iStride™ Device Used for Stroke Rehabilitation
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1. Rationale for the study, area of current scientific concern, and why the research is needed

Hemiparesis and other impairments are a frequent and disabling consequence of stroke and can lead to asymmetric and inefficient walking patterns. Training on a split-belt treadmill, which has two separate treads driving each leg at a different speed, can correct gait asymmetries post-stroke (Reisman et al. 2005, Reisman et al. 2007). However, the effects of split-belt treadmill training only partially transfer to everyday walking over ground and extended training sessions are required to achieve long-lasting effects (Reisman et al. 2009). Our previous studies suggest that the Gait Enhancing Mobile Shoe (GEMS) that has been developed in our laboratory can be used as an alternative gait training device for people with stroke (Handzic, Reed, and colleagues 2011, 2011, 2012, 2013).

The GEMS (Figure 1) mimics the actions of the split-belt treadmill, but can be used during over-ground walking and in one's own home, thus enabling long-term training. This GEMS does not require any external power and is completely passive; all necessary forces are redirected from the natural forces present during walking since it utilizes the wearer's weight to generate its movements. While the movements of the GEMS are similar to the split belt treadmill, and the GEMS generates a similar aftereffect, the efficacy of this shoe in modifying the gait of an individual with stroke is not yet verified. This research aims to test the GEMS on individuals with stroke to determine if the related effects that show up on healthy subjects can benefit individuals with stroke.

In this study, we will test the efficacy of the GEMS on individuals with stroke. Efficacy will be evaluated based on the change in gait coordination and also based on subjects' self-reported comfort on the device. We predict that the GEMS will result in changes to interlimb coordination of gait. Note that this is a efficacy study, not an effectiveness or safety study of the device; this distinction is made clear in a paper by Singal et al. (2014).

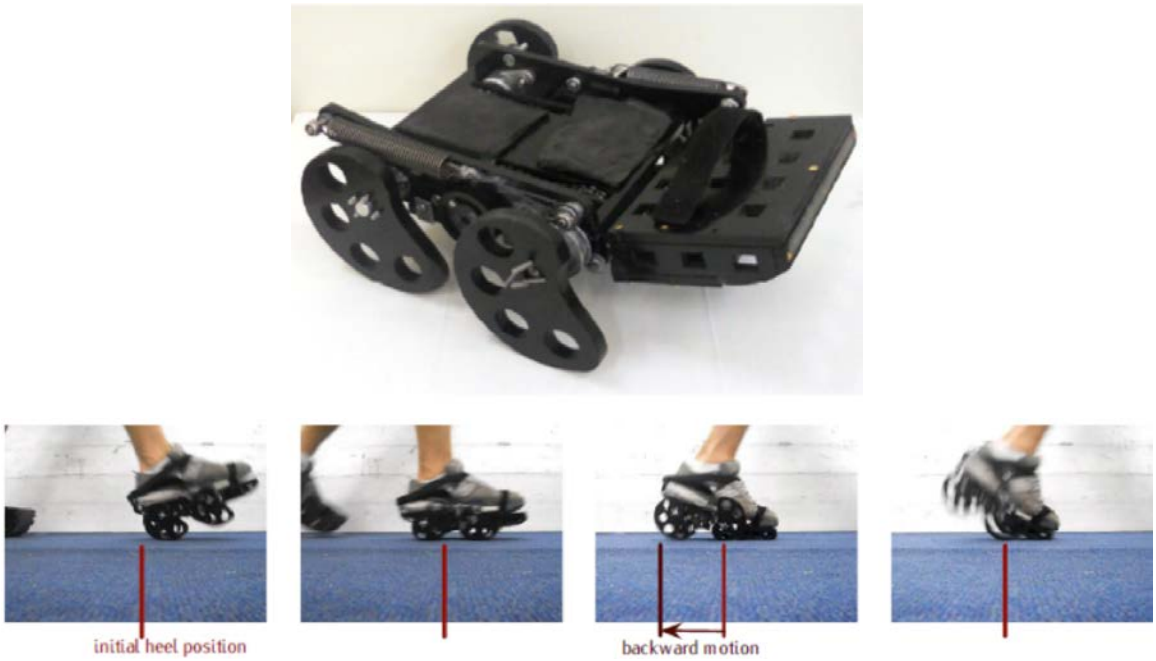

Figure 1: Gait Enhancing Mobile Shoe (GEMS). (top) Picture of GEMS – note that wheels are designed such that downward force (i.e. from standing) will cause them to rotate and move the shoe backwards, relative to the ground. (bottom) The motion of the GEMS from heel contact until toe off of walking. The GEMS was measured to have a smooth horizontal backward motion of approximately 6-8" (15-20 cm).

