Journal of Clinical and Translational Research
10.18053/Jctres/09.202302.004

ORIGINAL ARTICLE

Spatiotemporal gait and fatigue do not change when using common at-home gait tasks in patients with Facioscapulohumeral Muscular Dystrophy: a pilot study

Nicholas G. Murray[1]*, Marie Kelly[1], Vipul Lugade[2], Ryan Wuebbles[3], Madison Taylor[1], Douglas Powell[4], Takako Jones[3], Peter Jones[3]

1. Neuromechanics Laboratory, School of Public Health, University Of Nevada, Reno, United States of America
2. Decker College of Nursing and Health Sciences, Division of Physical Therapy, Binghamton University, New York, NY, United States of America
3. University of Nevada, Reno School of Medicine, Department of Pharmacology, Reno, NV, United States of America
4. University of Memphis, College of Health Sciences, Memphis, TN, United States of America

*Corresponding Author:
Nicholas Murray
Neuromechanics Laboratory, School of Public Health, University Of Nevada, Reno, 1664 N. Virginia Street m/s 0274, Reno, NV 89557, United States of America.
Tel: +1 775-682-8347
Fax: +1 775-784-1340
Email: nicholasmurray@unr.edu

Article information:
Received: December 20, 2022
Revised: January 23, 2023
Accepted: January 23, 2023

Journal of Clinical and Translational Research
10.18053/Jctres/09.202302.004

Abstract

Background: Facioscapulohumeral Dystrophy (FSHD) is the third most common muscular dystrophy, with para-spinal, trunk, and thigh muscles being affected earlier in the disease progression than previously believed. Gait declines are a possible marker of disease progression of FSHD, however, gait assessment typically requires patients to travel directly to a specific collection site. The introduction of smart-phone applications to measure gait may be a viable way of tracking longitudinal gait decline in FSHD. Yet it is not established which gait tasks are appropriate for this unique and varying population.
Aim: This paper investigates if three commonly used gait tasks in FSHD are appropriate for use in an at-home setting when collected using a smart-phone gait analyzer application.
Methods: Eight genetically confirmed FSHD individuals completed three gait tasks at-home using a custom made smart-phone gait analyzer application. These included the most common gait tasks reported in the FSHD literature 1) 12 consecutive walking trials over a ten-meter level surface, 2) 6 consecutive walking trials across a ten-meter level surface in the morning and afternoon (a minimum of 4 hours between testing) and 3) ambulating for as long as they can for 6-minutes. Two repeated measures ANCOVAs were used to examine velocity and cadence changes across the gait tasks while controlling for shoe type, surface, and the use of an assistive device. Three Wilcoxon Signed Ranks tests analyzed the delta self-reported fatigue score by each gait task.
Results: No significant difference was noted between the three gait tasks for gait velocity and cadence. FSHD patients self-reported that the 6-minute walk test was the most difficult, however, the delta fatigue score was not different between the gait tasks but had a moderate effect size compared to the 12 meter conservative walking. This is most likely due to the small and heterogeneous sample size but indicates the 6-minute walk test may be more physically demanding.
Conclusion: Patients with FHSD can successfully complete varying at-home walking protocols without eliciting a great deal of fatigue or significant change in spatiotemporal gait.
Relevance to patients: These three gait protocols could be used interchangeably for the evaluation of gait in FSHD at-home using the valid and reliable Gait Analyzer application. This will decrease the travel requirements for patients to attend in-person gait evaluations for research and clinical studies.

Keywords: Dystrophy, remote, applications, smart-phone, walking

Journal of Clinical and Translational Research
10.18053/Jctres/09.202302.004

1. Introduction

Facioscapulohumeral Dystrophy (FSHD) is the third most common muscular dystrophy affecting around 1:8,300-15,000 people in the world.[1] Although their lifespan is generally not impacted by the disease, FSHD patients suffer from slow progressive muscle weakness and loss of physical abilities [1]. Per clinical reports, the initial onset of disease often includes the facial, upper back, upper arms, and lower abdominal muscles [1]. Lower extremities of FSHD patients are also now a recognized aspect of disease pathogenesis, with muscle loss commonly observed in the tibialis anterior, hamstring, calf, and quadriceps muscle groups [1]. FSHD expressivity and penetrance is highly variable and asymmetric, with the earliest symptoms often going unnoticed and beginning in their early teens, followed by recognition and diagnosis in the second decade of life for males and the third decade for females [1]. Depending on age and disease progression, FSHD patients may suffer from scapular winging, loss of reachable space, abdominal protuberance, inability to perform a sit-up, foot drop, tripping, frequent falls, lumbar lordosis, and general muscle loss as well as other nonmuscular symptoms [1]. The personal, social and economic burden of this rare disease is immense and there is currently no cure or treatment available for FSHD patients [2]. However, clinical trials are underway and noninvasive metrics to track disease decline and therapeutic efficacy are sorely needed. One candidate marker is gait decline.

