Title

Assessing Ankle Proprioception using a Novel Robotic Device: Generalizability, Parameter Sensitivity, and Predictive Power for Stroke Rehabilitation

Author

Johnson, Christopher

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Assessing Ankle Proprioception using a Novel Robotic Device: Generalizability, Parameter Sensitivity, and Predictive Power for Stroke Rehabilitation

DISSERTATION

submitted in partial satisfaction of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

in Biomedical Engineering

by

Christopher Ameron Johnson

Dissertation Committee:
Professor David J Reinkensmeyer, Chair
Professor Zoran Nenadic
Assistant Professor Alexandra Voloshina

2024

DEDICATION

To my parents, grandparents and brothers' thanks for your love, support, and enthusiasm for my graduate studies.

To Breyah, the one and only, my best friend, my soon to be wife, thank you for supporting and loving me during the times when I needed it most. Words cannot explain how overjoyed I am to do this thing called life with you!

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ACKNOWLEDGEMENTS

To my advisor Dr. David Reinkensmeyer, thank you for giving me the opportunity to work in your lab and advising me through the years. I have learned so much from you and will continue to as we work together in the future. This entire experience has been better than I could ever imagined because you encouraged exploration and creativity which made me a better researcher, and further grew my interests in creating novel ideas, tools, and methods to help overcome challenges in the rehabilitation field. I couldn’t have asked for a better advisor, thank you so much! To the previous Biorobotics lab members, Quentin, Dylan, Marti, Merav, Veronica, and Shusuke thank you for the many conversations about research and the overall support in my early development as a graduate student. To Quentin, thank you for your extended friendship during our time as lab members and inspiration propelled me over the years. To Dylan, I appreciate your insight and commitment to our brainstorming sessions, you were always there to help me delineate the next steps in my work. To the current Biorobotics lab members Luis, Guillem, Caitlin, Andria, Josh, Sangjoon, and Juan, thank you for the continuous support throughout my final years. To Andria, thank you for the help in recruiting and testing participants that led to us collecting over 135 people in two years, and the many conversations about understanding proprioception. To the development of AMPD team Piyashi, Raksha, and Mark thank you for your help in developing AMPD. To Piyashi, thank you so much for the help since my first year in graduate school in programming AMPD and continuous dedication in ensuring that AMPD is safe. To the assessment and treatment team for the BCI -FES randomized control trial Jill, Vicky, Sharada, Olivia, Lucy, Dr. Do, and Dr. Nenadic thank you for the continuous support. To Dr. Do thank you for allowing me to use the data from this study to help advance the field in understanding ankle proprioception in stroke. To the additional UCI faculty and staff Dr. Sasha Voloshina, Dr. Tim Downing, Dr. Sharnnia Artis, Dr. Sari Mahon, Dr. Bruce Tromburg, Dr. Benard Choi thank you for the continuous support throughout my time in graduate school but also before entering graduate school and participating in summer programs at UCI. To Dr. Sari Mahon thank you for supporting me during my graduate studies and being a great help as I prepared to apply and enroll as a PhD student in 2019. To Dr. Sharnnia Artis, thank you for your continuous support in my success as a graduate student, your contributions and enthusiasm are greatly appreciated.

VITA

EDUCATION

University of California, Irvine

Ph.D. Biomedical Engineering Fall 2019 – Present

Courses: Biorobotics, Design for Human Movement, Sensory Motor Systems

Master of Science: Biomedical Engineering

February 2021

Hampton University

B.S. Electrical Engineering Fall 2014 - Spring 2019

Technical Electives: Circuit Design

RESEARCH EXPERIENCE

UC Irvine Biorobotics Lab, Graduate Student Researcher Fall 2019 - Present

Investigating ankle movement and sensation in walking to advance lower extremity stroke rehabilitation. Designed and built multiple bilateral ankle measuring proprioception devices to measure ankle movement and ankle sensation to gain a better understanding of proprioception in motor learning and movement execution.

Hampton University, Partnership for Research in Education and Materials (PREM), Undergraduate Research Assistant 2016-Spring 2019

Project 1 consisted of researching applications of Drug Delivery using Layer-by-Layer spraying techniques. Helped plan and participate in STEM outreach events and help cultivate new ideas and projects. Project 2 consisted of integrating photonics and devices. Built frequency modulation and amplitude modulated systems for optical communication.

UT, Austin, National Nanotechnology Coordinated Infrastructure Research Experience for Undergraduates (NNCI REU), Undergraduate Research Assistant Summer 2018

Investigated phononic spectroscopy of semiconductor Schottky contacts. Successfully developed a lock-in base differential measurement system to measure phonons in the far-infrared spectrum. Contributed to the development of a novel far-infrared laser

UC Irvine, Pathways to Biophotonics and Biomedical Engineering (PBBE), Undergraduate Research Assistant Summer 2017

Investigated ways to enhance the design and operation of a haptic interface device. Successfully reconstructed and integrated a haptic device from the 1980s that was used in NASA exploration with a computer.

PUBLICATIONS

Under Review or in Preparation:

1. “The weak relationship between ankle proprioception and gait speed after stroke: a robotic assessment study” **Neurorehabilitation and Neural repair (Under Review)**
2. “Generalization between passive and active robotic proprioception tests of the ankle: effects of

stroke and aging" **(In Preparation)**

3. "Reliability and validation of range of motion and dorsiflexion strength using an Ankle Proprioceptive Measuring Device" **(In Preparation)**
4. "Shared neural machinery in proprioceptive processing neural machinery in proprioceptive processing: joint specificity and generalization" **(In Preparation)**

Published

5. **Christopher A. Johnson,** Dylan S. Reinsdorf, David J. Reinkensmeyer, and Andria J. Farrens. "**Robotically quantifying finger and ankle proprioception: Role of range, speed, anticipatory errors, and learning**," 2023 45th Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), Sydney, Australia, 2023, pp. 1-5, doi: 10.1109/EMBC40787.2023.10340566.
6. Han Gil Seo, Seo Jung Yun, Andria J. Farrens, **Christopher A. Johnson**, and David J. Reinkensmeyer. **A Systematic Review of the Learning Dynamics of Proprioception Training: Specificity, Acquisition, Retention, and Transfer.** Neurorehabilitation and Neural repair. 2023
7. Veronica A. Swanson, **Christopher A. Johnson**, Daniel K. Zondervan, Susan J. Shaw and David J. Reinkensmeyer. **Exercise repetition rate measured with simple sensors at home can be used to estimate Upper Extremity Fugl-Meyer score after stroke.** Frontiers in Rehabilitation Sciences**.** 2023
8. V. Swanson, **C. Johnson**, D. Zondervan, N. Bayus, P. McCoy, Y.F. Ng, J. Schindele, D. Reinkensmeyer, S. Shaw. **Optimized home rehabilitation technology reduces upper extremity impairment compared to a conventional home exercise program: A randomized, controlled, single-blind trial in subacute stroke.** Neurorehabilitation and Neural Repair. 2023
9. E. Ramos Muñoz, V. Swanson, **C. Johnson**, R. Anderson, A. Rabinowitz, D. Zondervan, G. Collier, D. Reinkensmeyer. **Using large-scale sensor data to test factors predictive of perseverance in home movement rehabilitation: optimal challenge and steady engagement.** Frontiers in Neurology. 2022

CONFERENCE PRESENTATIONS AND POSTERS

Oral Presentations

1. Luis Garcia-Fernandez, Andria J. Farrens, **Christopher A. Johnson**, Joel C. Perry, Eric T. Wolbrecht, and David J. Reinkensmeyer, Member, IEEE. "A Novel Robotic Thumb Proprioception Assessment Reveals Thumb Localization is Coarse, Biased, and Rapidly Modified by Experience", at 2024 IEEE Haptics Symposium (HAPTICS)
2. Giacomo Zuccon, Kohl Foster Hertz, Lee Jaiswal McEligot, V. Reggie Edgerton, **Christopher Johnson**, David J. Reinkensmeyer. "Design of a Robot for Early-Stage Gait Rehabilitation". 2023 Socal Robotics Symposium.
3. **Christopher A. Johnson,** Dylan S. Reinsdorf, David J. Reinkensmeyer, and Andria J. Farrens. "Robotically quantifying finger and ankle proprioception: Role of range, speed, anticipatory errors, and learning" 45th Annual Internal Conference of the IEEE Engineering in Medicine & Biology Society (EMBC) July 24-27, 2023.
4. Dylan Reinsdorf, **Christopher Johnson**, David Reinkensmeyer. "Training Somatosensation with Proprioceptive Robots and Propriopixels" Accepted for ICORR, Computational Neurorehabilitation Session. September 24, 2021.

Poster Presentations

1. Luis Garcia-Fernandez, Andria J. Farrens, **Christopher A. Johnson**, Vicky Chan, Joel C. Perry, Eric T. Wolbrecht, and David J. Reinkensmeyer. "A Novel Robotic Thumb Proprioception Assessment Reveals Surprising Aspects of Proprioceptive Adaptation in Unimpaired and Stroke Participants" at the 2024 Society for the Neural Control of Movement (NCM)
2. AJ Farrens, M Torrecilla, L Garcia, **CA Johnson**, ET Wolbrecht, DJ Reinkensmeyer, D Gupta (November, 2023) "Behavioral and EEG Features of Finger Proprioception and Passive Movement: Effect of Error Feedback on Proprioception", at Society for Neuroscience.
3. Andria Farrens, Member, IEEE, David J. Reinkensmeyer, **Christopher A. Johnson.** "Comparing Finger and Ankle Proprioception with Two Robotic Tests" 45th Annual Internal Conference of the IEEE Engineering in Medicine & Biology Society (EMBC) July 24-27, 2023.
4. **Christopher A. Johnson**, Piyashi Biswas, Vicky Chan, Lucy Dodakian, Jill See, Po T. Wang, Andria J. Farrens, Zoran Nenadic, An H. Do, David J. Reinkensmeyer. "Ankle Proprioception After Stroke using a Novel Robotic Assessment" 45th Annual Internal Conference of the IEEE Engineering in Medicine & Biology Society (EMBC) July 24-27, 2023.
5. Veronica A. Swanson, **Christopher Johnson**, Naveen Khan, John Dzivak, Daniel K. Zondervan, Vicky Chan, Sarah D. Cowart, Mike L. Jones, David J. Reinkensmeyer. "Uptake Rates of a Sensor for Monitoring Home Exercise Programs for Physical Rehabilitation." Accepted for American Congress of Rehabilitation Medicine (ACRM). November 8-10, 2022.
6. Veronica A. Swanson, Edgar Ramos Muñoz, George H. Collier, Daniel K. Zondervan, Amanda Rabinowitz, Raeda K. Anderson, **Christopher Johnson**, David J. Reinkensmeyer. "Using Data from a Sensorized Therapeutic Exercise Platform to Understand Unsupervised Home Rehabilitation Perseverance: Effect of Steadiness of Use on Duration and Volume of Exercise." Accepted for Ann. APA Technology, Mind, and Society Conf. November 3-5, 2021.

TEACHING & MENTORSHIP

Visiting International Students, Project Mentor for "Low-Cost Ankle Proprioception Device" at Summer 2023
UC Irvine

- Purpose: Design device to measure ankle proprioception in acute and subacute stroke.

MAE 189: Senior Design Project, Project Mentor for "AirStep" Fall 2022- Spring 2023
UC Irvine Department of Mechanical and Aerospace Engineering

- Purpose: Design a rehabilitation device designed for assisting in leg rehabilitation while participant is in supine position.

MAE 189: Senior Design Project, Project Mentor for "Portable Shoulder Device" Fall 2022- Spring 2023
UC Irvine Department of Mechanical and Aerospace Engineering

- Purpose: Design and build a rehabilitation device designed for rehabilitating overhead reaching in stroke.

PACE, Graduate Mentor at UC, Irvine Summer 2020-2023

- Mentored a **c**ohort of 16 minority students about graduate school and their future steps.

ACES, Graduate Mentor at UC, Irvine Summer 2020-2022

- Mentored a **c**ohort of 16 minority students about graduate school and their future steps.

MAE 106: Mechanical Systems Laboratory, Teaching Assistant Spring 2020

UC Irvine Department of Mechanical and Aerospace Engineering

AWARDS

UC-HBCU Diversity Fellowship Summer 2017 - Present

- Initiative to increase HBCU graduates completing UC Ph.D. programs.
- Funding packages offered for at least four years of funding.

UC Irvine Minority Serving Institution Enhancement (MSIE) Award Spring 2019

ABSTRACT OF THE DISSERTATION

Assessing Ankle Proprioception using a Novel Robotic Device: Generalizability, Parameter Sensitivity, and Predictive Power for Stroke Rehabilitation

by
Christopher Ameron Johnson
Doctor of Philosophy in Biomedical Engineering
University of California, Irvine, 2024
Professor David J. Reinkensmeyer, Chair

Stroke is one of the leading causes of disability worldwide because it often creates both sensory and motor deficits, which impact the ability to complete activities of daily living such as walking. Rehabilitation therapy can promote recovery of movement after stroke, but response to rehabilitation is highly variable. Understanding this variability would help optimize treatment. Most assessments focus on the motor effects of stroke – such as hemiparesis – but there is emerging evidence that proprioceptive deficits play an important role in determining the response to movement rehabilitation after stroke. However, at present, there is a large diversity of techniques to measure proprioception, ranging from crude clinical assessments to complex robotic assessments. Further, it has been hypothesized that each assessment measures a different aspect of proprioception, such that generalization is minimal. Therefore, it is unclear which technique is best for gaining insight into movement rehabilitation. Here we focused on the ankle, a key joint for propulsion and balance. We designed and built an innovative robot for testing ankle proprioception and then used it to investigate the following questions: 1) How do proprioceptive errors depend

on assessment parameters such as range of motion (ROM) and speed of movement? 2) Do different ankle proprioceptive assessments generalize in persons with stroke? 3) Is there site (i.e. joint) specificity to proprioception? 4) How well do ankle proprioceptive assessments predict gait function in persons with stroke? To answer these questions, we implemented two robotic proprioceptive assessments, joint position reproduction and Crisscross. Joint position reproduction is a well-established proprioceptive assessment, and Crisscross is a novel assessment that has implementation advantages for people with stroke. First, we found that proprioceptive acuity depends on the assessment parameters, with anticipatory errors increasing at slower speeds and with ROM. Second, we found generalization between the assessments in older unimpaired and stroke impaired individuals, but not younger unimpaired individuals. Third, we found proprioceptive processing has a body-general attribute that is shared across the ankles and fingers, particularly for young unimpaired participants. Lastly, we found that proprioceptive impairment weakly predicted gait speed after stroke, even though proprioceptive impairment was independent of motor impairment. As a side note, we also validated the robot for use to measure ROM and strength after stroke, showing that it has comparable reliability to experienced therapists but advantages in terms of resolution for strength measurement. This work therefore validates a novel robotic assessment of ankle proprioception (Crisscross), confirms its generalizability, and demonstrates its ability to quantify the effect of proprioceptive impairment on gait function after stroke. This work also provided the infrastructure to predict response to gait training after stroke using quantitative measures of proprioception acuity.

CHAPTER 1: INTRODUCTION

Stroke is one of the leading causes of disability worldwide, creates both sensory and motor deficits, and impacts the ability to complete activities of daily living [1]. An estimated one in four people worldwide will experience a stroke in their lifetime [2], with approximately one third of strokes resulting in death [3], and an estimated 75% of survivors experiencing difficulty walking [4], [5]. One of the most common deficits after stroke is hemiparesis, the loss of volitional movement and weakness on one side of the body [1], but somatosensory deficits, which relate to the ability to feel skin touch (cutaneous sense) or sense joint position (proprioception), are also common [6]. Rehabilitation can promote recovery of lost function and independence after stroke, but the response to rehabilitation is highly variable [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18].

The human shank and foot complex is an intricate, multi-joint mechanism, which is fundamental for the interaction between the lower limb and ground during locomotion [19]. The ankle is one the most fragile portions in the human body and is easily injured in daily life when it experiences unexpected forces or loses sensory-motor capability [20]. To enhance understanding of gait neurorehabilitation, better knowledge of the physiological mechanics of the ankle complex still remains a crucial issue [19].

Foot drop is one of the most common gait dysfunctions arising from neurologic injuries and is especially common after stroke [21]. Foot drop arises from significant weakness of ankle and toe dorsiflexion during the swing phase of gait [22] and increases the risk of tripping and falling. To combat this, stroke-impaired individuals go through rehabilitation aimed at improving their lost ankle function. However, loss of ankle function often persists, and people are in need of ongoing rehabilitation even years after the stroke, contributing to the expected increase in the healthcare cost for post-stroke patients in the next decade [23]. In order to reduce the cost and increase the efficacy of post-stroke rehabilitation, it is crucial to determine methods that prove to provide the best outcomes for foot drop [24].

ANKLE REHABILITATION AFTER STROKE

Repeated, intensive physical therapy sessions are commonly prescribed in an attempt to restore the lost function in the ankle after stroke. These sessions require cooperative and intensive efforts from both therapists and patients [25], [26]. Selection of therapeutic procedures is often based on the subjective perception of the therapist instead of an objective evaluation of clinical data [27]. To address foot drop, the most commonly selected exercise is probably to practice dorsiflexing against elastic bands in order to strengthen the ankle dorsiflexion muscles, but compliance with this exercise can be partial because it is repetitive and monotonous. Further, this exercise does not specifically target the ankle somatosensory deficits that may also contribute to gait deficits, or the integration of ankle control into locomotor function. Even after physical therapy, between 30% and 60% of stroke survivors remain affected by gait function impairments [16], [28], with foot drop often being the primary cause [29].

When foot drop persists, ankle-foot orthoses (AFO) are the most popular assistive approach to address it. These brace-like plastic orthotic devices are designed to be applied externally to the ankle foot joint to prevent foot drop during swing phase of gait [30]. They have been shown to improve alignment of the ankle joint [31], increase walking speed [32], and reduce energy consumption during walking [33]. However, they have limitations, such as inhibiting normal push-off during walking [34], reducing gait adaptability [35], and encouraging muscle weakness and atrophy when used over the long term [30].

ROBOTIC TECHNOLOGY FOR GAIT REHABILITATION

There is a need for novel rehabilitation techniques that enable therapists to provide efficacious interventions without increasing the burden on staff and resources [36]. To try to achieve these goals, there has been a dramatic increase in the development of robotic rehabilitation technologies over the past 40 years [37]. Robotic devices can provide repetitive, systematic, and prolonged ankle rehabilitation treatment as compared to the manual therapy [21]. Robotic devices can also apply or assist in limb motions in multiple DOFs without physical therapists' intervention. Furthermore, robots can provide a rich stream of data that can potentially be used to facilitate patient diagnosis, customize therapies, and maintain patient records [25]. In a recent review of robotic rehabilitation, the authors summarized the results of several surveys given to physical and occupational therapist to gauge their opinions about rehabilitation robots [38]. They found that therapists had positive impressions of the devices because patients like to use them and because they perceive them as having potential to increase accessibility, autonomy, and comfort, and reduce costs [38].

Many robotic devices have been developed to assist in gait rehabilitation [39], [40]. These devices can be classified in two different ways. First, they can be wearable devices or grounded/platform-based devices. Wearable devices [39] are portable devices such as robotic orthoses and exoskeletons or active ankle-foot orthoses that are worn in order to assist in lower limb movement during the gait cycle, and can be used to for assessment, therapeutic, and assistive purposes. They must be lightweight and portable. Platform-based devices are mechanically grounded and can take the form of exoskeletons or end-effector devices for assisting in the gait cycle or single-joint devices. These devices can be used for assessment or therapy but are not worn for assistance in daily activities like walking. They typically are heavier and can use larger actuators that are mechanically grounded to provide better control fidelity.

A second way to view rehabilitation robots, as already partially alluded to in the above paragraph, is that they can be multi-joint or single-joint devices. Figure 1 shows different types of multi-joint robots. Numerous clinical trials have provided evidence that rehabilitative therapy conducted with all three types of multi-joint robots (grounded exoskeletons, end-effector devices, and wearable exoskeletons) can help improve gait function [39]. Figure 2 shows single-joint, platform-based devices. For these devices, participants are typically in a seated position and only one joint is actuated, with the most common joints being the ankle and the knee (Figure 2). This simplified set-up allows a high fidelity of motion control and sensing to be achieved, allowing a precise analysis of joint-based function. Platform-based, single-joint robots typically use large motors and have low portability. Further, because they focus on one joint, their ability to improve the more complex motor activity of gait is an open research question. However, in a recent review [41], the authors found that platform-based robots focused on ankle function indeed allow ankle function to be improved with repeated training, and that this resulted in improved gait function. As detailed in Chapter 2, this dissertation developed a novel platform-based robot to aid in the quantification of ankle sensory motor function after stroke.

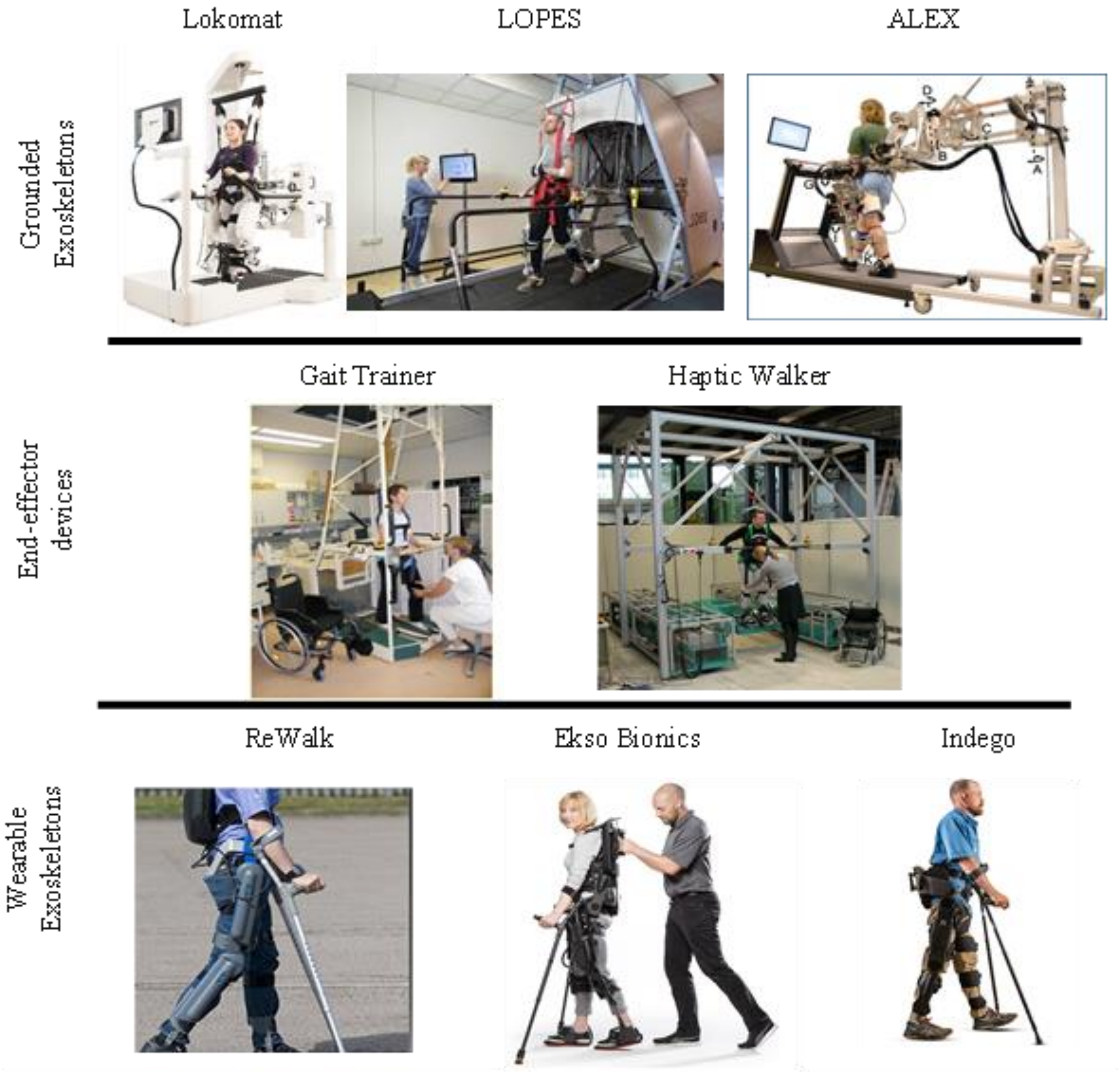

Figure 1 Multi-Joint Robotics for Gait Rehabilitation. The top row shows examples of grounded exoskeletons (Lokomat [218], LOPES [219], ALEX [220]). The middle row shows examples of end-effector devices (Gait Trainer [221], Haptic Walker [222]). The bottom row shows examples or wearable exoskeletons (Rewalk [223], Ekso Bionics [224], Indego [225]).

IMPORTANCE OF PROPRIOCEPTIVE ASSESSMEMENTS

Traditional approaches towards neurologic movement rehabilitation can be characterized as bottom-up approaches, where therapies are applied that act on the distal physical system (i.e. the limbs and joints at the "bottom" of the control system) aiming to

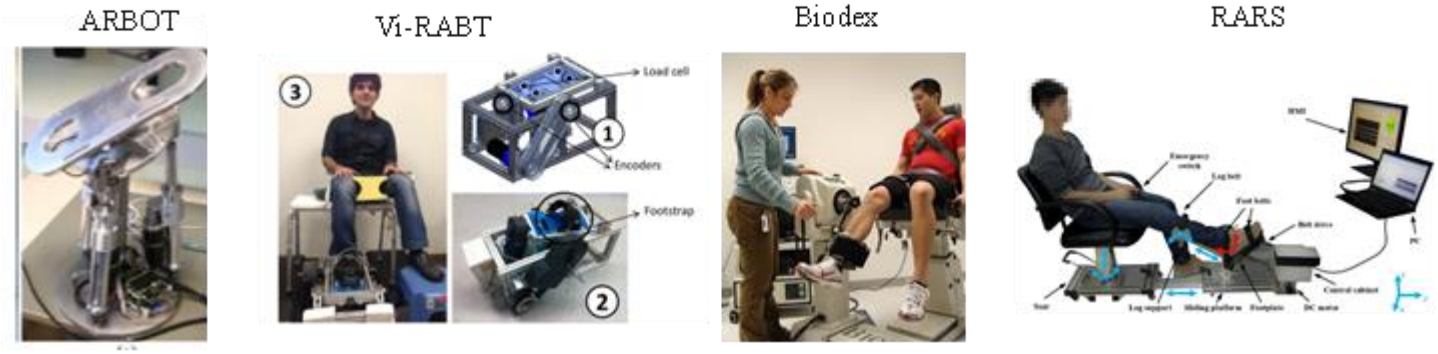

Figure 2 Single-Joint, Platform-Based Robots for Ankle Rehabilitation (ARBOT [226] , Vi-RABT [227], Biodex [228], RARS [229])

influence the neural system (i.e. the “top” of the control system), but an increasing number of researchers are pursuing a top-down approach, consisting of defining the rehabilitation therapies based on the state of the brain after stroke [42]. The increasing interest in top-down approaches can be attributed to the heterogeneity in stroke recovery [43], meaning not all participants benefit equally from therapy. Many randomized controlled trials (RCTs) have now shown that stroke survivors benefit different amounts from physical therapy [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18]. These RCTs raise the question, are there baseline clinical measurements that can be used as predictors of treatment response?

A variety of studies have found moderate correlations between treatment responders and measures of stroke location, neural connectivity, and neural activity [44], [45], [46], [47], [48], [49] . However, obtaining these neuroanatomical and neurophysiological measures is time consuming and expensive, because they typically rely on use of magnetic resonance imaging (MRI) systems or sophisticated electroencephalography (EEG) systems. A key, outstanding goal in rehabilitation science, therefore, is to identify predictors of treatment response that are simple to implement and therefore accessible for clinical practice.

A biological measurement that shows promise in predicting treatment responders is proprioception acuity. Proprioception is one’s ability to integrate sensory signals to determine body and limb position and movements in space [50]. Proprioception is thought to play a key role in motor learning by providing the feedback signals needed to guide learning [51], [52], [53] – in this, sense, proprioception might be considered a "top-level" signal used for motor performance. Recent studies have shown that proprioception acuity is a strong predictor of treatment response of the upper extremity after stroke [8], [11], [54], [55], but to our knowledge no studies have examined its ability to predict the treatment response to lower extremity therapy after stroke. Therefore, as described in detail below, this dissertation seeks to develop a novel test of ankle proprioception, in order to help to answer the question: does baseline lower extremity proprioception acuity predict gait rehabilitation treatment response?

Many tests for assessing proprioception have been developed using manual techniques, simple mechanical technologies, or robots [56], [57], [58], [59]. A recent review counted 1346 different types of proprioceptive measurements that fit within three classes: method of adjustment, where participants have to adjust the level of a stimulus to a reference; method of constant stimuli, where participants have to judge standard and comparison stimuli presented in pairings; and method of limits, where participants have to indicate the appearance or disappearance of a stimulus [56]. Horvath et al. also proposed a finger-grained classification system that clusters the measurement techniques based on the eight aspects of proprioception they target (e.g. perception of joint position, trajectory, velocity, force etc.) as well as the psychophysical paradigm they employ (method of adjustment, constant stimuli, or limits) [56]. Despite this plethora of proprioception measurement techniques, clinicians still rarely implement proprioception assessments in clinical practice. When they do, they typically rely on course indicators of proprioception, such as whether an individual can detect the direction of movement of a joint when their eyes are closed.

SUMMARY OF DISSERTATION

The impetus for this dissertation was to determine whether lower extremity proprioception acuity predicts responders to gait rehabilitation after stroke. This goal was identified in the context of a NIH-funded RCT at UCI that is using a brain computer interface (BCI) with functional electrical stimulation (FES) to treat footdrop of chronic stroke participants[1]. At the onset of the UCI BCI-FES RCT, we identified a need for a precise, valid test of ankle proprioception. I therefore endeavored to create the technical infrastructure needed to accurately assess ankle proprioception after stroke. As a secondary goal, we desired that the technical infrastructure could also aid in the assessment of two other fundamental aspects of ankle function – ankle range of motion and strength.

Chapter 2 describes the technical design and specifications of a novel robotic system for assessing ankle proprioception as well as ankle range of motion (ROM) and strength (or "maximum voluntary contraction" – MVC). The novel robotic system is a platform-based system called the Ankle Measuring Proprioception Device (AMPD).

Chapter 3 examines how the parameters of ankle proprioception assessments influence ankle proprioception acuity. This is an understudied area that has importance for understanding how failing to standardize parameters of proprioception testing may cause misrepresentation of proprioceptive integrity.

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[1] The BCI-FES RCT will finish after my planned dissertation completion. Therefore, while I will be involved in publishing the answer to the question "does baseline lower extremity proprioception acuity predict BCI-FES treatment response?", the plan is that this publication will be submitted when I am a postdoctoral fellow. My dissertation therefore focuses on the design and validation of a bilateral platform-based robot and implementing a novel proprioception assessment.

Chapter 4 presents the implementation of a novel ankle proprioception assessment called Crisscross using AMPD, as well as the results of a study aimed at determining the concurrent validity of Crisscross against a commonly used technique, joint position reproduction (JPR). We examined three populations: unimpaired young individuals, chronic post-stroke individuals, and unimpaired older individuals matched in age to the stroke participants.

Chapter 5 examines if the ability to utilize proprioceptive information at different joints is a body-general attribute or a site-specific attribute, that is, whether individuals who perform better/worse on a proprioceptive task at one joint are also those who perform better/worse at other joints.

Chapter 6 describes a study aimed at determining if AMPD is as effective as skilled therapists at quantifying ankle ROM and dorsiflexion MVC. We compared robotic test-retest reliability and validity in a group of 34 persons post-stroke to that of experienced therapists making the same measurements in the same persons using a goniometer and manual muscle testing. We also evaluated robotic test-retest reliability in 36 young and 26 older unimpaired adults.

Chapter 7 examined the relationship between ankle proprioception and gait function, as well as between ankle proprioception and ankle motor impairment, after stroke using AMPD-based robotic assessments in 39 persons in the chronic phase of stroke.

As will be shown, the results of these experiments demonstrate the reliability and validity of a novel platform-based robot (AMPD) for assessing ankle proprioception, as well as for assessing ankle ROM and MVC. They also provide novel insights into ankle proprioceptive function, including: indicating how assessment parameters affect proprioception acuity, identifying a component of proprioception processing that is body-general (i.e. shared between the fingers and ankles), and showing that baseline proprioception predicts gait speed post-stroke. Besides making these fundamental contributions, this work also lays the groundwork for determining whether lower extremity proprioception acuity predicts responders to gait rehabilitation after stroke.

CHAPTER 2: DESIGN OF AN ANKLE MEASURING PROPRIOCEPTIVE DEVICE (AMPD): A BI-IMPEDANCE ROBOT

SUMMARY OF CHAPTER

This chapter describes the design of a novel, bilateral, platform-based, robot for measuring sensory motor function of the ankles. We describe the mechanical and software design of Ankle Measuring Proprioceptive Device, including both a first version (AMPD 1.0) and a second version with several improvements (2AMPD). Both AMPD robots have two impedance states, mechanically rigid and mechanically transparent, which are chosen by manually engaging (locking) or disengaging (unlocking) the rack and pinion. In its rigid state, AMPD can be used to measure participants' maximum dorsiflexion strength and can independently move both ankles through participants' dorsiflexion and plantar flexion passive range of motion. In its mechanically transparent state, AMPD allows participants to move their ankles on their own volition with minimal resistance, disconnected from the motors. Use of a bi-impedance design thus allowed a high dynamic bandwidth (rigid or maximally backdriveable) with use of low-cost motors, and, in addition, simplified the control and safety of the robot. Further, with only two impedance states, we demonstrate how a variety of fundamental motor and sensory assessments can be completed.

INTRODUCTION

The human ankle joint is a complex bony structure within the human skeleton and plays a significant role in maintaining body balance during ambulation [60]. Because of this role, it is of significant interest to quantify ankle function in a variety of pathophysiological conditions, including during gait rehabilitation after stroke.

Over the past four decades, the use of robotic devices in rehabilitation has increased significantly [41]. Robotic devices allow application of controlled movements and provide appropriate forces during training [61], [62]. They can also continuously monitor movement performance to quantitatively assess outcomes and so that treatment can be objectively adapted to the patient's needs [62].

As reviewed in the introduction, robotic rehabilitation devices can be classified in two different ways. First, they can be wearable devices or grounded/platform-based devices. Wearable devices [39] are portable devices such as robotic orthoses and exoskeletons or active ankle-foot orthoses that are worn in order to assist in lower limb movement during the gait cycle, and can be used to for assessment, therapeutic, and assistive purposes. Platform-based devices are mechanically grounded and can take the form of exoskeletons or end-effector devices for assisting in the gait cycle or single-joint devices (**Error! Reference source not found.**). For wearable devices they must be lightweight and portable, and platform-based devices are typically heavier and can use larger actuators that are mechanically grounded to provide better control fidelity.

A second way to view rehabilitation robots is that they can be multi-joint or single-joint devices. For these devices, participants are typically in a seated position and only one joint is actuated, with the most common joints being the ankle and the knee (Figure 2). This simplified set-up allows a high fidelity of motion control and sensing to be achieved, allowing a precise analysis of joint-based function, but typically use large motors and have low portability.

Many platform-based robots that actuate a single joint, such as the ankle [63], [64], limits their flexibility for proprioceptive assessments, since a range of proprioceptive assessments involve comparing positions of two limbs. Platform-based robots that have implemented independent, bilateral support have typically used expensive and bulky motors, which also have safety concerns for clinical usage [65], [66]. We decided to take a different approach and design and build a two degree of freedom (DOF), dorsiflexion and plantarflexion, bilateral platform-based robot using low-cost, speed-limited, linear actuators (Figure 3). This chapter provides a technical description of the system hardware and software of the Ankle Measuring Proprioceptive Device (AMPD) robot, including an initial design and second design that improved on the first.