2. Background information, description of existing research, and information that is already known

In the United States, nearly 800,000 people suffer a stroke each year, and approximately two-thirds of these individuals survive (Lloyd-Jones et al. 2010). Many people suffer from significant and

long-lasting motor deficits that require rehabilitation. One such motor deficit that frequently occurs is hemiparesis, or a weakness on one side: among ischemic stroke survivors over 65 years old, half had some degrees of hemiparesis persisting over six months post-stroke (Kelly-Hayes et al. 2003). Lower limb hemiparesis leads to asymmetric walking patterns, called hemiparetic gait (Brandstater et al. 1983; Wall and Turnbull 1986). Specific characteristics of hemiparetic gait include asymmetries in temporal (e.g. swing time and double-support time) (Brandstater et al. 1983; Titianova and Tarkka 1995) and spatial (e.g. step length) (Balasubramanian et al. 2007) measures of interlimb coordination. That is, the timing and placement of the feet are not equal on the two sides.

The asymmetric nature of hemiparetic gait can have a large impact on functional walking ability. For example, swing phase asymmetry is a significant predictor of hemiparetic walking performance because it strongly correlates with stages of motor recovery, walking speed, and falls (Brandstater et al. 1983; Titianova and Tarkka 1995). Another measure of temporal asymmetry – double support duration – is similarly correlated with walking speed (Olney et al. 1994). In addition, spatial (e.g. step length) asymmetry is associated with decreased propulsive force on the paretic leg (Balasubramanian et al. 2007; Bowden et al. 2006), which limits forward motion of the body and reduces gait efficiency (Brouwer et al. 2009; Kahn and Hornby 2009). The importance of gait efficiency should not be understated – the elevated energy demands of hemiparetic gait combined with physical deconditioning post-stroke can greatly limit performance of activities of daily living, contributing to poor cardiovascular fitness and metabolic syndrome. In turn, this can increase the risks of a second stroke or cardiovascular event and is associated with increased morbidity and mortality rates (Ivey et al., 2005). Therefore, improving gait symmetry should be an important goal for therapy, to not only improve functional mobility and reduce injury, but also to enhance general health and well-being post-stroke.

Practicing walking on a split-belt treadmill can correct abnormal interlimb coordination of gait in individuals with hemiparesis following stroke or other central nervous system lesions (Reisman et al. 2005, Reisman et al. 2007). Asymmetric gait can manifest as a spatial asymmetry, in which steps taken on one side are longer than those on the other. It can also manifest as a temporal asymmetry, where the timing is uneven on the paretic and non-paretic sides. Temporal asymmetries are often measured as differences in the duration of double support periods, which are the amount of time both feet are simultaneously contacting the ground and are measured separately for the paretic and non-paretic sides. The GEMS is designed to cause changes in both spatial and temporal gait symmetry. We predict that the GEMS would cause the steps on the side with the GEMS to be larger since individuals would compensate for the backward rolling motion by placing their foot farther forward in stance, thus increasing the distance between the two feet. Similarly, since the stride is longer, it may also shorten the duration of stance relative to the other side. With shortened stance duration, the amount of time spent in double-support at the end of stance would likely decrease as well. An alternative is to have a GEMS that moves the foot forward, which would have the opposite effect, shortening steps and lengthening double-support durations of the foot that it is placed on. Therefore, the same effect could be obtained by using a backward-moving GEMS on the healthy-side foot as would be obtained using a forward-moving GEMS on the paretic-side foot. In this study, we will focus on the backward moving GEMS, as shown in Figure 1.