To successfully navigate their environment, individuals use a locomotion strategy to ensure appropriate balance, weight-bearing, and forward propulsion. Symmetry, timing, and mechanics observed in individual gait patterns can be used to assess fitness, strength, states of injury or repair, and even neurologic and muscle dysfunction [3]. Recent MRI findings from FSHD patients suggest that para-spinal, trunk, and thigh muscles are affected earlier in the disease process than previously believed [4–7]. Weakness of the trunk and lower extremity muscles, present in more than half of FSHD patient participants [7,8], can influence the ability to maintain an upright stance and perform locomotion [9,10]. This muscular weakness is correlated to an increased risk (≈5x) of falling [11], leading to an elevated risk of injury and/or a fear of falling [12]. Fear of falling results in decreased physical activity and increased

muscular disuse, subsequently reducing general health and overall quality of life [3,12]. With additional information regarding their gait pattern, FSHD patients may avoid or identify strategies to overcome these impairments. This may reduce the overall fear of falling and increase overall activity levels.

Many FSHD affected muscle groups are involved in gait and several studies have reported a decrease in walking speed, step length, step time, and step frequency in FSHD patients as measured using motion capture systems [13–15]. These deficits are characteristic of a more conservative gait strategy in an attempt to reduce the risk of falling [16]. Unfortunately, clinical spatiotemporal gait alterations appear to be dependent upon disease severity and may mask mild FSHD cases [15]. For example, those that are categorized as having mild muscular weakness in the pelvis or proximal legs based on the clinical severity scores (CSS) 23 of 30 were not different than healthy controls when assessed using common baseline spatiotemporal gait characteristics [13]. Conversely, among those within the moderate ($3.5 \leq CSS < 5$) muscular weakness classification, patients demonstrated an approximate 60% reduction in walking speed and significantly greater step time and reduced step length when compared to healthy controls [15].

Recent developments using more functional assessments of mobility, specifically the instrumented timed up and go (iTUG), suggests that certain gait characteristics can distinguish between mild and moderate classifications of FSHD compared to normative data [17,18]. Unfortunately, patients can obtain acceptable results during the iTUG even though their true functional capacity is poor [19]. Other research has attempted to overcome this issue by increasing the difficulty of over ground walking such as stepping over an obstacle [8,15] or using more advanced technology like force platforms to ascertain the lower-limb kinetics during gait propulsion [3]. Stepping over an obstacle is not always safe for participants and is at times nearly impossible for more advanced cases of FSHD. Our recent study into FSHD gait metrics [20] using Tekscan force pressure mats observed decreased cadence and gait velocity in FSHD patients relative to age, sex, height, and weight matched participants from the unaffected population. Our study confirmed the findings from other research groups, who used high-cost accelerometers and/or motion capture technology [3,15,17,18], which indicates that certain gait metrics

are now measurable indicators of FSHD disease progression [18]. However, the cost of motion capture and force platform technology is often high, it requires patients to travel directly to a specific collection site, and it relies on highly trained personnel to run the equipment and interpret the results. These barriers have led to relatively low numbers of patients included in these studies and a general lack of statistically significant data sets, particularly in the younger and milder FSHD populations. Therefore, finding a sensitive, portable, low cost, and reproducible method of performing FSHD gait assessments, which can be performed daily by individual FSHD patients without specialist supervision, will greatly reduce the cost of performing this important clinical outcome measure.

Modern smartphones are used by approximately 45% of the world's population [21] and are fairly accurate, depending on the internal accelerometers, in tracking gait features [22,23]. The Gait Analyzer [24] created by Control One LLC, has gained popularity as published research indicates it can accurately track gait of pathological and older adult populations [24–26]. This application was recently validated against a gold standard gait mat [26], acceptable levels of intrarater and interrater reliability [22], and sufficient validity when compared to motion capture [22]. To overcome the barrier of patient travel and to reduce the overall cost of potential clinical trials, it is important to use technology such as the Gait Analyzer to track gait performance at-home. However, this application has yet to be explored in this population alongside the lack of which gait task is the safest and most effective to monitor gait performance.

The purpose of this study was to analyze three commonly used gait tasks reported in the FSHD literature for use in an at-home setting for FSHD patients using a custom gait analyzer application, Gait Analyzer. It was hypothesized that the gait tasks would not change the spatiotemporal characteristics, specifically gait velocity and cadence. It was further hypothesized that fatigue would vary by gait task and the 6-minute walk test would elicit the greatest overall fatigue.

