Journal of Clinical and Translational Research 2022; 8(2): 166-175

Journal of Clinical and Translational Research

Journal homepage: http://www.jctres.com/en/home

ORIGINAL ARTICLE

Spatio-temporal gait differences in facioscapulohumeral muscular dystrophy during single and dual task overground walking - A pilot study

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ARTICLE INFO

Article history:
Received: October 27, 2021
Revised: December 29, 2021
Accepted: January 11, 2022
Published online: March 19, 2022

Keywords:
dual task paradigm
facioscapulohumeral muscular dystrophy
methylation, multilevel model
muscular dystrophy gait
Tekscan Strideway

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ABSTRACT

Background: Facioscapulohumeral muscular dystrophy (FSHD) is a rare genetic muscle disorder leading to progressive muscle loss over time. Research indicates that this progressive muscular atrophy can negatively impact spatio-temporal gait characteristics, but this is not always the case during early-onset or mild cases of the disease. In addition, the performance of a secondary task during overground walking may elucidate greater deficits in spatio-temporal characteristics of gait. However, such dual task effects on FSHD gait have not been studied thus far.

Aim: The current study aimed to (a) quantify changes in spatio-temporal gait parameters in individuals with FSHD using the Tekscan Strideway gait mat system, (b) measure the dual task (DT) effects on cadence and gait velocity during single task (ST) and DT overground walking in FSHD and healthy controls and (c) investigate the correlation between the gait parameters and the methylation status in FSHD.

Methods: Nine FSHD (M±SD=52.78±14.69 years) and nine nearly matched healthy controls (M±SD=50.11±16.18 years) performed five ST and five DT walking in a pseudo-randomized order. The DT included a serial 7's subtraction task from a random number between 50 and 100. Dependent variables: Cadence (steps/min) and gait velocity (cm/sec) were obtained from Tekscan Strideway (30 Hz, Boston, MA).

Results: The pairwise comparison indicated that cadence was significantly different for both ST (P<0.004) and DT (P<0.02) where FSHD showed lower cadence compared to controls. Gait velocity was also significantly lower for FSHD during ST (P<0.004) and DT (P<0.008). Multilevel modeling (MLM) approach revealed a group by task interaction for cadence (P<0.05) and gait velocity (P<0.001). The interaction showed a significant difference between ST and DT in controls for cadence and gait velocity. However, there was no difference between ST and DT in FSHD. Finally, a comparison of methylation percentage versus gait parameters revealed a significant negative correlation coefficient for cadence but not for gait velocity.

Conclusion: These results indicate specific pairwise differences in both ST and DT walking, observed in the gait parameters as decreased cadence and gait velocity during ST and DT. In addition, the MLM showed that controls exhibited the DT cost as expected but FSHD did not for cadence and gait velocity.

Relevance for Patients: ST appears to be sufficiently challenging in FSHD and results in overall declines in spatio-temporal characteristics of gait. Further research is needed to test this paradigm with early-onset or mild cases to track disease progression and its effects on ambulation.

1. Introduction

Facioscapulohumeral muscular dystrophy (FSHD) is the third most common autosomal dominant genetic muscle disorder resulting in progressive muscle weakness and loss (1, www.orpha.net, April 2020). FSHD is caused by misexpression of a toxic protein

DOI: http://dx.doi.org/10.18053/jctres.08.202202.007

called DUX4, specifically in skeletal muscle, from the terminal repeat of a contracted 4q35 D4Z4 array [1]. Initial FSHD patient symptoms often manifest in the lower abdominals, facial muscles, scapular stabilizers, upper arms, hamstrings, and tibialis anterior muscles [2,3]. Although expressivity can be highly variable, patient symptoms normally begin in the early teens with diagnosis occurring around the age of twenty [1]. With aging, FSHD patients display asymmetric muscle weakness surrounding their hip, knee, and ankle joints leading to a loss of static and dynamic balance [4,5]. This loss of static and dynamic postural control results in an alteration to posture, gait patterns, and an increased risk of falling which all correlate to a decrease in overall quality of life [5,6]. These quantitative functional parameters of FSHD patient disease progression may be promising clinical trial outcome measures for upcoming therapeutic interventions targeting Dux4 expression or activity.

Screening tools such as clinical severity scores (CSS) [7], muscle composition, magnetic resonance imaging [8,9], manual muscle test (MMT; [10]), isolated muscle strength, and molecular biomarkers [11-13] have been used to quantify FSHD disease severity. Patient-reported symptoms have also been examined to identify important demographics and clinical symptoms that are associated with disease burden and severity [14]. However, these tools and measures can be limiting as they are subjective, lack sensitivity, provide only qualitative information, do not emphasize functional capacity, and are insufficient in detecting mild changes occurring in annual disease progression [15].