Although the original idea of the GEMS is derived from the motion of the split-belt-treadmill, there are distinct differences between walking on the GEMS and walking on a split-belt treadmill with asymmetric belt velocities (Handzic and Reed, 2013). While the body's velocity relative to ground is zero on a split-belt treadmill, the relative velocity of the GEMS is non-zero and forward. The GEMS forces the wearer's foot forward or backward whereas the treadmill moves both feet backward, but at different speeds. For both the split-belt treadmill and the GEMS, the relative velocity between both feet is similar and the backward-moving GEMS takes the place of the faster tread. Our short-term study will examine how the motion of the shoe affects the change in gait.

We hypothesize that training over ground will lead to a change in the interlimb coordination in individuals with asymmetric gait and allow individuals to develop a more persistent symmetric gait.

There are several differences between training on ground and a treadmill, such as visual flow and vestibular information signaling forward movement that likely limit the expression of learning in the over-ground context when trained on a treadmill. Visual cues appear to be particularly important for context awareness (Keamey, 2003). Visual cues, coupled with prior experience, are so powerful that predictive postural responses cause an individual to stumble when stepping onto an escalator that is not moving (Reynolds and Bronstein 2003; Bronstein et al. 2009). The body has learned an internal model that expects an acceleration when stepping onto an escalator, but when that acceleration does not occur, the person stumbles. A recent study of split-belt walking showed that transfer to over-ground walking is enhanced when subjects are blindfolded during training on the treadmill and tested over ground (Torres-Oviedo and Bastian, 2010). Since blindfolding eliminates visual cues about the environment, this also suggests that vision is a key factor in determining the context-dependence of learning. Since it is not realistic to blindfold stroke patients during gait training, we designed the GEMS so that training could occur during over-ground walking, thus visual cues during training and later walking over ground would be the same.

Data from control subjects using an earlier version of the GEMS has been published (Handzic et al. 2011) and a video of this previous version can be found at http://reedlab.eng.usf.edu/publications/handzic2011GEMS.mp4. In this study, we found that this earlier version of the GEMS was capable of changing step length as predicted, however the previous design was too heavy and too tall to be considered practical for testing in stroke populations. The current version of the GEMS produces similar motion to the previous version, but it weighs less (~1 kg) and is shorter (~4.4 cm). We will test the efficacy of wearing the current GEMS on gait coordination during walking over ground on individuals with stroke. All walking will be performed while subjects are wearing a gait belt and are closely guarded by an experienced physical therapist to prevent falling. Subjects may wear a safety harness attached to the SOLO-STEP® System (Solo-Step, Sioux Falls, SD) if necessary. The effects of the GEMS on gait coordination will be compared to those induced on a split-belt treadmill.

The proposed project represents one of the first attempts to build a device that corrects walking symmetry while walking over ground. Not only would this allow people to experience gait corrections while performing normal movements, but the simplicity and relative low cost of these devices would also open up potential opportunities to train at home (for high-functioning individuals with supervision) and in clinics where a split-belt treadmill is not available. The studies outlined here will establish whether the GEMS is capable of changing interlimb coordination of gait, and whether individuals with stroke can use these devices for rehabilitation purposes. This work will thus build the foundation for future training studies examining the effectiveness of long-term use of the GEMS for improving symmetric walking patterns.

3. The research questions, objectives, and purpose

The question that this study targets is the modification of human walking patterns for use in stroke rehabilitation. It is our ultimate objective to show that the GEMS can change a person's temporal and spatial gait asymmetry into a symmetric gait. Our points of reference are results obtained by previous studies with split-belt treadmills. We are also interested in how altering the interface between a foot and the ground influences the adaptation to new walking patterns.

4. The study design including information that is needed to answer the research questions

The goal of this study is to test the efficacy of the Gait Enhancing Mobile Shoe (GEMS), which we hypothesize can be used to correct gait asymmetry in individuals with stroke. The study will be structured around subjects walking on the GEMS before and after which the subjects' gait is recorded and analyzed. The study design is within-subjects where each individual's gait will be compared before, during, and after the training period. There will be three phases of this research, tests on healthy individuals, a short-term training on individuals with stroke that lasts up to four

sessions and a long-term training on individuals with stroke that lasts four weeks with an initial visit prior to the start of training and two follow-up tests at one and three months.