2. Methods

2.1 Participants

Eight (3 female; total sample avg. age = 57±16 years) genetically confirmed FSHD individuals participated in this study. Participants were included based on a familial FSHD1 or FSHD2 genetic diagnosis with confirmed 4qAD4Z4 contractions of 9 repeat units and below (FSHD1) or SMCHD1 mutation (FSHD2) along with patient reported clinical symptoms. In addition, participants self-reported the diagnosis of FSHD via a trained clinician alongside the genetic testing. All participants self-reported that they were mostly active, could easily navigate their home environment, and were able to walk 6-mins continuously. All participants had to be free of lower extremity injury during the past 6-months, existing neurological disorder, and were able to complete the 3-week walking protocol. Participants were allowed to use assistive devices during the walking tasks such as ankle-foot-orthotics, single-arm crutch, cane walker, or similar devices. Participants were excluded if they used a walker, bilateral crutches or did not have any self-reported clinical symptoms. All participants provided written informed consent to the study procedures, which was approved by the University's Institutional Review Board, before enrollment in the study.

2.2 Procedures

2.2.1 Gait Tasks

Participants were mailed an Android LGK20 smartphone that was pre-loaded with a custom Gait Analyzer application and an adjustable activity belt (Rino Valley Running Belt Waist Pack). This application is commercially available for other populations, but with the unique needs of FSHD patients, the application was custom built for this study. Once the phone was received, participants were instructed to securely fashion the phone within the activity belt snugly across their waist at L3 or L4 while they performed the 3 walking tasks at random for 5 of the 7 days during the next 3-weeks. These included:

Task 1 – 12 consecutive trials over a ten-meter level surface (T1) [3,19]

Task 2 – 6 consecutive trials of ten meters level surface in the morning and afternoon (a minimum of 4 hours between testing) (T2) [17,18]

Task 3 - ambulating for as long as they can for 6-minutes (T3) [19]

Participants were instructed to rest between trials if needed, however, they were asked to consistently walk for 6-mins if able. For T1 and T2, participants started and stopped from a resting state between each trials. The resting state between trials allowed for the application to manually determine the end of a trial after a 3-second pause. Participants were asked 1) how they felt (Fatigue Scale [27]) before and after the protocol on a scale of 0 to 10, 2) the surface that they walked on, 3) shoe type, 4) what type of assistive device (if any) they used, 5) did they stop during the trials, if so how long and how many times, 6) did any adverse events occur during the trials such as cramps or loss of breath, and if so the precise nature and description of the adverse event, and 7) the last time they ate a meal. For the walking surface, shoe type, and assistive device, the application allowed them to take a picture of each to be stored which was analyzed by the research team along with recorded answers to the questions. Before any testing, the participants met with one of the researchers via video conferencing software to discuss the procedures, and fit of the device, perform a series of practice gait tasks, and answer any/all questions. Each participant verbally stated that they felt comfortable with the procedures and application after the researchers carefully watched/evaluated their practice gait trials via video conference. Furthermore, the leg length, which was measured from the medial malleolus to the anterior superior iliac spine, was acquired for each participant during this meeting. Each week, a phone call and email reminder were sent to each participant to check on their progress along with answering any questions. After the testing protocol, the research team met with the participants again to discuss the testing protocol and receive any/all feedback.

2.3 Epigenetics

Saliva samples were collected by mail, returned, and de-identified. Genomic DNA was prepared, bisulfite converted, and assayed using our FSHD epigenetic analysis to determine the DNA methylation of the shortest 4q35 D4Z4 array (DRA: D4Z4 reduced allele), as described [28]. Everyone has two chromosome 4s, and in FSHD1 only one is contracted. We assayed the epigenetic status for both the contracted and noncontracted chromosome 4s. With our assay, producing two distinct epigenetic pools, one the contracted array and one from the noncontracted array. By using the first quartile (Q1) methylation percentage, we are assessing the methylation level at 50% of the contracted chromosome 4q D4Z4 arrays [28,29].

2.4 Data Analysis

The "Gait Analyzer" application provided real-time gait spatiotemporal computations, with results saved to a tab-delimited file on the phone following the completion of each walking trial. Online calculations of step time, step length, gait velocity, and cadence, were computed as previously described using each step [22]. This application has high intrarater and interrater reliability [22], sufficient validity when compared to motion capture [22], and high validity and good to high test-retest reliability [26]. Specifically, tri-axial accelerations, which were collected at the smartphone's maximum sampling frequency (Android: SENSOR_DELAY_FASTEST; 95-105 Hz range), were resampled to 100 Hz, to ensure a constant sampling rate. The tri-axial acceleration data were filtered using a 4th order low-pass Butterworth filter with a 20Hz cutoff frequency, and AP accelerations further filtered using a 4th order low-pass Butterworth filter with a 20Hz cutoff frequency. Heel strikes were identified based on positive peaks in the AP direction, with step time (*ST*) calculated as the time difference between these steps. The step length (*SL*) was computed as

$$SL = 2 * \sqrt{2 * h * l - h^2} \qquad \text{(Eq 1)}$$

where *h* is the change in vertical position and *l* is the participant's leg length. The change in vertical position was calculated by double integrating the vertical acceleration, and subsequently filtering the result using a 4th order high-pass Butterworth filter with a 0.1 Hz cutoff frequency to remove integration drift across each step cycle. Step velocity (*SV*) across each step *I* was computed as

$$SV_i = \frac{SL_i}{ST_i} \quad \text{(Eq 2)}$$

with gait velocity reported as the average step velocity across all steps. Cadence was computed as the quotient of the number of steps and the total trial time, in units of steps/min.