Few studies have looked at quantitative outcome measures such as dynamic stability during walking in FSHD while crossing obstacles [16]. Here, Rijken *et al*. found that moderately affected FSHD individuals display greater declines in walking/obstacle navigation indicated by decreased speed, longer step time, and smaller step lengths. Moderately affected individuals also lack the ability to compensate for greater gait stability demands, which may increase the difficulties faced by FSHD individuals during external environmental navigation [16]. Similarly, researchers have used instrumented functional tests such as the timed up and go (iTUG) test using inertial sensors to measure longitudinal disease progression in FSHD [17,18]. While iTUG demonstrates increased sensitivity relative to traditional timed functional test (solely based on time to completion), no time-related changes were observed in the iTUG over 20.6 months between the two methods [17]. This suggests that quantitative evaluation metrics are necessary to understand gait impairments in FSHD; however, instrumented functional assessments may elucidate greater impairment and may be more promising to evaluate FSHD disease progression and ability decline. Further, the outcomes from the existing studies are also limited by a lack of similarity in the anthropometric variables between FSHD and control group participants [18,19]. This calls for stronger methodologically driven research paradigms that can narrow down specific declines in FSHD that highlight functional changes with disease progression.

Several technologies have been used to assess and quantify gait parameters in muscular dystrophies defining significant changes in time to completion, stride length, stride velocity, cadence, double support, turns and range of motion of the knee, trunk, and arm [18,20,21]. Recent work by Statland's group demonstrated decreases in stride length, stride velocity, trunk sagittal range of motion and arm swing over the course of 20.6 months in ten FSHD patients [17]. In general, FSHD patients have greater spatio-temporal gait characteristics (step time) and a decline in cadence and gait velocity indicating decreased performance alongside increased severity. Modifications to functional tasks using environmental changes such as obstacle crossing have been studied in FSHD [5]. Although these tasks are a good measure to understand affected abilities in FSHD, they can increase the risks of falls. Safer alternatives, such as the effects of performing a cognitive secondary task using a dual task (DT) paradigm, have not yet been explored on FSHD patient gait function.

DT methodology has been extensively used to assess cognitive-motor interference while walking [22]. This paradigm involves performing a secondary task such as talking, texting, or mental calculations that may cognitively challenge a primary task such as walking, cycling, and running. Several studies suggest a strong association between age and reduction in gait speed under DT conditions which is further influenced by individuals' cognitive state [22-24]. In addition, the DT effect has been well established in several clinical populations including concussions [25], Parkinson's disease [26,27], and aging [28].

In this study, we assess FSHD gait parameters using Tekscan Strideway, with single task (ST) and DT challenges, relative to anthropometrically (age, weight, gender, and height) matched controls. The Tekscan technology is a highly sensitive and time-efficient method of analyzing gait speed, foot pressures, and deviated center of forces. The Tekscan Strideway allows for easy, safe, and effective capture of unmodified FSHD gait. The DT with a cognitive secondary task may impose a new challenge to the already affected gait in FSHD. Therefore, the purpose of the current study was (a) to quantify changes in spatio-temporal gait parameters specifically, cadence and gait velocity in individuals with FSHD using the Tekscan Strideway gait mat system and (b) to measure the DT effects on cadence and gait velocity during ST and DT overground walking in FSHD and healthy controls. Our hypotheses were two-fold. First, we hypothesized that the Strideway gait mat system would be an appropriate tool to capture gait declines in FSHD. Secondly, we hypothesized that DT cognitive cost demands during FSHD patient walking would exacerbate gait parameter discrepancies relative to controls. Further, we investigated the correlation between the gait parameters and the methylation status in FSHD.

2. Materials and methods

2.1. Procedures

Before data collection, the institutional review board reviewed and approved the study protocol (University of Nevada, Reno, IRBNet ID 1322339-5). Nine genetically diagnosed FSHD (Type I) and nine anthropometrically (age, gender, height, and weight) matched healthy controls volunteered to participate in the gait study and a written consent was obtained before data

DOI: http://dx.doi.org/10.18053/jctres.08.202202.007

collection. All exclusion criteria were evaluated using a pre-approved medical history questionnaire. Exclusion criteria for all FSHD patients included: (a) inability to walk and stand on both feet for a minute, (b) individual with any type of muscular dystrophy other than genetically confirmed FSHD, (c) a history of concussions, (d) any lower extremity injuries in the last 6-months, and (e) mild-moderate cognitive decline. All controls were recruited by word of mouth and cross-verified to fit the anthropometric parameters (height, weight, and leg-length) and exclusion criteria and assessed using the same protocol as the FSHD participants.