SYSTEM HARDWARE

Ankle Measuring Proprioceptive Device 1.0

Foot pedals: The foot pedals of AMPD 1.0 attach to the left and right foot of the subject to allow dorsi-plantar flexion ankle movement of the left and right ankle (Figure 2). Each footplate is 12.0 inches (L) X 4.5 inches (W) X 0.25 inches (H) and is attached to a steel rotary shaft, and the rotary shaft is connected to the frame of the robot using rotational bearings. The foot pedal is 15 inches from the ground to allow for clearance for plantarflexion. The weight of each foot pedal is 1.86 pounds, which is similar to the weight of a hiking boot. However, a counterbalance weight was attached to each shaft to remove the weight of the foot pedal. The subject's feet are strapped on top of the footplate, with the shaft aligned to the lateral malleolus. Wood shim plates (1/8" thickness) are stacked to separate the sole of the foot from the footplate by the appropriate amount to align the malleolus. Foot straps (Reusable Cinch Straps, Amazon) are used to secure the patient's foot on the robotic footplate. A 3D printed heel was attached to the foot pedal, via Velcro, to prevent any lateral movement of the foot in the sagittal plane.

Transmission mechanism: Linear, ACME lead screw actuators (Progressive Automations, PA-04-8-400-HS-24VDC) with a 12-inch stroke were used based on their qualities of producing high amounts of force, having limited velocity, being compact, and being affordable ($176). The linear actuator was rated to provide a max load of 400 lbs. in the push and pull direction at a speed of 0.51 in/sec under no load conditions and 0.16 in/sec under full load conditions. As shown in Figure 4, a rack and pinion (NEXEN, 966819, 966800) was used to translate linear to rotational motion. This rack and pinion have a special feature that the pinion consists of bearing-supported rollers that rotate when they encounter the rack to reduce friction. This is particular of interest to us because it gives AMPD the ability

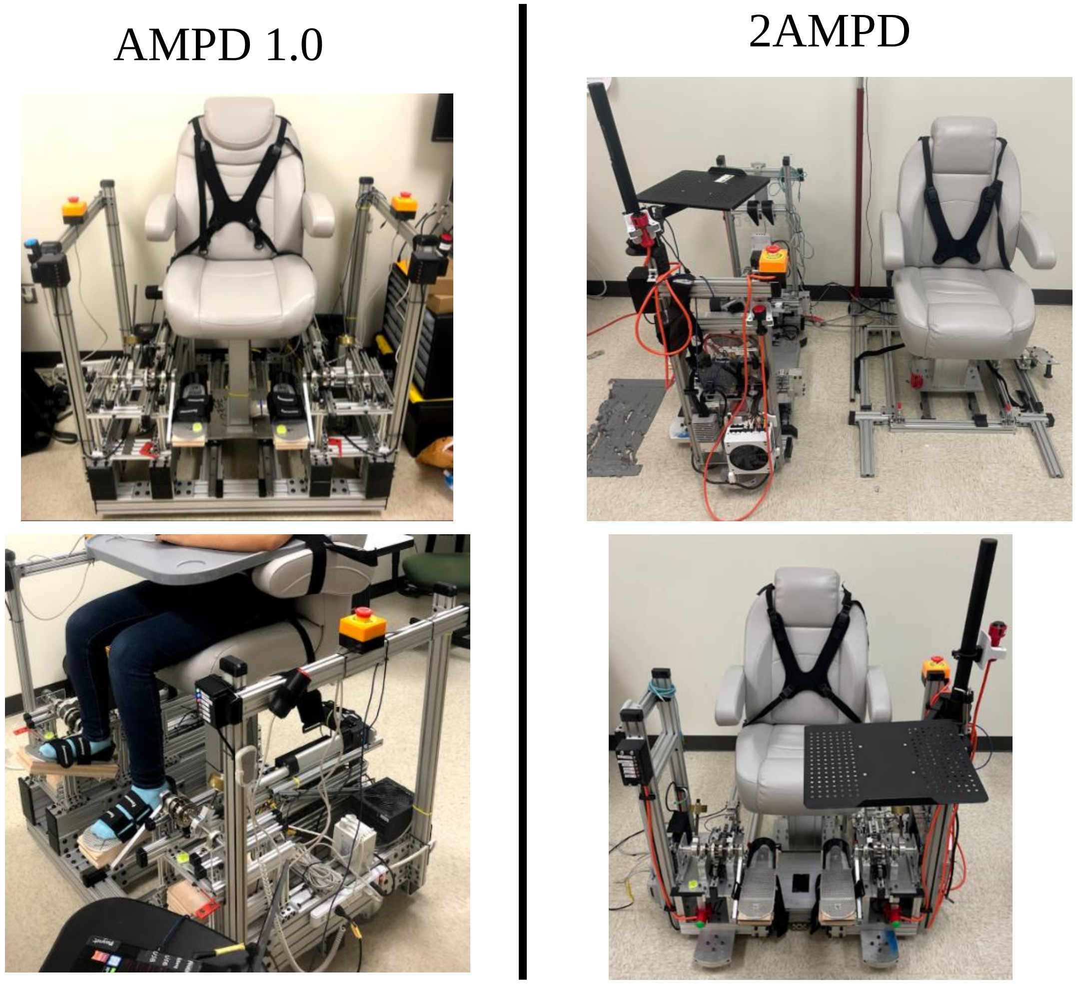


Figure 3. Photos of AMPD 1.0 (Left) and 2AMPD (Right)

to disengage and re-engage the rack and pinion without teeth binding, which can happen with a traditional rack and pinion system. The combination of a linear actuator and rack and pinion provides a full range of motion of dorsiflexion and plantarflexion.

Sensors and Microcontroller: The AMPD transmission mechanism was equipped with a compression and tension load cell (Interface, SMA-200) positioned between the linear actuator and rack to measure torque. In addition, an angular quadrature encoder (E6B2-C, 1024 P/R) was connected the rotary shaft to measure ankle angular position (Figure 4). A Teensy 4.0 (PJRC, Teensy) microcontroller was used as the control unit, both to read information from the sensors and to control the linear actuators.

Platform: AMPD incorporates an adjustable seat and an adjustable sliding platform. The seat consisted of a captain's boat chair (Pontoon, RCL-Gray) and a lifting column (Progressive Automations**,** FLT-03-2-1), that had optical distance sensors (4 meter, SEN-14722) to measure chair position. The sliding platform consisted of two linear bearing carriages (McMaster, 6713K14), two linear rails (McMaster, 6250K4), and a hand break (McMaster,1685N17). All these mechanisms were powered using a 750W computer power supply (Newegg, CAPSTONE 750M).

Improvements from AMPD 1.0 to 2AMPD

AMPD 2.0 is similar to AMPD 1.0, but with some usability improvements that were identified after extensive clinical testing with 17 individuals with a stroke in collaboration with expert physical therapists. First, AMPD 1.0 seat height was 33 inches, which required use of a stepping stool and introduced safety concerns during transfers of subjects with motor impairments. We reduced the height of the seat from 33 to 16 inches by designing AMPD 2.0 so that it could be separated into two independent pieces, a rollable structure that holds the transmission mechanisms and one for seating (Figure 4). The sitting piece has a 3-stage lifting column (TiMotion, **TL3**), which reduced the seating height drastically. Second, we reduced the size of the transmission mechanism by using a linear actuator (TiMOTION, TA16) with a 6 in stroke, which was rated to provide 1011 lbs-force pushing and 562 lbs-force pulling at a maximum speed of 2.2in/sec under no load conditions and 0.16 in/sec under max load conditions. This allowed us to reduce the amount of space needed for the transmission mechanism by placing the linear actuator underneath the rack and pinion system (**Figure *4***). Third, we improved the ease of switching of impedance states by having a latch that disengages the rack and pinion, to increase efficiency in transitioning between robotic assessments (active range of motion, maximum strength, etc) (Figure 4). This was achieved by allowing the horizontal mounting plate for the rack to rotate down in order to disengage the rack from the pinion after it is unlatched. Lastly 2AMPD is able to adjust the lateral distance between the feet. With AMPD 1.0 this distance was set to a fixed width of 12.5 inches, which is the average hip breadth during sitting obtained from anthropometric data [67]. However, use of a fixed width caused the knees to point slightly inward or outward dependent upon participants' size and posture.

Thus, the major parts of AMPD 2.0 (2AMPD) are an adjustable mechanical seat, an adjustable sliding platform that holds the footplates and transmission, a mechanism for adjusting distance between the feet, a transmission mechanism, footplates for both feet, and a control unit. The adjustable mechanical seat consisted of a captain's boat chair (Pontoon, RCL-Gray) and a 3-stage lifting column (TiMotion, **TL3**). The sliding platform consisted of two linear bearing carriages (McMaster, 6713K14), two linear rails (McMaster, 6250K4), and a hand break (McMaster,1685N17). The adjustable mechanism to adjust the width between the feet consisted of four linear bearing carriages (McMaster, 6713K14) and 4 linear rails (McMaster, 6250K4). Linear actuators were connected to the linear bearing carriages. The transmission mechanism consisted of a rack and roller pinion system (NEXEN, 966819, 966800), with the rack connected to the linear actuator (TiMOTION, TA16). The foot pedals were custom made from aluminum and drilled with a honeycomb of holes to reduce inertia during movement. A Teensy 4.1 (PJRC, TEENSY41) was used as the control unit.

Just like AMPD 1.0, 2AMPD has multiple sensors. The adjustable mechanical seat, sliding platform, and adjustable feet width are equipped with distance sensors (4 meter, SEN-14722) to measure chair position and feet width. The transmission mechanism is equipped with a compression and tension load cell (Interface, SMA-200) to measure torque and an angular quadrature encoder to measure ankle angular position (E6B2-C, 1024 P/R). Slide potentiometer was implemented (DigiKey, 2368-NTE74HC14-ND) to streamline the robot set up process, by setting the reference point for the incremental encoders without any operator intervention. All these mechanisms were powered using an 850W computer power supply (Newegg**,** P-9020188-NA**).**

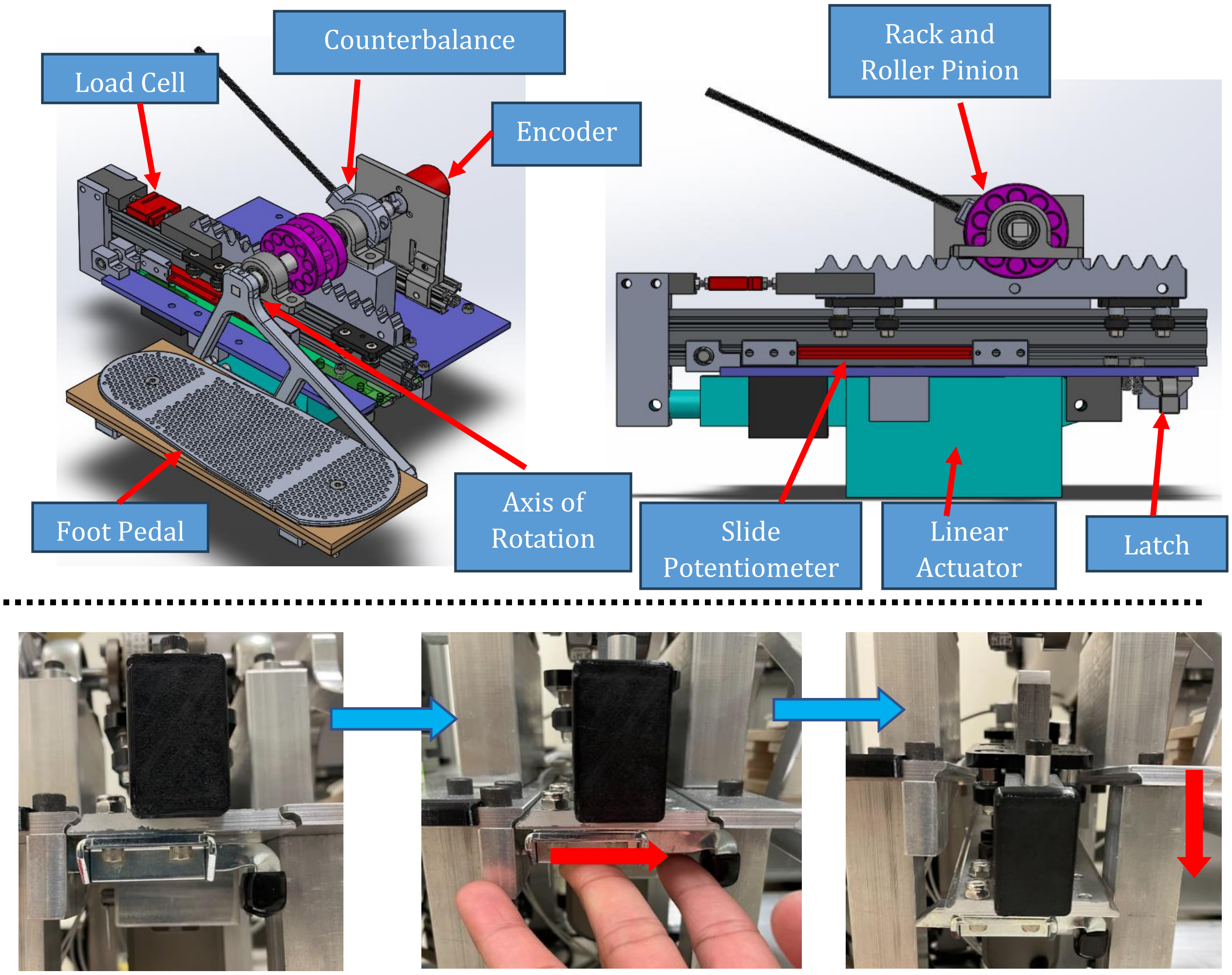


Figure 4. 2AMPD transmission mechanism and impedance state for the left ankle. Top: transmission mechanism with the foot pedal attached. Bottom: Operation of mechanism to transition between impedance states

SYSTEM SOFTWARE

Control System

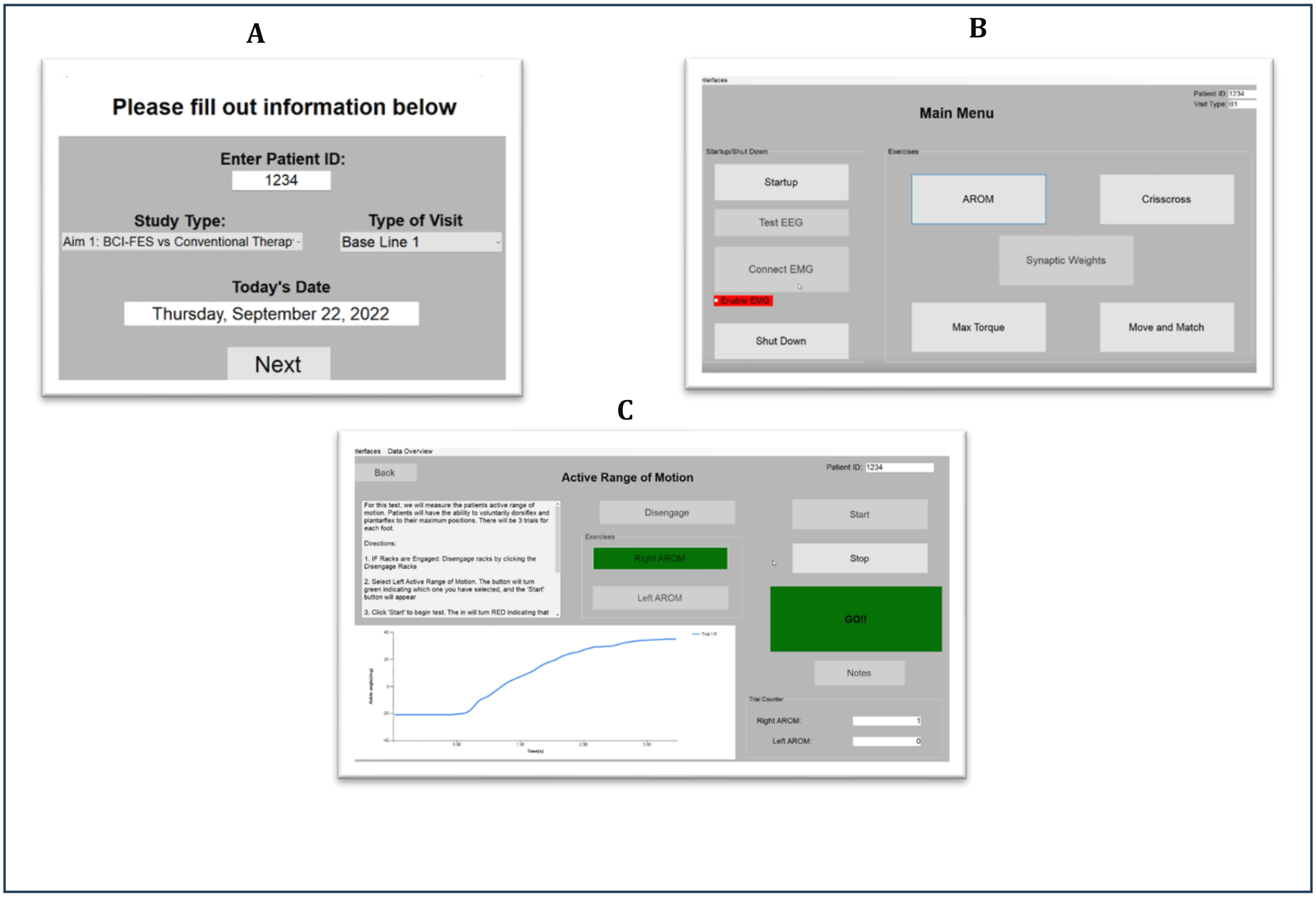
Both AMPD robots are programmed in C++. The linear actuators that move the foot are driven using pulse width modulation (PWM) from the Teensy microcontroller. During certain exercises AMPD must actuate the feet at certain speeds, therefore we implemented a velocity proportional-integral-derivative (PID) controller that modulates the PWM fed to the linear actuators by using the input of the encoders. The PID controller operates at 20Hz.

Graphical User Interface

A customized graphical user interface (GUI) was developed using Microsoft Visual Studious (C#) to control both robots. The initial page of the interface allows the operator to input the subject identification number and visit type (Baseline, Weekly, Followup, etc.), but the interface automatically enters the date from the computer to reduce user error (Figure 5A). On the main menu page AMPD showed four tasks that could be completed: active range of motion (AROM), maximum voluntary contraction (MVC), and two proprioception tests – Crisscross and joint position reproduction (JPR) (Figure 5B). Within each task window there are detailed instructions on how to run that specific task correctly. During each task data is plotted live in a window on the task screen for the operator to ensure data collection is of quality (Figure 5C). When each task is completed, the GUI displays the data and displays a notification box that the data has been saved. Also, the interface keeps track of the number of trials completed and gives therapists the ability to put in notes for specific or multiple trials. Figure 3 shows an example of the interface. The data generated from the trial is acquired at 200 Hz and stored on a laptop in a text file. The data variables saved from each trial are shown in Table 1.

Table 1 All Data Saved that AMPD outputs at 200Hz.

Left	Right
Angular Position (ticks)	Angular Position (ticks)
Torque (mV)	Torque (mV)
Torque Gain	Torque Gain
PWM fed to motor	PWM fed to motor
Intended Speed fed to PID	Intended Speed fed to PID
When motor is ON/OFF	When motor is ON/OFF
Rack Position (2AMPD)	Rack Position (2AMPD)
Time Data point was received (ms)	
TTL Sync Pulse	
JPR Matching Index	
Version of Prop Assessment	



Enter Patient ID: 1234

Study Type: Aim 1: BCI-FES vs Conventional Therap

Type of Visit: Base Line 1

Today's Date: Thursday, September 22, 2022

Patient ID: 1234

Visit Type: B1

Patient ID: 1234

For this test, we will measure the patients active range of motion. Patients will have the ability to voluntarily dorsiflex and plantarflex to their maximum positions. There will be 3 trials for each foot.

Directions:

1. IF Racks are Engaged: Disengage racks by clicking the Disengage Racks

2. Select Left Active Range of Motion. The button will turn green indicating which one you have selected, and the 'Start' button will appear

3. Click 'Start' to begin test. The in will turn RED indicating that

Right AROM: 1

Left AROM: 0

Figure 5 AMPD GUI from the perspective of the operator. **A)** Input of subject identification number, study type, type of visit and date. **B)** Main menu with all the exercises that could be completed. **C)** Example of active range of motion for the right ankle.

Conversion of Data from ticks and mV to Angle and Torque

The encoders on AMPD robots are optical quadrature incremental encoders. Incremental encoders are limited by only providing change in information, meaning each time they turn on the reference position must be set for each ankle. The reference position for us was neutral, the ankle is 90° in the sagittal plane between the foot and shank [68]. Each time the digital signal is high the Teensy increments or decrements by one, which we will call a tick, based on the rotation of the shaft. The resolution of these encoders is 12 bits, meaning there are 4096 ticks to complete a full 360° rotation. With this conversion we multiplied each tick by 0.088° to get angular position.

The load cells were positioned between the rack and linear motor to measure the compression and tension of the rack and roller pinion system. Both AMPD devices are able to modulate the gains of the amplification of the load cell signals to prevent saturation of voltage and damage to the Teensy through the use of multiplexers (Digikey, 296-2058-ND) and resistors. Using a low power instrumented amplifier (Digikey, INA125), we were able to receive the forces applied to the load cell in mV. We converted the analog signal in mV to

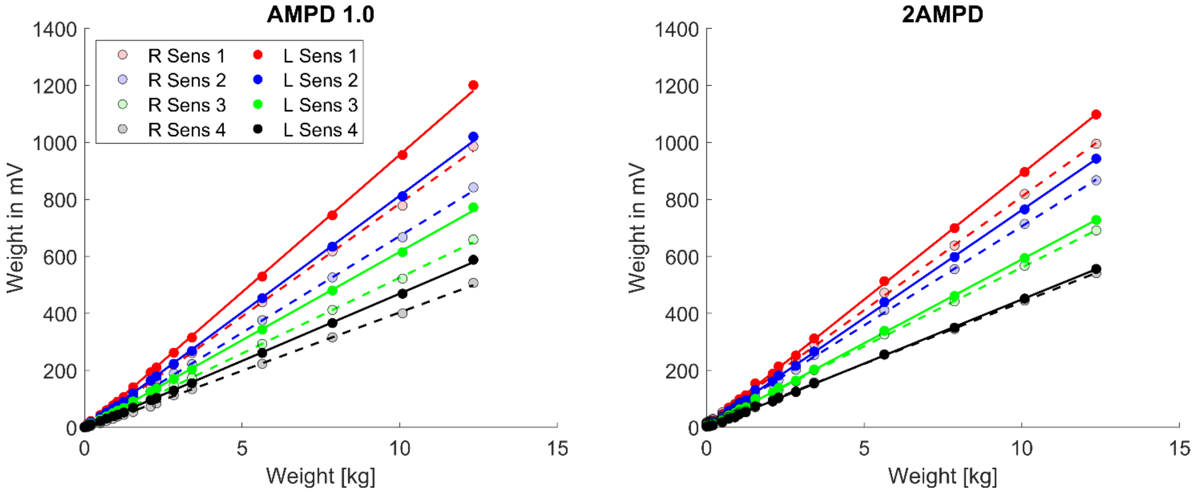


Figure 6. Linear Regressions between weight (kg) applied and mV from load cell for each foot pedal on each robot.

torque using equation: $torque = r * F * \cos(\theta)$. Where r is the radius, F is the force, and theta is the angle. The radius in this case was the moment arm from the center of the shaft to the front bolt of the foot pedal which was 0.21 meters. To obtain F, there were multiple steps involved. First, we converted from mV, output of load cell, to weight (kg), by hanging known weights of various sizes from the foot pedal and recording the output voltage (see Figure 6 and calibration equations from regression in Table 2). Lastly, we multiplied by acceleration. For theta we used the angular position from the encoder.

Table 2 Linear Regression equations for each robot for left and right ankle

	AMPD 1.0		2AMPD	
	Right	Left	Right	Left
Sensitivity 1 (Default)	y = 79.33 * x -7.76	y = 96.36 * x -7.21	y = 79.76 * x +12.33	y = 88.31 * x + 6.94
Sensitivity 2	y = 67.87 * x -7.35	y = 81.90 * x -5.96	y = 69.49 * x +10.59	y = 75.75 * x + 5.03
Sensitivity 3	y = 53.19 * x -6.50	y = 62.00 * x -4.16	y = 55.34 * x +7.96	y = 58.82 * x +1.15
Sensitivity 4	y = 40.95* x -6.09	y = 47.21 * x -2.88	y = 43.36* x +6.00	y = 44.99 * x -1.06

CONCLUSION

This chapter detailed the mechanical design and system software of two, 2-DOF, platform-based single joint robotic devices for measuring ankle function. Both robots were designed with the considerations of interactive safety and interface friendliness. Also, both robots have the ability to change impedance state fairly quickly, which gives us the ability to create a wide variety of ankle motor and sensory function assessments.

CHAPTER 3: EFFECT OF ROBOTIC TESTING PARAMETERS AND AGE ON ANKLE PROPRIOCEPTIVE ACUITY

SUMMARY OF THE CHAPTER

Robotic devices can be used to improve proprioceptive assessments, but there is a lack of knowledge about how programmable factors such as testing range and speed affect proprioceptive acuity. Little is also known about how age affects ankle proprioception acuity. To determine the influence of such factors, and how best to structure proprioceptive assessments across a range of ages, we studied ankle proprioception acuity using the Crisscross assessment with range and speed variations in 26 young (18-35 yrs) and 25 older (50-88 yrs) unimpaired participants in a single session. For both groups, testing a smaller range of motion significantly lowered proprioceptive error ($p < 0.001$). When we normalized error by the maximum possible error that could be achieved, range of motion no longer influenced acuity, providing a means to objectively compare errors from individuals with different testing ranges. While both groups had poorer acuity at slower speeds due to greater anticipatory errors ($p < 0.001$), older individuals performed significantly better at slow speeds, which we speculate may be due to differences in preferred ankle velocity during walking. Proprioceptive acuity significantly improved near the ends of the range of motion for young and older participants ($p<0.001$) with the greatest error in the mid-extension of the workspace. This is consistent with greater involvement of load and joint receptors at joint limits. Interestingly, across testing parameters, contrary to our expectations, aging did not significant deteriorate ankle proprioceptive acuity. In fact, older individuals showed higher acuity across speeds and crossing positions compared to young adults, particularly for timing error. These results show how the range and speed selected for a proprioceptive

test affect proprioceptive acuity and highlight the heightened role of anticipatory errors at slow speeds. Improvement in ankle proprioceptive acuity with aging is a novel finding that deserves further exploration.

INTRODUCTION

For the lower extremity, proprioceptive signals related to leg kinematics and loading are thought to play a key role in locomotor control and plasticity [69], [70], [71], [72]. In rehabilitation after stroke, impaired proprioception predicts poor motor recovery [8], [11], [54], [55]. It is also well known as humans age deterioration occurs to the sensorimotor system, which reduces sensory and motor performance and increases postural sway [73]. Balance loss and falls in older adults have been attributed to impaired lower limb proprioception [74], [75].

Given its important role in motor function, there is interest in improving techniques to quantify proprioception, to replace coarse, standard clinical assessments that are currently available [76]. In a previous review, authors outlined the benefits of using lower limb robotic devices for assessing proprioception because of high consistency in the protocol such as speed, points of limb contact, and timing between trials [77]. However, introducing robotic tools for assessing proprioception requires consideration of a broad design parameter space, forcing engineers and clinicians to make decisions about the particular testing parameters to use (e.g. speed and range), to optimize the goals of the assessment.

From neurophysiological studies, we know that proprioception is mediated by an array of proprioceptors, including cutaneous receptors, joint mechanoreceptors, muscle spindles, and Golgi tendon organs (GTOs) that show different sensitivities to speed and tendon stretch [78], [79]. For example, muscle spindles exhibit greater firing rates at greater speeds [80]. Similarly, towards the extremes of the range of motion, muscle/tendon stretch increases spindle, GTO, and joint receptor firing rates [81]. While several studies have examined how such parameters impact proprioceptive acuity in the upper extremity [73], [82], [83], few studies have looked at the influence of assessment parameters on proprioceptive acuity at the ankle and how sensitivity to such factors change with aging [84], [85].

To address this limitation, we applied a recently developed robotic proprioceptive assessment, called Crisscross, to the ankles. Crisscross requires participants to indicate when two joints are aligned as they are passively moved by the robot in a crossing pattern [86], [87], [88], [89]. With this assessment we can measure not only positional sensing errors, but also directional and timing related errors in position sense associated with motor planning and on-line monitoring of motor performance. This assessment has previously been validated for the fingers and was found to be sensitive to aging [86] and the presence of a prior stroke [89], and predicted the ability to benefit from robotic finger training after stroke [87], [88]. A key advantage of this assessment is that it does not require the participant to be able to move the limb being tested, such that mobility is not a confound in assessing proprioceptive acuity, nor does the test include a memory component, reducing the effect of cognitive factors.

In this study, we used Crisscross to evaluate the influence of assessment range of motion (ROM or “workspace”), speed, and crossing position on different quantification methods of proprioceptive acuity in young and older unimpaired adults. We hypothesized that smaller assessment ROM would elicit smaller errors, as errors would be bounded by the reduced workspace range. We expected proprioceptive acuity to improve at the kinematic extrema—near the edges of the test workspace— and with greater speeds due to greater engagement of spindles and GTOs in these conditions. Lastly, we hypothesized that older participants would have lower proprioceptive acuity compared to younger adults due to age-related deterioration to the sensorimotor system.

METHOD

Participants

Young adults, aged 18–35 years old, and older adults, aged 50–88 years old, were recruited for a single assessment session. Exclusion criteria were history of neurological injury, musculoskeletal damage to the ankles, or current injuries that affected participants ability to move or feel their ankles, or use of medication that would change how the brain perceived pain/movement. The local ethics committee approved this study, and written informed consent was obtained from each participant prior to participating, following procedures established by the University of California Irvine Institutional Review Board.

Proprioception Testing Protocol

We implemented the Crisscross assessment by using a robotic device to move the two ankle joints past each other and asking participants to push a button when they felt that their ankles were aligned. To test the effects of the assessment workspace and ankle movement speed, we created 4 different Crisscross tasks (see also Table 3), each comprised of total of 20 crossings.

Task 1 and 4: To test for ROM effects, we assessed participants using a workspace equal to their full passive ROM (Task 1) and workspace equal to half of their passive ROM (Task 4). We used the same speed parameters for each task.

Task 1,2, 3: To test how speed affects the proprioceptive performance, we applied a range of ankle movement speeds throughout the entire speed range achievable by AMPD: 2 to 20 deg/sec. We constrained the movement speeds of the AMPD to a lower range (2-8 deg/sec, Task 1), upper range (14-20 deg/sec, Task 2), or 70% of the speed range (6.5-20 deg/sec, Task 3). Four, equally spaced speeds were assessed in each task.

Table 3 Parameters experienced for each Crisscross task.

Task #	4 Speeds (deg/sec)	Ankle speeds per run	Crossing Workspace
1	[2:2:8]	Coupled	Full ROM
2	[14:2:20]	Coupled	Full ROM
3	[6.5:4.5:20]	Coupled	Full ROM
4	[2:2:8]	Coupled	50% of Full ROM

For each task, we programmed 2AMPD to passively move the ankle joints in opposing directions in an alternating crossing pattern with vision of the legs occluded (Figure 5). We instructed participants to press a button to indicate when they perceived their ankles to be at the same angular position. For all participants, before beginning the test, a trained operator assessed each participants' passive range of motion by manually moving both ankles to a comfortable maximum dorsiflexion and plantarflexion position. The assessment workspace was then calculated by taking the smaller extent of dorsiflexion between the two ankles, and the smaller extent of plantar flexion as well. The assessment workspace was then split into 5 sections, such that a single crossing occurred in each workspace section, >60% PF (extension), 60-20% PF (mid-extension), 20%PF - 20%DF (center), 20%-60%DF (mid-flexion) and >60% DF (flexion). This ensured an approximately uniform distribution of crossing position and speeds in the assessment workspace. Example of Crisscross assessment shown in Figure 7.

To ensure each participant understood the test, they first completed four crossing movements with vision of their feet, giving verbal confirmation that they understood the test. Then, with vision occluded participants performed each of the 5 tasks. Each participant received a different pseudo-randomized task order that ensured a uniform distribution of each task type (1, 2, 3, etc.) in each order (first, second, third, etc.) across participants, to decouple potential learning or fatigue effects from task-specific effects. Within each task the crossing positions and speeds were pseudo-randomized such that crossing position or speed

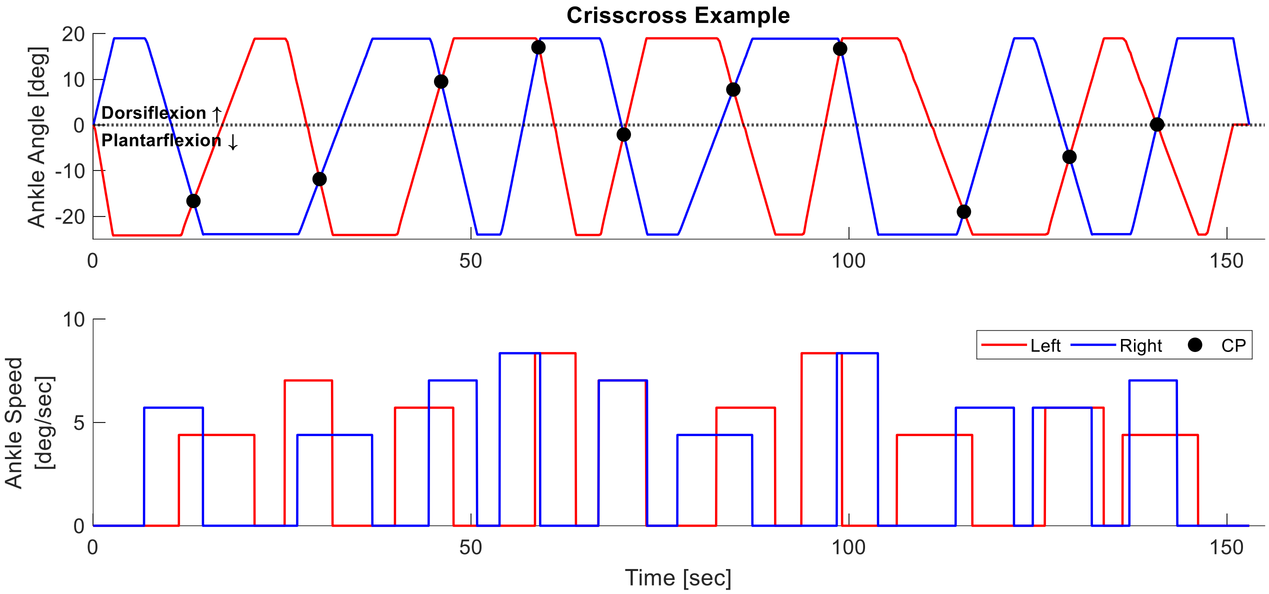


Figure 7. Example of Crisscross. The top figure is the ankle trajectories and crossing positions (denoted by circles) during Crisscross test generated by 2AMPD. Positive ankle angles correspond to dorsiflexion and negative number correspond to plantarflexion. The bottom figure is ankle speeds during Crisscross test generated by 2AMPD where the ankles can move at the same speed or independent speeds for a crossing trial. **CP** = Crossing Position

changed every trial, to ensure the assessment was unpredictable. For “Coupled” ankle speed tasks, participants experienced all four speeds in each workspace section.

STATISTICAL ANALYSIS

We quantified proprioceptive performance using absolute error, normalized absolute error, and timing error. Absolute error is defined as the absolute angular difference between the left and right ankle at the moment of button press. Normalized absolute error is defined by the absolute error divided by the maximum error that could be achieved. Timing error is defined as the difference between button press and actual crossing in time, with negative values signifying button presses before crossing position occurred and positive values signifying button presses after crossing position occurred. Crossings in which a participant did not press the button were excluded from analysis, meaning participants were not penalized for missing a crossing.