For the recorded images, all participants' footwear were coded as tennis shoes, boots, sandal or misc. (i.e. loafers or boat shoes) [30–32]. Walking surfaces were coded as concrete or wood surface [30]. Each participant was instructed to walk using the same footwear and surface across each trial if possible. During the task, we could not remove gait initiation and termination from the data due to ecological validity concerns. Prior research has not removed these gait characteristics and the research team felt it was important to keep them within the dataset [24–26].

2.5 Statistical Analysis

Each gait task trials across the 5 days were ensemble averaged by each week (T1=60 trials, T2=60 trials, and T3=5 trials that were ensemble averaged) for an overall velocity, cadence, and delta fatigue score (post-pre). Descriptive statistics were calculated for all three variables (velocity, cadence, and delta fatigue score) to create a direct comparison of mean and standard deviation along with the assessment of the normality of the data using skewness and kurtosis. If any variable was ±2.0 for skewness or kurtosis, it was considered abnormally distributed. From the descriptives, the data velocity and cadence data were considered parametric and without influential skewness while the delta fatigue score was skewed. Two repeated measures ANCOVAs were run to examine velocity and cadence changes across the gait tasks while controlling for shoe type, surface, and the use of assistive device.

Three Wilcoxon Signed Ranks tests analyzed the delta self-reported fatigue score by each gait task. All statistical analysis were performed by creating a model in Statistical Package for the Social Sciences (SPSS IBM, Armonk, NY 2019) with an *a priori* alpha of 0.05.

3. Results

Across all the walking conditions, 12.5% of participants used tennis shoes, 50.0% used boots, and 37.5% wore miscellaneous shoe types. 62.5% of the participants performed the gait tasks on concrete while 37.5% walked on a solid wood surface. Lastly, 62.5% did not use an assistive device while 37.5% used both an ankle foot orthotic and/or a walking cane. No participants used any type of crutches and no participants reported needing to rest between trials. All participants had eaten before the walking tasks, reported no adverse events and successfully completed all gait tasks (5 consecutive days for 3 weeks). All eight participants had genetically confirmed FHSD 1 and levels of DNA methylation consistent with FSHD (Q1 methylation ranges: 3.6 to 11.7; 4A or 4A/B).

3.1 Gait Velocity

For gait velocity, there was no significant effect of time ($F_{(2,3)}$=1.038, p=0.454, η^2=0.409), no significant interaction for time*shoe type ($F_{(2,3)}$=1.508, p=0.352, η^2=0.501), no significant interaction for time*walking surface ($F_{(2,3)}$=0.021, p=0.980, η^2=0.412) and no significant interaction for time*assistive device ($F_{(2,3)}$=0.052, p=0.950, η^2=0.034) (see Figure. 1). Overall, these results suggest that gait velocity did not change by the varying gait tasks when controlling for shoe type, walking surface or assistive device.

3.2 Cadence

For cadence, there was no significant effect of time ($F_{(2,3)}$=0.213, p=0.819, η^2=0.124), no

significant interaction for time*shoe type ($F_{(2,3)}$=0.050, p=0.952, η^2=0.032), no significant interaction for time*walking surface ($F_{(2,3)}$=0.213, p=0.820, η^2=0.124) and no significant interaction for time*assistive device ($F_{(2,3)}$=0.239, p=0.801, η^2=0.138) (see Figure. 2). These results suggest gait cadence did not change by the varying gait tasks. When controlling for shoe type, walking surface or assistive device.

3.3 Fatigue Score

For the fatigue score, there was no significant difference when comparing T1 to T2 (p=0.109, Cohen's d=0.71), T2 to T3 (p=0.144, Cohen's d=0.62) and T1 to T3 (p=0.500, Cohen's d=0.17) (see Figure 3). These results suggest that fatigue score did not change across the gait tasks, however, participants who reported fatigue indicated on an individual level that T2 elicited the least amount of fatigue followed by T1 and then T3.

4. Discussion

The purpose of this study was to analyze three different at-home gait tasks for use within FSHD patients using a custom gait analyzer application with the long-term goal of assessing gait as an outcome measure for FSHD clinical trials. The results suggest that gait velocity, cadence and fatigue score do not change by the type of gait task. The most important findings of this article indicate that the Gait Analyzer application can measure FSHD gait at-home and the three most common gait tasks used in FSHD research can be used interchangeably. Lastly, it is not necessary to have those with FSHD perform taxing gait tasks, like the 6-minute walk test, when they can perform more simple and less difficult gait tasks. This is important as at-home gait tasks should be some-what challenging, flexible, safe, and require as little effort from FSHD patients as possible to complete and reduce fall risk. Lastly,

The gait velocity in the current study was slower than normative data for usual gait speed [33] across all the varying gait tasks. This is not surprising given the self-reported clinical presentation of

symptoms reported by the patients and the diagnosis of FSHD. These data are similar to other findings in FSHD [3,15,17,18] that demonstrate slower gait velocity and increased cadence associated with FSHD. The declines in gait can be mainly attributed to dystrophy of the para-spinal, trunk, and thigh muscles which are affected earlier in the disease process than previously believed [4–7]. This influences the ability to maintain an upright stance, perform locomotion and is related to increased risk (5x) of falling. Our research suggests that FSHD can perform either of the gait protocols without inducing significant fatigue while the gait outcomes are relatively stable. These data provide a model for expansion research in a wider age range, onset of the disease, and clinical severity.