The testing protocol included a battery of initial assessments and the gait protocol. The initial assessments tested for any cognitive decline using the montreal cognitive assessment (MoCA; [29]), physical activity readiness using the questionnaire (PAR-Q and YOU; [30]), upper and lower extremity muscular strength using (MMT- 0-6 mild to moderate; 7-15 moderate to severe [10] from which the CSS was derived), functional test: Timed up and Go test (TUG; [31]) and Patient-Reported Outcomes Measurement Information System-57; [32]. These assessments were used to be consistent with a few previous FSHD studies that have evaluated functional tasks and gait [17].

Following the initial assessments, the participants completed the gait protocol (Figure 1) to evaluate spatio-temporal gait parameters using the Tekscan Strideway gait mat system (3.4 meters, 30 Hz, Tekscan, Inc., Model ×7.7, South Boston, Massachusetts, USA). For all gait testing, the interpreter asked participants to complete five ST and five DT (subtracting seven from a given random number between 50 and 100) barefoot walking at a self-selected pace in a pseudo-randomized order (Figure 1). The pseudo-randomized order was fixed for all participants; however, the number provided for each DT was fully randomized for all participants. During DT, participants were asked to say the answers out loud while walking and an interpreter evaluated the number of errors produced in the subtraction task. To be consistent with the previous studies Cadence (steps/min) and Gait velocity (cm/s) were selected as the dependent variables along with the behavioral outcome: total number of errors for DT.

Following the completion of the gait protocol, participants were given an option to volunteer to provide their saliva sample which was then processed to obtain the relevant 4q35A methylation. Prior studies have shown that the fundamental epigenetic dysregulation of the chromosome 4q35 D4Z4 locus leads to the pathogenic gene expression causing FSHD [33]. Hence, investigating the relevant 4q35A methylation will provide a link between gait parameters and epigenetic markers of FSHD.

2.2. Relevant 4q35A methylation

Genomic DNA samples extracted from saliva were bisulfite converted, amplified using primers specific for the distal 4qA and 4qA-L D4Z4 repeat regions, and then sequenced, as described [34]. The 4qA BSS assay analyzes 56 CpGs in the most telomeric D4Z4 RU on 4qA-containing chromosomes. A fraction of chromosomes characterized as 4qA are an allelic variant termed 4qA-L; these contain an additional 2kb of D4Z4 sequence at the distal repeat although the A-type subtelomere is unchanged. Thus, the 4qA-LBSS assay utilizes the same 4qA-specific reverse BS-PCR primers as the 4qA assay but analyzes a distinct set of 30 CpGs in the distal repeat on 4qA-L chromosomes [34]. To account for differences in the number of assayable 4q alleles in subjects (1 or 2), DNA methylation from this BSS assay is reported in methylation percentage quartiles for each linearly sequenced chromosome, calculated such that with n chromosomes ordered highest methylation to the lowest methylation, the first quartile (Q1) is methylation of the n/4-th chromosome. If n/4 is not an integer, then interpolation is used between the nearest values. Thus, the greater the n chromosomes assayed, the higher the confidence in the presented Q1 values. Q1 value less than 25% for 4qA assay and Q1 value < 30% for 4qA-L assay are characterized as FSHD.

2.3. Statistical analysis

All demographic variables were compared across groups as means and standard deviations (Table 1). Three different statistical analyses were performed. First, a paired samples t-test was used to compare each matched pair (FSHD and control) by task for each dependent variable (cadence and gait velocity) using the "ggplot2" package [35] and reported as p-values. Second, each dependent variable was separately analyzed using

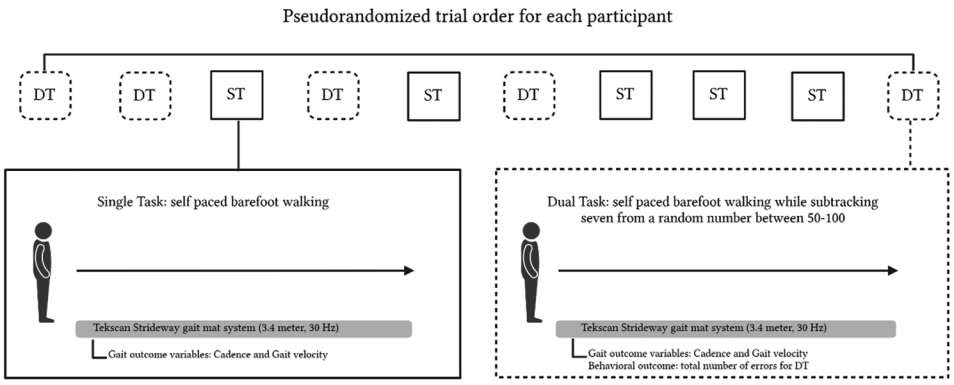

Figure 1. Experimental design. Each participant performed self-paced barefoot walking for each ST and DT in the gait protocol where the task order was pseudorandomized. The outcome variables for each task are described.