We conducted statistical analyses using Matlab R2023 and JMP Pro 16 software. Normality was tested using the Shapiro Wilks test. Since all data was normally distributed, we used parametric tests. A two-way ANOVA was performed to analyze the effect of task and age for each of the three metrics of proprioceptive acuity. To test for ROM effects, we compared Tasks 1 and 4. To assess the influence of specific speeds and crossing positions, we analyzed data from Tasks 1, 2, and 3. We defined crossing speed as the sum of the limb speed magnitudes (i.e. sum of left and right ankle speed magnitudes). We used an ANOVA to analyze the effect of crossing speed, crossing position and age on the three metrics of quantifying proprioceptive performance. If significant effects were found, we used a Tukey's

Honest Significant Difference (HSD) for post hoc analysis. We used an alpha level of 0.05 for all comparisons and correlations.

RESULTS

We assessed proprioceptive acuity over a range of robotic assessment parameters in 26 young, unimpaired participants (13 male, 13 female; mean ± SD, age = 24 ± 4 yrs) and 25 older, unimpaired participants (11 male, 14 female; age = 64 ± 10 yrs). All participants completed each task. We focus first on the younger participants and then compare the older participants. For each comparison statistic given below, we first performed an omnibus ANOVA as described in the methods to confirm the presence of a significant effect, then performed the post-hoc comparisons reported here.

Effect of workspace size

Absolute errors were significantly lower for the younger participants when Crisscross was conducted across the half workspace (Task 4) compared to the full workspace (Task 1) (Figure 8A, $p < 0.0001$). Timing errors were anticipatory and smaller for the half workspace (Figure 8B). When we normalized error by workspace size, there was no longer an effect of workspace size on error (Figure 8C, $p = 0.98$).

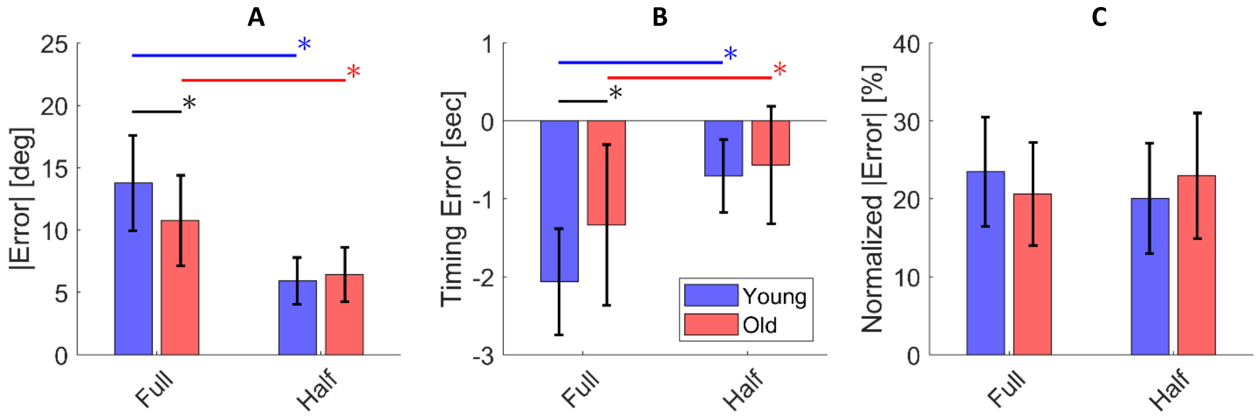


Figure 8 The averages of all three-quantification metrics for the effect of ROM in young and older participants. Error bars show +/- SD.

Since decreasing the testing workspace decreased proprioceptive error, we analyzed how error varied with the testing workspace set by the operator for each individual. The testing workspace varied across participants because it was based on each participant's passive ROM, which varied across participants (Figure 9A). We found that participants with larger ROM produced larger errors (r2 = 0.13, p < 0.008, Figure 9B). Further, we found that the ROM set by the operator for younger participants (average ± SD: 57.1°± 8.8°) was significantly greater than for older participants (51.1°±5.8°) (t-test, p = 0.005). When we normalized error by ROM, it no longer varied significantly with ROM (Figure 9C).

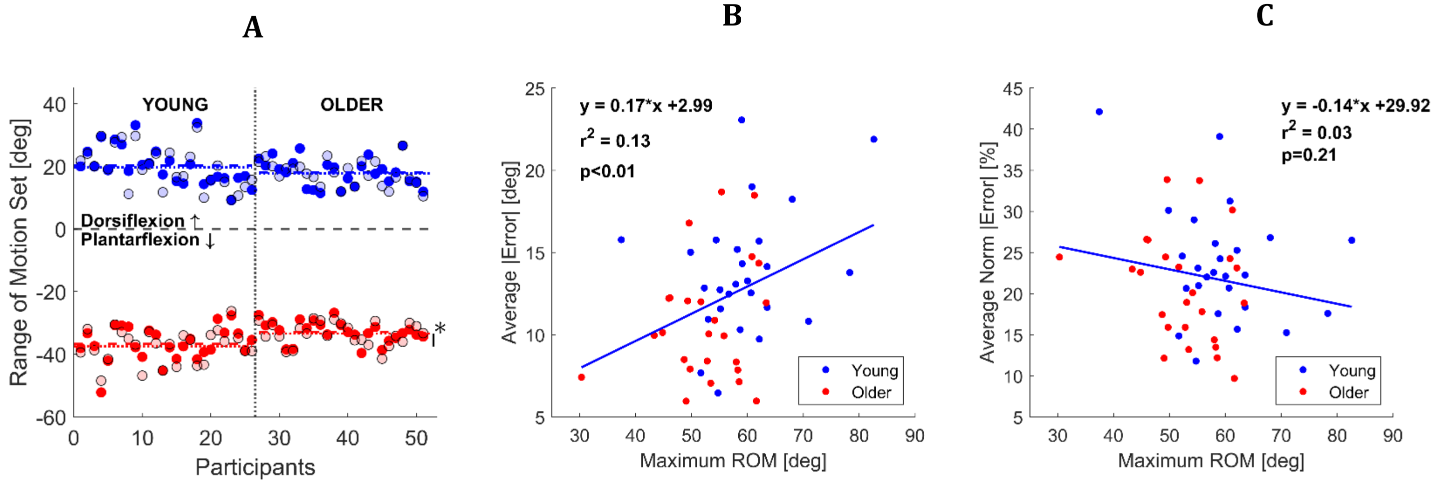


Figure 9. Relationship between ROM and absolute errors for young and older participants. A) Each participants set dorsiflexion and plantarflexion position for the left and right ankle. B) Maximum error that could have been achieved as a function of absolute average error. C) Maximum error that could have been achieved as a function of normalized absolute average error.

<u>Effect of speed and crossing position</u>

Both normalized and timing errors were greater at slower speeds (Figure 10A, 8B). Normalized error was maximal at mid-extension (Figure 10C). Timing error was anticipatory and increased significantly as crossing position moved to flexion, but the increase was small (Figure 10D, $p < 0.05$).

Effect of Age

Considering now the older participants, the general shape of the error curves in Figure 10 for the older participants (red lines) was similar to that of the younger participants (blue lines). However, some of the curves were significantly different. When they were different, it was always because older participants had better proprioceptive acuity, and the error measure that was most often different was timing error. For example, older participants had significantly lower absolute and timing errors for the full testing workspace (Task 1) (Figure 8A $p = 0.0043$, Figure 6B $p = 0.023$), but not the half workspace (Task 4) (Figure 8A $p = 0.92$, Figure 6B $p = 0.98$). Normalized error was not significantly different between young and old for the workspace experiment (Figure 8C $p > 0.40$).

When analyzing crossing speed, older participants had significantly smaller timing error between 4 deg/sec to 12 deg/sec (Figure 10B $p < 0.0001$); normalized errors were not significantly smaller (Figure 10A $p > 0.20$). For crossing position, older participants had significantly less anticipatory timing error in the middle of their ROM compared to younger participants (Figure 10D, $p < 0.02$), but again, normalized error was not significantly smaller (Figure 10C, $p > 0.20$).

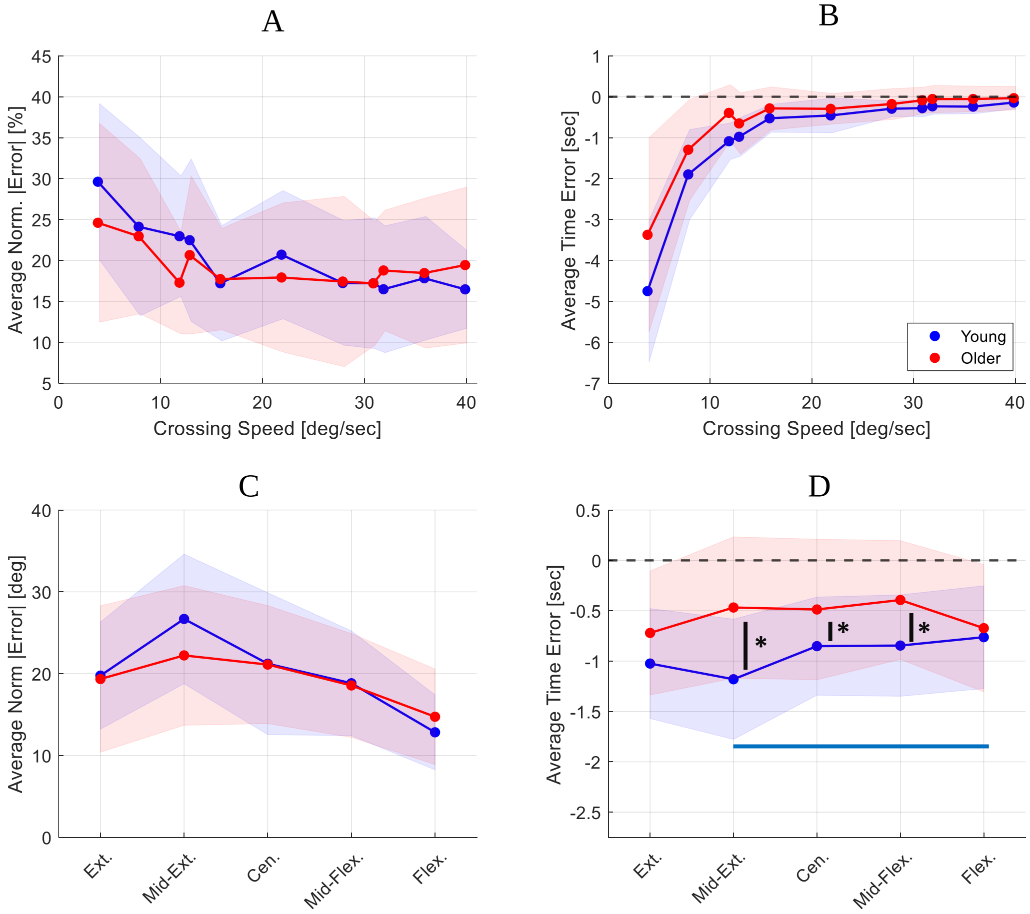


Figure 10 The effects of crossing speed and position for young and older participants. Row 1: Effect of relative crossing speed (x-axis) on normalized absolute error and timing error (y-axis). Row 2: Effect of crossing position (x-axis) on normalized absolute error and timing error (y-axis)

DISCUSSION

We investigated how programmable factors such as testing range and speed affected crossing and timing error for the ankle using Crisscross. We found that the testing workspace significantly influenced proprioceptive performance, with better performance in smaller testing workspaces. In addition, as we hypothesized, proprioception was better at greater speeds and at the kinematic extrema. However, our hypothesis that age would reduce proprioceptive acuity was incorrect. We will now discuss these results and their implication for ankle proprioceptive assessment.

Effect of Testing Workspace

Consistent with our results, it has previously been shown for the upper extremity, using a passive joint position reproduction task, that larger angular distances traveled induced greater matching positional errors [82], [90]. One hypothesis, that was stated in [82], is that the increased errors seen with larger movements reflect increased sensorimotor noise caused by larger movements [52]. Alternately, there may be a measurement saturation issue – if the testing workspace is only one degree of movement, then error cannot be greater than one degree; thus smaller workspaces necessarily must have smaller errors. A third possibility is that this phenomenon reflects some sort of neural recalibration, in which the nervous system senses the decreased range of motion and somehow adjusts sensitivity to the workspace.

In terms of proprioception testing methodology, these results show that quantifying ankle proprioception error without correcting for testing workspace may inflate proprioceptive acuity when the testing workspace is mall. We propose that normalized absolute error might be a better indication of proprioceptive acuity for individuals with different ankle ROM.

Effects of Crossing Speed

It was counterintuitive to us that proprioception acuity declined at slower speed. Estimating the position of ones limbs seems like it would be easier when they are moving more slowly. One possible explanation is that the proprioceptive system relies on velocity sensing and then integrates the sensed velocity to estimate position. Then, if there are increased velocity sensing errors or sensing noise at slower speed, this could explain the greater error. However, a model of position estimation based on velocity integration would need to explain why the timing errors at slow speeds are asymmetrical. That is, participants increasingly overly anticipated the crossing at slow speeds. The reason for this over-anticipation is an interesting question for future research.

Effect of Crossing Position

Proprioceptive error increased in the middle of the workspace compared to the ends. A possible explanation for this is that there was less engagement of spindle and GTO afferents in the mid-range due to less physical stretching of these afferents in this range.

Effect of Age

When we observed an effect of aging on proprioceptive error, it was in the opposite direction from what we expected: older adults had lower proprioceptive error. There was especially apparent for timing error at slower speeds. There is a is large body of work that has shown proprioceptive acuity decreases with aging [73], [74], [75], [91], and our finding is unique to our knowledge. We speculate that older adults' proprioceptive system was better tuned to sense slower speeds because older individuals tend to move at slower speeds compared to younger individuals. Studying this unexpected improvement in ankle proprioception with aging is an important direction for future research.

Designing the Most Sensitive Crisscross Assessment for Aging

We can use the results of this study to inform the design of the best Crisscross parameters to detect effects of age. We suggest using slower speeds, particularly in the 2 to 12 deg/sec speed range, because speeds above 16 deg/sec did not now show a consistent significant difference between young and old. However, with slower speed, greater variability was seen, so determining the number of crossings to complete in a trial is essential because too few trials can cause a misrepresentation of acuity. Also with slower speeds, attention may influence performance, so keeping the number of trials as small as possible may help maintain attention. We suggest a minimum of four attempts per speed is sufficient. Normalizing absolute error can be done to account for within subject differences in acuity due to variations in ankle ROM, however, timing error showed the most sensitivity to age.

CHAPTER 4: GENERALIZATION AND VALIDATION BETWEEN PASSIVE AND ACTIVE ROBOTIC TESTS OF THE ANKLE: EFFECTS OF STROKE AND AGING

SUMMARY OF THE CHAPTER

Assessing ankle proprioception is important for a variety of clinical conditions including during stroke rehabilitation but it is currently unclear how best to assess it. A fundamental issue in selecting a proprioceptive assessment is that different assessments target different aspects of proprioception; thus, it was recently observed that there appear to be no generalizable tests of proprioceptive accuracy (Horvath et al. 2023). Using the recommended Crisscross parameters stated in Chapter 3, we tested whether proprioceptive accuracy measured with Crisscross generalized to a more commonly used technique, a contralateral Joint Position Reproduction (JPR) test that required actively matching the position of the target ankle (which was moved in a random pattern by a robot) with the other ankle. We examined three populations: unimpaired, young individuals (N=42), individuals with gait impairment in the chronic phase post-stroke (N = 40), and unimpaired, older individuals matched in age to the stroke participants (N = 27). For the young group, Crisscross and JPR accuracy were uncorrelated, as expected ($p > 0.1$). However, for both the older and stroke groups, Crisscross and JPR were moderately correlated ($r = 0.56$, $p = 0.002$; $r = 0.55$, $p < 0.001$), respectively, indicating generalization between assessments in these populations. We also found that proprioception accuracy was significantly worse after stroke compared to age-matched controls (mean age = 64), as expected, but, unexpectedly, not in our older compared to younger group, suggesting that ankle proprioception accuracy was preserved into at least 60 years old. Further, accuracy was better for JPR than Crisscross in

all groups ($p < 0.01$). This suggests that actively moving the ankle during the assessment improved proprioceptive estimation, a finding consistent with the theory of prediction of limb position using a forward model. Finally, for the JPR test, when the robot stopped moving the target ankle and allowed individuals to statically match ankle positions, they did not reduce error. This suggests that proprioceptive accuracy is driven primarily by integrating velocity signals rather than by directly sensing position. These results indicate that different proprioception assessments can generalize under certain neurologic conditions (i.e. stroke-related injury and aging), and provide novel information about the role of age, active movement, and velocity-related signals in ankle proprioceptive accuracy.

INTRODUCTION

Proprioception is mediated by an array of proprioceptors, including cutaneous receptors, joint mechanoreceptors, muscle spindles, and Golgi tendon organs (GTOs). Multiple somatosensory brain areas process information from these proprioceptors [92]. It is common after stroke for proprioceptive deficits to be present when damage occurs to afferent pathways or to the neural circuits responsible for sensory integration and perception [93], [94], [95]. About a third to half of people have somatosensory deficits of the lower limb [96], [97], with somatosensory deficits and motor weakness resulting in worse functional outcomes at six months than motor weakness alone in stroke [98].

Proprioceptive impairment after stroke is thought to affect the control of muscle tone, disrupt postural reflexes, and impair spatial and temporal aspects of volitional movement [99]. For the upper extremity, proprioceptive impairment also predicts the ability to benefit from rehabilitative movement training, such as constraint-induced therapy [11] or robotic hand movement training [8], [18], [100]. This suggests that proprioceptive feedback plays an important role in mediating use-dependent plasticity after neurologic injury. For the lower extremity, proprioceptive impairment after stroke was found to be a predictor of balance ability, fall risk, gait symmetry, stride length, and walking endurance [72], [101]. Such findings have led to the suggestion that evaluating proprioception should be an important goal for understanding and improving rehabilitation in persons with stroke [59], especially in the ankle [56], [102], [103], [104], [105].

Many tests for assessing proprioception have been developed using manual techniques, simple mechanical technologies, or robots [56], [57], [58], [59]. Horvath et al. counted 1346 different types of proprioceptive measurements that fit within three classes: method of adjustment, where participants have to adjust the level of a stimulus to a reference; method of constant stimuli, where participants have to judge standard and comparison stimuli presented in pairings; and method of limits, where participants have to indicate the appearance or disappearance of a stimulus [56]. Horvath et al. also proposed a finger-grained classification system that clusters the measurement techniques based on the eight aspects of proprioception they target (e.g. perception of joint position, trajectory, velocity, force etc.) as well as the psychophysical paradigm they employ (method of adjustment, constant stimuli, or limits) [56].

In their review [56], Horvath et al. highlight what they term a “current misconception in the field”, i.e. “that results obtained with the use of one particular method with respect to one particular body part (e.g., joint, muscle) can be generalized.” Their analysis of previous studies suggests that proprioceptive accuracy exhibits both site-specificity and method-specificity. On the latter point, they found no studies reporting a significant correlation between different tests [106], [107], [108], [109], [110], [111], [112], [113], and many studies that reported test-dependent differences in specific proprioceptive abilities [83], [84], [114], indicating lack of concurrent validity. However, another recent meta-analysis that analyzed whether proprioceptive learning shows features similar to motor learning did find some evidence of generalization between assessments after learning [104]. Generalization is related to the concept of "concurrent validity" in assessment theory, which is exhibited when a test correlates with a previously validated test and justifies the use of the new test.

The studies analyzed in Horvath's review focused primarily on populations that were either young unimpaired individuals [16], [21]–[28] or individuals with peripheral nervous system rather than central nervous system (CNS) damage [14], [17]–[24]. Therefore, it remains unclear if age of damage to the CNS will induce a correlation between different types of proprioception measurements or will continue the trend of no correlation because of method-specificity. This is an important question to answer in order to rationally design proprioceptive assessment paradigms: how many types of assessments must one employ to adequately characterize proprioceptive ability?

Proprioception can be measured using active and passive movements, or via a combination of both, with, for example, an active limb being used to indicate the perceived position of a passively moved limb. When considering the selection of a proprioceptive assessment, tests that involve active motion might be preferred from the viewpoint of external (ecological) validity, as they may better reflect the individual's performance under a wider variety of everyday circumstances [56]. However, for individuals with movement impairments, such as persons post-stroke, passive movement proprioceptive methods may be advantageous, because motor impairments – which appear bilaterally [115], [116] – may confound the ability of an active limb to respond as desired. Using a passive proprioceptive assessment may also estimate a more basic aspect of proprioceptive integrity because sensing joint position after active motion is influenced by processes of sensorimotor integration and cognition as well as motor control [59], [82]. There are studies that used a bilateral assessment to reduce the influence of cognitive or memory impairment [82], but there are few or no bilaterally passive proprioceptive assessments. Therefore, with a view toward usage in stroke rehabilitation, we developed a novel proprioceptive assessment called Crisscross, which aims to reduce the influence of active movement deficits and memory impairment on the measurement of proprioceptive acuity [117] .

Crisscross combines components of movement discrimination, movement speed and direction sense, comparison between relative limb positioning in space, and discrete position matching (where by "discrete" we mean the test subject makes one proprioceptive judgment per each movement trial). Of note, Crisscross asks individuals to judge limb position relatively between to limbs, rather than by using proprio-visual reasoning to point to where the limb is perceived to be [118], [119]. Studies that have employed Crisscross to measure finger proprioception have found that the test is sensitive to aging [117] and presence of a prior stroke [18], and was the strongest predictor of the ability of individuals post-stroke to benefit from a three-week period of robotic finger training [8], [100].

Using the parameters recommended for Crisscross in Chapter 3, slower speeds, particularly in the 2 to 12 deg/sec speed range, we tested its ability to quantify ankle proprioception in unimpaired young individuals' post-stroke, and unimpaired, older individuals, comparing it to the results from a more commonly used type of proprioception test, a JPR test. Even though Crisscross and JPR are different types of assessments (e.g.

Crisscross is a passive assessment and JPR requires an active matching movement from the subject), they both require joint position estimation and reduce the need for memory-based matching. Based on the review by Horvath et al., we hypothesized that there would be limited or no generalization of proprioceptive accuracy measured with Crisscross and JPR for unimpaired, young individuals. However, we also hypothesized that damage to the proprioceptive system caused by stroke or aging should cause generalizable errors across these two proprioceptive assessments, since presumably these assessments must rely at least in part on some degree of shared neural machinery.

METHODS

Participants

Young participants, aged 18–35 years old, and older adults with ages selected to match the average age of our stroke participants, were recruited for a single assessment session. For these participants the exclusion criteria were: history of neurological injury, musculoskeletal damage to the ankles, current injuries that affected participants ability to move or feel either their ankles, or use of medication that would change how the brain perceived pain/movement. The dominant side was reported according participant responses to which leg they use to kick a ball. The local ethics committee approved this study, and written informed consent was obtained from each participant prior to participating, following procedures established by the University of California Irvine Institutional Review Board.

Persons in the chronic phase post-stroke (N = 40) who participated were enrolled in an ongoing clinical trial designed to evaluate the efficacy of a brain-computer-interface functional electrical stimulation system for treating foot drop (clinicaltrials.gov

NCT04279067). The inclusion criteria were as follows: age 18-80 years, radiologically confirmed stroke, with day of onset at least 26 weeks prior to day of randomization, gait velocity < 0.8 m/s using the 10 Meter Walk Test [120], foot-drop in affected limb, plantarflexor spasticity < 3 on Modified Ashworth Scale of Spasticity (MAS) [121], walk > 10 m (with or without ankle foot orthosis, and cane or walker permitted) at a supervised level. Only baseline proprioceptive measurements were used for analysis. The local ethics committee approved this study and written informed consent was obtained from each participant prior to participating, following the procedures established by the University of California Irvine Institutional Review Board.

A trained physical therapist assessed each participant with a battery of clinical assessments, shown in Table 1. For the MAS, ankle plantarflexion scores that were marked with a "+," an additional 0.5 points was added for calculations.

Robotic Device

Two versions of Ankle Measuring Proprioceptive Device (AMPD and 2AMPD, an improved version of AMPD) were used for this study. Chapter 2 describes these devices in detail, but here we briefly describe 2AMPD, which is similar to AMPD (see Figure 3) with some clinical usability improvements such as improved seating, robot mode switching, and adjustment of feet width. To use 2AMPD, participants sit in an upright position with the hip and knee bent at 90 degrees such that the shank is perpendicular to the ground, the center of the lateral malleolus is aligned to the rotational shaft of 2AMPD, and the feet are adjusted to be hip width. 2AMPD has two impedance states, mechanically rigid and mechanically transparent. In its rigid state, 2AMPD can individually assist and move both ankles, via motors (TiMOTION, TA16), through participants' natural dorsiflexion and plantar flexion passive range of motion. In its mechanically transparent state, 2AMPD allows participants to move their ankles on their own volition with minimal resistance. 2AMPD is equipped with angular quadrature encoders to measure ankle angular position (E6B2-C, 1024 P/R) and s-type load cells (Interface, SMA-200) to measure ankle force and then converted to ankle torque. Data is acquired at 200 Hz and stored on a laptop.

Crisscross Test

For the Crisscross test, 2AMPD drove the left and right ankles in opposing directions during a series of non-periodic ankle-crossings of different angular velocities (**Figure *11***A). For each ankle-crossing movement, participants were instructed to press a handheld button when they perceived their feet to be at the same angular position.

Chapter 3 describes how the ROM was set, but here we briefly describe the process. For all participants, before beginning the test, a trained experimenter assessed each participants' passive range of motion by manually moving the unimpaired and impaired ankle with 2AMPD in its mechanically transparent mode to a comfortable maximum dorsiflexion and plantarflexion position. The assessment workspace was then calculated by taking the smaller extent of dorsiflexion between the two ankles, and the smaller extent of plantar flexion as well. The assessment workspace was then split into 5 sections, such that a single crossing occurred in each workspace section, >60% PF (extension), 60-20% PF (mid-extension), 20%PF - 20%DF (center), 20%-60%DF (mid-flexion) and >60% DF (flexion). This ensured an approximately uniform distribution of crossings in the assessment workspace.

To ensure each participant understood the test, they first completed four crossing movements with vision of their feet, giving verbal confirmation that they understood the test.

Then, with vision occluded by a large lap table, each participant experienced two crossing attempts in each crossing workspace section in a randomized order, for a total of 10 crossover movements. Participants experienced four ankle speeds: 4.4, 5.7, 7.0, and 8.3 degrees/second (**Figure *11***B), which is in the recommended range stated in Chapter 3. Individual ankle speeds were randomized such that the impaired and unimpaired ankle mostly did not move at equal speeds.

Joint Position Reproduction (JPR) Test

Many variations in protocols for JPR have been proposed, some requiring active reproduction of a passively imposed movement. Here we implemented a passive-active contralateral JPR test, where the nondominant foot for unimpaired participants or impaired foot for participants post-stoke was passively driven by 2AMPD (the "target ankle"), and the dominant foot or unimpaired ankle (the "matching ankle") was actively moved by the participant to try to match the movement of the target ankle.

We designed the ankle joint trajectories to have two parts, which we term the dynamic and static periods (**Figure *11***C). The dynamic periods consisted of 2AMPD driving the target ankle at a constant velocity of 5°/s through its available dorsiflexion and plantarflexion range (Figure 1C). Participants were instructed to match angular position and speed using their matching ankle during these dynamic periods. Dynamic periods were randomly interrupted by static periods where the robot stopped moving the ankle at a pseudo-random set of positions distributed across the workspace. Participants were instructed to match the angular position of the stationary target ankle by making fine adjustments with their matching ankle. For each static period, unlimited time was given, and participants were instructed to press a handheld button when they perceived their feet to be at the same angular position. The robot returned to a dynamic period after they pushed the button. Just like Crisscross, all participants first performed a short practice test with vision of their feet allowed and gave verbal confirmation that they understood the test. Then, their vision of their feet was occluded with the lap table and the subsequent test lasted about 2 minutes.

Since Crisscross was completed before the JPR test, the passive range of motion of the target ankle used in Crisscross was used in the JPR test and 2AMPD drove the target ankle to 80% of the maximum dorsiflexion and plantarflexion positions. The static periods were selected by splitting the impaired ankle ROM into sections, >60% PF (extension), 60-10% PF (mid-extension), 10%PF – 60%DF (mid-flexion), >60%DF (flexion). One static period occurred in each section resulting in a total of 4 dynamic periods and 4 static periods.

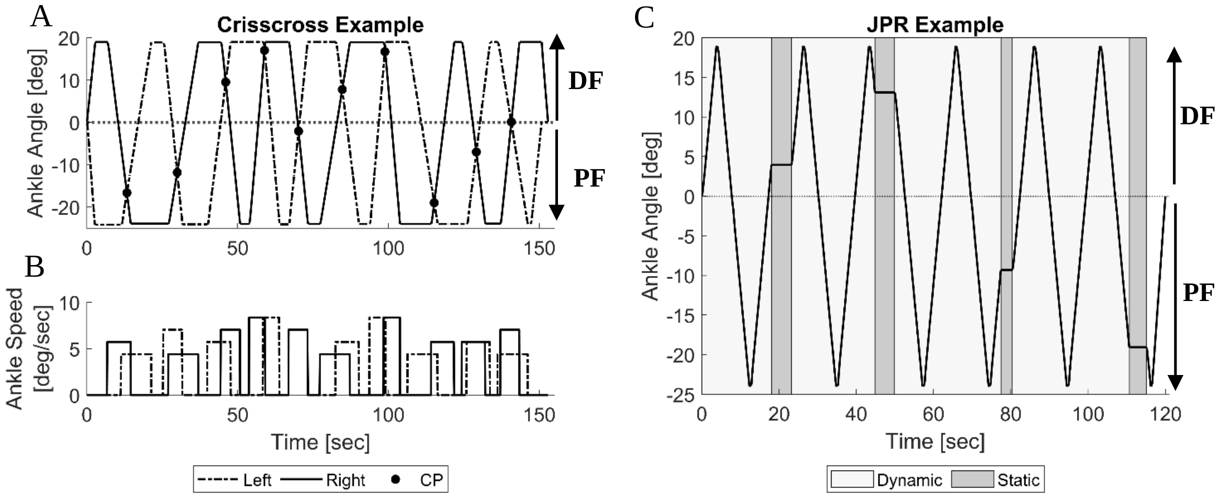


Figure 11 Examples of Crisscross and JPR tests. **A)** Ankle trajectories and crossing positions (denoted by circles) during Crisscross test generated by 2AMPD. Positive ankle angle corresponds to dorsiflexion. **B)** Ankle speeds during Crisscross test generated by 2AMPD. **C)** Unimpaired ankle trajectory during JPR test generated by 2AMPD, showing both dynamic and static periods. **DF** = Dorsiflexion Direction; **PF** = Plantarflexion Direction

Statistical analyses were conducted using Matlab R2023 software. Normality was tested using the Shapiro Wilks test. Since all data were normally distributed, we used parametric tests. To compare proprioceptive errors between assessments, a one-way ANOVA was performed to compare the effect of assessment on proprioceptive acuity. If significant effects were found, t-tests were used for post hoc analysis. To determine the relationship between assessments, Pearsons's correlation coefficient was calculated using the absolute error for all assessment measurements. An alpha level of 0.05 was used for all comparisons and correlations.

Proprioceptive acuity using Crisscross was quantified using absolute error. Absolute error was defined as the absolute angular difference between the left and right ankle at the moment of button press. Signed error was the angular difference between the left and right ankle at the moment of button press reflecting the button press occurring before (negative) the crossing or after crossing (positive). If a participant did not attempt to press the button on single or multiple crossing attempts, their average error was calculated using the crossing attempts where a button press happened. In general, we will use the term "error" to refer to the absolute error unless otherwise indicated.

Similarly, proprioceptive acuity using JPR was also quantified using absolute error. Absolute error here was defined as the absolute angular difference between the left and right ankle at the moment of button press for the static condition, and the absolute angular difference averaged across the dynamic condition. The coefficient of variation (CV), defined as the mean error divided by the standard deviation [122], was calculated for all assessments in each group.

RESULTS

42 unimpaired, young participants (25 male, 17 female; mean ± SD, age = 25 ± 4 yrs), 40 persons in the chronic phase of stroke (19 male, 15 female; age = 65 ± 10 yrs), and 27 older unimpaired participants, age-matched to the stroke participants (12 male, 15 female; age = 64 ± 10 yrs) participated, with characteristics as shown in **Table *4*** and **Table *5***. All young and older participants completed all tests. For the stroke participants, one participant did not press the button during the Crisscross test (apparently because they could not sense movement of their ankles) and was excluded from analysis resulting in a total of 39 participants (15 female/24 male). There was no significant difference in the average age between stroke and older participants (t-test, p =0.10).

Table 4 Clinical characteristics of stroke participants (N = 39)

	Average ± SD	**[Min Max]**
Age	60 ± 12	[27 76]
Days Post Stroke	1155 ± 1096	[201 4085]
[123] NIH Stroke Severity Scale [0 42]	6 ± 3	[2 16]
[124] Lower Extremity Fugl Meyer [0 34]	20 ± 3	[12 26]
[121]Modified Ashworth Score [0 4]	1.59 ± 0.48	[0 2]
[125] 6 min walk distance (meters)	113.3 ± 66.8	[0.20 298.50]
[120] 10 Meter Walk Test (m/s)	0.37 ± 0.24	[0 0.76]
[126] Montreal Cognitive Assessment [0 30]	23 ± 6	[1 29]
Ischemic/Hemorrhagic/Both	20/16/3	
Biological Sex M/F	24/15	

Table 5 Characteristics of unimpaired participants (N= 42, N= 27)

	# of Participants	Age [Max Min]	Sex	Dominance
Young	42	24 ± 4 [19 33]	25M/17F	39R/3L
Older	27	64 ± 10 [50 84]	12M/15F	23R/4L

Proprioception Assessment Results

Unimpaired, Young Participants

For Crisscross, unimpaired young participants pushed the button on 415 out of the 420 crosses. 37 of 42 participants pushed on all 10 crosses. One participant missed 2 crossing attempts, and 3 participants missed one crossing attempt. Of the 415 crossings attempted, participants pressed the button on average 0.9 $\pm$ 0.50 seconds before crossing indicating that they on average overly anticipated the moment their ankles would cross.

For JPR, during the dynamic period participants lagged the target on average 42%±10% of the time and led 58%±10% of the time (t-test, $p < 0.001$). The average speed at which participants moved the dominant ankle during the dynamic phase was 5.0°/s ±0.8°/s, which was not significantly different from the actual average speed of the of the nondominant ankle, 4.9°/s ±0.04°/s (p >0.70). Of the 168 static periods, 44% of button pressed occurred with the matching ankle below the target ankle position. Participants on average pressed the button 2.44 ± 1.3 seconds after the start of the matching period; the delay to button press was not significantly correlated with JPR static error (r = -0.16, p > 0.30).

The average absolute errors for the Crisscross, JPR static, and JPR dynamic tests were 11.2° ± 4.2° (CV: 38%), 5.8° ± 2.8° (CV: 48%), and 6.2° ± 2.3° (CV: 37%), respectively (Figure 2). A one-way ANOVA revealed that there was a statistically significant difference in proprioceptive acuity between at least two assessments (F(2,123) = 37.4, p < 0.001). Post hoc tests revealed that proprioceptive error using the Crisscross test was significantly higher than JPR dynamic error (p <0.0001) and JPR static error (p<0.0001) (Figure 12). There was no significant difference between JPR static and JPR dynamic error (p = 0.16, Figure 12).

Unimpaired, Older Participants

For Crisscross, unimpaired, older participants pressed the button on 268 out of the 270 crosses. Two participants missed one crossing attempt. Of the 268 crossings attempted, participants pressed the button on average 0.5 ± 0.6 seconds before crossing indicating that they on averaged overly anticipated the moment their ankles would cross, just like the younger individuals.