For T1, the data was similar to prior research with a slightly slower velocity (≈0.98 m/s compared to 0.92 m/s) but a similar cadence [3,19]. The slower velocity could be attributed to some participants using assistive devices along with not cropping the data during gait initiation and termination. For T2, the data followed a similar trend for T1 but mimicked data observed using a shorter (7-meter) timed-up-and-go task [17,18]. T2 did elicit the least amount of fatigue score and could be a viable measure for those with higher clinical severity or older FSHD patients. Lastly, during T3 slower gait velocity and reduced cadence were observed when compared to T1 and T2, however, this change was not significant. Clinically, T1 to T3 had a moderate effect size (Cohen's d = 0.42) while multiple patients self-reported T3 as being the most challenging and difficult of the protocols to complete. The 6-min walk test may be more appropriate for less affected FSHD patients but should elicit similar results to T1 and T2. It is the author's expectation that with a larger sample size and less heterogeneous population, the 6-min walk test self-reported delta fatigue score effect size would reduce. However, the moderate effect size should not be ignored, as it is a warning to clinicians that the 6-min walk test is physically demanding and could be unsafe for more affected FSHD patients. This study included individuals who could complete the 6-min walk test safely unsupervised by the study team. Future research should carefully consider if this test is necessary and appropriate due to the potential fall risk when not conducted in a highly controlled environment.

3.1 Limitations

Limitations to the current study included a small sample size and the inclusion of a wider range of patients (18 to 64 years of age). This can influence the spatiotemporal gait characteristics as it changes over time and within age groups. However, each patient was symptomatic and self-reported notable declines in overall gait function due to the disease. In general, adherence to longitudinal protocols like this study are extremely challenging within disease populations. These data may demonstrate how through the use of a smartphone device, it might be possible to reach larger groups of at-risk, vulnerable patients, who would otherwise not be tested. We had no ability to control the patient's current athletic ability including weekly exercise programs and it is possible that some individuals lead healthier lifestyles. Additionally, if the participants were not actively exercising this at-home walking protocol may have promoted physical activity and increased their gait capacity over time. The use of numerous trials for each protocol may have washed out any increase in gait capacity. Our future research will pursue a standard exercise protocol and/or an exercise log to track exercise capacity in order to control for exercise and reduce it as potential confounder in statistical analysis. Lastly, the inclusion of gait initiation and cessation data will decrease the overall gait velocity and increase the cadence but the data in this current study was very similar to existing research in FSHD populations.

Conclusions

Patients with FHSD can successfully complete varying walking protocols at-home without eliciting a great deal of fatigue or significant change in spatiotemporal gait. These three varying gait protocols could be used interchangeably for differing FSHD clinical severity. It is important to consider what is ideal for each FSHD patient given the progression of their disease, however, this study provides a preliminary survey of numerous commonly used gait tasks for this particular population with the inclusion of their particular walking aids. Future research will assess if gait mechanics change over time relative to disease progression and if gait can be used as a relevant outcome measure for drug efficacy in

clinical trials.

Acknowledgements

The authors would like to thank the FSHD subjects who participated and made this study possible. In addition, we thank the Neuromechanics Lab staff for their outstanding efforts on this project. This grant was partially funded by the Neuroscience COBRE NIGM P20GM103650.

Conflict of Interest Statement

The authors have received no funding from any company or private corporation to complete this research. The authors have no competing or conflicts of interest related to this project.

Journal of Clinical and Translational Research
10.18053/Jctres/09.202302.004

References

1. Hamel J, Tawil R. Facioscapulohumeral Muscular Dystrophy: Update on Pathogenesis and Future Treatments. Neurotherapeutics 2018;15:863-871.

2. Schepelmann K, Winter Y, Spottke AE, et al. Socioeconomic burden of amyotrophic lateral sclerosis, myasthenia gravis and facioscapulohumeral muscular dystrophy. J Neurol 2010;257:15-23.

3. Rijken NHM, van Engelen BGM, de Rooy JWJ, Weerdesteyn V, Geurts ACH. Gait propulsion in patients with facioscapulohumeral muscular dystrophy and ankle plantarflexor weakness. Gait Posture 2015;41:476-481.