DOI: http://dx.doi.org/10.18053/jctres.08.202202.007

a theory-driven two-level multilevel model (MLM; [36]) using the "lme4" package [37] in R v3.5.1 (R Core Team, 2018). The significant interactions were confirmed via Satterthwaite's degrees of freedom method implemented to the best fit model from lmerTest [38] and are reported as F values (significance) for each variable provided as a table. MLM was chosen over repeated measures analysis of variance (RM-ANOVA) for its capability to account for lack of independence between repeated observations on the same participant via the inclusion of random effect (upper-level specific intercepts and/or slopes), making it more flexible for incorporating unbalanced or incomplete data and investigating interactions that RM-ANOVA fails to account for [36]. Fixed effects were investigated for the task (level 1: "Task" ST and DT) and the participant for each group (level 2: "Group" control and FSHD), and the cross-level interaction between Task and Group. The reference category for Task was ST and Group was Control. The level of significance was set at $P<0.05$ *a priori*.

Finally, the DRA RQA (%) for each FSHD participant ($n=7$) was compared with their respective ST cadence and ST gait velocity values. Two of the FSHD patients and corresponding controls were removed from this data as their contracted allele was 4q35A-L which may have an altered epigenetic environment. Control participants ($n=7$) were graphed at identical DRA RQA% as a visual comparison using the "ggplot2" package [35] and reported as *P*-values. This was done to ensure that the slope was not dependent on age-related gait decline.

3. Results

To assess FSHD gait function parameters during ST and DT walking, nine FSHD patients and matched controls were recruited into this study. Average group characteristics for control and FSHD group (Table 1) or individual participant metrics (Supplementary Table 1) were gathered or scored on the day of assessment. FSHD patients recruited into the study represented a broad spectrum of ages and disease progression and thus controls were recruited to match age, weight, height, and gender for gait parameter assessments. During the visit, we conducted walking trials ($n=10$) for the ST and DT on all participants. Many gait metrics were collected by Tekscan, but after assessment, the primary changes between FSHD patients and controls occurred in cadence and gait velocity. In addition, standard MMT was assessed to produce a CSS [39], MoCA to assess cognitive state [40], and DNA in the saliva to assess D4Z4 reduced allele (DRA) relevant quartile 4qA (RQA) methylation assessments [41] (Supplementary Table 1). The FSHD group overall had a moderate CSS of 6 of which 55% had a mild to moderate severity score and 45% had a moderate to severe score (Table 1). Neither FSHD nor the control groups showed any cognitive decline ($P=0.21$) indicated by the high MoCA scores (Table 1).

Table 1. Participant demographics. The left column includes all variable for each group (control and FSHD) presented as Mean±SD following inclusion-exclusion criteria

Variables	Group, Mean±SD	
	Control ($n=9$)	FSHD ($n=9$)
Age (years)	50.11±16.18	52.78±14.69
Height (cm)	176.59±12.13	176.94±7.89
Weight (kg)	84.7±15.11	82.41±22.28
Average leg length (cm)	82.47±8.53	83.11±3.96
MoCA (score out of 30)	28.75±1.16	27.88±1.46
FSHD clinical severity (score out of 15)	0±0	6±3.24

SD: Standard deviation

3.1. Cadence

The initial pairwise comparison between each FSHD patient and their matched control showed a significantly different cadence for both ST ($P<0.004$) and DT ($P<0.02$) where FSHD demonstrated lower cadence compared to controls (Figure 2A and Table 2). The omnibus effect of group x task interaction was indicated to be significant through the MLM analyses (F (1, 191.04)=11.782, $P<0.001$; Figure 2B and Table 3) with *post hoc* analyses using the Satterthwaite's degrees of freedom indicating significant group and task main effects (Table 3).

3.2. Gait velocity

Akin to cadence, a similar pattern was observed for gait velocity. Specifically, gait velocity was significantly lower for FSHD during ST ($P<0.008$) and DT ($P<0.004$) in the pairwise comparison (Figure 3A and Table 2). The MLM analyses revealed a significant group x task interaction (F (1, 191.04)=26.05,

Table 2. Dependent variables. Mean±SD for cadence and gait velocity for groups (control and FSHD) for ST and DT conditions

Variables	Group, Mean (SD)			
	Control ($n=9$)		FSHD ($n=9$)	
	ST	DT	ST	DT
Cadence	103.97 (12.95)	84.13 (19.72)	82.49 (14.85)	69.69 (13.26)
Gait velocity	113.46 (20.80)	87.69 (28.33)	77.36 (29.18)	63.03 (24.39)