For JPR, during the dynamic period, participants lagged the target on average 45%±7% of the time and led 55%±7% of the time (t-test, p = 0.005). The average speed at which participants moved the dominant ankle during the dynamic phase was 4.9°/s ± 1.2°/s, which was not significantly different from the actual average speed of the of the nondominant ankle, 4.9°/s ±0.05°/s (p = 0.99). Of the 108 static periods, 57% of button presses occurred with the matching ankle below the target ankle position. Participants on average pressed the button 2.6 ± 1.5 seconds after the start of the matching period; the delay to button press was not significantly correlated with JPR static error (r = 0.15, p = 0.45).

The average absolute error for the Crisscross, JPR static, and JPR dynamic was 9.3° ± 3.5° (CV: 38%), 6.8° ± 2.9° (CV: 43%), and 6.7° ± 2.4°(CV: 36%), respectively (Figure 2). A one-way ANOVA revealed that there was a statistically significant difference in proprioceptive acuity between at least two assessments (F(2,78) = 37.4, p = 0.0027). Post hoc tests revealed that proprioceptive error using the Crisscross test was significantly higher than JPR dynamic error (p < 0.001) and JPR static error (p= 0.002) (Figure 12). There was no significant difference between JPR static and JPR dynamic error (p = 0.868, Figure 12).

Chronic Stroke Participants

Stroke participants pushed the button on 333 out of the 390 crosses. 23 participants attempted all 10 crosses. 16 participants missed at least 1 crossing, and, of these, 4 pushed the button on less than 50% of crossings. Of the 57 total crosses with no button press, 28 attempts were missed in the plantarflexion region and the remaining in the dorsiflexion region. A two way AVONA revealed no significant interaction between speed and crossing position (F(24,355) = 0.91, p = 0.60), and no main effects of speed (p = 0.06) and crossing position (p = 0.92). Of the 333 crossings attempted, participants pressed the button on average 0.3 ± 1.3 seconds before crossing indicating that they on average overly anticipated the moment their ankles would cross, like the unimpaired individuals.

For JPR, during the dynamic period, participants lagged the target on average 50%±14% of the time and led 50%±15% of the time (t-test, $p = 0.56$). The average speed at which participants moved the unimpaired ankle during the dynamic phase was 5.1°/s ±2.0°/s, which was not significantly different from the actual average speed of the of the impaired ankle, 5.1°/s ±0.03°/s ($p = 0.84$). Of the 156 static periods, 59% of button pressed occurred with the unimpaired ankle below the intended position. Participants on average pressed the button 5.6 ± 8.1 seconds after the start of the matching period; the delay to button press was not correlated with JPR static error ($r = 0.19$, $p > 0.2$).

The average absolute error for the Crisscross, JPR static, and JPR dynamic was 16.3° ± 7.2° (CV: 44%), 11.3° ± 7.1° (CV: 63%), and 11.2° ± 5.6° (CV: 50%), respectively (Figure 2). A one-way ANOVA revealed that there was a statistically significant difference in proprioceptive acuity between at least two assessments ($F(2,114) = 37.4$, $p = 0.008$). Post hoc tests revealed that proprioceptive error using the Crisscross test was significantly higher than JPR dynamic error ($p < 0.001$) and JPR static error ($p= 0.003$) (Figure 12). There was no significant difference between JPR static and JPR dynamic error ($p = 0.83$, Figure 12).

Impaired proprioception, defined as exhibiting a mean error that was greater than 2 SDs of the mean error in older unimpaired controls, was present in the following percentage of the participants with stroke: 49% for Crisscross, 33% for JPR Static, 41% for JPR Dynamic. The errors for the younger and older unimpaired participants were not significantly different for any assessment ($p > 0.05$, Figure 12), but interestingly the comparison between young and older participants using Crisscross bordered significance ($p = 0.056$). The errors for the individual's post-stroke were significantly greater for all assessments ($p < 0.0001$, Figure 12).

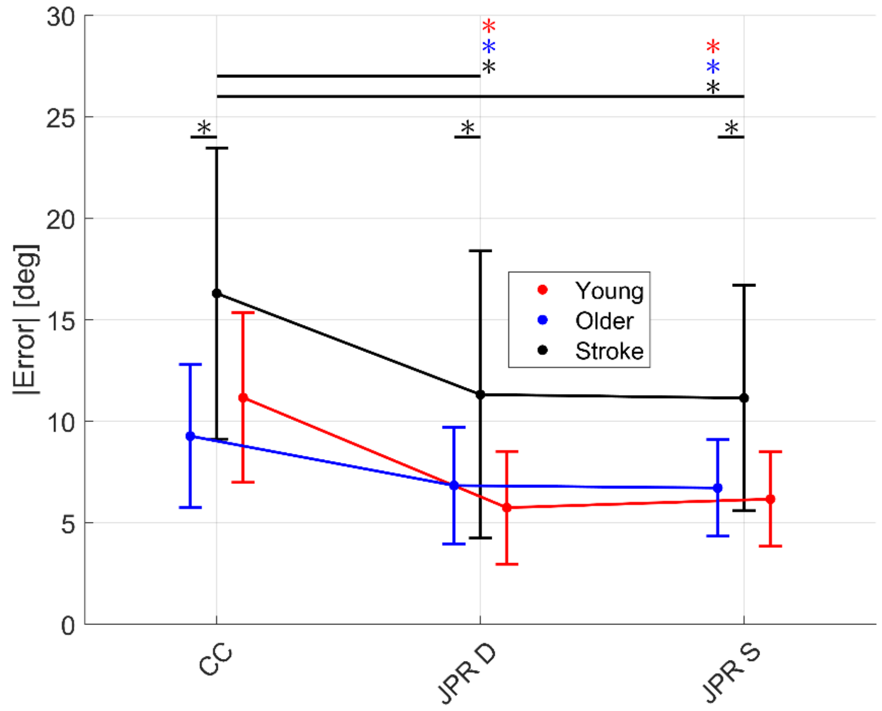


Figure 12 Average absolute error on Crisscross, JPR Static (JPR S), JPR Dynamic (JPR D) for all groups. *Denotes significant difference $p < 0.05$

Relationships Between Assessments

For young participants, Crisscross error was not significantly correlated with JPR static absolute error ($p = 0.95$) or JPR dynamic absolute error ($p = 0.67$). However, JPR static and JPR dynamic error were strongly correlated ($r = 0.73$, $p < 0.001$). Relationships are shown in Figure 13A, D, G.

In contrast, for older unimpaired participants, Crisscross error was moderately correlated with JPR static mean error ($r = 0.39$, $p = 0.04$) and JPR dynamic mean error (r =

0.56, p = 0.002). JPR static and dynamic error were strongly correlated (r = 0.85, p < 0.001). Relationships are shown in Figure 13B, E, H.

Similarly, for chronic stroke participants Crisscross error was moderately correlated with JPR static error (r = 0.55, p < 0.001) and JPR dynamic mean error (r = 0.54, p < 0.001), and JPR static and JPR dynamic mean error (r = 0.73, p < 0.001). Relationships are shown in Figure 13C,F,J.

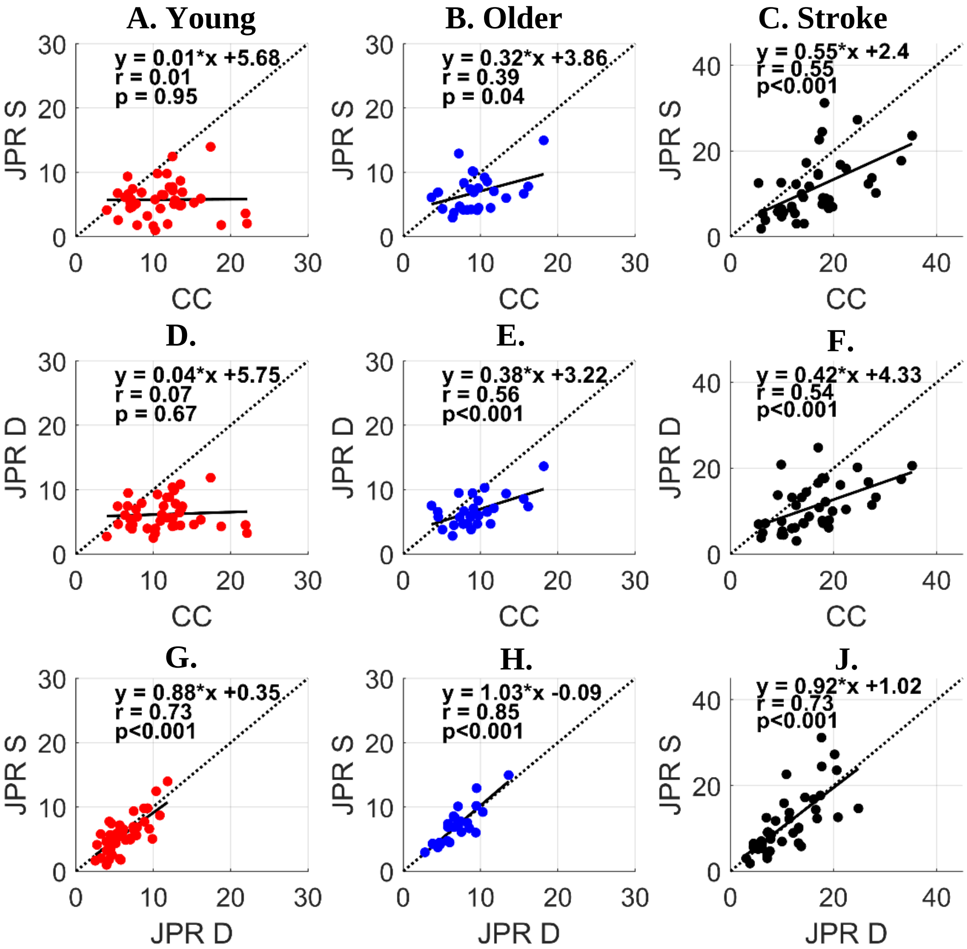


Figure 13 Relationships between Crisscross error (CC), JPR static error (JPR S), and JPR dynamic error (JPR D) for all groups. (A,D,G) Unimpaired, young participants. (B,E,H) Unimpaired, older participants. (C,F,J) chronic stroke participants.

DISCUSSION

We investigated if ankle proprioception error measured with a novel robotic assessment (Crisscross) is correlated with the error measured with a more established assessment (JPR). That is, we sought to ascertain if errors generalize across these different assessments, or, conversely do the errors fall within the trend of no apparent generalization between assessments noted by Horvath et al [56]. Further, we investigated if the degree of generalization depends on presence of stroke or aging. Consistent with the observation by Horvath et al. , Crisscross and JPR errors did not correlate in unimpaired young individuals. However, in individuals with nervous system damage due to stroke, or, with nervous system changes due to aging, they did correlate. This is consistent with our hypothesis of induced generalization between assessments due to alterations in the proprioceptive neural machinery needed for both assessments. We also found that in all groups Crisscross proprioceptive error was significantly higher compared to JPR proprioceptive error; thus, the passive assessment had greater error than the active assessment. Further, JPR static and dynamic error were highly correlated and JPR static error was not significantly less than JPR dynamic error, even though individuals were given extra time to better match the target ankle, which had stopped moving. As expected, stroke decreased ankle proprioceptive acuity, but, surprisingly, older age did not (although the effect neared significance). We will now discuss and interpret these results.

Limited generalization in ankle proprioception assessment in unimpaired, young adults

Using the classification scheme of proprioception tests proposed by Horvath et al., Crisscross and JPR both involve the detection of target joint position, movement and movement extent, trajectory, and velocity. One might expect the errors measured with each technique would correlate because similar aspects of proprioception are being tested, but we found this was not the case for unimpaired, young participants. This result reinforces the assertion that there is a rather rigorous method-specificity of proprioception assessments for unimpaired, young adults [56]. We note, however, that JPR static and dynamic error were strongly correlated for this population, indicating that there is a limit to method specificity. If the assessment methods are similar enough, a correlation in error can be observed.

We proposed previously that proprioception is a dynamic process that exhibits aspects of learning similar to motor learning [104]. In motor learning, it is well-known that the motor system builds a library of internal models of the dynamic environments with which it interacts (such as tools or objects), and, further, there is limited generalization between these models state in [127]. When experiencing a new proprioceptive test, the sensory system must transform afferent information from cutaneous receptors, joint mechanoreceptors, muscle spindles, and Golgi tendon organs into an estimation of limb position and movement [92]. This conversion is based on an internal model of the sensor dynamics that is tuned over time by experience, likely using visual input for calibration [128]. If proprioceptive internal models are task-dependent, one would expect a high degree of method specificity in proprioceptive assessment, since each new proprioceptive assessment is essential a new sensory "task".

Why did the assessments generalize in older adults and after stroke?

It is well known that, as we age, aspects of both the peripheral and central nervous systems change that are broadly relevant to proprioception. Peripheral changes include decreased number and function of muscle spindles [129], cutaneous receptors [130], and joint receptors [131]. Normal aging also affects the conductive function of central somatosensory pathways [132], induces neurochemical changes in the brain related to synaptic transmission [133], and causes progressive loss of dendrites in the motor cortex [134]. Neuroimaging studies in older adults have related decreased proprioceptive function to decreased right-sided subcortical activity and structural changes, most notably in the right putamen [135], [136]. There is substantial variability in each of these age-related changes across individuals. Since these changes are widespread and structural, one might expect them to affect proprioception in a general way, inducing the correlation between errors measured with Crisscross and JPR that we observed. Individuals with more severe age-related changes would be expected to exhibit larger errors in both tests, while individuals with less severe age-related changes would be expected to exhibit smaller errors in both tests.

Similarly, widespread structural damage in somatosensory systems caused by stroke may account for the correlation in Crisscross and JPR error after stroke. Stroke frequently impairs grey matter responsible for sensory motor processing [137] as well as white matter tracts that conduct sensory neural signals [138]. The somatosensory system must use this neural machinery during any proprioceptive assessment. Further, estimating the relative position of the two ankles requires interhemispheric connectivity and communication. Several studies have observed an increased influence of the lesioned hemisphere onto the contra-lesional hemisphere during motor tasks [139]. Since, again, there is high variability in the amount of damage caused by stroke and the resulting changes in neural activation and interhemispheric balance, one would expect individuals with greater stroke-related damage to exhibit larger errors in both proprioception tests examined here, with individuals with less damage exhibiting smaller errors, thereby inducing the observed correlation.

Interestingly, one might expect that stroke would induce a stronger correlation between proprioceptive errors than aging would, since the neural damage caused by stroke is seemingly more severe than that caused by normal aging. For example, the motor deficits of the stroke participants in the current study (such as hemiparesis) were clearly greater than those of the age-matched controls. Stroke did cause a larger proprioceptive error than aging, on average, but the strength of the correlation of errors for the two assessments was comparable. This may suggest that the effects of aging on ankle proprioception are highly variable.

Effect of age on ankle proprioception

Although aging induced a correlation between proprioceptive errors measured with Crisscross and JPR, the mean proprioceptive error in the unimpaired, older participants (with mean age of 64) was not significantly greater than that of the younger participants (with mean age of 23). Admittedly, this result was nearly significant ($p = 0.059$), but, nevertheless, this surprised us, as we expected a strong effect of age because of the numerous reports of decrease in proprioception acuity in various limbs with aging [91], [117], [140]. All of our unimpaired, older participants were ambulatory and were active and in good health. It may be that regular walking helps preserve ankle proprioceptive acuity, at least into the 60s. In future work we will increase our sample size by testing even older individuals to better determine the possible effects of aging on ankle proprioception acuity.

Proprioceptive errors were significantly smaller during the active assessment

When participants were asked to actively match the position of their passively moved target ankle with their tracking ankle (i.e. during JPR), they were able to sense their ankle positions more accurately than when both ankles were passively moved (i.e. during Crisscross). The speeds of ankle movement during the two assessments were slightly different, with the Crisscross speeds ranging from 4.4 to 8.3 deg/sec per ankle, and the JPR speed set to a constant 5 deg/sec. Thus, one possibility is that the experience of slightly greater speeds on some trials during Crisscross caused an increase in mean error. Contradicting this possibility, however, are preliminary analyses we have performed in which we found that Crisscross error actually decreases at higher speeds shown in Chapter 3 and [84].

A possible explanation is that during passive movement, when muscles are not active, fusimotor activity and the sensory feedback from muscle spindles are diminished [141]. In active movement control, fusimotor drive and muscle spindle feedback are both involved, although input from muscle spindles is considered to play a more dominant role [142]. Because of the difference between engagement and disengagement of fusimotor activity, contribution of central control may be different. The contention is that when a body part is moved by an external force (passive movement) information about ankle position is derived primarily from feedback provided by receptors sensitive to joint position and movement.

Participants could not further reduce error when the target ankle stopped moving

Surprisingly, for all subjects, JPR dynamic and static error strongly correlated with each other, and the mean dynamic and static errors were not significantly different from one another. This indicates that participants were unable to further reduce tracking error during the static period, even though their target ankle had stopped moving and they were given unlimited time for static periods. This indicates that the brain's estimate of ankle position is not improved by information received when the ankle is not moving, which, in turn, seems to suggest that velocity-related information is primarily used to estimate ankle position. That is, if the nervous system only sensed ankle velocity, then integrated velocity to estimate position, it would explain this result. Physiologically, this could correspond to a greater dependence on primary (type IA) spindle afferents than on secondary (type II afferents), since the former are velocity sensitive and the latter are position sensitive[129], [143].

Validation of an ankle proprioception assessment for stroke

The present results can also be viewed as a validation of Crisscross as a new technique for assessing ankle proprioception. In the Introduction, we mentioned that generalization is related to the concept of "concurrent validity" in assessment theory, which is exhibited when a test correlates with a previously validated test and justifies the use of the new test. Crisscross showed concurrent validity with the more commonly used JPR test. Further, Crisscross was sensitive to the presence of stroke (although not aging, see above discussion). Thus, this study validated ankle proprioception using Crisscross in two ways.

Why propose another assessment technique when there are already so many? Crisscross has advantages relative to many existing proprioception assessments such as not requiring active movement in the tested limbs, being relatively rapid to administer, and producing a continuous measure of ankle proprioception acuity (as opposed to, for example, threshold detection techniques). Further, Crisscross requires that the test subject reference the position of one ankle to the position of the other, rather than to a visual target, as in some assessment techniques (reg Gassert); this may make it a more “basic” test of proprioception, unconfounded by visual calibration processing.

CHAPTER 5: SHARED NEURAL MACHINERY IN PROPRIOCEPTIVE PROCESSING: COMPARISON OF ACUITY BETWEEN THE ANKLES AND FINGERS

SUMMARY OF THE CHAPTER

It is unclear if the ability to utilize proprioceptive information at different joints is a body-general attribute or a site-specific attribute, that is, whether individuals who perform better/worse on a proprioceptive task at one joint are also those who perform better/worse at other joints. To provide clarity we assessed the ankle and finger proprioception acuity of 26 young (< 35 yrs) and 25 older (>50 yrs) unimpaired participants using the Crisscross test. For both limbs, acuity was poorer for slower movements due to greater anticipatory errors. Proprioceptive acuity was better for the fingers than the ankle ($p < 0.01$). Ankle proprioception acuity was moderately correlated with finger proprioception acuity in both young and older participants ($r = 0.43$ and 0.49, respectively, for normalized crossing error, $p < 0.03$). These results indicate that there is a body-general component to proprioceptive processing.

INTRODUCTION

As discussed earlier in this dissertation, Horvath et al. [56] highlighted what they term a “current misconception in the field”, i.e. “that results obtained with the use of one particular method with respect to one particular body part (e.g., joint, muscle) can be generalized.” Their analysis of previous studies suggests that proprioceptive accuracy exhibits both site-specificity and method-specificity. On the former point they have reported a few studies that used a joint position discrimination (AMEDA) test and assessed multiple joints on the body (eg, ankle, knee, shoulder, and fingers), but found no correlation in proprioceptive acuity between different joints in the same participant [144], [145].

In Chapter 4, we found method-generalizability for proprioception acuity in the ankles, but only for persons with stroke and older individuals – an exception to Horvath's observation. Here, we investigated site-specificity using a simple, passive proprioceptive assessment (Crisscross) to test the possibility that proprioceptive acuity is related between joints. Previous studies addressing this question were based on AMEDA, an active proprioceptive assessment that is completed under load bearing conditions, which adds to the complexity of processing proprioceptive and may have masked effects.

METHODS

Participants

A total of 26 young and 25 old unimpaired participants, ages 18 - 35 years and 50-88 yrs, respectively, were recruited for a single finger testing and a single ankle testing session. Exclusion criteria included history of neurological injury, musculoskeletal damage, or current injuries that affected participants ability to move or feel either their fingers and/or ankles. The dominant side was determined using the Edinburg handedness inventory [146], and only the dominant hand was used for proprioceptive testing. The local ethics committee approved this study, and each participant provided consent prior to participating, following procedures established by the University of California Irvine Institutional Review Board.

Robotic Devices

To assess finger proprioception, we used the FINGER robot (Figure 14) [147]. FINGER uses two eight-bar mechanisms to independently move each finger through a natural curling trajectory between 0 and 60 degrees of metacarpophalangeal flexion (i.e. from full extension towards a flexed posture).

To assess ankle proprioception, we used the Ankle Measuring Proprioceptive Device (AMPD) (Figure 14). AMPD is a novel platform-based ankle device that is composed of an adjustable mechanical seat and sliding platform, a transmission mechanism, robotic footplates for both feet, and a control unit. AMPD has two impedance states, mechanically rigid and mechanically transparent, which allows for multiple ankle assessments to be done across participants' entire range of motion.

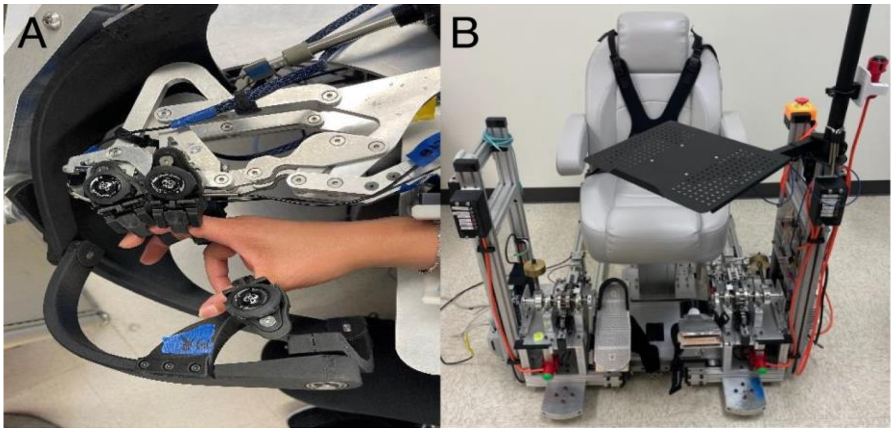


Figure 14. Robots used to implement Crisscross. A) FINGER uses two linkages controlled by linear actuators to move the index and middle fingers through a natural curling motion. The thumb was not used in this study. B) AMPD uses two linear actuators attached to footplates to move the ankles in plantar flexion and extension.

Experimental Design

Participants participated in a single finger session and a single ankle session, collected on two separate days spaced 3-10 days apart (mean = 7 days). We randomized the limb selected for the first session. Within each session, participants experienced multiple proprioceptive assessments. To remove the potential of learning, each participant received a pseudo-randomized task order that ensured a uniform distribution of each task type (1, 2, 3, etc.) in each order (first, second, third, etc.). Within each task the crossing positions and speeds were pseudo-randomized such that crossing position or speed changed every trial, to ensure the assessment was unpredictable. Both for finger and ankle assessments, 5 tasks were completed, however only Tasks 1 and 2 were used for this analysis because limb speeds were matched (Table 6).

To ensure they understood Crisscross, at the start of each session participants performed a familiarization task consisting of 6 crossings with vision of the limb. After this, participants gave a verbal confirmation of task understanding. Each subsequent Crisscross consisted of 20 trials with a trial defined as a single crossing, without vision. Participants performed the finger assessment with their dominant hand.

Table 6 Parameters experienced for each Crisscross task.

Task #	**4 Speeds (deg/sec)**	**Ankle speeds per run**	**Crossing Workspace**
1	[2:2:8]	Coupled	Full ROM
2	[14:2:20]	Coupled	Full ROM

STATISTICAL ANALYSIS

We quantified proprioceptive performance using normalized absolute error and timing error. Normalized absolute error is defined by the absolute error divided by the maximum error that could be achieved. Timing error is defined as the difference between button press and actual crossing in time, with negative values signifying button presses before crossing position has occurred and positive values signifying button presses after crossing position has occurred. We defined relative crossing speed as the summed absolute limb speeds (i.e. sum of left and right ankle speed magnitudes). Crossings in which a participant did not press the button were excluded from analysis, meaning participants were not penalized for missing a crossing.

We examined the distributions of proprioceptive performance and found they did not violate normality (Shapiro-Wilk test, $p > 0.05$) and therefore used ANOVA and follow-up t-tests for comparison between finger and ankle acuity. We used Pearson correlations to establish relationships between finger and ankle proprioceptive acuity. Analyses were performed using MATLAB (version 2023a, Mathworks) and JMP Pro 17. Significance was considered at $p < 0.05$.

RESULTS

We assessed ankle and finger proprioceptive acuity in 26 young, unimpaired participants (13 male, 13 female; mean ± SD, age = 24 ± 4 yrs) and 25 older, unimpaired participants (11 male, 14 female; age = 64 ± 10 yrs). All participants completed each task. One older participant was removed from the analysis due to fatigue during their finger assessments. Therefore, a total of 24 older participants were included for this analysis.

Joint Specificity

We first looked to see if the fingers and ankles behave similarly in terms of proprioceptive acuity at different speeds. For the fingers, both age groups exhibited significantly lower anticipatory errors as speed increased ($p < 0.01$). Normalized error significantly decreased with speed in young ($p = 0.002$) but not older participants ($p = 0.093$). For the ankle, as reported in Chapter 3, anticipatory and normalized errors decreased as speed increased ($p < 0.0001$). Thus, in general, acuity improved at faster speeds for both the fingers and ankles for both age groups.

Next, we asked: which part of the body has better proprioceptive acuity? Finger proprioception acuity was significantly lower in both groups for both normalized and anticipatory errors (Figure 15, p < 0.01).

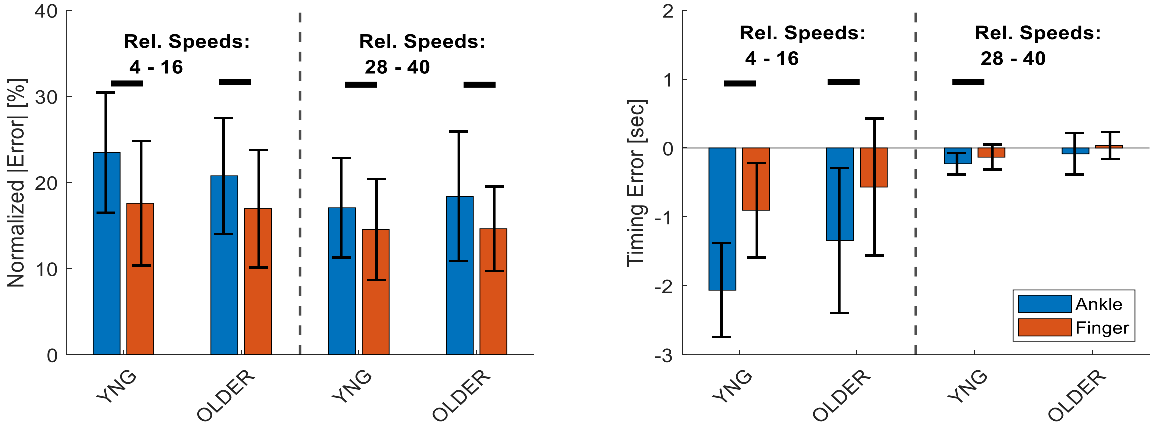


Figure 15 Average performance for task 1 and task 2 for the fingers and ankle.

Body General Proprioception

Finally, we posed the question, is there a body-general component to proprioceptive processing or is or is it joint specific? Both finger and ankle proprioception error were moderately correlated for both normalized ($r = 0.46$, $p = 0.0008$) and timing errors ($r = 0.48$, $p = 0.0004$) (Figure 16A, 3D).

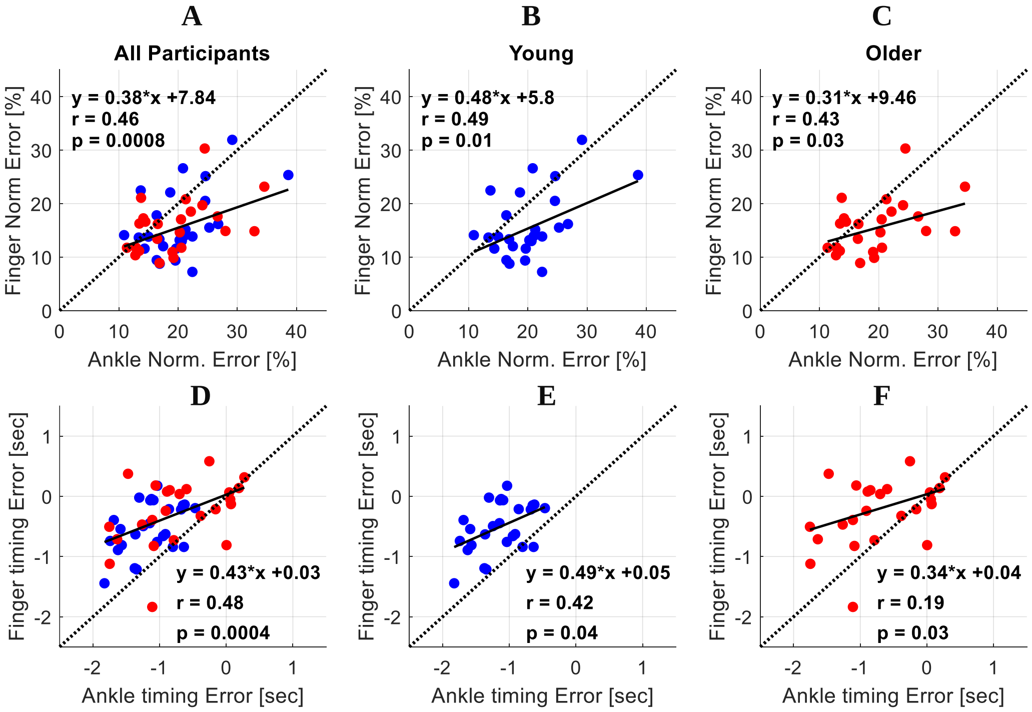


Figure 16 Relationships between ankle and finger proprioception.

DISCUSSION

Here we sought to determine if finger and ankle proprioception acuities generalize in young and older adults; that is, whether they are related in each individual. To our knowledge, we are the first to show that ankle and finger proprioception acuity are moderately correlated and, therefore, that proprioception is processed to some extent as a body-general attribute.

We briefly suggest two possible explanations. First, this result is consistent with the idea that there are shared neural resources for the way proprioceptive information from widely separate body parts is processed. For example, in any proprioception test, there is a cognitive/decision making component. Perhaps it is this capability of this cognitive component that is unique to each individual and thus body-general. Another possibility is that there are genetic variations in the density or functioning of afferent receptors in the periphery, which could also account for the body-general finding.

We also found that proprioceptive error is higher at slower speeds for Crisscross, due to greater anticipatory errors, and that older adults had lower error – these findings were discussed in Chapter 3. Another finding was that the fingers have higher proprioceptive acuity than the ankles, which we anticipated due to the well-known greater density of somatosensory receptors in the finger skin, tendons, and muscles [148].

CHAPTER 6: RELIABILITY AND VALIDATION OF RANGE OF MOTION AND MAXIMUM DORSIFLEXION STRENGTH USING AMPD

SUMMARY OF THE CHAPTER

In rehabilitation research, the lack of sensitive and reliable outcome measures can hamper the results of clinical trials aimed at determining the efficacy of new treatments, if changes due to the intervention under study fail to be detected. Robotic devices are being suggested as a possible means to improve evaluation of motor function in a wide variety of conditions, but it remains unclear if they are as effective as skilled therapists in quantifying basic clinical outcomes. Here, we used a platform-based robotic device to evaluate two fundamental aspects of ankle function – active range of motion (dorsi-plantar flexion AROM) and strength (dorsiflexion maximum voluntary contraction – MVC) while sitting. We compared robotic test-retest reliability across two days in a group of 34 persons post-stroke to that of experienced therapists making the same measurements in the same persons using a goniometer and manual muscle testing. standard error of measurement (SEM) and minimal detectable change (MDC) was calculated for each test. We also evaluated robotic test-retest reliability in 36 young and 26 older unimpaired adults. For AROM, test-retest reliability was high and comparable for both the robot and therapist (ICC > 0.94). For MVC, test-retest reliability was lower, but slightly higher for the robot (ICC: 0.89) than therapist (ICC: 0.86), and the robot provided finer resolution of measurement. Dorsiflexion ROM measured by the therapist was highly correlated with that measured by the robot ($r > 0.65, p < 0.0001$), but significantly less, on average, than that in the robot for both active ($p < 0.001$) and passive ($p < 0.0001$) ROM. Test-retest reliability was lower for young (ICC > 0.76) compared to older populations (ICC > 0.91) for both AROM and MVC using AMPD. As a side analysis, we

evaluated three different ways to quantify ROM and MVC (first trial, average of three trials, max of three trials) and found comparable test-retest reliability between average and max of three, but lower reliability for first trial, particularly for persons post-stroke. Further, we provide a table of these measurements as a database of reference values for ROM and MVC for young, older, and persons post-stroke, both male and female. We conclude that, like a skilled therapist, a robot can be highly reliable for evaluating ankle ROM but captures a larger ROM possibly due to the supportive, mechanical constraint it provides to the ankle.

INTRODUCTION

Stroke can affect different functions in different individuals, leaving residual impairments of varying severity that individuals often learn to address with a variety of compensatory strategies [149]. Impairments in ankle joint motion and strength are particularly common, which negatively impacts gait and balance function [150], [151], [152]. Assessing ankle function is critical in detecting and diagnosing gait deficits, monitoring treatment progression, and guiding treatment plans [153], [154].

Two key assessments often completed by physical therapists to assess ankle motor function are passive and active range of motion (PROM and AROM) and maximum voluntary contraction (MVC). The methods for measuring ankle ROM can be broadly classified into three categories: goniometry, weight-bearing, and instrumented techniques [155], but the most commonly used technique in the clinic is a goniometer. Goniometers are inexpensive and convenient but require the greatest degree of technical proficiency, due to the necessity of aligning the axis with the joint fulcrum and positioning the two arms with established reference points, a process that is even more complicated during PROM measurements when the therapist must hold the goniometer while manually moving the joint [153], [156]. For assessing MVC, there are many methods and tools, but the most commonly used technique in the clinic is the Manual Muscle Test, as it is quick and easy to perform [157]. However, its reliability is low because its grading depends on subjective assessment of force, which can be influenced by the examiner's muscle strength and temporal variations is force production [158]. With these challenges of assessing ROM and muscle strength, alternative methods have been proposed focused on use of various electromechanical technologies (see review [159]).

Within the last couple of decades there has been an increase in using robotic devices for neurorehabilitation training in clinical centers [160], [161], [162]. Besides using them for movement training, translational researchers in neurorehabilitation have proposed the use of robotic devices to overcome some of the limitations in traditional clinical assessments [77]. Robotic devices are being suggested as a possible means to improve evaluation of motor function in a wide variety of conditions as they can provide an accurate (e.g. able to measure exact body position/force applied) and objective (not relying as strongly on observer judgement) measurement [77], [160]. Even though robotic devices may fill these gaps, a challenge for the acceptance of new, robot-based assessments in clinical practice is the lack of information on their validity and reliability [160], [163]. For example, it currently remains unclear if robots are as effective as skilled therapists in quantifying basic clinical outcomes such as ROM and MVC.

Reliability is commonly assessed with the Intra-class Correlation Coefficient (ICC) and the Standard Error of Measurement (SEM). The ICC targets the relative reliability (the degree to which individuals maintain their position in a sample over repeated measurements), while the SEM measure's absolute reliability (the degree to which repeated measurements vary for individuals) [164]. For validity, the general approach is testing for correlations between the novel, instrumented measures and clinical scores in order to find which measured parameters are able to reconstruct established clinical tests (concurrent validity).