4. Dahlqvist JR, Vissing CR, Thomsen C, Vissing J. Severe paraspinal muscle involvement in facioscapulohumeral muscular dystrophy. Neurology 2014;83:1178-1183.

5. Mul K, Vincenten SCC, Voermans NC, et al. Adding quantitative muscle MRI to the FSHD clinical trial toolbox. Neurology 2017;89:2057-2065.

6. Regula JU, Jestaedt L, Jende F, Bartsch A, Meinck HM, Weber MA. Clinical Muscle Testing Compared with Whole-Body Magnetic Resonance Imaging in Facio-scapulo-humeral Muscular Dystrophy. Clin Neuroradiol 2016;26:445-455.

7. Rijken NHM, van der Kooi EL, Hendriks JCM, et al. Skeletal muscle imaging in facioscapulohumeral muscular dystrophy, pattern and asymmetry of individual muscle involvement. Neuromuscul Disord 2014;24:1087-1096.

8. Rijken NHM, van Engelen BGM, de Rooy JWJ, Geurts ACH, Weerdesteyn V. Trunk muscle involvement is most critical for the loss of balance control in patients with facioscapulohumeral muscular dystrophy. Clin Biomech 2014;29:855-860.

9. Halliday SE, Winter DA, Frank JS, Patla AE, Prince F. The initiation of gait in young, elderly, and Parkinson's disease subjects. Gait Posture 1998;8:8-14.

10. Horak FB, Henry SM, Shumway-Cook A. Postural perturbations: new insights for treatment of balance disorders. Phys Ther 1997;77:517-533.

11. Horlings CGC, Munneke M, Bickerstaffe A, et al. Epidemiology and pathophysiology of falls in facioscapulohumeral disease. J Neurol Neurosurg Psychiatry 2009;80:1357-1363.

12. Pieterse AJ, Luttikhold TB, de Laat K, Bloem BR, van Engelen BG, Munneke M. Falls in patients with neuromuscular disorders. J Neurol Sci 2006;251:87-90.

13. Iosa M, Mazzà C, Frusciante R, et al. Mobility assessment of patients with facioscapulohumeral dystrophy. Clin Biomech 2007;22:1074-1082.

14. Iosa M, Mazzà C, Pecoraro F, Aprile I, Ricci E, Cappozzo A. Control of the upper body movements during level walking in patients with facioscapulohumeral dystrophy. Gait Posture 2010;31:68-72.

15. Rijken NHM, van Engelen BGM, Geurts ACH, Weerdesteyn V. Dynamic stability during level

walking and obstacle crossing in persons with facioscapulohumeral muscular dystrophy. Gait Posture 2015;42:295-300.

16. Powell DW, Blackmore SE, Puppa M, et al. Deep brain stimulation enhances movement complexity during gait in individuals with Parkinson's disease. Neurosci Lett 2020;728:133588

17. Huisinga J, Bruetsch A, Mccalley A, et al. An instrumented timed up and go in facioscapulohumeral muscular dystrophy. Muscle Nerve 2018;57:503-506.

18. Statland JM, Karanevich A, Bruetsch A, Huisinga J. A pilot study of the responsiveness of wireless motion analysis in facioscapulohumeral muscular dystrophy. Muscle Nerve 2019;60:590-594.

19. Rijken NH, van Engelen BG, Weerdesteyn V, Geurts AC. Clinical Functional Capacity Testing in Patients With Facioscapulohumeral Muscular Dystrophy: Construct Validity and Interrater Reliability of Antigravity Tests. Arch Phys Med Rehabil 2015;96:2201-2206.

20. Alphonsa S, Wuebbles R, Jones T, Pavilionis P, Murray N. Spatio-temporal gait differences in facioscapulohumeral muscular dystrophy during single and dual task overground walking - A pilot study. Transl Res 2022;8:166-175.

21. Smartphone users 2026. Accessed November 17, 2021. https://www.statista.com/statistics/330695/number-of-smartphone-users-worldwide/

22. Silsupadol P, Teja K, Lugade V. Reliability and validity of a smartphone-based assessment of gait parameters across walking speed and smartphone locations: Body, bag, belt, hand, and pocket. Gait Posture 2017;58:516-522.

23. Wong JS, Jasani H, Poon V, Inness EL, McIlroy WE, Mansfield A. Inter- and intra-rater reliability of the GAITRite system among individuals with sub-acute stroke. Gait Posture 2014;40:259-261.

24. Lugade V, Fortune E, Morrow M, Kaufman K. Validity of using tri-axial accelerometers to measure human movement—Part I: Posture and movement detection. Medical Engineering & Physics 2014;36:169-176.

25. Howell DR, Seehusen CN, Wingerson MJ, Wilson JC, Lynall RC, Lugade V. Reliability and Minimal Detectable Change for a Smartphone-Based Motor-Cognitive Assessment: Implications for Concussion Management. J Appl Biomech 2021;37:380-387.