ST: Single task; DT: Dual task; SD: Standard deviation

Table 3. Parameter Estimates for the MLM regarding Cadence (steps/min)

Cadence (steps/min)				
Fixed Effects	Est (SE)	Wald Sig	F (df)	SW Sig.
(Intercept)	104.42 (4.57)	***		
Group (ref = Control)			8.46 (1)	*
FSHD	-21.94 (6.47)	***		
Task (ref = ST)			144.56 (1)	***
DT	-19.98 (1.95)	***		
Group x Task	7.08 (2.73)	**	6.71 (1)	*
Random Effects	Var			
Intercept	171.52			
Residual	82.04			

*** p<0.001, ** p<0.01, * p<0.05
Wald sig uses a normal distribution whereas the SW sig utilizes the Satterthwaite's method for type III tests of fixed effects
Sample size = 176 observations on 18 participants

DOI: http://dx.doi.org/10.18053/jctres.08.202202.007

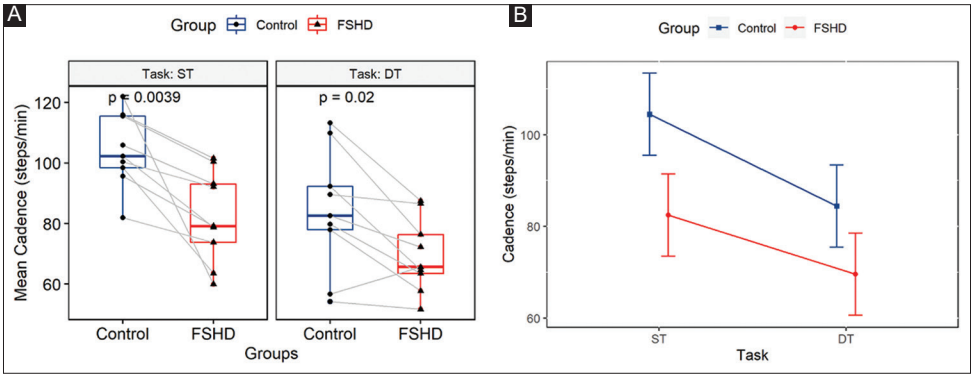

Figure 2. Pairwise and group comparison for cadence during ST and DT. (A) Pairwise comparisons of cadence (steps/min) for each FSHD participant with the specific matched control are represented as individual lines. The data are matched for each individual pair separately for ST and DT. Individual pairwise test results for each task are reported as *P*-values. (B) MLM model fit for cadence (steps/min) is shown as estimated marginal mean cadence for ST and DT for Control and FSHD groups. Error bars indicate standard error.

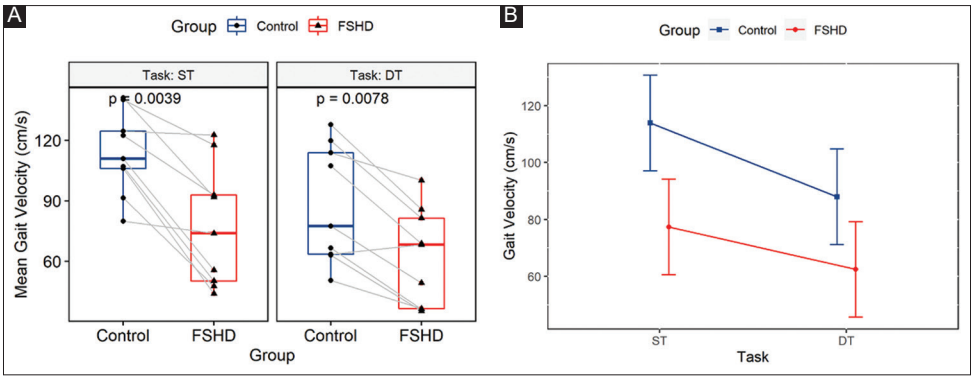

Figure 3. Pairwise and group comparison for gait velocity during ST and DT. (A) Pairwise comparisons of mean gait velocity (cm/s) for each FSHD participant with the specific matched control are represented as individual lines. The data are matched for each individual pair separately for ST and DT. Individual pairwise test results for each task are reported as p values. (B) MLM model fit for gait velocity (cm/s) is shown as estimated marginal mean gait velocity for ST and DT for Control and FSHD groups. Error bars indicate standard error.

P<0.001). Further, the *post hoc* analyses showed significant group and task main effects for gait velocity indicating that FSHD was different from controls and ST was different from DT. The results for the best fit model for gait velocity are verified and confirmed by the visual inspections in Figure 3B and reported in Table 4.