A related methodological question is how many measurements are needed to ensure reliability and how those measures should be processed (e.g. maximum or average). Many studies report ankle ROM and MVC data from an average of three readings; few have quantified the reliability/validity of a single or average measures of ROM and MVC [155], [157]. Therefore, we sought to clarify this issue as well.

Toward these ends, we used the custom-developed, bilateral, platform-based robot described in Chapter 2 (AMPD) to evaluate two fundamental aspects of ankle function – dorsi-plantar flexion ROM and MVC while sitting. First, we tested if robotic assessment is as reliable as assessment by a skilled therapist in quantifying these basic clinical outcomes. Secondly, we also compared the first trial versus maximum of three trials versus average of three trials approaches for reliability. Lastly, we sought to establish concurrent validity between clinical and robotic assessments. We hypothesized that the platform-based robot would provide both reliable and valid measurements of ankle ROM and dorsiflexion MVC.

METHODS

Participants

Young, unimpaired participants, aged 18–35 years old, and older, unimpaired adults with ages selected to match the average age of our stroke participants, were recruited for two assessment sessions. For young and older adults, the exclusion criteria were: history of neurological injury, musculoskeletal damage to the ankles, or current injuries that affected participants ability to move or feel either their ankles, and use of medication that would change how the brain perceived pain/movement. Leg dominance was determined by asking which foot participants preferred to kick a ball with.

Participants who were post-stroke were enrolled in an ongoing clinical trial designed to evaluate the efficacy of a brain computer interface, functional electrical stimulation system for treating footdrop (Clinicatrials.gov, NCT04279067). The inclusion criteria were as follows: Age 18-80 years, radiologically confirmed stroke, with day of onset at least 26 weeks prior to day of randomization, Gait velocity < 0.8 m/s, footdrop in affected limb, plantarflexor spasticity < 3 on modified Ashworth Scale, walk > 10 m (with or without ankle foot orthosis (AFO), and cane or walker permitted) at a supervised level.

The local ethics committee approved this study, and written informed consent was obtained from each participant prior to participating, following procedures established by the University of California Irvine Institutional Review Board.

Ankle Measuring Proprioceptive Device

Two versions of Ankle Measuring Proprioceptive Device (AMPD and 2AMPD, an improved version of AMPD) were used for this study. Here we briefly describe 2AMPD, which is similar to AMPD (see Figure 3) with some clinical usability improvements such as improved seating, impedance mode switching, and control of feet width. Quickly, 2AMPD is a bilateral ankle robot device that has 2 impedance states, mechanically rigid and mechanically transparent, which are chosen by manually locking or unlocking the rack and roller pinion system. This allows for multiple assessments to be done on the AMPD.

Experimental Protocol

For all participants, ROM and MVC were measured in two sessions, 3 to 10 days apart, using AMPD. For only the post-stroke participants only, a skilled PT assessed ROM and MVC in these two sessions as well. Three skilled PTs participated in this study, each with 20+ years of experience in assessing motor function after stroke. For the post-stroke participants enrolled in the clinical trial, no treatment occurred between the first and second assessments.

To measure ROM and MVC with AMPD, all participants sat in an upright position with their hips and knees bent at 90 degrees such that the shanks was perpendicular to the ground and the feet were hip width. The feet were strapped to the AMPD footplates after wood shims were added to the footplates to align the lateral malleolus to the rotational shaft of AMPD. Once participants were in the correct seated position, the chair position was recorded and saved so it could be used for the second session of measurements. Standardized instructions and a demonstration were provided before each ankle test.

For measuring ROM, AMPD was placed in its mechanically transparent state. For AROM measurements participants were instructed to dorsiflex the ankle to their maximum position without lifting the heel off the foot pedal, and then transition to their maximum plantarflexion position without internally rotating the hip. A single trial consisted of each maximum position held for ~3 seconds. All participants performed three trials on each ankle and 15 seconds of rest was given between each trial. For stroke participants, three trials were performed on the nonparetic ankle first to aid in understanding the task and then the paretic ankle was measured. For measuring the paretic ankle PROM, the PT moved the paretic ankle by rotating the foot pedal, dorsiflexing until firm resistance was encountered without inducing discomfort. That position was saved, and only one trial was completed.

For measuring dorsiflexion MVC, AMPD was placed in its mechanically rigid state with the ankles locked at an angle of 90° in the parasagittal plane. Participants were asked to gradually dorsiflex one ankle until they reached maximum effort and hold for three seconds. Like AROM measurements, participants performed three trials on each ankle. For participants who were post-stroke, three trials were performed on the nonparetic ankle first to aid understanding of the task and then the paretic ankle was measured.

For the post-stroke participants, a PT also manually assessed ROM (both PROM and AROM) and MVC. The post-stroke participants were seated on a gurney in an upright position with the hip and knee bent at 90 degrees such that the shank was perpendicular to the ground and the feet suspended in the air.

For measuring the dorsiflexion AROM using the goniometer, the PT positioned the goniometer so that the rotation axis rested over the center of the lateral malleolus. They aligned the stationary goniometer arm parallel to the longitudinal axis of the fibula, and the mobile arm parallel to the longitudinal axis of the fifth metatarsal bone. The therapist measured the paretic ankle dorsiflexion AROM three times to the nearest degree. A similar procedure was used to measure PROM, but in this case the therapist manually dorsiflexed the ankle with their knee to the felt end of the ROM and three trials was performed.

For the manual muscle test, the PT asked each stroke participant to dorsiflex as strongly as possible and rated the generated force using the Medical Research Council Scale (0-5) [165]. Only one trial was performed.

STATISTICAL ANALYSIS

Statistical analyses were conducted using Matlab R2023 and JMP Pro 16 software. AROM and dorsiflexion strength data was analyzed using 3 different metrics, first trial completed, maximum of the 3 trials, and the average of 3 trials. The intraclass correlation coefficient with 95% confidence intervals (CI) was calculated using a two-way mixed effects with a single rater [166] to assess the test–retest reliability (session 1 compared to session 2 measurements) for each. To evaluate the agreement between goniometer and AMPD measurements, a two-way random effects with a single rater [20]. Reliability was defined as values less than 0.5 are indicative of poor reliability, values between 0.5 and 0.75 indicate moderate reliability, values between 0.75 and 0.9 indicate good reliability, and values greater than 0.90 indicate excellent reliability [166]. SEM was calculated using the standard deviation (SD), where SEM = SD * $\sqrt{1-ICC}$, and minimal detectable change at 95% confidence level was computed using the formula MDC = SEM * 1.96 * $\sqrt{2}$ [167].

To assess validity, Pearsons's correlation coefficient was calculated, and a paired t-test was used to compare AMPD and goniometer measurements. The correlations and comparisons done are as followed: the average of 3 trials of dorsiflexion AROM was averaged across session 1 and session 2 for AMPD and therapist, the first measure of dorsiflexion PROM for AMPD and therapist, and the first measure of dorsiflexion MVC for AMPD and MMT from the first session was used. Paired t-tests were used for comparing validation measurements.

To compare between timepoints (first, second session), leg dominance (dominant, nondominant), age (Young, Older), sex (female, male), we used a four-way repeated measures ANOVA. For chronic stroke participants a three-way repeated measures ANOVA was used to compare timepoints (first/second session), ankle impairment (impaired/unimpaired), sex (female, male). If significant effects were found, a Tukey's Honest Significant Difference (HSD) test were used for post hoc analysis, and Cohens d was used to determine effect size, with a value of 0.8 considered a large effect, 0.5 to be a medium and 0.2 to be a small effect [168]. The level of statistical significance was set at $p < 0.05$.

RESULTS

Participants

36 young, unimpaired participants (23 male, 13 female; mean ± SD, age = 25 ± 4 yrs), 24 older, unimpaired participants (10 male, 12 female; age = 65 ± 10 yrs, p = 0.16, t-test), and 34 persons in the chronic phase of stroke (19 male, 15 female; age = 65 ± 10 yrs) performed ankle ROM and MVC assessments during two sessions that were on average 7 ± 2 days apart, using AMPD. The participants who were post-stroke also were assessed by a PT for ankle ROM and MVC using a goniometer and manual muscle testing (MMT), respectively. Demographics of the unimpaired participants are shown in Table 7 and clinical characteristics of the participants who were post-stroke are shown in Table 8. Figure 17 gives an overview of the AROM and dorsiflexion MVC measurements for all participants.

Table 7 Characteristics of unimpaired participants (N = 36, N = 26)

	# of Participants	Age [Max Min]	Sex	Dominance
Young	36	25 ± 4 [19 33]	23M/13F	34R/2L
Older	26	64 ± 10 [50 84]	10M/16F	22R/4L

Table 8 Clinical characteristics of stroke participants (N = 36)

	Average ± SD	**[Min Max]**
Age	60 ± 12	[27 78]
Days Post Stroke	1114 ± 1027	[201 4085]
[123] NIH Stroke Severity Scale [0 42]	6 ± 3	[2 16]
[124] Lower Extremity Fugl Meyer [0 34]	20 ± 4	[12 28]
[121]Modified Ashworth Score [0 4]	1.6 ± 0.5	[0 2]
[125] 6 min walk distance (meters)	107.9 ± 66.2	[0.20 298.50]
[120] 10 Meter Walk Test (m/s)	0.36 ± 0.24	[0 0.76]
[126] Montreal Cognitive Assessment [0 30]	22 ± 6	[1 30]
Ischemic/Hemorrhagic/Both	16/16/2	
Biological Sex M/F	19/15	
Age	12R/22L	

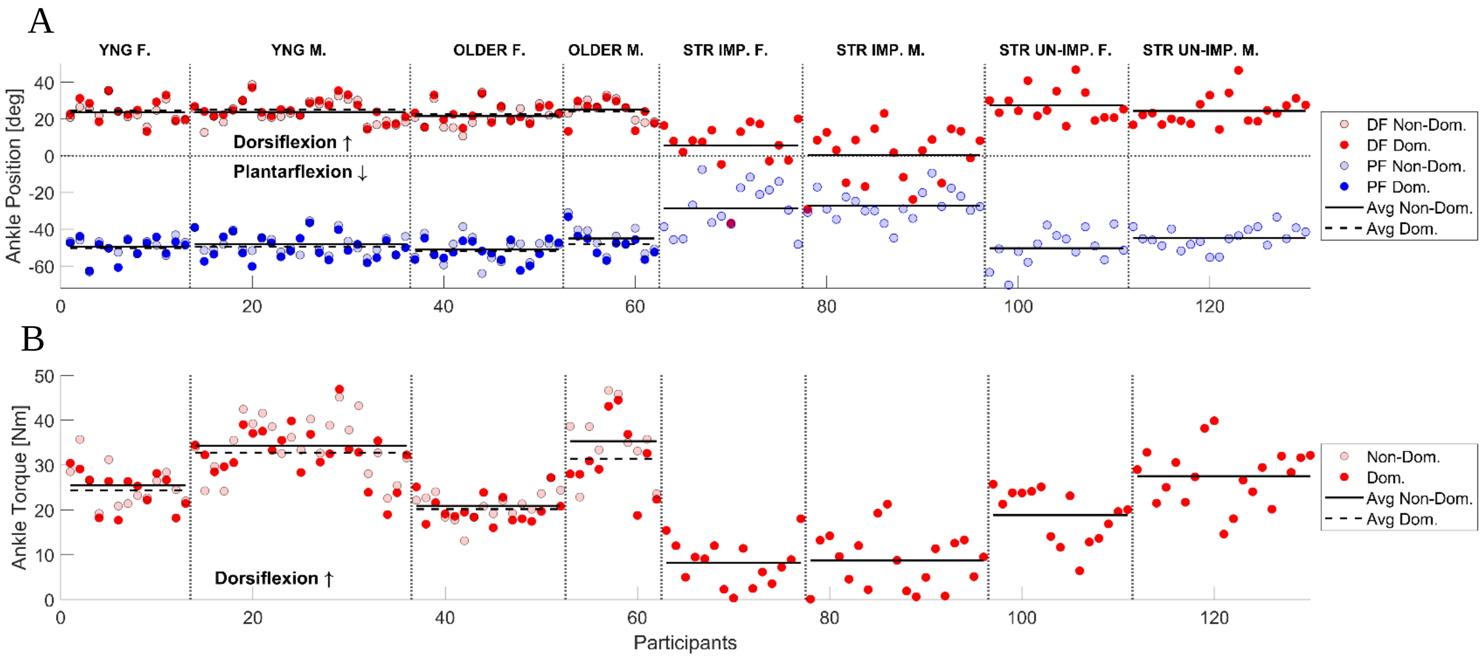


Figure 17 Average AROM and dorsiflexion MVC using AMPD for all groups at session 1 but broken up by sex and leg dominance. A) AROM dorsiflexion and plantarflexion positions for the dominant and non dominant ankle. B) Dorsiflexion MVC for the dominant and non-dominant ankle. The dotted and solid black lines represent the averages for the dominant and non-domant ankle. **DF:** Dorsiflexion, **PF**: Plantarflexion, **Non-Dom:** Non-dominant, **Dom:** Dominant

Test-Retest Reliability of Therapist-Based Compared to Robot-Based Measurement of Ankle AROM and MVC

Of key interest for this study was the test-retest reliability of the ankle ROM and MVC measurements taken by therapists compared with those taken with the robot (Table 9). To re-iterate, we obtained therapist test-retest data only for the participants with a stroke, so this analysis was only possible for individuals post-stroke. Further, while therapists measured AROM at two sessions, they measured PROM at only one session, so only analysis of AROM was possible. Overall, the therapist and robot measurements of ankle AROM and dorsiflexion MVC both showed excellent test-retest reliability: ICCs were always 0.86 or above (**Table 9**). However, the MDC was typically lower for the therapists because stroke participants had greater variability using AMPD (±7.8°) from session 1 to session 2 causing the SEM and MDC to being higher compared to the change variability for therapist (±0.3°) for forsiflexion AROM. The SEM and MDC are zero because values did not reach a point of 1, which also suggest how insensitive the MMT is.

Table 9 Summary of test-retest reliability of AMPD and goniometer measurements. ICC intraclass correlation coefficient, SEM standard error of measurement, MDC minimal detectable change for the average of 3 trials, maximum of 3 trials, and first trial

	Stroke		
	ICC [95% CI]	**SEM**	**MDC**
AROM Dorsiflexion Position (Impaired Ankle)			
Avg	R: 0.92 [0.84 0.96] T: 0.95 [0.90 0.98]	R: 2.2 T: 1.3	R: 6.2 T: 3.7
Max	R: 0.91 [0.83 0.96] T: 0.95 [0.90 0.98]	R: 2.3 T: 1.4	R: 6.4 T: 3.7
First	R: 0.92 [0.86 0.96] T: 0.94 [0.87 0.97]	R: 2.0 T: 1.8	R: 5.4 T: 4.9
Dorsiflexion MVC (Impaired Ankle)			
First	R: 0.89 [0.77 0.94] T: 0.86 [0.72 0.93]	R: 1.3 T: 0.0	R: 3.5 T: 0.0

Validity of Robot-Based Compared to Therapist-Based Measurement of Ankle ROM and MVC

We next were interested in the concurrent validity of the robot-based measurements. Thus, we analyzed how well the dorsiflexion AROM, PROM, and MVC measurements taken with AMPD correlated with the same measurements taken by the therapist. Again, we performed this analysis only for the post-stroke participants. All correlations between AMPD and therapist were significant and moderate to strong (Figure 18, $r > 0.48$, $p < 0.002$). This supports concurrent validity of the three measures.

However, as can been seen in Figure 18A and 16B, the dorsiflexion ROM measured with the robot was larger than that with the goniometer. These post-stroke participants were able to achieve on average 18.2 ± 9.9 degrees more dorsiflexion when measuring AROM and 3.9 ± 6.0 degrees more when measuring participants dorsiflexion PROM, which were both significantly different, with a large effect size for dorsiflexion AROM ($p < 0.0001$, $d = 1$) and a medium effect for PROM ($p < 0.0001$, $d = 0.63$).

As for maximum dorsiflexion strength, although the robotic and therapist measures of MVC were significantly correlated, there was poor segregation of the MMT scores relative to the robotic scores. Individuals scoring 0 on the MMT fell with the range of AMPD MVC values of individuals scoring 1, and the same was true for the individual who scored a 2 on the MMT. That is, using this data, we could not define a range of AMPD MVC scores that clearly defined a 0, 1, or 2 MMT rating. The most that can be said is that the average ankle torque produced using AMPD increased for subjects that were scored a 0, 1, or 2 (3.4 ± 3.7 Nm, 9.2 ± 5.2 Nm, and 19.3 Nm, respectively) (Figure 18C). Subjects that were scored a 0 on the MMT had significantly lower ankle dorsiflexion MVC compared to subjects that were scored a 1 ($p = 0.01$). These results highlight the rather coarse nature of MMT.

Reliability of Robotic Measures for Unimpaired Participants and Comparison of Three Analysis Techniques

We also used the robot to obtain test-retest reliability of ROM and MVC for young and older, unimpaired participants. Test-retest reliability was also high for these participants: ICCs were always 0.89 or above (Table 10). There was no observable, systematic difference in reliability for young unimpaired, older unimpaired, and post-stroke participants.

Table 10 also presents the results of using either the average of 3, max, or first calculation methods. ICCs were nearly always high, except for the first calculation method for AROM plantarflexion position for individuals with stroke. Table 10 also provides the SEM and MDC for each measurement technique.

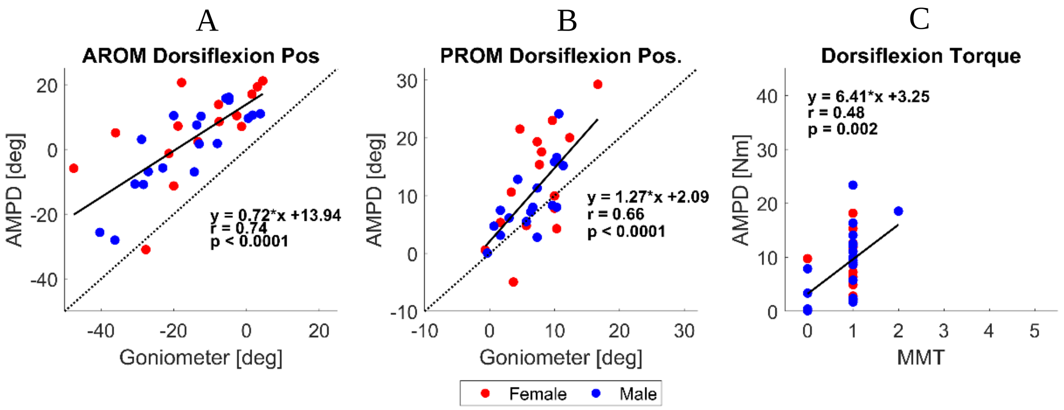


Figure 18 Relationship between clinical measurements (x-axis) and AMPD measures (y-axis) of chronic stroke participants impaired ankle. We used the average of 3 calculation for dorsiflexion AROM, the first measure for dorsiflexion PROM (since only one measure was taken by the therapists), and the first measure for dorsiflexion MVC (since again only one measure was taken by the therapists). Data is always from the first evaluation session.

Table 10 Summary of test-retest reliability of AMPD. ICC intraclass correlation coefficient, SEM standard error of measurement, MDC minimal detectable change, for the average of 3 trials, maximum of 3 trials, and first trial

	Young			**Older**			**Stroke**		
Method	**ICC [95% CI]**	**SEM**	**MDC**	**ICC [95% CI]**	**SEM**	**MDC**	**ICC [95% CI]**	**SEM**	**MDC**
AROM Dorsiflexion Position									
Avg	0.91 [0.85 0.95]	0.9	2.6	0.96 [0.90 0.98]	0.5	1.4	0.96 [0.94 0.98]	1.2	3.5
Max	0.90 [0.82 0.94]	1.1	3.2	0.95 [0.90 0.97]	0.6	1.6	0.96 [0.93 0.97]	1.3	3.5
First	0.89 [0.82 0.94]	1.2	3.4	0.95 [0.89 0.97]	0.6	1.5	0.96 [0.94 0.98]	1.2	3.3
AROM Plantarflexion Position									
Avg	0.94 [0.90 0.96]	0.6	1.8	0.93 [0.87 0.96]	0.9	2.5	0.96 [0.94 0.98]	1.0	2.7
Max	0.93 [0.89 0.96]	0.8	2.3	0.93 [0.88 0.96]	0.9	2.4	0.95 [0.93 0.97]	1.2	3.3
First	0.92 [0.87 0.95]	1.0	2.7	0.92 [0.86 0.95]	1.0	2.8	0.73 [0.56 0.83]	6.7	18.6
Dorsiflexion MVC [Nm]									
Avg	0.96 [0.94 0.98]	0.5	1.4	0.95 [0.91 0.97]	0.8	2.3	0.97 [0.95 0.98]	0.6	1.8
Max	0.96 [0.93 0.97]	0.6	1.6	0.95 [0.91 0.97]	0.9	2.5	0.97 [0.95 0.98]	0.6	1.8
First	0.91 [0.89 0.95]	1.2	3.3	0.93 [0.87 0.96]	1.1	3.2	0.94 [0.90 0.96]	1.2	3.4

Comparison of First to Second Session

An interesting question is whether individuals improved in their values from one session to the next. First starting with AROM measurements, the average dorsiflexion and plantarflexion change in AROM position using AMPD from session 1 session 2 for young and older unimpaired participants was 1.3°±3.2° and 1.2°±2.4, which for dorsiflexion showed statistically significant difference for both groups ($p < 0.001$) but had a small effect ($d < 0.20$) (Table 11), suggesting that there is systemic bias, but it is negligible. The average change from session 1 to session 2 for plantarflexion was 0.1°±3.1° for young and 0.7°±3.3° for older participants, which were not significantly different for both groups ($p > 0.3$) (Table 11), suggesting there was not systemic biases for measuring plantarflexion AROM. For stroke participants the average change in dorsiflexion and plantarflexion AROM for the impaired and unimpaired 0.6°± 7.8° and 0.3°± 2.7°, respectively higher dorsiflexion positions using the paretic ankle but produced 0.3°± 2.7° lower dorsiflexion positions using the nonparetic ankle, which were non-significant ($p > 0.5$) (Table 11), suggesting there was not systemic biases for measuring AROM in stroke. These results further strengthen that AMPD is a reliable device for measuring AROM.

For dorsiflexion MVC measurements young and older participants slightly increased their dorsiflexion torque from session 1 to session 2 by an average of 0.05 ± 2.6 Nm and 0.3±3.6 Nm, respectively. For stroke participants from session 1 to session 2, the average change increased for the unimpaired ankle by 1.0 ± 3.7 Nm but decreased for the impaired ankle by 0.1 ± 3.3 Nm (Table 11). For all groups there not a significant difference session 1 and session 2 measurements ($p > 0.4$). Just like AROM measurements, these results further strengthen that AMPD is a reliable device for measuring dorsiflexion MVC.

Comparison of Stroke to Unimpaired Age Matched Adults

Another interesting question is whether stroke impaired any of the measurements. Within stroke participants impaired ankle had significantly less AROM and dorsiflexion strength compared to the unimpaired ankle ($p < 0.0001$). Interestingly, comparing stroke participant unimpaired ankle to unimpaired controls AROM showed that stroke participants unimpaired AROM was comparable to unimpaired age matched controls ($p > 0.4$), however when looking at dorsiflexion strength, stroke participants produced significantly less dorsiflexion torque compared to controls ($p< 0.001$) (Table 11). This suggests that there are motor deficits on the impaired ankle but also the unimpaired side is affected as well.

Comparison of Older to Younger Unimpaired Adults

A final interesting question is whether aging impaired any of the measurements. For AROM measurements young participants showed that their dominant side achieved significantly larger dorsiflexion plantarflexion position compared to their nondominant side ($p < 0.04$), but no significant difference in leg dominance within older participants ($p = 0.52$). Also, no significant differences were found between young and older participants dorsiflexion positions ($p > 0.1$), which might suggest that age related declines are not present for AROM within this sample size.

For dorsiflexion MVC measurements, young and older participants produced significantly larger dorsiflexion toque with their non-dominant ankle compared to the dominant ankle ($p < 0.001$). Interestingly, there were no significant differences between young and old MVC measurements ($p > 0.5$), which might suggest that age related declines are not present for dorsiflexion within this sample size.

Table 11 Session 1 and Session 2 average dorsiflexion and plantarflexion AROM position and dorsiflexion MVC for each ankle per group.

	Young		Old		Stroke	
	Dom.	Non-Dom.	Dom.	Non-Dom.	Impaired	Unimpaired
AROM Dorsiflexion Position [°]						
Test 1	A: 25.04°±5.8 F: 24.8°± 6.4° M: 25.2°±5.6°	A: 23.8°±6.0° F: 23.7° ± 5.2° M: 23.8°±6.5°	A:23.2°±6.0° F: 22.8°±5.6° M:24.0°±6.7°	A: 23.0°±6.1 F: 21.6°± 6.3° M: 25.2°±5.4°	A: 2.7°±7.8° F: 5.6°± 14.2° M: 0.4°± 14.7°	A:25.8°±8.2 F: 27.6°± 8.6° M: 24.4°± 7.9°
Test 2	A: 26.4°±5.9° F: 25.8°±6.4° M: 26.7°±5.7°	A: 25.0°±6.4° F: 25.1°± 7.1° M: 24.9°±6.2°	A:24.7°±7.0° F: 24.9°±7.8° M: 24.3°±5.8°	A:24.0°±6.7° F: 23.1°±7.0° M: 25.4°±6.3°	A: 3.3°±13.6° F: 5.6°± 14.6° M: 1.5°± 12.9°	A:25.5°±7.5° F: 25.7°± 8.4° M: 25.4°± 6.9°
Change in mean	A:1.3°±2.7° F: 1.0°±3.5° M: 1.5°±2.2°	A:1.2 °± 3.7° F: 1.3°±4.7° M: 1.1°± 3.1°	A: 1.3°± 2.8° F: 2.1°± 2.9° M: 0.4°±1.6°	A: 1.0°± 2.1° F: 2.1°± 2.9° M: 0.2°±2.5°	A: 0.6°± 7.8° F: 0.0°± 7.6° M: 1.1°± 8.1°	A: -0.3°± 2.7° F: -1.9°± 4.2° M: 1.0°± 4.1°
AROM Plantarflexion Position [°]						
Test 1	A: -49.8°±6.3° F: -50.2°± 5.9° M: -49.6°±6.6°	A: -48.5°±5.5° F: -49.5°±5.3° M: -48.0°± 5.7°	A: -50.5°±6.3° F: -51.9°±5.5° M -48.2°±7.1°	A: -48.7°±7.6° F: -51.1°± 6.9° M:-45.0°±7.4°	A: -27.9°±10.5° F: -28.7°± 13.2° M: -27.2°± 8.0°	A: -47.2°±8.0° F: -50.3°± 9.4° M: -44.8°± 5.8°
Test 2	A: -49.75°±7.0° F: -49.8°± 7.6° M: -49.7°± 6.8°	A: -48.3°±6.2° F: -49.9°± 6.1° M: -47.4°± 6.2°	A: -49.2°±5.3° F: -50.3°± 5.3° M:-47.3°±5.0°	A: -48.6°±6.1° F: 50.1°±6.1° M:-46.2°±5.5°	A: -28.1°±12.0° F: -27.0°± 15.6° M: -28.9°± 8.5°	A: -46.8°±8.4° F: -49.4°± 10.3° M: -44.7°± 6.0°
Change in mean	A:0.1°±2.8° F: 0.4°±2.9° M: -0.1°± 2.8°	A:0.2°±3.4° F: -0.4°± 3.0° M: 0.5°±3.6°	A:1.3°±3.3° F: 1.6°± 3.6° M: 0.9°± 2.9°	A:0.1°±3.2° F: 1.0°± 3.1° M: -1.2°± 3.0°	A: -0.2°±6.4° F: 1.7°± 6.8° M: -1.7°± 5.7°	A:0.4°±3.5° F: 0.8°± 3.3° M: 0.0°± 3.7°
Dorsiflexion Maximum Strength [Nm]						
Test 1	A:29.7±6.7 F:24.4 ±4.3 M: 32.8±5.9	A:31.1±7.3 F: 25.5±4.7 M: 34.3±6.5	A:24.5±7.8 F: 20.2±3.2 M: 31.4±8.2	A:26.5±9.0 F:20.9 ±3.3 M: 35.3±7.9	A: 8.5±5.7 F: 8.2±5.1 M: 8.7±6.3	A:23.7±7.6 F: 18.8±5.9 M: 27.5±6.5
Test 2	A:29.8±6.7 F: 25.1±5.2 M: 32.5±6.0	A:31.1±6.6 F:25.6 ±4.9 M: 34.3±5.4	A:24.6±6.9 F: 21.5±3.6 M: 30.0±7.7	A:26.8±9.0 F: 22.2±4.1 M: 34.3±9.7	A:8.4±5.4 F: 8.2±5.9 M: 8.5±5.3	A:22.7±7.4 F: 18.3±5.4 M: 26.2±7.1
Change in mean	A: 0.1±2.5 F: 0.8±2.0 M: -0.3±2.7	A:0.0±2.8 F: 0.2±1.9 M: -0.1±3.3	A:0.3±3.3 F: 1.3±2.6 M: -1.4±3.9	A:0.4±3.9 F:1.2 ±2.6 M: -1.0±5.3	A: -0.1 ± 3.3 F: 0.0±3.1 M: -0.2±3.4	A: 1.0 ± 3.7 F: -0.5±2.9 M: -1.3±4.3

DISCUSSION

A first objective of this study was to determine if robotic assessments are as reliable as assessment by a skilled therapist in quantifying these basic clinical outcomes. Second, we sought to establish concurrent validity between clinical and robotic assessments. Third, we compared the first trial versus maximum of three trials versus average of three trials approaches for reliability. Fourth, we further analyzed validity of the robot measurements by determining if they could detect the effect of stroke or aging on ROM and MVC. Lastly, we provide a database of reference values for ROM and MVC for young, older, and persons post-stroke, both male and female, and as expected, stroke significantly decreased ROM and MVC; aging had a smaller but significant effect.

Our hypothesis was correct that AMPD can provide reliable and valid measurements of ankle motor function. We will now discuss our results.

Reliability And Validity

Both AMPD had excellent test-retest reliability across all groups for AROM (ICC > 0.90), and therapist-based measurement using the goniometer also showed excellent test-retest reliability (ICC = 0.94-0.95) and is consistent with those obtained by other authors in unimpaired participants [155], [156], [169]. These results suggest that both tools can be used to measure ankle AROM without failure during a given time period. However, the agreement between goniometer and AMPD measurements were poor (ICC = 0.38) for AROM, which suggests that AMPD is reliable within itself, and therapist-based measurements are reliable within itself. One reason for poor agreement may be due to stroke participants achieving a significantly greater dorsiflexion position using AMPD. For maximum dorsiflexion strength, AMPD had excellent test-retest reliability across all groups for (ICC > 0.91), and therapist-based measurement using MMT showed excellent but lower test-retest reliability (ICC = 0.86). These findings are consistent with those obtained by other authors for older [170], [171] and young [157] unimpaired adults.

Most studies report ankle ROM and MVC results from an average of 3 readings [156], [157], [172], and a few have quantified the potential benefit of single versus average measures of ROM [155], but to our knowledge none have demonstrated the potential benefit of the first trial versus maximum of three trials versus the average of 3 measures for test-retest reliability. The average of 3 trials provided slightly better test-retest reliability metrics compared to the first trial or the maximum of the three trials for AROM and dorsiflexion MVC assessments, but the maximum of 3 trials was very close. This shows that using an average or maximum of 3 trials gives very similar results and can be used interchangeably. This was also shown to be true for goniometer measurements. The test-retest reliability estimates obtained using the average of trials showed the best test-retest reliability metrics compared to a single measurement is consistent with those obtained by [155].

For validity, moderate to strong relationships exist between goniometer and AMPD measurements, suggesting that AMPD is able to measure similar aspects of ankle dorsiflexion positions using a goniometer. This device may be a valuable tool for routine ROM of motion monitoring in clinical settings. A significantly moderate relationship between ankle dorsiflexion torque and MMT exists, but this may be driven by the fact that all participants were rated below a 2, with one participant being rated a 2. Manual muscle testing is inherently subjective and cannot reliably distinguish subtle differences in strength [173], [174].

AMPD Elicits greater dorsiflexion ROM

Stroke participants produced significantly higher dorsiflexion AROM and PROM positions on AMPD compared to goniometer measurements. There are many possible explanations on why subjects produced greater AROM dorsiflexion positions using AMPD, 1) subtalar and foot position, specifically pronation, may allow the ankle to achieve greater angles of dorsiflexion ROM [175], 2) AMPD provides support of the bottom which can give increased cutaneous afferents during movement, which can drive force output and control

[176], 3) Due to cortical damage, stroke survivors can lose the ability to move their joints independently, which result in abnormal coupled pathophysiological movement patterns, also called synergies [77]. The loss of independent control of joint moments is caused by involuntary co-activation of muscles over multiple joints [177]. Brunnstrom [178] defined two often occurring pathophysiological synergies in the lower extremities, extension synergy, consisting of internal rotation, adduction and extension of the hip, extension of the knee, and plantar flexion and inversion of the ankle, and flexion synergy consisting of external rotation, abduction, and flexion of the hip, flexion of the knee and dorsal flexion and eversion of the ankle. Because dorsiflexion is considered a flexion synergy, stroke participants may have been activating multiple muscles that may have caused their foot to lift perpendicular to the ground causing a greater dorsiflexion measurement using AMPD.

Limitation

This study has multiple limitations. First, we did not assess unimpaired subjects AROM using a goniometer. This would have given us greater clarity on the validity between AMPD and goniometer measurements. Second, we did not assess any participants that scored greater than a 3 on the MMT, because of the exclusion criteria of the RCT. This would have helped determine if the relationship would have continued to trend linearly with muscle torque measured with AMPD. Lastly, we did not perform inter-rater reliability testing. It has been shown that technical proficiency influences the reliability of ankle ROM measurements [156], [179], and doing this would determine if AMPD is resistant to PTs technical level.

CHAPTER 7: ESTABLISHING RELATIONSHIPS BETWEEN ANKLE PROPRIOCEPTION, GAIT IMPAIRMENT, AND ANKLE MOTOR IMPAIRMENT AFTER STROKE: A ROBOTIC ASSESSMENT STUDY

SUMMARY OF THE CHAPTER

Ankle proprioceptive deficits are common after stroke and have been found to occur independently of ankle motor impairments. Despite this independence, some studies have found that ankle proprioceptive deficits predict gait function, consistent with the concept that somatosensory input plays a key role in gait control. Other studies, however, have not found a relationship, possibly because of variability in proprioception assessments. Robotic assessments of proprioception offer improved consistency and sensitivity. Here, we quantified ankle proprioception using two different robotic tests (joint position reproduction – JPR, and crisscross – CC) in 39 persons in the chronic phase of stroke. We then analyzed the extent to which these robotic proprioception measures predicted gait speed, measured over a long distance (6-minute walk test - 6MWT) and a short distance (10-meter walk test - 10mWT). We also studied the relationship between robotic proprioception measures and lower extremity motor impairment, quantified with measures of ankle strength, active range of motion, and the lower extremity Fugl-Meyer exam. Impairment in ankle proprioception was present in 87% of the participants. Ankle proprioceptive acuity measured with JPR was weakly correlated with gait speed measured with the 6MWT ($\rho = -0.34$, $p = 0.039$) but not the with the 10mWT. Ankle proprioceptive acuity was not correlated with lower extremity motor impairment ($p > 0.2$). These results confirm the presence of a weak relationship between ankle proprioception and gait after stroke that is independent of motor impairment.

INTRODUCTION

There is a large body of evidence linking lower extremity (LE) motor impairment to gait function in patients with stroke [1], [180], [181]. For example, strength of the impaired ankle has often been found to be a strong predictor of gait velocity [1], [181]. However, when it comes to LE sensory deficits predicting gait function, results are less clear.