The tests on healthy people will consist of either one or two training sessions on the GEMS and/or split-belt treadmill with one pre-screening test to evaluate subjects' gait patterns. Some of the sessions will be used to optimize the motion of the GEMS and the after-effects prior to testing on individuals with stroke. Some of the sessions will be directly compared to the split-belt treadmill.

The short-term training will consist of three training sessions performed in one week with a gait evaluation on the last day and a pretest with initial fitting of the shoe the week before. One or two of the training sessions may be replaced with training on the split-belt treadmill in place of training on the GEMS to allow for a direct comparison in the change in gait.

The long-term training will consist of four weeks of training with three training sessions performed each week. Gait evaluations will be performed the week before the first training, periodically during training (no more than once per week), and followup tests at one and three months after final training. An assessment of the subjects ability to adapt to a split-belt treadmill may be conducted at the start and/or end of the experiment to allow a direct comparison of their gait.

The training sessions for the testing on healthy individuals and the short- and long-term trainings on individuals with stroke will consist of up to forty minutes of training over up to eight shorter sessions of walking on the GEMS with breaks between walking sessions and as needed if the subject requests an additional break. Subjects will place the GEMS on their foot in which they have the shortest step length, as measured during the pre-training gait analysis. This is typically the healthy side foot. The GEMS will encourage them to take larger steps with that foot. The total training sessions will be no longer than one hour. For split-belt treadmill sessions, the format will be exactly the same, but they will walk on a split-belt treadmill instead of the GEMS with the faster tread moving on the same foot that would wear the GEMS in the over-ground walking sessions.

A study physician or an advanced registered nurse practitioner (ARNP) will perform medical screening for the subjects that will participate in the stroke portion of this study to determine if potential subjects had one or more cerebral strokes without other medical conditions (e.g., other neurological, orthopedic, etc.) that would affect or explain the subjects' walking or limb movement. Clinical assessments will consist of vision, proprioception, pressure sensation, cognition using Folstein Mini-Mental Status Exam (Folstein et al. 1975), and lower extremity motor function test using Fugl-Meyer Assessment (Fugl-Meyer et al., 1975). Six Minute Walk Test and Timed Up and Go Test (Andersson et al., 2006) will be performed to assess changes in subjects' aerobic capacity and risk of falls, respectively, following training. Healthy subjects will be asked to walk and a pre-test of their gait asymmetry will be evaluated.

To measure gait, a ProtoKinetics Zeno Walkway (ProtoKinetics, Havertown, PA) or a motion capture system will be used. The Zeno Walkway calculates the desired gait parameters after an individual walks across it. For motion capture, we will use infrared-emitting markers placed bilaterally on different parts of the body, such as the shoulder (acromion process), pelvis (iliac crest), hip (greater trochanter), knee (lateral joint space), ankle (lateral malleolus), and toe (5th metatarsal head), to record 3D position data. The motion capture system will record the movement of these markers at 120 Hz. In addition, pressure switches may be taped to the bottom of the shoes, beneath the heel and toe, to measure durations of swing and stance phases

Our main analysis will be to compare the amount of learning (i.e. deviations from symmetry post-adaptation) to normal baseline symmetry. This will be done using a repeated measures ANOVA to compare baseline gait symmetry at the start of the experiment to post-adaptation at the end of the experiment and on the 1 and 3 month follow-ups. We will quantify the amount of adaptation and the change in gait asymmetry by comparing the magnitude of step length and double support differences during baseline, at the beginning of training, during training, and after training. During a symmetric gait, step lengths on each side are the same; during an asymmetric gait, step lengths are different. These measures are standard accepted measures for measuring gait asymmetries.

5. Sample size

Preliminary studies with three healthy test subjects showed statistical data that indicated that the minimum number of subjects for this study is 18 (Handzic et al. 2011). We powered the t-test between pre-training and post-training data. We calculated an effect size of 0.68 for step length difference, resulting in an estimated sample size of 18 subjects. We are planning two experiments, a short-term and a long-term, so we expect to need 36 total subjects to show the necessary statistical power for each. The preliminary test with healthy subjects was approved under the Einstein Healthcare Network IRB HN4365, and other preliminary tests with healthy subjects were conducted under USF IRB Pro00001858. Similarly, for the healthy person study, we expect to need a sample size of 18 subjects.