3.3. Relationship of DRA RQA methylation percentage versus gait

The DRA RQA percentage for each FSHD participant (*n*=7) was compared with their respective ST cadence (Figure 4A) and ST gait velocity (Figure 4B) values. Two of the FSHD patients and corresponding controls were removed from this data as their contracted allele was 4q35A-L which may have an altered epigenetic environment. Control participants (*n*=7) were graphed at identical DRA RQA% (Figure 4A and B) as a visual comparison and to ensure that the slope was not dependent on age related gait decline. Participants with higher methylation exhibited lower cadence (Figure 4A) in the FSHD group, with a significant negative correlation coefficient for cadence (R=–0.72, *P*=0.066). Gait velocity did not appear to be impacted by DRA RQA methylation percentage as the slope appeared unaltered relative to controls (Figure 4B).

3.4. DT response errors

Incorrect responses were recorded during each DT trial gait assessment and graphed as the number of errors made during the serial 7 subtraction. Despite the average trial response number from FSHD participants typically being higher due to the extended gait times, FSHD had fewer errors with subtracting 7's relative to the matched controls. The graphical representations of these differences are reported in Figure 5.

4. Discussion

In this study, we quantified the changes in spatio-temporal gait parameters (cadence and gait velocity) in individuals with FSHD using the Tekscan Strideway gait mat system and evaluated the changes during ST and DT overground walking in individuals with FSHD compared to their healthy matched controls. Our ST results (particularly Table 2) are consistent with previous studies [5,17] and support our first hypothesis that the Strideway gait mat system proved to be an appropriate tool to capture gait declines in FSHD. Our results confirm gait declines in FSHD, observed as lower cadence and gait velocity in ST. This is likely

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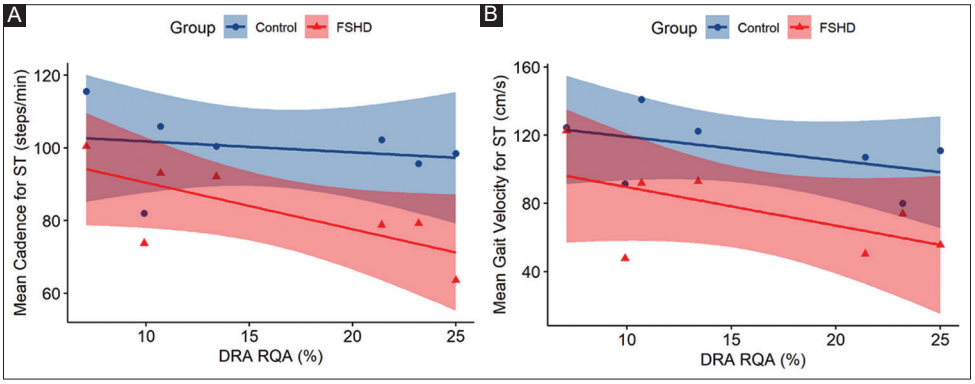

Figure 4. Relationship of DRA RQA methylation percentage versus mean cadence and gait velocity during ST. The regression plots depict the mean cadence (A) and gait velocity (B) value during ST for each participant in the FSHD group relative to their DRA RQA methylation percentage. Controls were graphed as if they possessed identical DRA RQA methylation percentages to their FSHD counterparts. Lines indicate the slope of this relationship for each group. Data are jittered to show the intersection of the DRA RQA methylation percentage and mean cadence for each participant for each group. The data reveal a greater negative slope for ST cadence in FSHD compared to controls (A) but no change in gait velocity (B).

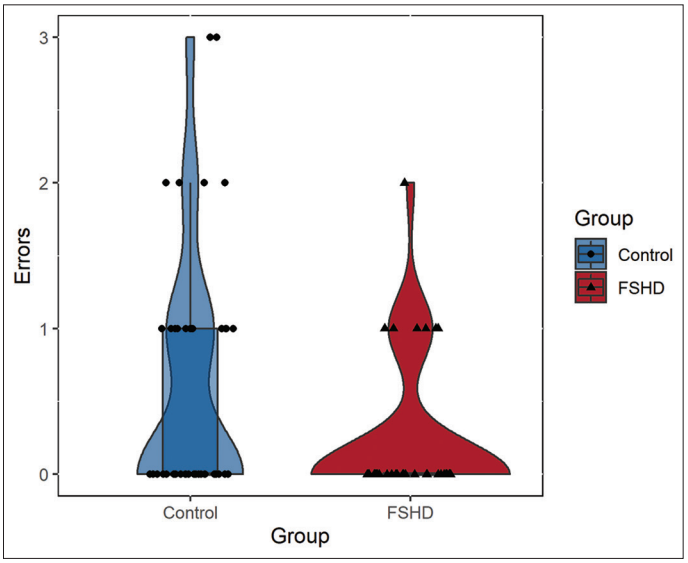

Figure 5. Greater performance errors in controls compared to FSHD. The box plot indicates median and quartile (q1, q3) range of performance errors during DT with whiskers noting the range of values (min, max and outliers) for the control and FSHD groups. The violin plot shows the smoothed probability density of the overall performance for each group. Data are jittered to show the number of errors for each participant for each group. The data reveal better performance by FSHD compared to controls indicated as lower number of errors.