Proprioceptive impairment after stroke is thought to affect the control of muscle tone, disrupt postural reflexes, and impair spatial and temporal aspects of volitional movement [99]. For the upper extremity, proprioceptive impairment also predicts the ability of persons who have experienced a stroke to benefit from rehabilitative movement training, such as constraint-induced therapy [11] or robotic hand movement training [8], [18], [100]. This suggests that proprioceptive feedback plays an important role in mediating use-dependent plasticity. For the LE, proprioceptive signals related to leg kinematics and loading are thought to play a key role in locomotor control and plasticity [69], [70], [71], [72].

Unlike for ankle strength, however, studies have typically found no association [96], [182], [183], [184] or only weak associations between LE sensation and gait function, quantified as gait velocity [184], [185], balance ability [96], [101], [185], falls [96], [185], and endurance [186] (Table 12). One reason may be the wide variety in methods used to quantify proprioceptive acuity [96], [182], [183], [184]. Several studies that found no relationship have used available clinical assessments, such as the modified Nottingham Sensory Assessment [96] and the sensory scale of the Fugl Meyer Assessment [182], [184], which provide basic information on an individual's ability to perceive movement and/or its direction on an ordinal scale as "absent", "impaired", or "normal" [187]. These clinical assessments of sensory impairment have limited accuracy and responsiveness [185], [187].

Other assessments for LE proprioception have been developed using robotics [56], [58] to address these limitations. Robotic assessments for both sensory and motor impairments are more objective (not relying as strongly on observer judgement) and accurate (e.g. able to measure exact body position/force applied), because they can deliver precise, reproducible stimuli and then measure the response to those stimuli [188].

Table 12 Summary of studies of the relationship between LE sensation and gait function after stroke.

Study (# of Participants)	Measure of Lower Extremity Sensation	Measure of Gait Function	Correlation Result
Nadeau et al. 1999 (16)	LEFM	9mWT	r = 0.14
Hsu et al. 2003 (26)	LEFM	6mWT	r = 0.4*
Lee et al. 2005 (11)	TDPM (robot)	6MWT	r = 0.63 to 0.77*
Lin 2005 (21)	JPR (robot)	6mWT	r = -0.021
Gorst et al. 2018 (32)	Gradient Dscr and Step Height Dscr (robot)	10mWT Balance – COP	r = -0.40 to -0.60* r = -0.43 to -0.44*
Gorst et al. 2019 (163)	EmNSA	Falls Efficacy Scale Balance - Centre of force 10mWT	r = -0.22* r = -0.20* r = 0.09
Cho et al. 2021 (57)	JPR (robot)	Berg Balance Scale	r = -0.40*

Abbreviations: LEFM = Lower Extremity Fugl Meyer; **TDPM** = Threshold to Detection of Passive Motion; **JPR** = Joint Position Reproduction; **Dscr** = Discrimination; **EmNSA** = Erasmus MC modified version of the Nottingham Sensory Assessment; **COP** = Center of Pressure; **r** = Spearman's rank correlation; **r** = Pearson's correlation; ***** denotes significant relationship ($p < 0.05$)

Here, we sought to clarify the relationship between ankle proprioception and gait function after stroke using robotic assessments of ankle proprioception. We used a custom-built robotic device to implement a commonly used type of proprioception test, a Joint Position Reproduction (JPR), as well as more novel proprioception assessment, Crisscross, which we recently developed to measure proprioception acuity of the fingers [117]. JPR asks individuals to copy the motion imposed on one ankle by the robotic device by actively moving their other ankle in a matching motion. Crisscross reduces the motor demand on individuals by asking them to simply push a button when they feel their ankles cross each other, as the ankles are driven through their plantar/dorsi flexion range of motion using a robotic device. Crisscross combines components of movement discrimination, movement speed and direction sense, comparison between relative limb positioning in space, and discrete position matching (where by "discrete" we mean the test subject makes one proprioceptive judgment per each movement trial). Studies that employed Crisscross with a robotic exoskeleton to measure finger proprioception have found that the test is sensitive to aging [117] and presence of a prior stroke [18], and that it predicted stroke subjects' ability to benefit from a three-week period of robotic finger training [8], [100]. For our measure of gait function, we focused on standardized measures of gait speed over long and short distances.

METHODS

Participants and Clinical Assessments

Chronic stroke participants were enrolled in an ongoing clinical trial designed to evaluate the efficacy of a brain-computer-interface, functional electrical stimulation system for treating foot drop. The inclusion criteria were as follows: Age 18-80 years, radiologically confirmed stroke, with day of onset at least 26 weeks prior to day of randomization, Gait velocity < 0.8 m/s, foot-drop in affected limb, plantarflexor spasticity < 3 on modified Ashworth Scale, walk > 10 m (with or without ankle foot orthosis (AFO), and cane or walker permitted) at a supervised level. Only baseline measurements were used for analysis.

A trained physical therapist assessed each participant. The following measures were taken: National Institutes of Health Stroke Scale (NIHSS) [123], [189], [190], Lower Extremity Fugl Meyer (LEFM) [124], [191], [192], [193], [194], 6 minute walk test (6MWT) [125], [195], [196], 10 Meter Walk Test (10mWT) [120], [197], [198], Nottingham Assessment of Somato-Sensations (NSA) [199], [200], Montreal Cognitive Assessment (MoCA) [126], [201] and Modified Ashworth Scale of Spasticity (MAS) [121], [202], [203]. MAS ankle plantarflexion scores that were marked with a "+," an additional 0.5 points was added for calculations.

For comparison, we recruited age-matched controls who had not experienced a stroke. Exclusion criteria were: history of neurological injury, musculoskeletal damage, or current injuries that affected participants ability to move or feel either their ankles, use of medication that would change how the brain perceived pain/movement. For both stroke and age matched participants the local ethics committee approved this study, and written informed consent was obtained from each participant prior to participating, following procedures established by the University of California Irvine Institutional Review Board.

Robotic Device

Two versions of Ankle Measuring Proprioceptive Device (AMPD and 2AMPD, an improved version of AMPD) were used for this study. Chapter 2 describes these devices in detail, but here we briefly describe 2AMPD, which is similar to AMPD (Figure 3) with some clinical usability improvements such as improved seating, robot mode switching, and adjustment of feet width. To use 2AMPD, participants sit in an upright position with the hip and knee bent at 90 degrees such that the shank is perpendicular to the ground, the center of the lateral malleolus is aligned to the rotational shaft of 2AMPD, and the feet are adjusted to be hip width. 2AMPD has two impedance states, mechanically rigid and mechanically transparent. In its rigid state, 2AMPD can individually assist and move both ankles, via motors (TiMOTION, TA16), through participants' natural dorsiflexion and plantar flexion passive range of motion. In its mechanically transparent state, 2AMPD allows participants to move their ankles on their own volition with minimal resistance. 2AMPD is equipped with angular quadrature encoders to measure ankle angular position (E6B2-C, 1024 P/R) and s-type load cells (Interface, SMA-200) to measure ankle force and then converted to ankle torque. Data is acquired at 200 Hz and stored on a laptop.

Lower Extremity Motor Impairment and Gait Function Measurements

Standardized instructions and a demonstration were provided before each ankle impairment test, active range of motion and maximum dorsiflexion strength. For active range of motion (AROM) tests, 2AMPD was placed in its mechanically transparent state and participants were instructed to dorsiflex the ankle to their maximum position and then transition to their maximum plantarflexion position. A single trial consisted of each maximum position held for 3 seconds. Three trials were first performed on the unimpaired ankle for understanding and then the impaired ankle completed the three trials. 15 seconds of rest was given between each trial.

For maximum dorsiflexion strength, 2AMPD was placed in its mechanically rigid state with the ankle in neutral, i.e., an angle of 90° in sagittal plane between foot and shank [204]. Participants were asked to gradually dorsiflex until maximum effort was given and held for 3 seconds. The participant performed three trials with the unimpaired ankle first, and then three with the impaired ankle. 15 seconds of rest was given between each trial.

Standardized instructions and a demonstration were provided before each walk test. Each walk test was performed without participants wearing an ankle-foot orthosis. For the

10mWT, the time in seconds to walk the middle 6-meter section of a 10-meter walkway was used to compute comfortable walking speed. Timing started when the participant's first foot crossed the 2-m mark and stopped when the first foot crossed the 8-meter mark, though the participant continued to walk to the 10-meter mark [120]. Participants performed 5 repetitions, and no encouragement was given during the test.

For the 6MWT the test was performed in a corridor, and the participant was instructed to, at a comfortable pace, cover as much as ground they could during the six-minute testing period [196]. The total distance in meters was measured. Participants completed this test once, and no encouragement was given during the test.

Crisscross Test

For the Crisscross test, 2AMPD drove the left and right ankles in opposing directions during a series of non-periodic ankle-crossings of different angular velocities (Figure 9A). For each ankle-crossing movement, participants were instructed to press a handheld button when they perceived their feet to be at the same angular position.

Chapter 3 describes how the ROM was set, but here we briefly describe the process. For all participants, before beginning the test, a trained experimenter assessed each participants' passive range of motion by manually moving the unimpaired and impaired ankle with 2AMPD in its mechanically transparent mode to a comfortable maximum dorsiflexion and plantarflexion position. The assessment workspace was then calculated by taking the smaller extent of dorsiflexion between the two ankles, and the smaller extent of plantar flexion as well. The assessment workspace was then split into 5 sections, such that a single crossing occurred in each workspace section, >60% PF (extension), 60-20% PF (mid-extension), 20%PF - 20%DF (center), 20%-60%DF (mid-flexion) and >60% DF (flexion).

This ensured an approximately uniform distribution of crossings in the assessment workspace.

To ensure each participant understood the test, they first completed four crossing movements with vision of their feet, giving verbal confirmation that they understood the test. Then, with vision occluded by a large lap table, each participant experienced two crossing attempts in each crossing workspace section in a randomized order, for a total of 10 crossover movements. Participants experienced four ankle speeds: 4.4, 5.7, 7.0, and 8.3 degrees/second (Figure 11B), which is in the recommended range stated in Chapter 3. Individual ankle speeds were randomized such that the impaired and unimpaired ankle mostly did not move at equal speeds.

Joint Position Reproduction (JPR) Test

Many variations in protocols for JPR have been proposed, some requiring active reproduction of a passively imposed movement. Here we implemented a passive-active contralateral JPR test, where impaired foot for participants post-stoke was passively driven by 2AMPD (the “target ankle”), and the unimpaired ankle (the “matching ankle”) was actively moved by the participant to try to match the movement of the target ankle.

We designed the ankle joint trajectories to have two parts, which we term the dynamic and static periods (Figure 11C). The dynamic periods consisted of 2AMPD driving the target ankle at a constant velocity of 5°/s through its available dorsiflexion and plantarflexion range (Figure 11C). Participants were instructed to match angular position and speed using their matching ankle during these dynamic periods. Dynamic periods were randomly interrupted by static periods where the robot stopped moving the ankle at a pseudo-random set of positions distributed across the workspace. Participants were instructed to match the angular position of the stationary target ankle by making fine adjustments with their matching ankle. For each static period, unlimited time was given, and participants were instructed to press a handheld button when they perceived their feet to be at the same angular position. The robot returned to a dynamic period after they pushed the button. Just like Crisscross, all participants first performed a short practice test with vision of their feet allowed and gave verbal confirmation that they understood the test. Then, their vision of their feet was occluded with the lap table and the subsequent test lasted about 2 minutes.

Since Crisscross was completed before the JPR test, the passive range of motion of the target ankle used in Crisscross was used in the JPR test and 2AMPD drove the target ankle to 80% of the maximum dorsiflexion and plantarflexion positions. The static periods were selected by splitting the impaired ankle ROM into sections, >60% PF (extension), 60-10% PF (mid-extension), 10%PF – 60%DF (mid-flexion), >60%DF (flexion). One static period occurred in each section resulting in a total of 4 dynamic periods and 4 static periods.

STATISTICAL ANALYSIS

Ankle Proprioceptive Acuity

Proprioceptive acuity using Crisscross was quantified using absolute error, defined as the absolute angular difference between the left and right ankle at the moment of button press. If a participant did not attempt to press the button on single or multiple crossing attempts, their average error was calculated using only the crossings where a button press happened. Similarly, proprioceptive acuity using JPR was also quantified using absolute error. Absolute error here was defined as the absolute angular difference between the left and right ankle at the moment of button press for the static condition, and the absolute angular difference averaged across the dynamic condition.

Ankle Motor Impairment

For AROM and maximum dorsiflexion strength tests, only the impaired ankle was considered. The maximum dorsiflexion and plantarflexion position of the 3 trials were averaged. Then the maximum dorsiflexion and plantarflexion position was summed together for a total active range value. For maximum strength, the maximum torque produced in each trial was taken and averaged across all three trials for the impaired ankle.

Gait Function

The 5 repetitions for the 10mWT were first converted to a velocity (meters/sec), and then averaged. For the 6MWT, the total distance was used in all gait function analysis. If stroke participants were unable to complete the 10mWT or 6MWT without an AFO, they were given zero for each test they could not complete.

Statistical analyses were conducted using Matlab R2023 software. Each output parameter was independently tested for normality using Shapiro Wilks test. The 10mWT and maximum dorsiflexion strength were not normally distributed ($p < 0.05$), but 6mWT, active range of motion, and LEFM were normally distributed ($p > 0.05$). Since not all data series proved to be normally distributed, we used non-parametric tests, Wilcoxon rank-sum test for comparison and Spearmans's rank order for correlation. An alpha level of 0.05 was used for all comparisons and correlations.

RESULTS

Participants

Thirty-nine people in the chronic phase of stroke (mean age 59.8 ± 11.7 SD; 15 female/24 male) participated in the study. 27 were left side affected and 12 were right side affected. Table 4 provides a demographic and clinical overview of the participants. Sixteen non-impaired, age-matched (64.6±11.11 yrs; 7F/9M) controls were included. 12 participants were right-side dominant, and 4 participants were left-side dominant.

Table 4 Clinical characteristics of stroke participants (N = 39)

	Average ± SD	**[Min Max]**
Age	60 ± 12	[27 76]
Days Post Stroke	1155 ± 1096	[201 4085]
NIH Stroke Severity Scale [0 42]	6 ± 3	[2 16]
Lower Extremity Fugl Meyer [0 34]	20 ± 3	[12 26]
Modified Ashworth Score [0 4]	1.59 ± 0.48	[0 2]
6 min walk distance (meters)	113.3 ± 66.8	[0.20 298.50]
10MWT (m/s)	0.37 ± 0.24	[0 0.76]
Montreal Cognitive Assessment (MoCA) [0 30]	23 ± 6	[1 29]
Ischemic/Hemorrhagic/Both	20/16/3	
Biological Sex M/F	24/15	

Overview of Proprioception Assessment Results

For Crisscross, stroke participants pushed the button on 333 out of the 390 crosses. 23 participants attempted all 10 crosses they were presented. 16 participants missed at least 1 crossing, and, of these, 4 pushed the button on less than 50% of crossings. Of the 57 total crosses with no button press, 29 attempts were missed in the plantarflexion region and the remaining in the dorsiflexion region. Of the 333 crossings attempted, participants pressed the button on average 0.3 ± 1.3 seconds before crossing indicating that they on average overly anticipated the moment their ankles would cross. The average absolute error for the Crisscross test was 16.3°±7.2°.

For JPR, during the dynamic period participants lagged the target on average 50%±15% of the time and led 50%±15% of the time. The average speed at which participants moved the unimpaired ankle during the dynamic phase was 5.1°/s ± 2.0°/s, which was not significantly different from the average speed of the impaired ankle that they were trying to track as the robot moved it (5.0°/s ±0.2°/s, p = 0.99). Of the 156 static periods, 59% of button presses occurred with the unimpaired ankle below the intended position. Participants on average pressed the button 5.6 ± 8.0 seconds after the start of the matching period. The delay to button press was positively correlated with JPR static error (R = 0.32, p = 0.046); thus, participants who took longer to press the button to indicate they had matched their ankle positions exhibited greater error. The average absolute error for JPR Static and JPR Dynamic was 11.3°±7.1° and 11.2°±5.6°, respectively.

For age matched participants their average Crisscross error, JPR Static error, and JPR Dynamic error were: 9.6° ± 3.5°, 6.1° ± 2.3°, 6.2° ± 2.0°, respectively. Impaired proprioception, defined as exhibiting a mean error that was greater than 2 SDs of the mean error in healthy controls, was present in the following percentage of the participants with stroke: 87% for Crisscross, 74% for JPR Static, 76% for JPR Dynamic.

Relationship between Robotic Assessments of Ankle Proprioception and Gait Speed

Together, the two robotic proprioceptive assessments produced three measures of proprioceptive error: Crisscross error, JPR dynamic error, and JPR static error. The two clinical assessments of gait function produced two measures of gait speed, one based on 10 meters of walking (i.e. the 10mWT) and one based on six minutes of walking (i.e. the 6MWT). The average gait velocity for the 10mWT and meters walked for 6MWT was 0.37 ± 0.24 meters per second and 113.3 ± 66.8 meters, respectively. Table 1 shows the average values for each measure, while Figure 19 shows graphs of the measures of ankle proprioception versus the measures of gait speed. The only significant correlation was between JPR Dynamic proprioceptive error and 6MWT (JPR Static: r = -0.34, p = 0.039, Figure 19F). JPR Dynamic error was nearly significantly related to gait speed in the 10mWT (r = -0.28, p = 0.09, Figure 19C) and Crisscross error was nearly significantly related to 6MWT distance (r = -0.29, p = 0.08, Figure 19D).

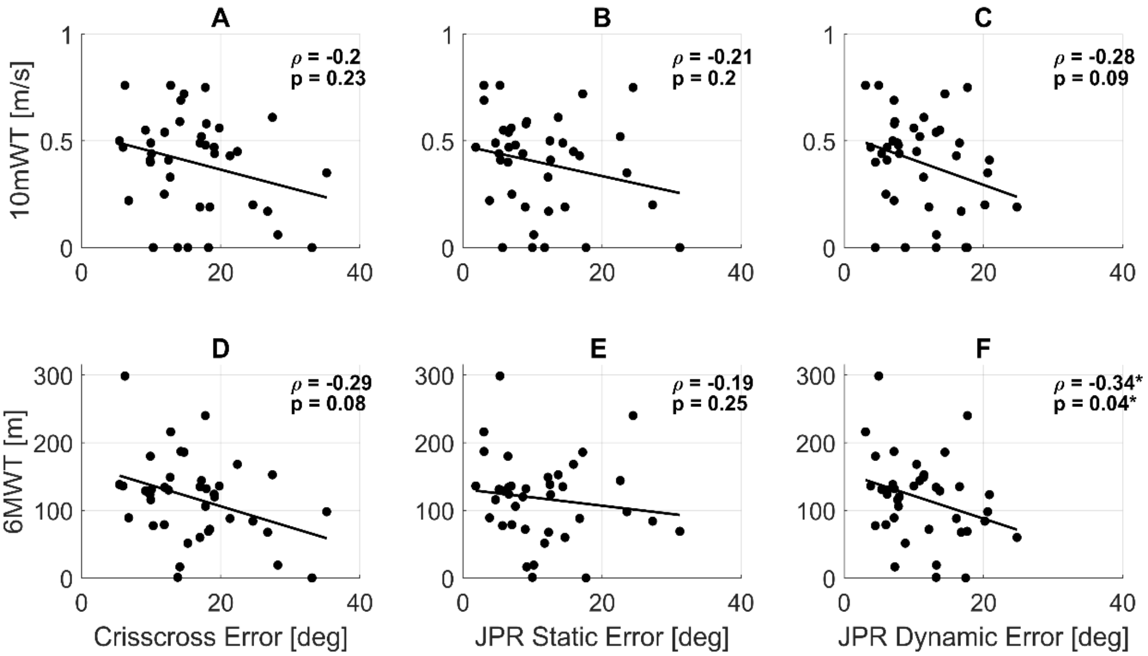


Figure 19 Relationship between three robotic measures of ankle proprioception (x axis) and two measures of measures and gait function (y axis). **A, B, C:** Average 10mWT gait velocity versus proprioceptive error. **D, E, F:** 6MWT distance versus proprioceptive error. Statistics from applying Spearman's correlation are shown. **Abbreviations:** ***10mWT***: 10-meter walk test; ***6MWT:*** 6-minute walk test; * denotes $p < 0.05$

Relationship between Robotic Assessment of Ankle Proprioception and Lower Extremity Motor Impairment

The average AROM for the impaired ankle was 31.7° ± 16.7°. The average maximum dorsiflexion strength was 9.7 ± 7.4 N/m. The average LEFM score was 20 ± 3 (out of a possible 34, Table 13). Figure 20 shows graphs relating ankle proprioception error to measures of ankle motor impairment. No significant relationships were found between ankle proprioception and ankle motor impairment ($p > 0.2$).

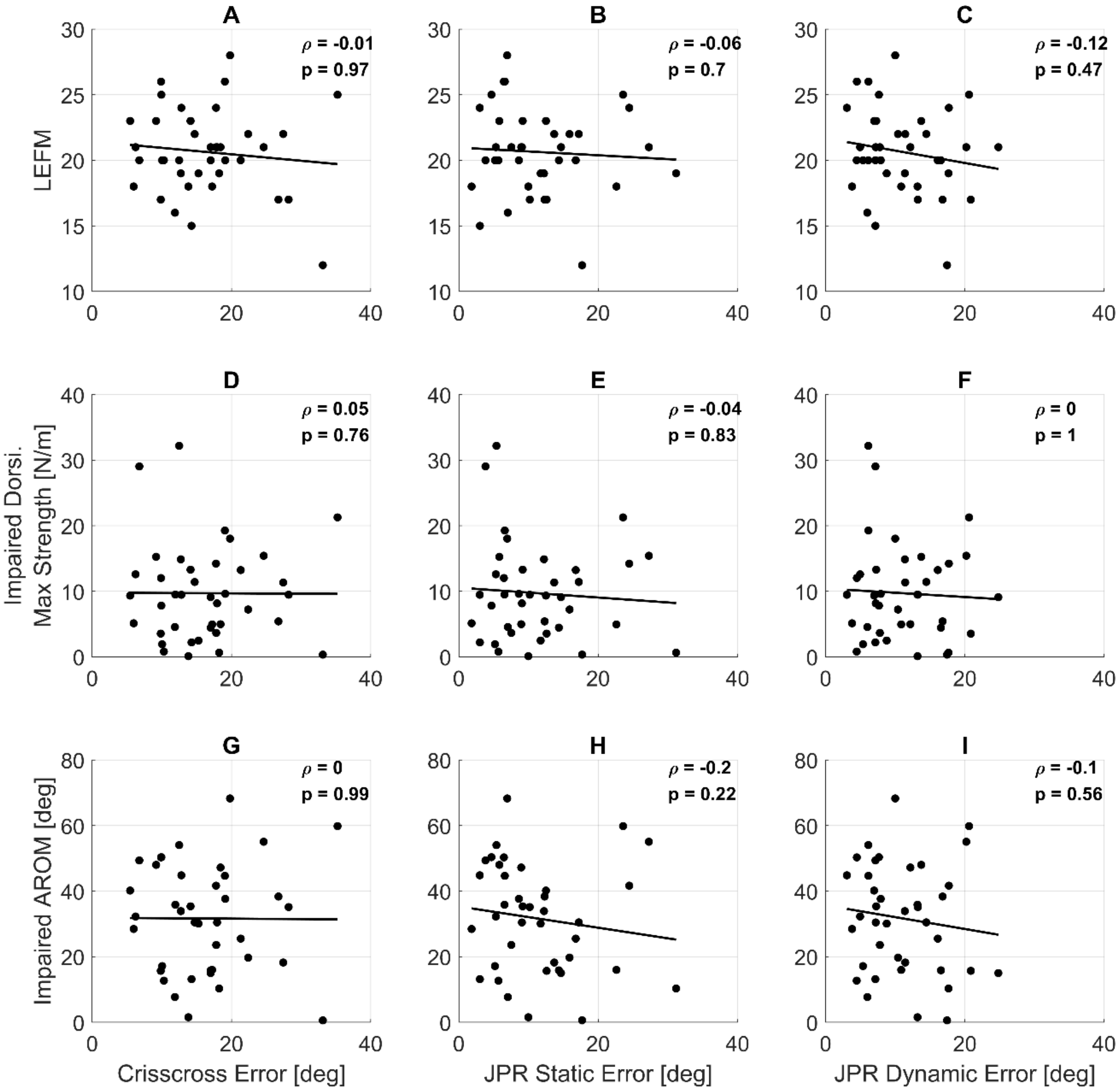


Figure 20 . Relationship between three robotic measures of ankle proprioception (x axis) and three measures of measures of LE motor impairment (y axis) **D, E, F:** Impaired dorsiflexion maximum strength as a function of proprioceptive error. **G, H, I:** Impaired AROM as a function of proprioceptive error.
Abbreviation: LEFM: Lower Extremity Fugl Meyer; AROM: Active Range of Motion; * $p < 0.05$

DISCUSSION

Gait function is a key factor in determining the level of independent mobility during activities of daily living after stroke [205]. Identifying the specific motor and sensory impairments that influence gait function is of great interest in stroke rehabilitation research, in part because this knowledge helps guide treatment. In this study, we quantified ankle proprioceptive ability of 39 individuals in the chronic phase of stroke. Using a novel robotic device we implemented two bilateral proprioceptive tests, a joint position reproduction (JPR) test similar to previously developed JPR tests, and the Crisscross test, which here we applied to the measurement of ankle proprioception after stroke for the first time. Using a 2SD criteria relative to age-matched controls, we found that ankle proprioception deficits were common in our participants, being present in approximately 75-90% of individuals we tested, depending on the specific test and error measure. We investigated the relationships between the magnitude of the proprioceptive error measured with these tests and gait function, quantified as gait speed across long and short distances. We found only one significant but weak relationship between ankle proprioceptive acuity (measured with JPR dynamic error) and gait function (measured with the 6MWT). We also found that ankle proprioception acuity was not significantly related to three measures of LE motor impairment (ankle AROM, ankle dorsiflexion strength, and LEFM score). We discuss first the significance of these results then limitations and directions for future research.

Relationship between Ankle Proprioception and Gait Function

After stroke, significant but weak associations between LE sensation and gait impairment have sometimes been observed [96], [101], [184], [185], [186] but not always [96], [182], [183], [184] (see Table 12). This is somewhat surprising as there is a large body of research that has identified the importance of LE sensory input for locomotion plasticity [69], [70], [71], [72]. It has been suggested that the inconsistency in findings may be explained by the variation in methods used to quantify proprioception [96], [185]. Here we applied two robotic ankle proprioception assessments methods, hoping that the improved consistency and sensitivity provided by robotics might more definitively answer this question. Yet we still found a mixture of significant, moderately insignificant, or insignificant correlation results depending on the test, the measure of proprioceptive error, and the measure of gait function; in all cases the putative correlations were weak in magnitude. This result would be explained if: 1) there is only a weak relationship between proprioception and gait function after stroke; and 2) there is high variability in proprioception acuity between individuals after stroke. Then, regardless of the sensitivity of the proprioception test, one would expect to find weak correlations, and that the statistical significance would depend on the particular sample of participants.

Why might the relationship between ankle proprioception and gait function after stroke be weak? One possibility is that, while normal gait function relies on ankle proprioception, individuals who lose ankle proprioception learn to compensate using other sensory pathways. Ankle proprioception is thought to rely mostly on information from muscle spindles [206], but if spindle pathways are damaged then the locomotor control system could substitute information from cutaneous and load related afferents, which are modulated during gait due to loading and weight-shifting [207]. Furthermore, the central nervous system (CNS) may also reduce reliance on somatosensory information and increase reliance of visual and vestibular inputs [96]. The relative contribution of somatosensory, visual, and vestibular sensory inputs changes in response to individual, task, and environmental factors [60], [208]. Measuring gait function in the dark after stroke might reveal a greater dependence on loss of integrity of leg proprioception.

Why is there high variability in ankle proprioceptive function after stroke? The neuroanatomical damage due to stroke is highly variable in its location and extent; somatosensory structures are sometimes affected and at other times spared. Further, ankle proprioception testing relies on cognitive abilities such as attention and working memory, which are commonly impaired post-stroke [209] and confounded by fatigue [210]. These impairments may further increase proprioceptive testing variability.

Relationship between Ankle Proprioception and Lower Extremity Motor Impairment

Consistent with other studies [96], [182], [183], [184] we did not find a significant relationship between ankle proprioception and LE motor impairment in our sample of persons with a stroke. No relationship we tested had a significance value less than 0.2. It might be that other measures of LE motor impairment might lead to significant results, but the three we tested here – active ROM, dorsiflexion strength, and LEFM score – are widely used and clinically relevant. A more likely possibility is that the neural tracts and circuits supporting ankle proprioception are anatomically distinct from those supporting LE motor function. Thus, when a stroke destroys ankle proprioceptive circuitry, it is unlikely to damage LE motor circuitry in a proportional way. Although the LE motor and somatosensory representations in primary motor and somatosensory cortex neighbor each other [211], [212], sensory-motor control of LE motion during walking is to some degree offloaded to the spinal cord [213], [214], [215]. Thus, damage to cortical sensory-motor areas may induce LE sensory deficits but have smaller consequences for gait function.

Limitations

This study has several limitations. First, while the sample size of 39 is considered adequate in statistical theory for performing correlation analysis [216], increasing the sample size might make the detection of any weak correlative relationships more robust. Second, we deployed only two specific proprioceptive tests, and only measured proprioceptive acuity at the ankle joint. A recent review by Horvath et al., highlights that errors measured with different proprioceptive assessments or at different joints do not appear to generalize, at least for young unimpaired persons and persons with peripheral nervous system damage, suggesting that each proprioceptive assessment tests a different aspect of proprioception [56]. If different proprioceptive assessments test different underlying mechanisms, changing the method of proprioceptive assessment may change the result. Third, there may be aspects of gait function with which ankle proprioception is more strongly related. For example, this study did not test walking in dark conditions or include an assessment specifically focused on balance [16], although we would expect deficits in balance should be reflected in gait speed.

CHAPTER 8: CONCLUSION

The lack of understanding concerning the high variability of stroke impaired individuals' response to movement rehabilitation is a major gap in stroke rehabilitation research that was identified at the start of this dissertation. Understanding this variability can potentially reduce the cost and increase the efficacy of post-stroke rehabilitation. A biological measurement that shows promise in predicting treatment responders is proprioception. Therefore, in this dissertation, we designed and validated robotic assessment infrastructure for supporting an NIH-funded RCT at UCI that is using a brain computer interface (BCI) with functional electrical stimulation (FES) to treat footdrop of chronic stroke participants. At the onset of the UCI BCI-FES RCT, we identified a need for a precise, valid test of ankle proprioception. The robotic technology described in this description provided this proprioception test, as well as several novel insights into ankle proprioception and ankle sensory motor assessment.

SUMMARY OF NOVVEL CONTRIBUTIONS OF THE DISSERTATION

We began by describing the design and specifications of the novel, platform-based robot called Ankle Measuring Proprioception Device (AMPD) (Chapter 2). AMPD was designed for assessing ankle proprioception as well as ankle range of motion (ROM) and strength (MVC). We described in detail the mechanical and software systems for both version 1 (AMPD 1.0) and version 2 (2AMPD). The key design concept behind both AMPD robots is that they have two impedance states, mechanically rigid and mechanically transparent, which are chosen by manually engaging (locking) or disengaging (unlocking) the rack and pinion. This allows a high dynamic bandwidth (rigid or maximally backdriveable) with use of low-cost motors. In addition, this design approach simplified the control and safety of the robot, making it well suited for use in the ongoing BCI-FES trial. With these two robots we implemented in the ankles for the first time Crisscross, a sensory assessment that is more advantageous to use in the stroke population with motor control impairments, as well as more common proprioceptive assessment, joint position reproduction.

Using AMPD, we generated new insights into how the parameters of ankle proprioception assessments influence ankle proprioception acuity (Chapter 3). When it comes to implementing a new proprioception assessment, a major question arises, what parameters do I need to control for? Without understanding the parameter space, a misrepresentation of proprioceptive integrity can be elicited. Therefore, we varied the speed at which the ankles moved and the size of workspace for 26 young and 25 older unimpaired participants. Testing a smaller range of motion significantly lowered proprioceptive error ($p < 0.001$) in both groups, but normalizing the error by the maximum possible error that could be achieved caused range of motion to no longer influence acuity. This is because, for Crisscross, proprioceptive acuity linearly scales with range of motion ($r2 = 0.13$, $p < 0.0008$). Normalized Crisscross error provides a means to objectively compare errors from individuals with different testing ranges. We also determined that ankle proprioception has poorer acuity at slower speeds due to greater anticipatory errors ($p < 0.001$). Further, proprioceptive acuity significantly improved near the ends of the range of motion for young and older participants ($p<0.001$) with the greatest error in the mid-extension of the workspace, which could indicate greater involvement of load and joint receptors in this situation. Lastly, across testing parameters, contrary to our expectations, aging did not significantly deteriorate ankle proprioceptive acuity, which warrants further investigation. With this improved understanding of how range of motion and speed affect proprioceptive acuity, we used similar slower speeds to evaluate the validity of Crisscross in a subsequent study.

Specifically, we studied the concurrent validity of Crisscross against a commonly used technique, joint position reproduction (JPR) in young and older unimpaired participants, and participants in the chronic phase of stroke, where the older unimpaired participants were age-matched to the stroke participants (Chapter 4). Previous studies have led to the assertion that proprioception acuity is method-specific [56], [144], [145], causing a potential problem for selecting an assessment for a clinical trial. First, we determined proprioception accuracy was significantly worse after stroke compared to age-matched controls as expected. However, older participants did not have significantly worse proprioceptive acuity compared to younger participants, suggesting that ankle proprioception accuracy was preserved into at least 60 years old. Second, we determined that proprioceptive acuity was significantly better when using an active proprioception assessment (JPR) ($p < 0.05$), suggesting actively moving the ankle during the assessment improved proprioceptive estimation. Third, we found that generalization occurred between Crisscross and JPR error in older and stroke participants, but not in young participants. This demonstrated a level of generalization in these populations, and suggesting neural machinery vulnerable to aging or stroke is shared between assessments. Last, the data suggested that proprioceptive accuracy is driven primarily by integrating velocity signals rather than by directly sensing position for JPR. These results demonstrated that Crisscross is a valid ankle proprioceptive assessment, and that both the Crisscross and JPR proprioceptive assessments provide novel information about the role of age, active movement, and velocity-related signals in ankle proprioceptive accuracy.

Zooming out and looking at proprioception from a holistic view, we posed the question: is proprioception a body general attribute or a site-specific attribute? That is, to what extent do individuals who perform better/worse on a proprioceptive task at one joint also perform better/worse at other joints (Chapter 5). Previous studies have led to the assertion that proprioception is not only method-specific but also site-specific [56], [144], [145]. Therefore, using our passive assessment Crisscross, we assessed ankle and finger proprioception acuity for 26 young and 25 older unimpaired participants, and determined that, first, as expected, finger acuity is significantly better for the fingers than the ankles ($p < 0.01$). Second, ankle proprioception acuity was weakly correlated with finger proprioception acuity in young and older participants ($r = 0.40 – 0.49$, $p < 0.05$). These results indicate that there is a body-general component to proprioceptive processing in young and older unimpaired individuals.

AMPD was designed for assessing ankle proprioception as well as ankle range of motion (ROM) and strength (or "maximum voluntary contraction" – MVC. Now focusing on ankle ROM and strength, we questioned if AMPD is as effective as skilled therapists at quantifying ankle ROM and dorsiflexion MVC (Chapter 6). In 34 persons post-stroke we measured robotic test-retest reliability and validity and compared them to experienced therapists making the same measurements in the same persons using a goniometer and manual muscle testing. To further test the reliability of AMPD, we included 36 young and 26 older unimpaired adults. Like a skilled therapist, AMPD is highly reliable for evaluating ankle ROM but captures a larger ROM possibly due to the foot pedal support at the ankle. Also, AMPD has an advantage in both reliability and resolution for measuring MVC.