In addition, initial testing on individuals with stroke has been approved and conducted under the Einstein Healthcare Network IRB HN4365. The protocol described here is similar, but will be performed at USF and the training will involve multiple sessions, as opposed to the earlier studies that involved a single session.

According to the 2006 American Community Survey, the percentage of females in the adult population in Hillsborough County is slightly greater than male adults (51.3% and 48.7% respectively). We have no reason to think that women and men will differ in their abilities on any of these tasks. As such, we expect to enroll approximately the same number of men and women.

6. Inclusion and exclusion criteria

We will recruit individuals with stroke for this study. Since the focus of this project is to ultimately use this device to help stroke survivors, we will recruit both young adults and older adults. Inclusion criteria includes:

1) age 21-80
2) one or more cerebral strokes
3) a stroke at least 6 months prior to enrollment
4) gait asymmetry, but able to walk independently
5) no evidence of uncompensated hemianopsia, tested by using Pedretti's method (Pedretti 1985)
6) no evidence of severe (greater than 16 in the Folstein Mini-Mental Status Exam) cognitive impairment (Folstein et al. 1975) or language dysfunction that would interfere with understanding the instructions
7) no evidence of neglect, tested by being asked to copy a simple drawing of a house (Gregory and Aitkin 1971)

Exclusion criteria includes:

1) orthopedic or pain conditions
2) uncontrolled seizures
3) metal implants (stents, clips, pacemaker)
4) pregnancy
5) any condition that makes balance unstable
6) require a walker to walk
7) uncorrected visual impairments

We will also recruit healthy individuals for this study; our target subject demographic includes healthy persons of age range between 18 to 50 with no major interlimb coordination abnormalities. The exclusion criteria includes the following from the above exclusion criteria list: 1, 2, 3, 4, 5, 6, 7, & 8.

7. The expected results of the research

This study will enhance rehabilitation methods used for lower limb rehabilitation, which is currently administered with a split-belt treadmill and other traditional methods. This method aims to improve upon existing methods and to also eventually enable a home-based solution. The study results will be submitted to rehabilitation, neuroscience, and engineering publications for dissemination to researchers and clinicians who are interested in using and expanding this method.

8. Roles of study staff

This study is being conducted at USF by Kyle B. Reed, Ph.D., Seok Hun Kim, P.T., Ph.D., David Rose, M.D., Ismet Handzic, and Andrea Bozeman, ARNP. Specific roles include:

- Dr. Reed will be responsible for overseeing the study and help with testing and data analysis.
- Dr. Kim will be conduct consenting, training, testing, and data analysis.
- Dr. Rose will provide medical oversight for all study subjects, screening, consenting.
- Mr. Handzic will assist with testing, data analysis, and device maintenance.
- Ms. Bozeman will conduct screening and consenting.

9. Sites

The research will be conducted at the University of South Florida at the following on-campus sites:

9) USF School of Physical Therapy & Rehabilitation Sciences (3515 E. Fletcher Ave.; Tampa, FL 33612). This location will be used for recruitment, screening, consenting, training, and assessment.
10) USF Physical Therapy Center (13330 USF Laurel Dr.; Tampa, FL 33612). This location will be used for training and assessment.
11) USF South Tampa Center for Advanced Healthcare (2 Tampa General Circle; Tampa, FL 33606). This location will be used for recruitment, screening, and consenting.
12) USF Center for Assistive, Rehabilitation & Robotics Technologies (3720 Spectrum Blvd., Suite 114; Tampa, FL 33612). This location will be used for assessment.

10. Potential risks to the subjects

The risks for this study are slightly higher than regular walking over ground and include the possibility of falling. The risk can be compared to walking on high-heeled shoes. To minimize this risk, subjects are wearing a gait belt and are closely guarded by an experienced physical therapist. If necessary, subjects may wear a safety harness attached to the SOLO-STEP® System (Solo-Step, Sioux Falls, SD) designed to support people in the event of a fall. As such, the combined risks associated with this study are minimal.

11. The potential benefits to subjects

There is potential for subjects to improve their gait patterns, which is our hypothesis regarding this method. It may not change their gait, so there may be no benefit to subjects.