26. Marie K, Jones P, Wuebbles R, Lugade V, Taylor M, Pavilionis P, Cipriani D, Murray NG. Novel FSHD Gait Analyzer smart phone application is reliable and valid in measuring spatio-temporal gait. Measurement 2022;192:110882.

27. Kim E, Lovera J, Schaben L, Melara J, Bourdette D, Whitham R. Novel method for measurement of fatigue in multiple sclerosis: Real-Time Digital Fatigue Score. J Rehabil Res Dev 2010;47:477-484.

28. Jones TI, Yan C, Sapp PC, et al. Identifying diagnostic DNA methylation profiles for facioscapulohumeral muscular dystrophy in blood and saliva using bisulfite sequencing. Clin Epigenetics 2014;6:23.

29. Jones TI, King OD, Himeda CL, et al. Individual epigenetic status of the pathogenic D4Z4 macrosatellite correlates with disease in facioscapulohumeral muscular dystrophy. Clin Epigenetics

2015;7:37.

30. Dobson JA, Riddiford-Harland DL, Bell AF, Steele JR. Work boot design affects the way workers walk: A systematic review of the literature. Appl Ergon. 2017;61:53-68. doi:10.1016/j.a

31. Martinez-Santos A, Preece S, Nester CJ. Evaluation of orthotic insoles for people with diabetes who are at-risk of first ulceration. J Foot Ankle Res 2019;12:35.

32. Sun X, Lam WK, Zhang X, Wang J, Fu W. Systematic Review of the Role of Footwear Constructions in Running Biomechanics: Implications for Running-Related Injury and Performance. J Sports Sci Med 2020;19:20-37.

33. Bohannon RW, Wang YC. Four-Meter Gait Speed: Normative Values and Reliability Determined for Adults Participating in the NIH Toolbox Study. Arch Phys Med Rehabil 2019;100:509-513.

Journal of Clinical and Translational Research
10.18053/Jctres/09.202302.004

Figures

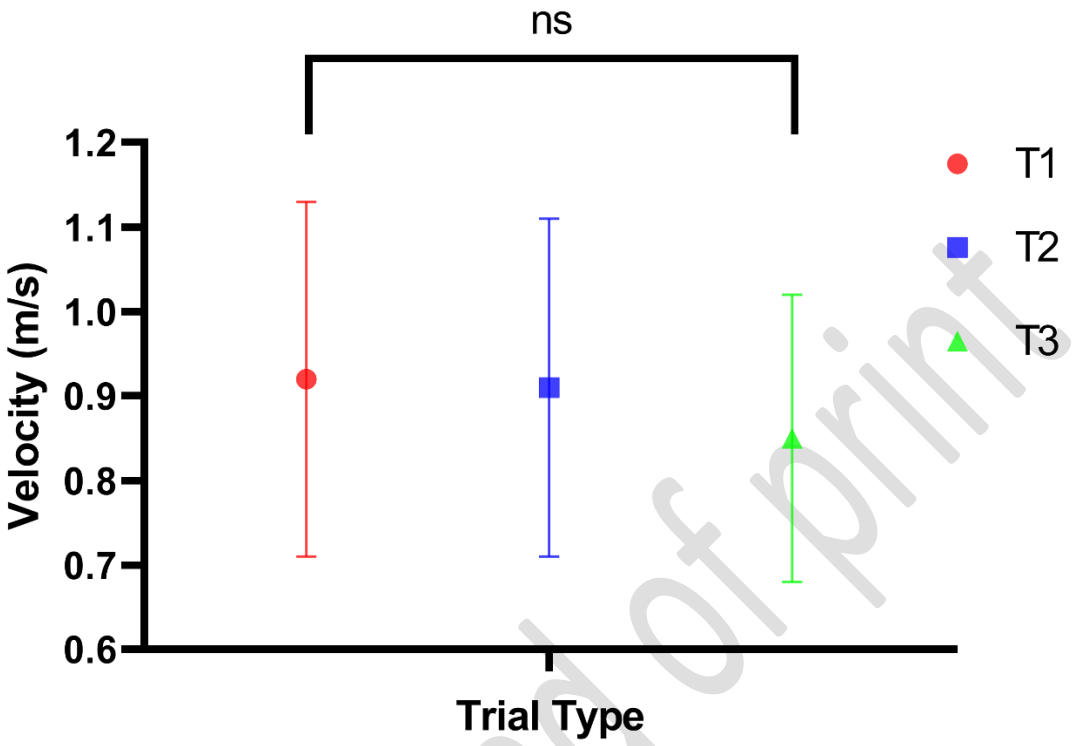

Figure 1. **Gait Analyzer App average FSHD patient gait velocity by gait task.** No statistical difference between the FSHD gait tasks was observed. These data are approximately a 33% reduction in gait velocity compared to normative data. T1 = 12 trials of 10 meters, T2 = 6 trials of 10 meters in the morning and afternoon, T3 = six minute walk test.