Finally, we sought to understand how our novel assessment, Crisscross, and a commonly used assessment, JPR, relate to ankle motor impairment and gait function after stroke (Chapter 7). We assessed 39 individuals in the chronic phase of stroke and found proprioceptive acuity measured with JPR was moderately correlated with gait speed, but ankle proprioceptive acuity using either proprioceptive assessment did not correlate with lower extremity motor impairment. These results confirm the presence of a weak relationship between ankle proprioception and gait after stroke that is independent of motor impairment.

Together these results demonstrate the reliability and validity of a novel platform-based robot (AMPD) for assessing ankle proprioception, as well as for assessing ankle ROM and MVC. Also, these results for the first time provide insight into on how ankle proprioceptive assessment parameters affect proprioception acuity, identifying a component of proprioception processing that is body-general (i.e. shared between the fingers and ankles), and showing that baseline proprioception predicts gait speed in a group of 39 person's post-stroke. Ultimately, besides making these fundamental contributions, this work also lays the groundwork for determining whether lower extremity proprioception acuity predicts responders to gait rehabilitation after stroke. At the time of writing of this dissertation, AMPD has been used to evaluate proprioception, ROM, and MVC in over 40 individuals post-stroke who have enrolled in the ongoing BCI-FES RCT at UCI.

FUTURE WORK

We briefly identify three important directions for future research on ankle proprioception using robotics technology.

There are a large number of research studies that have that found age degrades proprioception [74], [75], [117], [217]. Interestingly, we found the opposite for the ankle: older individuals had better proprioceptive acuity, particularly when measured as timing error using Crisscross. Future work should add a group of middle-aged participants, similar to [117], as well as very old participants, to determine if this finding is caused by inclusion of older participants in the younger range of aging (50 to 60 yrs). Understanding the factors that preserve ankle proprioceptive acuity into aging is another important direction for future research.

Future work could also create computational models representing proprioceptive assessments. Currently there is a lack of computational models that explain the known features of ankle proprioception acuity, to which this dissertation contributed several new findings. Models could combine aspects of neurophysiological factors and cognition to explain the observed patterns in young and older unimpaired participants, and then apply these models to individuals post-stroke. Modeling proprioception would improve our mechanistic understanding of sensory function and suggest further experiments.

Lastly, future work should determine if ankle proprioception acuity predicts response to movement rehabilitation. As described above, we have collected a large data set to answer this question as part of the BCI-FES RCT at UCI, which is scheduled to complete in 2024. Once the trial completes, we will analyze how well Crisscross results predict changes in gait speed after therapy. AMPD could also be used in other populations with motor and sensory impairments, such as individuals with cerebral palsy or spinal cord injury, to determine if Crisscross is a sensitive and effective assessment in these populations as well.

REFERENCES

[1] B. F. Mentiplay, B. Adair, K. J. Bower, G. Williams, G. Tole, and R. A. Clark, “Associations between lower limb strength and gait velocity following stroke: A systematic review,” *Brain Inj*, vol. 29, no. 4, pp. 409–422, Apr. 2015, doi: 10.3109/02699052.2014.995231.

[2] V. L. Feigin *et al.*, “Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019,” *Lancet Neurol*, vol. 20, no. 10, pp. 795–820, 2021, doi: https://doi.org/10.1016/S1474-4422(21)00252-0.

[3] E. S. Donkor, “Stroke in the 21st Century: A Snapshot of the Burden, Epidemiology, and Quality of Life,” *Stroke Res Treat*, vol. 2018, 2018, doi: 10.1155/2018/3238165.

[4] P. W. Duncan *et al.*, “Body-weight-supported treadmill rehabilitation after stroke,” *N Engl J Med*, vol. 364, no. 21, pp. 2026–2036, May 2011, doi: 10.1056/NEJMOA1010790.

[5] J. W. Sturm, H. M. Dewey, G. A. Donnan, R. A. L. Macdonell, J. J. McNeil, and A. G. Thrift, “Handicap After Stroke: How Does It Relate to Disability, Perception of Recovery, and Stroke Subtype?,” *Stroke*, vol. 33, no. 3, pp. 762–768, Mar. 2002, doi: 10.1161/hs0302.103815.

[6] Y. Yu, Y. Chen, T. Lou, and X. Shen, “Correlation Between Proprioceptive Impairment and Motor Deficits After Stroke: A Meta-Analysis Review,” *Front Neurol*, vol. 12, p. 688616, Jan. 2022, doi: 10.3389/FNEUR.2021.688616/BIBTEX.

[7] J.-E. Cho, J.-H. Shin, and H. Kim, “Does electrical stimulation synchronized with ankle movements better improve ankle proprioception and gait kinematics in chronic stroke? A randomized controlled study,” *NeuroRehabilitation*, vol. Preprint, no. Preprint, pp. 1–11, May 2022, doi: 10.3233/NRE-220018.

[8] J. B. Rowe, V. Chan, M. L. Ingemanson, S. C. Cramer, E. T. Wolbrecht, and D. J. Reinkensmeyer, “Robotic Assistance for Training Finger Movement Using a Hebbian Model: A Randomized Controlled Trial,” *Neurorehabil Neural Repair*, vol. 31, no. 8, pp. 769–780, Aug. 2017, doi: 10.1177/1545968317721975.

[9] K. Narayan Arya, R. Verma, R. Garg, V. Sharma, M. Agarwal, and G. Aggarwal, “Topics in Stroke Rehabilitation Meaningful Task-Specific Training (MTST) for Stroke Rehabilitation: A Randomized Controlled Trial Meaningful Task-Specifi c Training (MTST) for Stroke Rehabilitation: A Randomized Controlled Trial,” *Top Stroke Rehabil*, vol. 19, no. 3, pp. 193–211, 2012, doi: 10.1310/tsr1903-193.

[10] C. Colomer, E. Noé, and R. Llorens, “Mirror therapy in chronic stroke survivors with severely impaired upper limb function: A randomized controlled trial”.

[11] S.-W. Park, S. L. Wolf, S. Blanton, C. Winstein, and D. S. Nichols-Larsen, “The EXCITE Trial: Predicting a Clinically Meaningful Motor Activity Log Outcome,” 2008, doi: 10.1177/1545968308316906.

[12] C. D. Gordon, R. Wilks, and A. McCaw-Binns, “Effect of aerobic exercise (walking) training on functional status and health-related quality of life in chronic stroke survivors: A randomized

controlled trial," *Stroke*, vol. 44, no. 4, pp. 1179–1181, Apr. 2013, doi: 10.1161/STROKEAHA.111.000642/FORMAT/EPUB.

[13] C. Globas *et al.*, "Chronic Stroke Survivors Benefit From High-Intensity Aerobic Treadmill Exercise: A Randomized Controlled Trial," *Neurorehabil Neural Repair*, vol. 26, no. 1, pp. 85–95, doi: 10.1177/1545968311418675.

[14] A. L. Faria, M. S. Pinho, and S. Bermúdez I Badia, "A comparison of two personalization and adaptive cognitive rehabilitation approaches: a randomized controlled trial with chronic stroke patients", doi: 10.1186/s12984-020-00691-5.

[15] G. Kwakkel *et al.*, "Effects of Unilateral Upper Limb Training in Two Distinct Prognostic Groups Early after Stroke: The EXPLICIT-Stroke Randomized Clinical Trial," *Neurorehabil Neural Repair*, vol. 30, no. 9, pp. 804–816, Oct. 2016, doi: 10.1177/1545968315624784/FORMAT/EPUB.

[16] C. J. Winstein *et al.*, "Effect of a Task-Oriented Rehabilitation Program on Upper Extremity Recovery Following Motor Stroke: The ICARE Randomized Clinical Trial," 2009, doi: 10.1001/jama.2016.0276.

[17] S. Mudge, P. A. Barber, and N. S. Stott, "Circuit-Based Rehabilitation Improves Gait Endurance but Not Usual Walking Activity in Chronic Stroke: A Randomized Controlled Trial," *Arch Phys Med Rehabil*, vol. 90, no. 12, pp. 1989–1996, Dec. 2009, doi: 10.1016/J.APMR.2009.07.015.

[18] M. L. Ingemanson *et al.*, "Neural Correlates of Passive Position Finger Sense After Stroke," *Neurorehabil Neural Repair*, vol. 33, no. 9, pp. 740–750, Sep. 2019, doi: 10.1177/1545968319862556.

[19] A. Leardini, J. J. O'Connor, and S. Giannini, "Biomechanics of the natural, arthritic, and replaced human ankle joint," *J Foot Ankle Res*, vol. 7, no. 1, pp. 1–16, Feb. 2014, doi: 10.1186/1757-1146-7-8/FIGURES/12.

[20] X. Zeng, G. Zhu, M. Zhang, and S. Q. Xie, "Reviewing Clinical Effectiveness of Active Training Strategies of Platform-Based Ankle Rehabilitation Robots," *J Healthc Eng*, vol. 2018, p. 2858294, 2018, doi: 10.1155/2018/2858294.

[21] S. Hussain, P. K. Jamwal, and M. H. Ghayesh, "State-of-the-art robotic devices for ankle rehabilitation: Mechanism and control review," *Proc Inst Mech Eng H*, vol. 231, no. 12, pp. 1224–1234, Dec. 2017, doi: 10.1177/0954411917737584/ASSET/IMAGES/LARGE/10.1177_0954411917737584-FIG2.JPEG.

[22] M. G. Alvarez-Perez, M. A. Garcia-Murillo, and J. J. Cervantes-Sánchez, "Robot-assisted ankle rehabilitation: a review," *Disabil Rehabil Assist Technol*, vol. 15, no. 4, pp. 394–408, May 2020, doi: 10.1080/17483107.2019.1578424.

[23] E. J. Benjamin *et al.*, "Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association," *Circulation*, vol. 139, no. 10, pp. e56–e528, Mar. 2019, doi: 10.1161/CIR.0000000000000659.

[24] B. Hobbs and P. Artemiadis, “A Review of Robot-Assisted Lower-Limb Stroke Therapy: Unexplored Paths and Future Directions in Gait Rehabilitation,” *Front Neurorobot*, vol. 14, p. 529640, Apr. 2020, doi: 10.3389/FNBOT.2020.00019/BIBTEX.

[25] N. Tejima, “Advanced Robotics Rehabilitation robotics: a review Noriyuki Tejima Rehabilitation robotics: a review,” *Advanced Robotics*, vol. 14, no. 7, pp. 551–564, 2000, doi: 10.1163/156855301742003.

[26] H. I. Krebs *et al.*, “Rehabilitation robotics: Performance-based progressive robot-assisted therapy,” *Auton Robots*, vol. 15, no. 1, pp. 7–20, Jul. 2003, doi: 10.1023/A:1024494031121/METRICS.

[27] P. K. Jamwal, S. Q. Xie, S. Hussain, and J. G. Parsons, “An Adaptive Wearable Parallel Robot for the Treatment of Ankle Injuries,” *IEEE/ASME Transactions on Mechatronics*, vol. 19, no. 1, pp. 64–75, 2014, doi: 10.1109/TMECH.2012.2219065.

[28] P. W. Duncan *et al.*, “Body-Weight-Supported Treadmill Rehabilitation after Stroke A bs t r ac t,” *N Engl J Med*, vol. 364, pp. 2026–2062, 2011.

[29] H. S. Jørgensen, H. Nakayama, H. O. Raaschou, and T. S. Olsen, “Recovery of walking function in stroke patients: the Copenhagen Stroke Study,” *Arch Phys Med Rehabil*, vol. 76, no. 1, pp. 27–32, 1995, doi: 10.1016/S0003-9993(95)80038-7.

[30] F. Alnajjar, R. Zaier, S. Khalid, and M. Gochoo, “Trends and Technologies in Rehabilitation of Foot Drop: A Systematic Review,” *Expert Rev Med Devices*, vol. 18, no. 1, pp. 31–46, Jan. 2021, doi: 10.1080/17434440.2021.1857729.

[31] H. Abe, A. Michimata, K. Sugawara, N. Sugaya, and S.-I. Izumi, “Improving Gait Stability in Stroke Hemiplegic Patients with a Plastic Ankle-Foot Orthosis,” *Tohoku J Exp Med*, vol. 218, no. 3, pp. 193–199, 2009, doi: 10.1620/tjem.218.193.

[32] H. Gök, A. Küçükdeveci, H. Altinkaynak, G. Yavuzer, and S. Ergin, “Effects of ankle-foot orthoses on hemiparetic gait,” *Clin Rehabil*, vol. 17, no. 2, pp. 137–139, Mar. 2003, doi: 10.1191/0269215503cr605oa.

[33] M. Alam, I. A. Choudhury, and A. Bin Mamat, “Mechanism and Design Analysis of Articulated Ankle Foot Orthoses for Drop-Foot,” *The Scientific World Journal*, vol. 2014, p. 867869, 2014, doi: 10.1155/2014/867869.

[34] A. Vistamehr, S. A. Kautz, and R. R. Neptune, “The influence of solid ankle-foot-orthoses on forward propulsion and dynamic balance in healthy adults during walking,” *Clinical Biomechanics*, vol. 29, no. 5, pp. 583–589, 2014, doi: https://doi.org/10.1016/j.clinbiomech.2014.02.007.

[35] R. van Swigchem, M. Roerdink, V. Weerdesteyn, A. C. Geurts, and A. Daffertshofer, “The capacity to restore steady gait after a step modification is reduced in people with poststroke foot drop using an ankle-foot orthosis,” *Phys Ther*, vol. 94, no. 5, pp. 654–663, 2014, doi: 10.2522/PTJ.20130108.

[36] Q. Miao, M. Zhang, C. Wang, and H. Li, “Towards optimal platform-based robot design for ankle rehabilitation: The state of the art and future prospects,” *J Healthc Eng*, vol. 2018, 2018, doi: 10.1155/2018/1534247.

[37] D. J. Reinkensmeyer, L. Marchal-Crespo, and V. Dietz, *Neurorehabilitation technology*, Third edition. Cham: Springer, 2022.

[38] P. Babu, M. Ratti, R. Rescinito, and M. Panella, “Platform-Based Robot-Assisted Rehabilitation,” Apr. 2022.

[39] A. Rodríguez-Fernández, J. Lobo-Prat, and J. M. Font-Llagunes, “Systematic review on wearable lower-limb exoskeletons for gait training in neuromuscular impairments,” *Journal of NeuroEngineering and Rehabilitation 2021 18:1*, vol. 18, no. 1, pp. 1–21, Feb. 2021, doi: 10.1186/S12984-021-00815-5.

[40] P. K. Jamwal, S. Hussain, and S. Q. Xie, “Review on design and control aspects of ankle rehabilitation robots,” *Disabil Rehabil Assist Technol*, vol. 10, no. 2, pp. 93–101, Mar. 2015, doi: 10.3109/17483107.2013.866986.

[41] P. Babu, M. Ratti, R. Rescinito, K. Vanhaecht, and M. Panella, “Effectiveness of Platform-Based Robot-Assisted Rehabilitation for Musculoskeletal or Neurologic Injuries: A Systematic Review,” *Bioengineering*, vol. 9, Mar. 2022, doi: 10.3390/bioengineering9040129.

[42] J. M. Belda-Lois *et al.*, “Rehabilitation of gait after stroke: A review towards a top-down approach,” *J Neuroeng Rehabil*, vol. 8, no. 1, pp. 1–20, Dec. 2011, doi: 10.1186/1743-0003-8-66/METRICS.

[43] D. Alvarado Flores, A. Pollock, F. Maissan, P. Langhorne, J. Bernhardt, and G. Kwakkel, “Stroke Care 2 Stroke rehabilitation Related papers Mot or Recovery Aft er St roke: a Syst emat ic Review Out come measures in physiot herapy management of pat ient s wit h st roke: a survey int o self-report e… Stroke Care 2 Stroke rehabilitation,” *Lancet*, vol. 377, pp. 1693–702, 2011, Accessed: Oct. 29, 2022. [Online]. Available: http://www.ebrsr.com

[44] R. S. Marshall, E. Zarahn, L. Alon, B. Minzer, R. M. Lazar, and J. W. Krakauer, “Early imaging correlates of subsequent motor recovery after stroke,” *Ann Neurol*, vol. 65, no. 5, pp. 596–602, May 2009, doi: 10.1002/ANA.21636.

[45] R. Lindenberg, L. L. Zhu, T. Rüber, and G. Schlaug, “Predicting functional motor potential in chronic stroke patients using diffusion tensor imaging,” *Hum Brain Mapp*, vol. 33, no. 5, pp. 1040–1051, May 2012, doi: 10.1002/HBM.21266.

[46] K. R. Crafton, A. N. Mark, and S. C. Cramer, “Improved understanding of cortical injury by incorporating measures of functional anatomy”, doi: 10.1093/brain/awg159.

[47] R. Pineiro *et al.*, “Relating MRI changes to motor deficit after ischemic stroke by segmentation of functional motor pathways,” *Stroke*, vol. 31, no. 3, pp. 672–679, 2000, doi: 10.1161/01.STR.31.3.672/FORMAT/EPUB.

[48] E. R. Buch, S. Rizk, P. Nicolo, L. G. Cohen, A. Schnider, and A. G. Guggisberg, “PREDICTING MOTOR IMPROVEMENT AFTER STROKE WITH CLINICAL ASSESSMENT AND DIFFUSION TENSOR IMAGING,” 1924.

[49] C. Stinear, “Prediction of recovery of motor function after stroke,” *Lancet Neurol*, vol. 9, no. 12, pp. 1228–1232, Dec. 2010, doi: 10.1016/S1474-4422(10)70247-7.

[50] S. Hillier, M. Immink, and D. Thewlis, “Assessing Proprioception: A Systematic Review of Possibilities,” *Neurorehabil Neural Repair*, vol. 29, no. 10, pp. 933–949, Nov. 2015, doi: 10.1177/1545968315573055.

[51] D. McNamee and D. M. Wolpert, “Internal Models in Biological Control,” *Annu Rev Control Robot Auton Syst*, vol. 2, no. Volume 2, 2019, pp. 339–364, 2019, doi: https://doi.org/10.1146/annurev-control-060117-105206.

[52] C. M. Harris and D. M. Wolpert, “Signal-dependent noise determines motor planning,” *Nature 1998 394:6695*, vol. 394, no. 6695, pp. 780–784, Aug. 1998, doi: 10.1038/29528.

[53] K. P. Körding and D. M. Wolpert, “Bayesian integration in sensorimotor learning,” *Nature*, vol. 427, no. 6971, pp. 244–247, 2004, doi: 10.1038/nature02169.

[54] I. L. Yeh *et al.*, “Effects of a robot-aided somatosensory training on proprioception and motor function in stroke survivors,” *J Neuroeng Rehabil*, vol. 18, no. 1, pp. 1–11, Dec. 2021, doi: 10.1186/S12984-021-00871-X/FIGURES/5.

[55] M. A. Dimyan *et al.*, “Baseline Predictors of Response to Repetitive Task Practice in Chronic Stroke,” *Neurorehabil Neural Repair*, vol. 36, no. 7, pp. 426–436, Jul. 2022, doi: 10.1177/15459683221095171/ASSET/IMAGES/LARGE/10.1177_15459683221095171-FIG1.JPEG.

[56] Á. Horváth, E. Ferentzi, K. Schwartz, N. Jacobs, P. Meyns, and F. Köteles, “The measurement of proprioceptive accuracy: A systematic literature review,” *J Sport Health Sci*, Apr. 2022, doi: 10.1016/J.JSHS.2022.04.001.

[57] L. A. Connell and S. F. Tyson, “Measures of sensation in neurological conditions: a systematic review,” *http://dx.doi.org/10.1177/0269215511412982*, vol. 26, no. 1, pp. 68–80, Oct. 2011, doi: 10.1177/0269215511412982.

[58] J. Han, G. Waddington, R. Adams, J. Anson, and Y. Liu, “Assessing proprioception: A critical review of methods,” *Journal of Sport and Health Science*, vol. 5, no. 1. Elsevier B.V., pp. 80–90, Mar. 01, 2016. doi: 10.1016/j.jshs.2014.10.004.

[59] S. Hillier, M. Immink, and D. Thewlis, “Assessing Proprioception: A Systematic Review of Possibilities,” *Neurorehabil Neural Repair*, vol. 29, no. 10, pp. 933–949, Nov. 2015, doi: 10.1177/1545968315573055.

[60] I. V. Bonan, F. Gaillard, S. Tasseel Ponche, A. Marquer, P. P. Vidal, and A. P. Yelnik, “Early post-stroke period: A privileged time for sensory re-weighting?,” *J Rehabil Med*, vol. 47, no. 6, pp. 516–522, Jun. 2015, doi: 10.2340/16501977-1968.

[61] H. I. Krebs, N. Hogan, M. L. Aisen, and B. T. Volpe, “Robot-aided neurorehabilitation,” *IEEE Transactions on Rehabilitation Engineering*, vol. 6, no. 1, pp. 75–87, 1998, doi: 10.1109/86.662623.

[62] N. Elangovan, I.-L. Yeh, J. Holst-Wolf, and J. Konczak, “A robot-assisted sensorimotor training program can improve proprioception and motor function in stroke survivors,” in *2019 IEEE*

16th International Conference on Rehabilitation Robotics (ICORR), 2019, pp. 660–664. doi: 10.1109/ICORR.2019.8779409.

[63] L. W. Forrester, A. Roy, H. I. Krebs, and R. F. Macko, "Ankle training with a robotic device improves hemiparetic gait after a stroke," *Neurorehabil Neural Repair*, vol. 25, no. 4, pp. 369–377, May 2011, doi: 10.1177/1545968310388291.

[64] A. B. Farjadian, M. Nabian, A. Hartman, and S.-C. Yen, "Vi-RABT: A Platform-Based Robot for Ankle and Balance Assessment and Training," *J Med Biol Eng*, vol. 38, no. 4, pp. 556–572, 2018, doi: 10.1007/s40846-017-0332-3.

[65] A. C. Schouten, T. A. Boonstra, F. Nieuwenhuis, S. F. Campfens, and H. van der Kooij, "A Bilateral Ankle Manipulator to Investigate Human Balance Control," *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, vol. 19, no. 6, pp. 660–669, 2011, doi: 10.1109/TNSRE.2011.2163644.

[66] S. M. Forster, R. Wagner, and R. E. Kearney, "A bilateral electro-hydraulic actuator system to measure dynamic ankle joint stiffness during upright human stance," in *Proceedings of the 25th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (IEEE Cat. No.03CH37439)*, 2003, pp. 1507-1510 Vol.2. doi: 10.1109/IEMBS.2003.1279630.

[67] C. C. Gordon *et al.*, "2012 ANTHROPOMETRIC SURVEY OF U.S. ARMY PERSONNEL: METHODS AND SUMMARY STATISTICS," 2014.

[68] T. B. Palmer, K. Akehi, R. M. Thiele, D. B. Smith, A. J. Warren, and B. J. Thompson, "Dorsiflexion, Plantar-Flexion, and Neutral Ankle Positions During Passive Resistance Assessments of the Posterior Hip and Thigh Muscles," *J Athl Train*, vol. 50, no. 5, p. 467, May 2015, doi: 10.4085/1062-6050-49.6.04.

[69] V. R. Edgerton *et al.*, "Retraining the injured spinal cord," *J Physiol*, vol. 533, no. Pt 1, p. 15, May 2001, doi: 10.1111/J.1469-7793.2001.0015B.X.

[70] T. Fujita *et al.*, "Functions necessary for gait independence in patients with stroke: A study using decision tree," *Journal of Stroke and Cerebrovascular Diseases*, vol. 29, no. 8, p. 104998, Aug. 2020, doi: 10.1016/J.JSTROKECEREBROVASDIS.2020.104998.

[71] F. S. F. Chia, S. Kuys, and N. Low Choy, "Sensory retraining of the leg after stroke: systematic review and meta-analysis," *Clin Rehabil*, vol. 33, no. 6, pp. 964–979, Jun. 2019, doi: 10.1177/0269215519836461/ASSET/IMAGES/LARGE/10.1177_0269215519836461-FIG4.JPEG.

[72] C. Wutzke, V. Mercer, and M. Lewek, "Influence of Lower Extremity Sensory Function on Locomotor Adaptation Following Stroke: A Review," *Top Stroke Rehabil*, vol. 20, no. 3, pp. 233–240, Jan. 2013, doi: 10.1310/TSR2003-233.

[73] H. Piitulainen, S. Seipäjärvi, J. Avela, T. Parviainen, and S. Walker, "Cortical Proprioceptive Processing Is Altered by Aging," *Front Aging Neurosci*, vol. 10, 2018, [Online]. Available: https://www.frontiersin.org/articles/10.3389/fnagi.2018.00147

[74] X. Chen and X. Qu, "Age-Related Differences in the Relationships Between Lower-Limb Joint Proprioception and Postural Balance," *Hum Factors*, vol. 61, no. 5, pp. 702–711, Aug. 2018, doi: 10.1177/0018720818795064.

[75] M. Henry and S. Baudry, "Age-related changes in leg proprioception: implications for postural control," *J Neurophysiol*, vol. 122, no. 2, pp. 525–538, Jun. 2019, doi: 10.1152/jn.00067.2019.

[76] J. Han, G. Waddington, R. Adams, J. Anson, and Y. Liu, "Assessing proprioception: A critical review of methods," *Journal of Sport and Health Science*, vol. 5, no. 1. Elsevier B.V., pp. 80–90, Mar. 2016. doi: 10.1016/j.jshs.2014.10.004.

[77] S. Maggioni *et al.*, "Robot-aided assessment of lower extremity functions: A review," *Journal of NeuroEngineering and Rehabilitation*, vol. 13, no. 1. BioMed Central Ltd., pp. 1–25, Aug. 02, 2016. doi: 10.1186/s12984-016-0180-3.

[78] S. C. Gandevia, L. A. Hall, D. I. McCloskey, and E. K. Potter, "Proprioceptive sensation at the terminal joint of the middle finger.," *J Physiol*, vol. 335, no. 1, pp. 507–517, 1983, doi: 10.1113/jphysiol.1983.sp014547.

[79] U. Proske and S. C. Gandevia, "The proprioceptive senses: their roles in signaling body shape, body position and movement, and muscle force.," *Physiol Rev*, vol. 92, no. 4, pp. 1651–97, 2012, doi: 10.1152/physrev.00048.2011.

[80] N. Kakuda and M. Nagaoka, "Dynamic response of human muscle spindle afferents to stretch during voluntary contraction," *J Physiol*, vol. 513, no. Pt 2, p. 621, Dec. 1998, doi: 10.1111/J.1469-7793.1998.621BB.X.

[81] A. Prochazka, "Proprioception: clinical relevance and neurophysiology," *Curr Opin Physiol*, vol. 23, p. 100440, 2021, doi: 10.1016/j.cophys.2021.05.003.

[82] D. J. Goble, "Proprioceptive acuity assessment via joint position matching: from basic science to general practice," *Phys Ther*, vol. 90, no. 8, pp. 1176–1184, Aug. 2010, doi: 10.2522/PTJ.20090399.

[83] D. J. Goble and S. H. Brown, "Dynamic proprioceptive target matching behavior in the upper limb: Effects of speed, task difficulty and arm/hemisphere asymmetries," *Behavioural Brain Research*, vol. 200, no. 1, pp. 7–14, Jun. 2009, doi: 10.1016/J.BBR.2008.11.034.

[84] C. A. Johnson, D. S. Reinsdorf, D. J. Reinkensmeyer, and A. J. Farrens, "Robotically quantifying finger and ankle proprioception: Role of range, speed, anticipatory errors, and learning." Accessed: Nov. 15, 2023. [Online]. Available: https://arinex.com.au/EMBC/pdf/full-paper_1006.pdf

[85] K. M. Refshauge, R. Chan, J. L. Taylor, and D. I. McCloskey, "Detection of movements imposed on human hip, knee, ankle and toe joints," *J Physiol*, vol. 488 (Pt 1), no. Pt 1, pp. 231–241, Oct. 1995, doi: 10.1113/JPHYSIOL.1995.SP020961.

[86] M. L. Ingemanson, J. B. Rowe, V. Chan, E. T. Wolbrecht, S. C. Cramer, and D. J. Reinkensmeyer, "Use of a robotic device to measure age-related decline in finger proprioception," *Exp Brain Res*, vol. 234, no. 1, pp. 83–93, 2016, doi: 10.1007/s00221-015-4440-4.

[87] M. L. Ingemanson, J. R. Rowe, V. Chan, E. T. Wolbrecht, D. J. Reinkensmeyer, and S. C. Cramer, "Somatosensory system integrity explains differences in treatment response after stroke," *Neurology*, vol. 92, no. 10, pp. E1098–E1108, 2019, doi: 10.1212/WNL.0000000000007041.

[88] J. B. Rowe, V. Chan, M. L. Ingemanson, S. C. Cramer, E. T. Wolbrecht, and D. J. Reinkensmeyer, "Robotic Assistance for Training Finger Movement Using a Hebbian Model: A Randomized Controlled Trial," *Neurorehabil Neural Repair*, vol. 31, no. 8, pp. 769–780, 2017, doi: 10.1177/1545968317721975.

[89] M. L. Ingemanson *et al.*, "Neural Correlates of Passive Position Finger Sense After Stroke," *Neurorehabil Neural Repair*, vol. 33, no. 9, pp. 740–750, 2019, doi: 10.1177/1545968319862556.

[90] J. Lönn, A. G. Crenshaw, M. Djupsjöbacka, J. Pedersen, and H. Johansson, "Position sense testing: Influence of starting position and type of displacement," *Arch Phys Med Rehabil*, vol. 81, no. 5, pp. 592–597, May 2000, doi: 10.1016/S0003-9993(00)90040-6.

[91] M. Henry and S. Baudry, "Age-related changes in leg proprioception: Implications for postural control," *J Neurophysiol*, vol. 122, no. 2, pp. 525–538, Aug. 2019, doi: 10.1152/JN.00067.2019/ASSET/IMAGES/LARGE/Z9K0071951360003.JPEG.

[92] A. Prochazka, "Proprioception: clinical relevance and neurophysiology," *Curr Opin Physiol*, vol. 23, p. 100440, 2021, doi: 10.1016/j.cophys.2021.05.003.

[93] S. E. Findlater *et al.*, "Lesion locations associated with persistent proprioceptive impairment in the upper limbs after stroke," 2018, doi: 10.1016/j.nicl.2018.10.003.

[94] U. Proske and S. C. Gandevia, "The proprioceptive senses: Their roles in signaling body shape, body position and movement, and muscle force," *Physiol Rev*, vol. 92, no. 4, pp. 1651–1697, Oct. 2012, doi: 10.1152/PHYSREV.00048.2011/ASSET/IMAGES/LARGE/Z9J0041226360016.JPEG.

[95] Y. Yu, Y. Chen, T. Lou, and X. Shen, "Correlation Between Proprioceptive Impairment and Motor Deficits After Stroke: A Meta-Analysis Review," *Front Neurol*, vol. 12, p. 688616, Jan. 2022, doi: 10.3389/FNEUR.2021.688616/BIBTEX.

[96] T. Gorst *et al.*, "The prevalence, distribution, and functional importance of lower limb somatosensory impairments in chronic stroke survivors: a cross sectional observational study," *Disabil Rehabil*, vol. 41, no. 20, pp. 2443–2450, Sep. 2019, doi: 10.1080/09638288.2018.1468932.

[97] L. A. Connell, N. B. Lincoln, and K. A. Radford, "Somatosensory impairment after stroke: frequency of different deficits and their recovery," *Clin Rehabil*, vol. 22, no. 8, pp. 758–767, Aug. 2008, doi: 10.1177/0269215508090674.

[98] A. T. Patel, P. W. Duncan, S.-M. Lai, and S. Studenski, "The relation between impairments and functional outcomes poststroke," *Arch Phys Med Rehabil*, vol. 81, no. 10, pp. 1357–1363, 2000, doi: https://doi.org/10.1053/apmr.2000.9397.

[99] J. E. Aman, N. Elangovan, I. L. Yeh, and J. Konczak, “The effectiveness of proprioceptive training for improving motor function: A systematic review,” *Front Hum Neurosci*, vol. 8, no. JAN, p. 119864, Jan. 2015, doi: 10.3389/FNHUM.2014.01075/ABSTRACT.

[100] M. L. Ingemanson, J. R. Rowe, V. Chan, E. T. Wolbrecht, D. J. Reinkensmeyer, and S. C. Cramer, “Somatosensory system integrity explains differences in treatment response after stroke,” *Neurology*, vol. 92, no. 10, pp. E1098–E1108, Mar. 2019, doi: 10.1212/WNL.0000000000007041.

[101] J.-E. Cho and H. Kim, “Ankle Proprioception Deficit Is the Strongest Factor Predicting Balance Impairment in Patients With Chronic Stroke,” *Arch Rehabil Res Clin Transl*, vol. 3, no. 4, p. 100165, Dec. 2021, doi: 10.1016/J.ARRCT.2021.100165.

[102] J.-E. Cho, J.-H. Shin, and H. Kim, “Does electrical stimulation synchronized with ankle movements better improve ankle proprioception and gait kinematics in chronic stroke? A randomized controlled study,” *NeuroRehabilitation*, vol. 51, pp. 259–269, 2022, doi: 10.3233/NRE-220018.

[103] A. Roy, L. W. Forrester, R. F. Macko, and H. I. Krebs, “Changes in passive ankle stiffness and its effects on gait function in people with chronic stroke,” vol. 50, no. 4, pp. 555–572, 2013, doi: 10.1682/JRRD.2011.10.0206.

[104] H. G. Seo, S. J. Yun, A. J. Farrens, C. A. Johnson, and D. J. Reinkensmeyer, “A Systematic Review of the Learning Dynamics of Proprioception Training: Specificity, Acquisition, Retention, and Transfer,” *Neurorehabil Neural Repair*, Oct. 2023, doi: 10.1177/15459683231207354/ASSET/IMAGES/LARGE/10.1177_15459683231207354-FIG4.JPEG.

[105] B. H. Dobkin, A. Firestine, M. West, K. Saremi, and R. Woods, “Ankle dorsiflexion as an fMRI paradigm to assay motor control for walking during rehabilitation”, doi: 10.1016/j.neuroimage.2004.06.008.

[106] N. Elangovan, A. Herrmann, and J. Konczak, “Assessing Proprioceptive Function: Evaluating Joint Position Matching Methods Against Psychophysical Thresholds,” 2014, Accessed: Aug. 29, 2022. [Online]. Available: https://academic.oup.com/ptj/article/94/4/553/2735670

[107] A. De Jong, S. L. Kilbreath, K. M. Refshauge, and R. Adams, “Performance in different proprioceptive tests does not correlate in ankles with recurrent sprain,” *Arch Phys Med Rehabil*, vol. 86, no. 11, pp. 2101–2105, Nov. 2005, doi: 10.1016/j.apmr.2005.05.015.

[108] K. R. Grob, M. S. Kuster, S. A. Higgins D G Lloyd, H. Yata, S. A. Higgins, and D. G. Lloyd, “THE JOURNAL OF BONE AND JOINT SURGERY Lack of correlation between different measurements of proprioception in the knee,” *J Bone Joint Surg [Br]*, vol. 84, pp. 614–622, 2002.

[109] D. Kiran, M. Carlson, D. Medrano, and D. R. Smith, “Correlation of three different knee joint position sense measures,” *Physical Therapy in Sport*, vol. 11, no. 3, pp. 81–85, Aug. 2010, doi: 10.1016/J.PTSP.2010.06.002.

[110] H. Kaynak, M. Altun, and S. Tok, “Effect of Force Sense to Active Joint Position Sense and Relationships between Active Joint Position Sense, Force Sense, Jumping and Muscle Strength,” 2019, doi: 10.1080/00222895.2019.1627280.

[111] B. Arnold, C. L. Docherty, B. L. Arnold, S. M. Zinder, K. Granata, and B. M. Gansneder, “Relationship between two proprioceptive measures and stiffness at the ankle,” *Journal of Electromyography and Kinesiology*, vol. 14, pp. 317–324, 2004, doi: 10.1016/S1050-6411(03)00035-X.

[112] N. Elangovan, A. Herrmann, and J. Konczak, “Assessing proprioceptive function: evaluating joint position matching methods against psychophysical thresholds,” *Phys Ther*, vol. 94, no. 4, pp. 553–561, 2014, doi: 10.2522/PTJ.20130103.