12. Human subjects considerations

a. Description of the informed consent process

Upon initial contact, the study coordinator will send the consent form to potential subjects when they inquire about the study. This will allow them to review the consent form without feeling rushed and will give them a better opportunity to discuss study participation with a friend or family member.

When individuals arrive to the study site, the informed consent discussion will be through a private meeting between a designated member of the research study and the potential subject.

The potential subject will be given ample time to consider their participation in the study and to ask any questions they may have. They may take it home with them if they need more time and then return to USF if they are interested in participating. If the individual agrees to participate, they will sign all informed consent documents and be given a copy to retain.

The written consent form will contain all of the elements required by the Western Institutional Review Board (WIRB) as well as adherence to all federal requirements. The primary information on the consent form will include, but is not limited to, name of sponsor, explicit study procedures, risks and benefits, subject rights, consent to use data, and study contact information. Each page will contain the most recent stamped WIRB approval printed on each page of the form. It will be written in language that is understandable to the subject. The original signed consent form will be retained in the study subject's file in a locked filing cabinet in the office of a study staff member, and stored for a period of 5-years in accordance with USF IRB policy after which time paper records will be shredded.

b. Safeguards to protect potentially vulnerable subjects

All subjects for this study will have at least normal cognitive function as described in the inclusion requirements. Care will be taken to make sure potential subjects will understand the risks and that they may not receive any benefits from this study.

c. Privacy and confidentiality

The signed consent forms will be kept confidential and stored in a secured location, while any soft data collected will be stored on a desktop computer in a USF laboratory with password protection. The data will be anonymized and combined with data from other experiments, so the data will not be identifiable throughout the study and in all reports generated from this data.

d. Compensation

Subjects will be paid $6 plus reimbursement for travel for each completed study visit and parking passes will be provided. If they do not complete the study, they will be paid for the visits completed. They will be paid within 30 days of the end of their participation in the study.

No compensation will be provided for the healthy participants.

e. Withdraw from the research study

We will discontinue testing if the subject reports or we observe signs of discomfort or fatigue that interfere with their participation in the experiment. In any of these circumstances, the experiment will immediately stop and the subject will be compensated for his/her time. Please note that the likelihood of participants experiencing these symptoms during the experiment is not greater than in their everyday lives (e.g. during walking). Since we are performing repeated-measures statistical tests, it is essential to obtain all measures from each subject. Therefore, if a subject is unable to complete the experiment, we will remove the data from analysis. Also, if a subject requests that his/her data be withdrawn, we will delete it all electronic files from our records and destroy any paper records.

13. Data and safety monitoring plan.

The collected data will be coded so no personally identifying information will ever be attached to the data. The lookup table will be stored separately from the data. Only Dr. Kim and Dr. Reed will have access to the data and the lookup table. No one but the PI (Kyle Reed) and study staff will have access to the data used in this study. The data will be recorded to spreadsheet and/or text files. Shortly after the experiment, the data will be analyzed for completeness and integrity. It will then be copied to a remote secure server and backed up. Once a subject's experiment has been verified, it will only be looked at as part of all experiments performed in conjunction with this set of experiments, all of which will be anonymous. The analysis of the entire data set (all subjects) will occur after each experiment.

14. Research funding information

This study will be funded by Moterum LLC, which is a company that evaluates technologies related to rehabilitation with the intention of commercializing viable technologies and bringing them to market. The company will not be involved in the evaluation of the GEMS.

Moterum LLC has entered into an agreement to license two patents from USF, which have Dr. Reed and Mr. Handzic listed as the inventors:

- USF 13B154PR_Handzic filed in Feb. 2014: "SYSTEMS AND METHODS FOR DESIGNING KINETIC SHAPES". This is a provisional patent for a method to generate a spiral-shaped wheel that generates a known horizontal force or moment when a vertical force is applied on it. It can be used to specify the shape of wheels that redirect forces and can also be used to define the roll-over shape of a foot with the ground to alter the interaction and resulting gait.
- USF 11B170PR filed in Feb. 2012: "GAIT ALTERING SHOE". This patent is for a shoe that generates a backward or forward motion when the user steps down on the shoe. The shoe can be used for rehabilitation of individuals with stroke, specifically for correcting their asymmetric gait, and also for healthy individuals to increase their forward progression with each step.