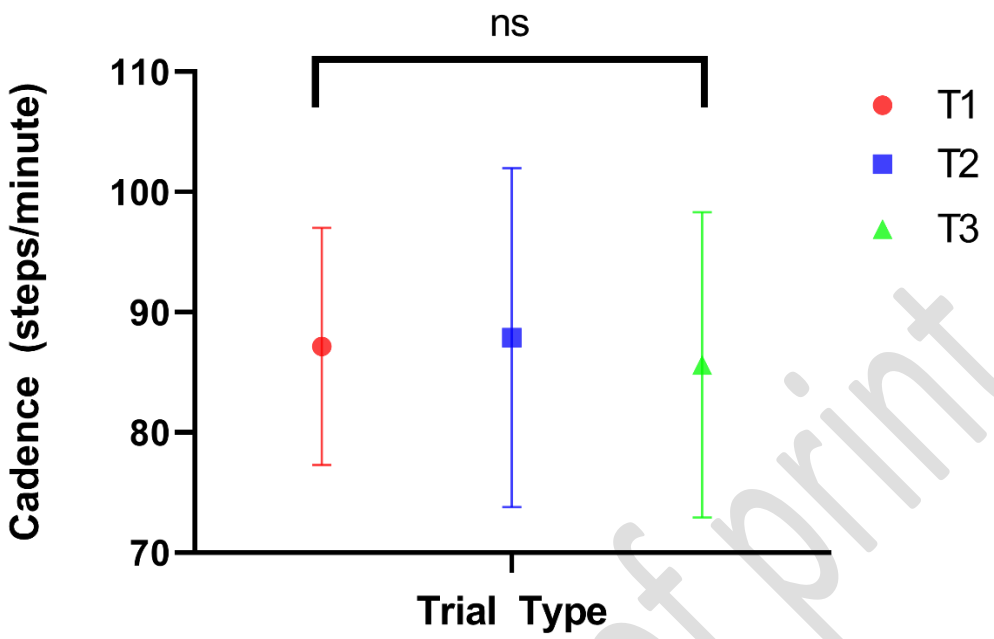

Figure 2. **Gait Analyzer App average FSHD patient cadence by gait task.** No statistical difference between the FSHD gait tasks was observed. T1 = 12 trials of 10 meters, T2 = 6 trials of 10 meters in the morning and afternoon, T3 = six minute walk test.

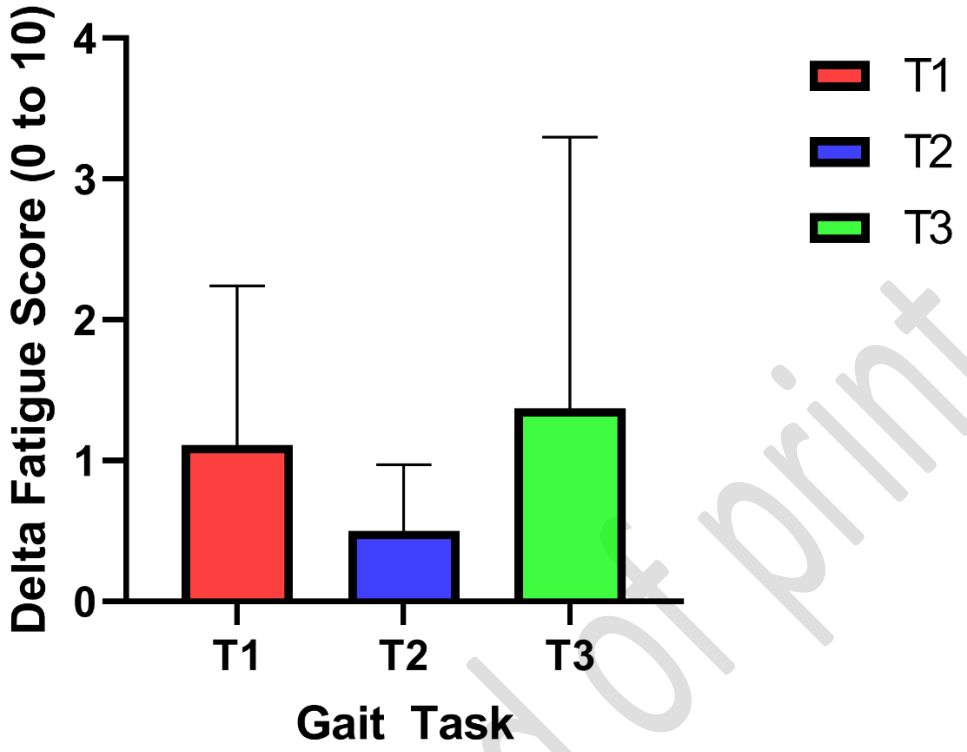

Figure 3. **Average delta fatigue score by gait task.** No statistical difference was noted between the gait tasks, however, T1 compared to T3 demonstrate a moderate effect size (Cohen's d= 0.41). T1 = 12 trials of 10 meters, T2 = 6 trials of 10 meters in the morning and afternoon, T3 = six minute walk test.