Table 4. Parameter Estimates for the MLM regarding gait velocity (cm/s) for Control and FSHD

Gait velocity (cm/s)				
Fixed Effects	**Est (SE)**	**Wald Sig**	**F (df)**	**SW Sig.**
(Intercept)	113.89 (8.56)	***		
Group (ref = Control)			6.67 (1)	*
FSHD	-36.53 (12.10)	**		
Task (ref = ST)			204.33 (1)	***
DT	-25.94 (2.03)	***		
Group x Task	11 (2.86)	***	14.79 (1)	***
Random Effects	Var			
Intercept	640.50			
Residual	89.70			

***p<0.001, **p<0.01, *p<0.05
Wald sig uses a normal distribution whereas the SW sig utilizes the Satterthwaite's method for type III tests of fixed effects
Sample size = 176 observations on 18 participants

a direct consequence of the underlying muscular dystrophy on lower extremity muscles which is further supported by the CSS scores. Our reported cadence and gait velocity outcomes (Table 2) were consistent with recent work by Statland *et al.* 2019 where they reported baseline FSHD cadence as 94.7 (14.3) (steps/min) and gait velocity to be 62.3 (12.9) (%stature/s) [17].

Our second hypothesis that DT cognitive cost demands during FSHD patient walking would exacerbate gait parameter discrepancies relative to controls was incorrect. We provide preliminary evidence to indicate that FSHD gait may not be affected by secondary task demands to the same extent as it affects healthy participants. FSHD patients displayed overall declines in cadence and gait velocity, for both ST and DT gait assessments compared to their matched controls. However, a greater decline in the gait metrics was imposed by the cognitive DT costs was observed in healthy control participants. Surprisingly, we observed that FSHD patients outperformed controls in DT, as indicated by a low number of subtraction errors. There are several potential explanations for this observed paradigm. The first is that FSHD patients may have greater real-world experience with cognitive tasks during locomotion due to the necessity for fall prevention. Constant DT would be unnecessary or easier for healthy controls and might include tasks such as environmental mapping, obstacle recognition, terrain optimization, and locating ramps or handrails. Alternatively, this lack of DT percentage cost could be a manifestation of lower ST gait function present in FSHD patients, and the ability to easily perform cognitive DT while walking at lower speeds. It will be interesting to see which of these DT paradigms is correct with further experimentation. Finally, it is possible that this ST/DT paradigm could be useful in

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the detection of mild FSHD outcome measures, but a much larger and more diverse sample is required for this expansion research.

Our findings of an inverse correlation between individual FSHD patient cadence and DRA RQA methylation percentage were interesting. The use of DRA RQA methylation for FSHD diagnostic and/or prognostic purposes is controversial [42] but warrants further exploration. While a larger patient cohort is needed to truly begin drawing conclusions on how methylation status relates to gait function, it is interesting that we found an inverse correlation in cadence which differed from controls. There is a possibility that methylation percentages may be prognostic for the FSHD patient gait parameter decline, at least for gait cadence during ST. This is certainly worth exploring in future studies, as a greater understanding of the impact of methylation on FSHD disease penetrance and presentation would be extremely useful for therapeutic clinical trials.

In this study, we have provided new evidence to demonstrate gait as a clinical assessment tool for FSHD patients. The Tekscan technology could easily be adapted by researchers or clinicians as clinical outcome measures for FSHD patients. Further, the dual statistical model analysis approach, pairwise and MLM, suggest that greater study significance may be achieved by matching anthropometric parameters between pairs of FSHD patients and healthy controls. To the best of our knowledge, smaller cohort studies have previously failed to recruit controls to match patient characteristics/anthropometrics, leading to potentially artificial variability in comparisons between groups. In addition, our outcome measures were directly obtained as pressure changes on a gait mat that has not yet been evaluated in the FSHD population. Both major factors may enhance the ability to ascertain more accurate measurements and comparisons in future FSHD gait research.

5. Conclusion

The absence of DT cost in cadence and gait velocity in FSHD compared to their healthy matched controls, open new research questions to explore. Our findings suggest that cognitive dual-task demands may not affect individuals with FSHD as compared to their controls and this may be an interesting dynamic assessment while evaluating individuals with FSHD. Further research is needed to test this paradigm with early-onset or mild cases to track disease progression and its effects on ambulation. Finally, our study provides preliminary evidence with ST and DT protocols that researchers can incorporate into clinical trials to understand the effectiveness of drugs on muscle degeneration in FSHD. Such non-invasive biomarkers are essential in detecting functional changes, further aiding in understanding disease progression in FSHD.