In addition to the patents, Dr. Reed has been asked to serve on the Scientific Advisory Board for Moterum LLC, which includes a yearly honorarium and stock options in the company. A conflict of interest management plan has been put in place and approved by USF.

15. Research references

Andersson AG, Kamwendo K, et al. How to identify potential fallers in a stroke unit: validity indexes of 4 test methods. J Rehabil Med, 2006, 38(3): 186-191.

Balasubramanian C, Bowden M, Neptune R, and Kautz S. Relationship between step length asymmetry and walking performance in subjects with chronic hemiparesis. Arch Phys Med Rehabil 88, 43-49 (2007).

Bowden M, Balasubramanian C, Neptune R, and Kautz S. Anterior-posterior ground reaction forces as a measure of paretic leg contribution in hemiparetic walking. Stroke 37, 872-876 (2006).

Brandstater M, de Bruin H, Gowland C and Clark B. Hemiplegic gait: analysis of temporal variables. Arch Phys Med Rehabil 64, 583-587 (1983).

Bronstein A, Bunday K, and Reynolds R, What the broken escalator phenomenon teaches us about balance. Ann N Y Acad Sci, vol. 1164, pp. 82-88, May 2009.

Brouwer B, Parvataneni K, and Olney S. A comparison of gait biomechanics and metabolic requirements of over ground and treadmill walking in people with stroke. Clin Biomech (Bristol, Avon) 24, 729-734 (2009).

Bunday K and Bronstein A., Visuo-vestibular Influences on the Moving Platform Locomotor Aftereffect", J Neurophysiol 99: 1354- 1365, 2008.

Folstein M, Folstein S and McHugh P. (1975), "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician", Journal of Psychiatric Research 12, 189-198

Folstein M, Folstein S, and McHugh P. (1975), "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician", Journal of Psychiatric Research 12, 189-198 (PMID: 1202204)

Fugl-Meyer AR, Jaasko L, Leyman I, Olsson S, Steglind S. The post-stroke hemiplegic patient. 1. a method for evaluation of physical performance. Scand J Rehabil Med, 1975, 7(1):13-31.

Grasso R, Bianchi L, and Lacquaniti F, Motor Patterns for Human Gait: Backward Versus Forward Locomotion, J. Neurophysiol, vol. 80, no. 4, pp. 1868-1885, 1998.

Gregory M and Aitkin J. (1971), “Assessment of parietal lobe function in hemiplegia”, Occup Ther, 34:9.

Gregory M, and Aitkin J. (1971), “Assessment of parietal lobe function in hemiplegia”, Occup Ther, 34:9.

Handzic I and Reed K, "Comparison of the Passive Dynamics of Walking on Ground, Tied-belt and Split-belt Treadmills, and via the Gait Enhancing Mobile Shoe (GEMS)," Proc. of the 13th Intl. Conf. on Rehabilitation Robotics (ICORR), Seattle, USA, June, 2013.

Handzic I, Barno E, Vasudevan E, and Reed K. "Design and Pilot Study of a Gait Enhancing Mobile Shoe," Journal of Behavioral Robotics, Special Issue on Assistive Robotics, Vol. 2, Num. 4, pp. 193-201, 2011.

Handzic I, Vasudevan E, and Reed K, "Developing a Gait Enhancing Mobile Shoe to Alter Over-Ground Walking Coordination," Proc. of IEEE Intl. Conf. on Robotics and Automation (ICRA), St. Paul, USA, May, 2012.

Handzic I, Vasudevan E, and Reed K, ”Motion Controlled Gait Enhancing Mobile Shoe for Rehabilitation,” Proc. of the 12th Intl. Conf. on Rehabilitation Robotics (ICORR), Zurich, Switzerland, June, 2011.

Honeycutt C, Sushko J, and Reed K, Asymmetric passive dynamic walker, in Proc. IEEE Int. Conf. Rehabilitation Robotics, 2011.

Ivey F, Macko R, Ryan A, and Hafer-Macko C. Cardiovascular health and fitness after stroke. Top Stroke Rehabil 12, 1-16 (2005).

