Patient is unable to perform protocol requirements
3. Patient demonstrates a change in medical condition
4. Patient experiences an adverse event that makes continuation in the protocol unsafe
5. PI determines that continuation in the study would not be appropriate
6. Other

Study Risks:

1. This is a study of walking performance therefore risk of falling is present. This risk is similar to the risk one would undertake while participating in outpatient physical therapy for walking training following stroke. It will be mitigate by study personnel maintain contact with the participant during walking, transitions and stair climbing. Participants will be encouraged to

wear their most comfortable walking shoes and will be walking in a well-lit, open environment.

2. While the adhesive materials used in this study are latex free, the risk of skin irritation is present. Skin irritation could arise from the tape used to fix the motion capture markers, the EMG sensors or from the HWA device itself rubbing on the skin. This risk will be discussed with the participants during the process of obtaining informed consent and they will be instructed to inform study personnel if they experience itching or irritation. Participants who demonstrate somatosensory impairment may not feel skin irritation. Those participants will receive a visual skin check in areas of possible irritation midway through the assessments. Adjustments to the size and fitting of the HWA will be conducted to address skin irritation including the possibility of adding additional padding or other measures to reduce irritation.
3. The HWA device delivers a maximum 4 Nm of torque to the legs during walking. There is a chance that the device could malfunction during use, which could cause a loss of stability or balance. To mitigate this risk study personnel will maintain contact with study participants during device use.
4. There is a possible risk that study participants may develop muscle soreness from the walking or stair climbing they will perform in as part of the assessments. To mitigate this risk participants will be given scheduled rest periods during the protocol and allowed to take additional rest if they choose.

Statistical considerations and Data Management

Study design

This study has a within-subjects design in which walking parameters including kinematics and muscle activity will be collected from participants during two testing sessions. For practical reasons a non-probability sample will be used. Pseudo randomization of participants into two groups will be used to control, in part, for the effect of order of testing on study outcomes.

Sample Size

The sample size for this study was calculated based on the assumption of detecting a meaningful difference in peak knee flexion angle (primary hypothesis) between the control and HWA walking conditions. To detect a mean difference of 5 degrees with a standard deviation of 5 degrees using a two-sided test and significance level of 5%, power of 80%, would require 10 participants. To allow for a 20% dropout rate 12 participants will be recruited. At the mid point of participant testing (6 participants) sample size will be recalculated and the sample adjusted if necessary to achieve appropriate power for the primary aims.

Data analysis plan

The measures collected for each subject in each condition will be compared within and across participants using paired t-tests and ANOVA. The alpha level will be set at $p<0.05$ to indicate statistical significance.

Data Management

Participant data collected in this study will be kept completely confidential and in compliance with HIPPA requirements. Participants will be assigned a study ID, all data collection forms and tools will use study ID therefore data will be de-identified. Data will be stored in locked cabinets, electronic data will be kept on secure, password protected computers. Data will be retained securely for three years after study publication.

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