6. Limitations

A major limitation in the current study is with respect to the sample size. First, due to the nature of recruitment and the availability of FSHD participants, the sample size was low. Secondly, we saw an overall variability in the FSHD sample. This is however a common limitation seen in many FSHD studies as the variability in the FSHD population is mainly contributed by the nature of disease severity and the rate of disease progression. This variance is further affected by age which makes monitoring biomechanical changes a challenge. Therefore, longitudinal quantification of spatio-temporal gait changes is necessary to answer gait changes as influenced by secondary task demands (cognitive, motor, and environmental) to quantify the nature of disease severity in FSHD. Future studies should consider longitudinal quantification and bigger sample size to help mitigate such variability by grouping the patients based on disease severity and FSHD disease-specific variables and comparing the outcome variables to the individual baseline.

Acknowledgments

We would like to thank Dr. Peter Jones for his continued guidance, patient recruitment, and advice with this study.

Conflict of interest

None of the authors have any professional relationships with companies that may benefit from this publication. The results of this study do not constitute an endorsement by Tekscan or any other organizations. The results of this study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

Funding

Dr. Takako Jones was funded by NIH/NIAMS R01AR062587.

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Journal of Clinical and Translational Research 2022; 8(2): 166-175

Journal of Clinical and Translational Research

Journal homepage: http://www.jctres.com/en/home

ORIGINAL ARTICLE

Spatio-temporal gait differences in facioscapulohumeral muscular dystrophy during single and dual task overground walking - A pilot study

Supplemental Table 1. Descriptive data for each individual FSHD patient and their matched controls.

Participant #	Gender	Age of onset (yrs)	Age at enrollment (yrs)	Weight (kg)	Height (cm)	Right leg length (cm)	Left leg length (cm)	Mean LL (cm)	Predicted Haplotype	DRA RQA (%)	MoCA (score out of 30)	FSHD clinical severity (score out of 15)	Response errors for DT
FSHD 1	M	~17	54	66.8	182.88	84	84.5	84.25	4A161/4B163, 10A166/10A166	23.2	29	5	1
Control 1	M	NA	50	81	177.8	81.5	81	81.25	NA	NA	30	0	4
FSHD 2	M	~46	78	85.1	182.88	81	80	80.5	4A161/4*172, 10A166/10A166	21.4	28	8	3
Control 2	M	NA	78	84	181	85	85.5	85.25	NA	NA	28	0	0
FSHD 3	M	NA	63	72.7	171.45	88	83	85.5	4A161/4B163, 10A166/10A166	10.7	30	5	0
Control 3	M	NA	68	76.4	181	90	89	89.5	NA	NA	29	0	2
FSHD 4	F	16	32	47.9	164.59	79	79	79	4A161/4A161, 10A166/10A166	7.1	27	2	0
Control 4	F	NA	32	53.7	163.5	74.5	73.5	74	NA	NA	30	0	2
FSHD 5	M	17	47	119.5	178	85	84	84.5	4A161/4A161-L, 10A166/10B161T	25	26	6	0
Control 5	M	NA	43	97.5	190	92.5	93.5	93	NA	NA	29	0	4
FSHD 6	M	17	64	106.55	186.5	86	87	86.5	4A161/4A166, 10A166/10A166	9.9	26	9	2
Control 6	M	NA	55	108.6	186	88.5	87.5	88	NA	NA	28	0	1
FSHD 7	F	11	51	95.8	165.64	75	76	75.5	4A161/4A161-L, 10A166/10A166	NA	28	12	0
Control 7	F	NA	47	88.4	151	65	65.5	65.25	NA	NA	27	0	10
FSHD 8	M	14	33	65.2	179	84.5	84.5	84.5	4A161/4B163, 10A166/10A166	13.4	29	2	1
Control 8	M	NA	26	82.6	183	85.5	85.5	85.5	NA	NA	30	0	0
FSHD 9	M	NA	53	82.1	181.5	87	88.5	87.75	4A161/4B163, 10A166/10A166	25	29	5	1
Control 9	M	NA	52	90.1	176	80	81	80.5	NA	NA	28	0	3

= number; FSHD = Facioscapulohumeral muscular dystrophy; Yrs = years; LL = Leg Length; DRA = D4Z4 reduced allele; RQA = relevant quartile 4qA; MoCA = Montreal Cognitive Assessment; DT = Dual task; NA = Not Available

DOI: http://dx.doi.org/10.18053/jctres.08.202202.007