Kahn J and Hornby T. Rapid and long-term adaptations in gait symmetry following unilateral step training in people with hemiparesis. Phys Ther 89, 474-483 (2009).

Keamey R, Context dependence of intrinsic and reflex contributions to ankle stiffness, in Proc. of 1st International IEEE EMBS Conf. on Neural Engineering, March 2003, pp. 434-437.

Kelly-Hayes M, et al. The influence of gender and age on disability following ischemic stroke: the Framingham study. J Stroke Cerebrovasc Dis 12, 119-126 (2003).

Krakauer J, Ghilardi M, and Ghez G, Independent learning of internal models for kinematic and dynamic control of reaching. Nature Neuroscience, vol. 2, pp. 1026-1031, 1999.

Lam T, Anderschitz M, and Dietz V, Contribution of feedback and feedforward strategies to locomotor adaptations, J. Neurophysiol, vol. 95, pp. 766-773, 2006.

Lam T, Wolstenholme C, and Yang J, How do infants adapt to loading of the limb during the swing phase of stepping? Journal of Neurophysiology, vol. 89, no. 4, pp. 1920-1928, 2003.

Lloyd-Jones D et al. on behalf of the American Heart Association Statistics Committee & Stroke Statistics Subcommittee Heart Disease and Stroke Statistics--2010 Update: A Report From the American Heart Association Circulation, 2010, 121, e46-215

Lou J and Bloedel J, A new conditioning paradigm: Conditioned limb movements in locomoting decerebrate ferrets, Neuroscience Letters, vol. 84, no. 2, pp. 185 - 190, 1988.

Morton S and Bastian A, Cerebellar Contributions to Locomotor Adaptations during Splitbelt Treadmill Walking, J. Neurosci., vol. 26, no. 36, pp. 9107-9116, 2006.

Olney S, Griffin M, and McBride I. (1994), “Temporal, Kinematic, and Kinetic Variables Related to Gait Speed in Subjects With Hemiplegia: A Regression Approach”, Physical Therapy 74(9), 872-885.

Pedretti L and Early M. (1985), Occupational therapy, CV Mosby.

Pedretti L and Early M. (1985), Occupational therapy, CV Mosby.

Perry J, Gait Analysis: Normal and pathological function, N. S. Inc., Ed. Thorofare, 1992, vol. 50.

Reinkensmeyer D, Emken J, and Cramer S, Robotics, motor learning, and neurologic recovery, Annu. Rev. Biomed. Eng., vol. 6, pp. 497- 525, 2004.

Reisman D, Wityk R, and Bastian A, Split-belt treadmill walking adaptation in post-stroke hemiparesis, J. Neurologic Physical Therapy, vol. 29, p. 196, 2005.

Reisman D, Wityk R, Silver K, and Bastian A, Locomotor adaptation on a split-belt treadmill can improve walking symmetry post-stroke, Brain, vol. 130, no. 7, pp. 1861-1872, 2007.

Reisman D, Wityk R, Silver K, and Bastian A, Splitbelt treadmill adaptation transfers to overground walking in persons poststroke. Neurorehabil Neural Repair, vol. 23, no. 7, pp. 735-744, Sep 2009.

Reynolds R and Bronstein A, The broken escalator phenomenon aftereffect of walking onto a moving platform. Exp Brain Res, vol. 151, no. 3, pp. 301-308, Aug 2003.

Singal A, Higgins P, and Waljee A. "A Primer on Effectiveness and Efficacy Trials." Clinical and translational gastroenterology 5.1 (2014): e45.

Titianova E and Tarkka I. (1995), “Asymmetry in walking performance and postural sway in patients with chronic unilateral cerebral infarction”, Journal of rehabilitation research and development 32, 3236-244.

Torres-Oviedo G and Bastian A. "Seeing is believing: effects of visual contextual cues on learning and transfer of locomotor adaptation." The Journal of Neuroscience 30.50 (2010): 17015-17022.

Wall J and Turnbull G. Gait asymmetries in residual hemiplegia. Arch Phys Med Rehabil 67, 550-553 (1986).

Whittle M, Gait Analysis: An Introduction. Elsevier Health Sciences, 1998.