[113] N. Yang, G. Waddington, R. Adams, and J. Han, “Joint position reproduction and joint position discrimination at the ankle are not related,” *Somatosens Mot Res*, vol. 37, no. 2, pp. 97–105, Apr. 2020, doi: 10.1080/08990220.2020.1746638.

[114] A. L. Yoss, · Bennett, I. Zuck, J. A. Yem, and W. G. Darling, “High proprioceptive acuity in slow and fast hand movements,” vol. 240, pp. 1791–1800, 2022, doi: 10.1007/s00221-022-06362-2.

[115] E. Yalcin, M. Akyuz, B. Onder, A. Kurtaran, S. Buyukvural, and S. Ozbudak Demir, “Position Sense of the Hemiparetic and Non-Hemiparetic Ankle after Stroke: Is the Non-Hemiparetic Ankle also Affected?,” *Eur Neurol*, vol. 68, no. 5, pp. 294–299, Nov. 2012, doi: 10.1159/000342025.

[116] C. L. Yang, R. A. Creath, L. Magder, M. W. Rogers, and S. M. C. Waller, “Impaired posture, movement preparation, and execution during both paretic and nonparetic reaching following stroke,” *J Neurophysiol*, vol. 121, no. 4, pp. 1465–1477, Apr. 2019, doi: 10.1152/JN.00694.2018/ASSET/IMAGES/LARGE/Z9K0041950100006.JPEG.

[117] M. L. Ingemanson, J. B. Rowe, V. Chan, E. T. Wolbrecht, S. C. Cramer, and D. J. Reinkensmeyer, “Use of a robotic device to measure age-related decline in finger proprioception,” *Exp Brain Res*, vol. 234, no. 1, pp. 83–93, Jan. 2016, doi: 10.1007/s00221-015-4440-4.

[118] M. Zbytniewska-Mégret *et al.*, *Feasibility, usability and effectiveness of a robot-assisted finger proprioception therapy*. 2024. doi: 10.21203/rs.3.rs-3916719/v1.

[119] M. Zbytniewska *et al.*, “Reliable and valid robot-assisted assessments of hand proprioceptive, motor and sensorimotor impairments after stroke,” *J Neuroeng Rehabil*, vol. 18, no. 1, pp. 1–20, Dec. 2021, doi: 10.1186/S12984-021-00904-5/TABLES/1.

[120] K. Severinsen, J. K. Jakobsen, K. Overgaard, and H. Andersen, “Normalized muscle strength, aerobic capacity, and walking performance in chronic stroke: a population-based study on the potential for endurance and resistance training,” *Arch Phys Med Rehabil*, vol. 92, no. 10, pp. 1663–1668, Oct. 2011, doi: 10.1016/J.APMR.2011.04.022.

[121] G. Lee, S. An, Y. Lee, D. Lee, and D. S. Park, “Predictive factors of hypertonia in the upper extremity of chronic stroke survivors,” *J Phys Ther Sci*, vol. 27, no. 8, p. 2545, Aug. 2015, doi: 10.1589/JPTS.27.2545.

[122] Ö. Öken, G. Yavuzer, S. Ergöçen, Z. R. Yorgancioglu, and H. J. Stam, “Repeatability and variation of quantitative gait data in subgroups of patients with stroke,” *Gait Posture*, vol. 27, no. 3, pp. 506–511, Apr. 2008, doi: 10.1016/J.GAITPOST.2007.06.007.

[123] S. E. Kasner, “Clinical interpretation and use of stroke scales,” *Lancet Neurol*, vol. 5, no. 7, pp. 603–612, Jul. 2006, doi: 10.1016/S1474-4422(06)70495-1.

[124] S. J. Page, E. Hade, and A. Persch, “Psychometrics of the wrist stability and hand mobility subscales of the Fugl-Meyer assessment in moderately impaired stroke,” *Phys Ther*, vol. 95, no. 1, pp. 103–108, Jan. 2015, doi: 10.2522/PTJ.20130235.

[125] U. B. Flansbjer, A. M. Holmbäck, D. Downham, C. Patten, and J. Lexell, “Reliability of gait performance tests in men and women with hemiparesis after stroke,” *J Rehabil Med*, vol. 37, no. 2, pp. 75–82, Mar. 2005, doi: 10.1080/16501970410017215.

[126] T. B. Cumming, D. Lowe, T. Linden, and J. Bernhardt, “The AVERT MoCA Data: Scoring Reliability in a Large Multicenter Trial,” *Assessment*, vol. 27, no. 5, pp. 976–981, Jul. 2020, doi: 10.1177/1073191118771516/ASSET/IMAGES/LARGE/10.1177_1073191118771516-FIG3.JPEG.

[127] A. Rezazadeh and M. Berniker, “Force field generalization and the internal representation of motor learning,” *PLoS One*, vol. 14, no. 11, pp. e0225002-, Nov. 2019, [Online]. Available: https://doi.org/10.1371/journal.pone.0225002

[128] N. B. Debats, H. Heuer, and C. Kayser, “Visuo-proprioceptive integration and recalibration with multiple visual stimuli,” *Scientific Reports 2021 11:1*, vol. 11, no. 1, pp. 1–12, Nov. 2021, doi: 10.1038/s41598-021-00992-2.

[129] E. Kararizou, P. Manta, N. Kalfakis, and D. Vassilopoulos, “Morphometric study of the human muscle spindle,” *Anal Quant Cytol Histol*, vol. 27, no. 1, pp. 1–4, 2005, [Online]. Available: https://www.scopus.com/inward/record.uri?eid=2-s2.0-14344252474&partnerID=40&md5=f7fe58c9c23618f381dbd8b091b4b3aa

[130] M. F. Bruce, “The relation of tactile thresholds to histology in the fingers of elderly people.,” *Journal of Neurology, Neurosurgery &amp; Psychiatry*, vol. 43, no. 8, p. 730, Aug. 1980, doi: 10.1136/jnnp.43.8.730.

[131] Y. Morisawa, “Morphological study of mechanoreceptors on the coracoacromial ligament*,” *Journal of Orthopaedic Science*, vol. 3, no. 2, pp. 102–110, 1998, doi: https://doi.org/10.1007/s007760050029.

[132] M. Tanosaki, I. Ozaki, H. Shimamura, M. Baba, and M. Matsunaga, “Effects of aging on central conduction in somatosensory evoked potentials: evaluation of onset versus peak methods,” *Clinical Neurophysiology*, vol. 110, no. 12, pp. 2094–2103, 1999, doi: https://doi.org/10.1016/S1388-2457(99)00193-5.

[133] R. Strong, “Neurochemical changes in the aging human brain: Implications for behavioral impairment and neurodegenerative disease,” *Geriatrics*, vol. 53, no. 1 SUPPL., pp. S9–S12, 1998, [Online]. Available: https://www.scopus.com/inward/record.uri?eid=2-s2.0-0031709338&partnerID=40&md5=51c4702f616150f528aff687e6bc2696

[134] S. Nakamura, I. Akiguchi, M. Kameyama, and N. Mizuno, “Age-related changes of pyramidal cell basal dendrites in layers III and V of human motor cortex: A quantitative Golgi study,” *Acta Neuropathol*, vol. 65, no. 3–4, pp. 281–284, 1985, doi: 10.1007/BF00687009.

[135] D. J. Goble *et al.*, “Brain activity during ankle proprioceptive stimulation predicts balance performance in young and older adults,” *Journal of Neuroscience*, vol. 31, no. 45, pp. 16344–16352, 2011, doi: 10.1523/JNEUROSCI.4159-11.2011.

[136] D. J. Goble *et al.*, “The neural basis of central proprioceptive processing in older versus younger adults: An important sensory role for right putamen,” *Hum Brain Mapp*, vol. 33, no. 4, pp. 895–908, Apr. 2012, doi: 10.1002/HBM.21257.

[137] E. Abela *et al.*, “Grey matter volumetric changes related to recovery from hand paresis after cortical sensorimotor stroke,” *Brain Struct Funct*, vol. 220, no. 5, pp. 2533–2550, 2015, doi: 10.1007/s00429-014-0804-y.

[138] Y. Wang, G. Liu, D. Hong, F. Chen, X. Ji, and G. Cao, “White matter injury in ischemic stroke,” *Prog Neurobiol*, vol. 141, pp. 45–60, 2016, doi: https://doi.org/10.1016/j.pneurobio.2016.04.005.

[139] M. Allegra, C. Favaretto, N. Metcalf, M. Corbetta, and A. Brovelli, “Stroke-related alterations in inter-areal communication,” 2021, doi: 10.1016/j.nicl.2021.102812.

[140] F. Ribeiro and J. Oliveira, “Aging effects on joint proprioception: the role of physical activity in proprioception preservation,” *European Review of Aging and Physical Activity*, vol. 4, no. 2, pp. 71–76, 2007, doi: 10.1007/s11556-007-0026-x.

[141] J. Han, J. Anson, G. Waddington, and R. Adams, “Proprioceptive performance of bilateral upper and lower limb joints: side-general and site-specific effects,” *Exp Brain Res*, vol. 226, pp. 313–323, 2013, doi: 10.1007/s00221-013-3437-0.

[142] B. T. Zazulak, T. E. Hewett, N. P. Reeves, B. Goldberg, and J. Cholewicki, “The Effects of Core Proprioception on Knee Injury: A Prospective Biomechanical-Epidemiological Study,” *Am J Sports Med*, vol. 35, no. 3, pp. 368–373, Mar. 2007, doi: 10.1177/0363546506297909.

[143] B. B. Edin and A. B. Vallbo, “Dynamic response of human muscle spindle afferents to stretch,” *J Neurophysiol*, vol. 63, no. 6, pp. 1297–1306, Jun. 1990, doi: 10.1152/jn.1990.63.6.1297.

[144] J. Han, J. Anson, G. Waddington, and R. Adams, “Proprioceptive performance of bilateral upper and lower limb joints: side-general and site-specific effects,” *Exp Brain Res*, vol. 226, no. 3, pp. 313–323, May 2013, doi: 10.1007/S00221-013-3437-0.

[145] G. Waddington and R. Adams, “Ability to discriminate movements at the ankle and knee is joint specific,” *Percept Mot Skills*, vol. 89, no. 3 Pt 1, pp. 1037–1041, 1999, doi: 10.2466/PMS.1999.89.3.1037.

[146] R. C. Oldfield, “The assessment and analysis of handedness: The Edinburgh inventory,” *Neuropsychologia*, vol. 9, no. 1, pp. 97–113, Mar. 1971, doi: 10.1016/0028-3932(71)90067-4.

[147] H. Taheri *et al.*, “Design and preliminary evaluation of the FINGER rehabilitation robot: Controlling challenge and quantifying finger individuation during musical computer game play,” *J Neuroeng Rehabil*, vol. 11, no. 1, pp. 1–17, 2014, doi: 10.1186/1743-0003-11-10.

[148] V. B. Mountcastle, *The Sensory Hand: Neural Mechanisms of Somatic Sensation*. Harvard University Press, 2005. [Online]. Available: https://books.google.com/books?id=WOmqKSheygYC

[149] J. E. Harris, J. J. Eng, D. S. Marigold, C. D. Tokuno, and C. L. Louis, "Relationship of Balance and Mobility to Fall Incidence in People With Chronic Stroke," *Phys Ther*, vol. 85, no. 2, pp. 150–158, Feb. 2005, doi: 10.1093/PTJ/85.2.150.

[150] P. Y. Lin, Y. R. Yang, S. J. Cheng, and R. Y. Wang, "The Relation Between Ankle Impairments and Gait Velocity and Symmetry in People With Stroke," *Arch Phys Med Rehabil*, vol. 87, no. 4, pp. 562–568, Apr. 2006, doi: 10.1016/J.APMR.2005.12.042.

[151] S. S. Ng and C. W. Hui-Chan, "Contribution of Ankle Dorsiflexor Strength to Walking Endurance in People With Spastic Hemiplegia After Stroke," *Arch Phys Med Rehabil*, vol. 93, 2012, doi: 10.1016/j.apmr.2011.12.016.

[152] D. Kunkel, J. Potter, and L. Mamode, "A cross-sectional observational study comparing foot and ankle characteristics in people with stroke and healthy controls," *Disabil Rehabil*, vol. 39, no. 12, pp. 1149–1154, Jun. 2017, doi: 10.1080/09638288.2016.1189605.

[153] M. Abdalla Alawna, B. H. Unver, and E. O. Yuksel, "The Reliability of a Smartphone Goniometer Application Compared With a Traditional Goniometer for Measuring Ankle Joint Range of Motion".

[154] M. Rabelo, G. S. Nunes, N. M. Da Costa Amante, M. De Noronha, and E. Fachin-Martins, "Reliability of muscle strength assessment in chronic post-stroke hemiparesis: a systematic review and meta-analysis," *Top Stroke Rehabil*, vol. 23, no. 1, pp. 26–35, 2016, doi: 10.1179/1945511915Y.0000000008.

[155] J. Wilken, R. Smita, M. Estin, C. Saltzman, and H. John Yack, "A new device for assessing ankle dorsiflexion motion: reliability and validity," *J Orthop Sports Phys Ther*, vol. 41, no. 4, pp. 274–280, 2011, doi: 10.2519/JOSPT.2011.3397.

[156] M. M. Konor, S. Morton, J. M. Eckerson, and T. L. Grindstaff, "RELIABILITY OF THREE MEASURES OF ANKLE DORSIFLEXION RANGE OF MOTION," *Int J Sports Phys Ther*, vol. 7, no. 3, p. 279, Jun. 2012, Accessed: Mar. 24, 2024. [Online]. Available: /pmc/articles/PMC3362988/

[157] S. Y. Cho, Y. Myong, S. Park, M. Cho, and S. Kim, "A portable articulated dynamometer for ankle dorsiflexion and plantar flexion strength measurement: a design, validation, and user experience study," *Sci Rep*, vol. 13, no. 1, p. 22221, 2023, doi: 10.1038/s41598-023-49263-2.

[158] F. N. Bittmann, S. Dech, M. Aehle, and L. V. Schaefer, "Manual Muscle Testing—Force Profiles and Their Reproducibility," *Diagnostics*, vol. 10, no. 12, Dec. 2020, doi: 10.3390/DIAGNOSTICS10120996.

[159] M. Zhang, T. C. Davies, Y. Zhang, S. Xie, and E. Phd, "Reviewing effectiveness of ankle assessment techniques for use in robot-assisted therapy," vol. 51, no. 4, pp. 517–534, 2014, doi: 10.1682/JRRD.2013.03.0066.

[160] O. Lambercy, S. Maggioni, L. Lünenburger, R. Gassert, and M. Bolliger, “Robotic and Wearable Sensor Technologies for Measurements/Clinical Assessments,” 2016, pp. 183–207. doi: 10.1007/978-3-319-28603-7_10.

[161] J. Mehrholz, S. Thomas, C. Werner, J. Kugler, M. Pohl, and B. Elsner, “Electromechanical-assisted training for walking after stroke,” *Cochrane Database Syst Rev*, vol. 5, no. 5, May 2017, doi: 10.1002/14651858.CD006185.PUB4.

[162] I. Díaz, J. J. Gil, and E. Sánchez, “Lower-Limb Robotic Rehabilitation: Literature Review and Challenges,” *Journal of Robotics*, vol. 2011, p. 759764, 2011, doi: 10.1155/2011/759764.

[163] E. A. S. Duncan and J. Murray, “The barriers and facilitators to routine outcome measurement by allied health professionals in practice: A systematic review,” *BMC Health Serv Res*, vol. 12, no. 1, pp. 1–9, May 2012, doi: 10.1186/1472-6963-12-96/FIGURES/2.

[164] G. Atkinson and A. M. Nevill, “Statistical methods for assessing measurement error (reliability) in variables relevant to sports medicine,” *Sports Medicine*, vol. 26, no. 4, pp. 217–238, Sep. 1998, doi: 10.2165/00007256-199826040-00002/METRICS.

[165] R. P. Kleyweg, F. G. A. Van Der Meché, and P. I. M. Schmitz, “Interobserver agreement in the assessment of muscle strength and functional abilities in Guillain-Barré syndrome,” *Muscle Nerve*, vol. 14, no. 11, pp. 1103–1109, Nov. 1991, doi: 10.1002/MUS.880141111.

[166] T. K. Koo and M. Y. Li, “A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research,” *J Chiropr Med*, vol. 15, no. 2, p. 155, Jun. 2016, doi: 10.1016/J.JCM.2016.02.012.

[167] J. P. WEIR, “QUANTIFYING TEST-RETEST RELIABILITY USING THE INTRACLASS CORRELATION COEFFICIENT AND THE SEM,” *The Journal of Strength & Conditioning Research*, vol. 19, no. 1, 2005, [Online]. Available: https://journals.lww.com/nsca-jscr/fulltext/2005/02000/quantifying_test_retest_reliability_using_the.38.aspx

[168] J. Cohen, “Statistical Power Analysis for the Behavioral Sciences,” *Statistical Power Analysis for the Behavioral Sciences*, May 2013, doi: 10.4324/9780203771587.

[169] A. Gatt and N. Chockalingam, “Validity and reliability of a new ankle dorsiflexion measurement device,” *Prosthet Orthot Int*, vol. 37, no. 4, pp. 289–297, Dec. 2012, doi: 10.1177/0309364612465886.

[170] C. Y. Wang, S. L. Olson, and E. J. Protas, “Test-retest strength reliability: Hand-held dynamometry in community-dwelling elderly fallers,” *Arch Phys Med Rehabil*, vol. 83, no. 6, pp. 811–815, Jun. 2002, doi: 10.1053/APMR.2002.32743.

[171] H. B. Menz, A. Tiedemann, M. M.-S. Kwan, M. D. Latt, C. Sherrington, and S. R. Lord, “Reliability of Clinical Tests of Foot and Ankle Characteristics in Older People,” *J Am Podiatr Med Assoc*, vol. 93, no. 5, pp. 380–387, 2003, doi: 10.7547/87507315-93-5-380.

[172] J. J. Eng, C. M. Kim, and D. L. MacIntyre, “Reliability of lower extremity strength measures in persons with chronic stroke,” *Arch Phys Med Rehabil*, vol. 83, no. 3, pp. 322–328, Mar. 2002, doi: 10.1053/APMR.2002.29622.

[173] E. Frese, M. Brown, and B. J. Norton, "Clinical reliability of manual muscle testing. Middle trapezius and gluteus medius muscles," *Phys Ther*, vol. 67, no. 7, pp. 1072–1076, 1987, doi: 10.1093/PTJ/67.7.1072.

[174] R. W. Bohannon, "Manual muscle testing: does it meet the standards of an adequate screening test?," *Clin Rehabil*, vol. 19, no. 6, pp. 662–667, Sep. 2005, doi: 10.1191/0269215505CR873OA.

[175] J. W. Youdas, C. L. Bogard, and V. J. Suman, "Reliability of goniometric measurements and visual estimates of ankle joint active range of motion obtained in a clinical setting," *Arch Phys Med Rehabil*, vol. 74, no. 10, pp. 1113–1118, Oct. 1993, doi: 10.1016/0003-9993(93)90071-H.

[176] J. T. Choi, J. Lundbye-Jensen, C. Leukel, and J. B. Nielsen, "Cutaneous mechanisms of isometric ankle force control," *Exp Brain Res*, vol. 228, no. 3, pp. 377–384, Jul. 2013, doi: 10.1007/S00221-013-3570-9/FIGURES/3.

[177] N. D. Neckel, N. Blonien, D. Nichols, and J. Hidler, "Abnormal joint torque patterns exhibited by chronic stroke subjects while walking with a prescribed physiological gait pattern," *J Neuroeng Rehabil*, vol. 5, no. 1, pp. 1–13, Sep. 2008, doi: 10.1186/1743-0003-5-19/FIGURES/7.

[178] S. BRUNNSTROM, "Movement therapy in hemiplegia," *A neurophysiological approach*, 1970, Accessed: May 04, 2024. [Online]. Available: https://cir.nii.ac.jp/crid/1574231875545213568.bib?lang=en

[179] S. E. Munteanu, A. B. Strawhorn, K. B. Landorf, A. R. Bird, and G. S. Murley, "A weightbearing technique for the measurement of ankle joint dorsiflexion with the knee extended is reliable," *J Sci Med Sport*, vol. 12, no. 1, pp. 54–59, 2009, doi: https://doi.org/10.1016/j.jsams.2007.06.009.

[180] S. I. Lin, L. J. Hsu, and H. C. Wang, "Effects of Ankle Proprioceptive Interference on Locomotion After Stroke," *Arch Phys Med Rehabil*, vol. 93, no. 6, pp. 1027–1033, Jun. 2012, doi: 10.1016/J.APMR.2012.01.019.

[181] P. Y. Lin, Y. R. Yang, S. J. Cheng, and R. Y. Wang, "The Relation Between Ankle Impairments and Gait Velocity and Symmetry in People With Stroke," *Arch Phys Med Rehabil*, vol. 87, no. 4, pp. 562–568, Apr. 2006, doi: 10.1016/J.APMR.2005.12.042.

[182] S. Nadeau, A. B. Arsenault, D. Gravel, and D. Bourbonnais, "ANALYSIS OF THE CLINICAL FACTORS DETERMINING NATURAL AND MAXIMAL GAIT SPEEDS IN ADULTS WITH A STROKE1," *Am J Phys Med Rehabil*, vol. 78, no. 2, 1999, [Online]. Available: https://journals.lww.com/ajpmr/fulltext/1999/03000/analysis_of_the_clinical_factors_determining.7.aspx

[183] S. I. Lin, "Motor function and joint position sense in relation to gait performance in chronic stroke patients," *Arch Phys Med Rehabil*, vol. 86, no. 2, pp. 197–203, Feb. 2005, doi: 10.1016/J.APMR.2004.05.009.

[184] A. L. Hsu, P. F. Tang, and M. H. Jan, “Analysis of impairments influencing gait velocity and asymmetry of hemiplegic patients after mild to moderate stroke,” *Arch Phys Med Rehabil*, vol. 84, no. 8, pp. 1185–1193, Aug. 2003, doi: 10.1016/S0003-9993(03)00030-3.

[185] T. Gorst, J. Freeman, K. Yarrow, and J. Marsden, “Assessing lower limb position sense in stroke using the gradient discrimination test (GradDT™) and step-height discrimination test (StepDT™): a reliability and validity study,” *Disabil Rehabil*, 2018, doi: 10.1080/09638288.2018.1554008.

[186] M. J. Lee, S. L. Kilbreath, and K. M. Refshauge, “Movement detection at the ankle following stroke is poor,” *Australian Journal of Physiotherapy*, vol. 51, no. 1, pp. 19–24, Jan. 2005, doi: 10.1016/S0004-9514(05)70049-0.

[187] Q. Huang, B. Zhong, N. Elangovan, M. Zhang, and J. Konczak, “A Robotic Device for Measuring Human Ankle Motion Sense,” *IEEE Trans Neural Syst Rehabil Eng*, vol. 31, pp. 2822–2830, 2023, doi: 10.1109/TNSRE.2023.3288550.

[188] M. Zbytniewska *et al.*, “Reliable and valid robot-assisted assessments of hand proprioceptive, motor and sensorimotor impairments after stroke,” *Journal of NeuroEngineering and Rehabilitation 2021 18:1*, vol. 18, no. 1, pp. 1–20, Jul. 2021, doi: 10.1186/S12984-021-00904-5.

[189] L. B. Goldstein, C. Bertels, and J. N. Davis, “Interrater reliability of the NIH stroke scale,” *Arch Neurol*, vol. 46, no. 6, pp. 660–662, 1989, doi: 10.1001/ARCHNEUR.1989.00520420080026.

[190] L. B. Goldstein and G. P. Samsa, “Reliability of the National Institutes of Health Stroke Scale. Extension to non-neurologists in the context of a clinical trial,” *Stroke*, vol. 28, no. 2, pp. 307–310, 1997, doi: 10.1161/01.STR.28.2.307.

[191] P. W. Duncan, M. Propst, and S. G. Nelson, “Reliability of the Fugl-Meyer assessment of sensorimotor recovery following cerebrovascular accident,” *Phys Ther*, vol. 63, no. 10, pp. 1606–1610, 1983, doi: 10.1093/PTJ/63.10.1606.

[192] K. J. Sullivan *et al.*, “Fugl-Meyer assessment of sensorimotor function after stroke: standardized training procedure for clinical practice and clinical trials,” *Stroke*, vol. 42, no. 2, pp. 427–432, Feb. 2011, doi: 10.1161/STROKEAHA.110.592766.

[193] J. H. Lin, I. P. Hsueh, C. F. Sheu, and C. L. Hsieh, “Psychometric properties of the sensory scale of the Fugl-Meyer Assessment in stroke patients,” *Clin Rehabil*, vol. 18, no. 4, pp. 391–397, Jun. 2004, doi: 10.1191/0269215504CR737OA.

[194] J. L. Crow and B. C. Harmeling-Van Der Wel, “Hierarchical properties of the motor function sections of the Fugl-Meyer assessment scale for people after stroke: a retrospective study,” *Phys Ther*, vol. 88, no. 12, pp. 1554–1567, Dec. 2008, doi: 10.2522/PTJ.20070186.

[195] J. J. Eng, P. / Ot, A. S. Dawson, and K. S. Chu, “Submaximal Exercise in Persons With Stroke: Test-Retest Reliability and Concurrent Validity With Maximal Oxygen Consumption,” 2004, doi: 10.1016/S0003-9993(03)00436-2.

[196] G. H. Guyatt *et al.*, “The 6-minute walk: a new measure of exercise capacity in patients with chronic heart failure,” *Can Med Assoc J*, vol. 132, no. 8, p. 919, Apr. 1985, Accessed: Jan. 17, 2024. [Online]. Available: /pmc/articles/PMC1345899/?report=abstract

[197] M. G. Bowden, C. K. Balasubramanian, A. L. Behrman, and S. A. Kautz, “Validation of a speed-based classification system using quantitative measures of walking performance poststroke,” *Neurorehabil Neural Repair*, vol. 22, no. 6, pp. 672–675, Nov. 2008, doi: 10.1177/1545968308318837.

[198] U. B. Flansbjer, A. M. Holmbäck, D. Downham, C. Patten, and J. Lexell, “Reliability of gait performance tests in men and women with hemiparesis after stroke,” *J Rehabil Med*, vol. 37, no. 2, pp. 75–82, Mar. 2005, doi: 10.1080/16501970410017215.

[199] T. B. Scalha, E. Miyasaki, N. M. F. V. Lima, and G. Borges, “Correlations between motor and sensory functions in upper limb chronic hemiparetics after stroke,” *Arq Neuropsiquiatr*, vol. 69, no. 4, pp. 624–629, 2011, doi: 10.1590/S0004-282X2011000500010.

[200] L. A. Connell, N. B. Lincoln, and K. A. Radford, “Somatosensory impairment after stroke: frequency of different deficits and their recovery,” *Clin Rehabil*, vol. 22, no. 8, pp. 758–767, 2008, doi: 10.1177/0269215508090674.

[201] J. Toglia, K. A. Fitzgerald, M. W. O’Dell, A. R. Mastrogiovanni, and C. D. Lin, “The Mini-Mental State Examination and Montreal Cognitive Assessment in persons with mild subacute stroke: relationship to functional outcome,” *Arch Phys Med Rehabil*, vol. 92, no. 5, pp. 792–798, May 2011, doi: 10.1016/J.APMR.2010.12.034.

[202] T. Kaya, A. Goksel Karatepe, R. Gunaydin, A. Koc, and U. Altundal Ercan, “Inter-rater reliability of the Modified Ashworth Scale and modified Modified Ashworth Scale in assessing poststroke elbow flexor spasticity,” *Int J Rehabil Res*, vol. 34, no. 1, pp. 59–64, Mar. 2011, doi: 10.1097/MRR.0B013E32833D6CDF.

[203] J. M. Gregson, M. Leathley, A. P. Moore, A. K. Sharma, T. L. Smith, and C. L. Watkins, “Reliability of the Tone Assessment Scale and the modified Ashworth scale as clinical tools for assessing poststroke spasticity,” *Arch Phys Med Rehabil*, vol. 80, no. 9, pp. 1013–1016, 1999, doi: 10.1016/S0003-9993(99)90053-9.

[204] M. Germanotta *et al.*, “Spasticity measurement based on tonic stretch reflex threshold in children with cerebral palsy using the pediAnklebot,” *Front Hum Neurosci*, vol. 11, p. 240744, May 2017, doi: 10.3389/FNHUM.2017.00277/BIBTEX.

[205] T. Shinohara and S. Usuda, “Association of Ability to Rise from Bed with Improvement of Functional Limitation and Activities of Daily Living in Hemiplegic Inpatients with Stroke: a Prospective Cohort Study,” *J Phys Ther Sci*, vol. 22, no. 1, pp. 29–34, 2010, doi: 10.1589/JPTS.22.29.

[206] U. Proske and S. C. Gandevia, “The Proprioceptive Senses: Their Roles in Signaling Body Shape, Body Position and Movement, and Muscle Force,” *Physiol Rev*, vol. 92, no. 4, pp. 1651–1697, Oct. 2012, doi: 10.1152/physrev.00048.2011.

[207] S. I. Lin, “Motor function and joint position sense in relation to gait performance in chronic stroke patients,” *Arch Phys Med Rehabil*, vol. 86, no. 2, pp. 197–203, Feb. 2005, doi: 10.1016/j.apmr.2004.05.009.

[208] R. J. Peterka, “Sensorimotor integration in human postural control,” *J Neurophysiol*, vol. 88, no. 3, pp. 1097–1118, 2002, doi: 10.1152/JN.2002.88.3.1097.

[209] S. L. Crichton, B. D. Bray, C. McKevitt, A. G. Rudd, and C. D. A. Wolfe, “Patient outcomes up to 15 years after stroke: survival, disability, quality of life, cognition and mental health,” *J Neurol Neurosurg Psychiatry*, vol. 87, no. 10, pp. 1091–1098, Oct. 2016, doi: 10.1136/JNNP-2016-313361.

[210] M. Acciarresi, J. Bogousslavsky, and M. Paciaroni, “Post-stroke fatigue: epidemiology, clinical characteristics and treatment,” *Eur Neurol*, vol. 72, no. 5–6, pp. 255–261, Apr. 2014, doi: 10.1159/000363763.

[211] H. Raju and P. Tadi, “Neuroanatomy, Somatosensory Cortex,” *StatPearls*, Nov. 2022, Accessed: Jan. 24, 2024. [Online]. Available: https://www.ncbi.nlm.nih.gov/books/NBK555915/

[212] M. R. Borich, S. M. Brodie, W. A. Gray, S. Ionta, and L. A. Boyd, “Understanding the role of the primary somatosensory cortex: Opportunities for rehabilitation,” *Neuropsychologia*, vol. 79, pp. 246–255, Dec. 2015, doi: 10.1016/J.NEUROPSYCHOLOGIA.2015.07.007.

[213] J. B. Nielsen, “Sensorimotor integration at spinal level as a basis for muscle coordination during voluntary movement in humans,” *J Appl Physiol*, vol. 96, no. 5, pp. 1961–1967, May 2004, doi: 10.1152/JAPPLPHYSIOL.01073.2003/ASSET/IMAGES/LARGE/ZDG0050430880004.JPEG.

[214] V. Dietz, “Spinal cord pattern generators for locomotion,” *Clinical Neurophysiology*, vol. 114, no. 8, pp. 1379–1389, Aug. 2003, doi: 10.1016/S1388-2457(03)00120-2.

[215] M. P. Côté, L. M. Murray, and M. Knikou, “Spinal control of locomotion: Individual neurons, their circuits and functions,” *Front Physiol*, vol. 9, no. JUN, p. 340854, Jun. 2018, doi: 10.3389/FPHYS.2018.00784/BIBTEX.

[216] J. Fraenkel, N. Wallen, and H. Hyun, *How to Design and Evaluate Research in Education*, vol. 60. 2011.

[217] R. K. Raw, G. K. Kountouriotis, M. Mon-Williams, and R. M. Wilkie, “Movement control in older adults: Does old age mean middle of the road?,” *J Exp Psychol Hum Percept Perform*, vol. 38, no. 3, pp. 735–745, Jun. 2012, doi: 10.1037/A0026568.

[218] G. Colombo, M. Wirz, and V. Dietz, “Driven gait orthosis for improvement of locomotor training in paraplegic patients,” *Spinal Cord*, vol. 39, no. 5, pp. 252–255, 2001, doi: 10.1038/SJ.SC.3101154.

[219] J. F. Veneman, R. Kruidhof, E. E. G. Hekman, R. Ekkelenkamp, E. H. F. Van Asseldonk, and H. Van Der Kooij, “Design and evaluation of the LOPES exoskeleton robot for interactive gait rehabilitation,” *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, vol. 15, no. 3, pp. 379–386, Sep. 2007, doi: 10.1109/TNSRE.2007.903919.

[220] S. K. Banala, S. H. Kim, S. K. Agrawal, and J. P. Scholz, "Robot assisted gait training with active leg exoskeleton (ALEX)," *IEEE Trans Neural Syst Rehabil Eng*, vol. 17, no. 1, pp. 2–8, Feb. 2009, doi: 10.1109/TNSRE.2008.2008280.

[221] S. Hesse, D. Uhlenbrock, C. Werner, and A. Bardeleben, "A mechanized gait trainer for restoring gait in nonambulatory subjects," *Arch Phys Med Rehabil*, vol. 81, no. 9, pp. 1158–1161, 2000, doi: 10.1053/apmr.2000.6280.

[222] H. Schmidt, C. Werner, R. Bernhardt, S. Hesse, and J. Krüger, "Gait rehabilitation machines based on programmable footplates," *J Neuroeng Rehabil*, vol. 4, no. 1, pp. 1–7, Feb. 2007, doi: 10.1186/1743-0003-4-2/FIGURES/3.

[223] A. Esquenazi, M. Talaty, A. Packel, and M. Saulino, "The ReWalk powered exoskeleton to restore ambulatory function to individuals with thoracic-level motor-complete spinal cord injury," *Am J Phys Med Rehabil*, vol. 91, no. 11, pp. 911–921, Nov. 2012, doi: 10.1097/PHM.0B013E318269D9A3.

[224] E. Strickland, "Good-bye, wheelchair," *IEEE Spectr*, vol. 49, no. 1, pp. 30–32, Jan. 2012, doi: 10.1109/MSPEC.2012.6117830.

[225] C. Hartigan *et al.*, "Mobility Outcomes Following Five Training Sessions with a Powered Exoskeleton," *Top Spinal Cord Inj Rehabil*, vol. 21, no. 2, pp. 93–99, Mar. 2015, doi: 10.1310/SCI2102-93.

[226] J. A. Saglia, N. G. Tsagarakis, J. S. Dai, and D. G. Caldwell, "Control strategies for patient-assisted training using the ankle rehabilitation robot (ARBOT)," *IEEE/ASME Transactions on Mechatronics*, vol. 18, no. 6, pp. 1799–1808, 2013, doi: 10.1109/TMECH.2012.2214228.

[227] A. B. Farjadian, M. Nabian, A. Hartman, and S. C. Yen, "Vi-RABT: A Platform-Based Robot for Ankle and Balance Assessment and Training," *J Med Biol Eng*, vol. 38, no. 4, pp. 556–572, Aug. 2018, doi: 10.1007/S40846-017-0332-3/TABLES/4.

[228] N. A. S. Taylor, R. H. Sanders, E. I. Howick, and S. N. Stanley, "Static and dynamic assessment of the Biodex dynamometer," *Eur J Appl Physiol Occup Physiol*, vol. 62, no. 3, pp. 180–188, May 1991, doi: 10.1007/BF00643739/METRICS.

[229] Z. Zhou, Y. Zhou, N. Wang, F. Gao, K. Wei, and Q. Wang, "A proprioceptive neuromuscular facilitation integrated robotic ankle–foot system for post stroke rehabilitation," *Rob Auton Syst*, vol. 73, pp. 111–122, Nov. 2015, doi: 10.1016/J.ROBOT.2014.09.023.