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Hip flexor fatigue limits walking in Charcot-Marie-Tooth disease

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Abstract

Charcot–Marie–Tooth (CMT) disease results in distal lower limb weakness that affects walking. In this study we assess the role of the hip flexors in compensating for distal weakness while walking and the effects of prolonged walking on these putative compensatory strategies. Eighteen subjects with CMT disease were compared with 14 matched controls while they walked on a treadmill to a predetermined point of perceived effort. A significant reduction was observed in peak hip flexor velocity during walking and hip flexor maximal voluntary contraction. In a second session following selective fatigue of the hip flexors, hip flexor velocity decreased immediately on walking, and walking duration was greatly reduced. This study suggests that hip flexors compensate for distal weakness and that fatigue in the hip flexors can limit walking duration. Treatments directed toward improving proximal muscle strength may therefore help to delay onset of hip flexor fatigue and thus prolong walking duration.

Charcot–Marie–Tooth (CMT) disease is a relatively common hereditary condition that affects 36 in 100,000 people.¹⁰ The most common types of CMT disease have an autosomal-dominant inheritance and are further classified into type 1 (demyelinating) and type 2 (axonal). Despite variations in the genes that cause CMT disease, the phenotype tends to have a similar pattern characterized by a slow decline in distal muscle strength and sensation due to degeneration of the longer peripheral nerves. Distal muscle wasting causes the classic inverted champagne bottle appearance of the lower portion of the leg. A pes cavus foot deformity is also frequently observed due to an imbalance in strength between the tibial muscle groups.^{3,4} In contrast, the proximal limb muscles are less affected in most cases, although they are still weak compared to normative data.⁵

During normal walking the ankle plantarflexor muscles generate nearly all of the positive work in late stance. Studies modeling the effects of individual muscles during walking suggest that the role of the plantarflexors is to progress the trunk and initiate the swing phase by accelerating the leg forward in combination with the hip flexor muscle group.^{17,18,27} In conditions where the distal leg muscles are weakened it has been suggested that the hip flexors compensate for the reduced contribution from the plantarflexors and take over the role of swing initiation. In those with ankle plantarflexor weakness following stroke, for example, maximum walking speed is related to the strength of the hip flexors.^{16,19} Further,

in those with diabetic peripheral neuropathy and distal leg weakness, there is an earlier onset of hip flexion at the end of the stance phase.¹⁵

In this study we assess the effect of prolonged walking on this putative hip compensatory strategy in CMT patients. It was hypothesized that prolonged walking would lead to fatigue of the hip flexor muscles and a deterioration in the compensatory strategy that would in turn limit walking time and distance. To assess this we first measured the change in hip flexor strength and kinematics with prolonged walking. Second, we assessed the effect of specifically fatiguing the hip flexors on subsequent walking kinematics and walking endurance.

Methods

Subjects

Individuals with CMT disease were recruited from the genetic peripheral neuropathy clinic at the National Hospital for Neurology and Neurosurgery (M.M.R.). Inclusion requirements were clinically definite CMT disease (many patients but not all had genetic confirmation) and the ability to walk 100 m in at least 10 minutes. Subjects were excluded if they had a history of other neurological impairment, cardiac dysfunction, orthopnea, orthopedic lower limb impairment unrelated to CMT disease, and lower limb or back pain exceeding 7 out of 10 on a visual-analog scale. Healthy control subjects were recruited for comparison in the first study and were matched for age, gender, weight, and height. All subjects participated after granting informed written consent and with the approval of the local ethics committee in accord with the Helsinki Declaration (1975).

Clinical Measures

Isometric strength of the lower limb muscles was measured using strain gauges attached to a fixed frame. Starting positions were standardized (see Table 2), and the proximal limb segment was fixed using straps. The muscle groups tested were the hip flexors and extensors, knee extensors, plantarflexors, and dorsiflexors. The peak maximal voluntary contraction (MVC) from three attempts was recorded. Subjects were additionally screened for scoliosis and foot deformity.

Light touch sensation was measured by testing the ability to feel the application of a 10-g monofilament at 10 locations on the plantar aspect of the foot (Neuropen; Owen Mumford, Oxford, UK). Vibration threshold was tested over the lateral malleolus and medial border of the first hallux using a biothesiometer (120 Hz; Bio-medical Instrument Co., Newbury, Ohio).⁶ The vibration amplitude was alternatively increased and decreased, and the average threshold of three trials was recorded.

Resting heart rate and blood pressure were taken prior to the walking task (MX3 Plus; Omron-Healthcare, Milton-Keynes, UK). Forced expiratory volume in 1 second (FEV₁), forced vital capacity (FVC), and peak expiratory flow rate (PEF) were measured using a spirometer (One Flow FVC; Medisave, Weymouth, UK).

Self-reported fatigue and health status were measured using the Fatigue Severity Scale (FSS) and the Short Form-36 (SF-36) questionnaire.^{12,24}

Session 1

Myometry: MVC of the hip flexors and plantarflexors was taken before and immediately after a treadmill walking test. Additionally, to check for motivational influences, a hand-held dynamometer was used to measure grip MVC. To measure the hip flexor MVC, subjects sat

in a customized chair with their thighs fully supported and their hips at 50° flexion, with the pelvis and chest constrained by straps. Straps were placed over the distal thigh, passed through the seat of the chair, and linked to strain gauges mounted on a rigid frame directly below. The positions of the myometry straps were marked to aid reliable placement. To calculate the hip flexor moment, the moment arm was measured from the greater trochanter to the center of the strap. Plantarflexor MVC was measured with the participant sitting with the knees and ankles at 90°. The thigh and shank were constrained using adjustable bars, and the foot was secured in a stirrup that was in series with a frame-fixed strain gauge. To calculate the plantarflexor moment, the moment arm was measured from the lateral malleolus to the midpoint of the stirrup. All tests of MVC were performed within 2 minutes of the subject completing the treadmill test. Repeatability testing of this method demonstrated good agreement between trials with an intraclass correlation coefficient of 0.83.

Treadmill Test: Subjects with CMT disease first performed a 10-m timed walk to ascertain their normal gait speed and cadence. They then walked on a motorized treadmill at the same speed. As this was a test of the subject's everyday walking endurance, any orthoses normally used by the subject were worn during the test. If subjects usually used a stick or had marked balance difficulties, light upper limb support was allowed. An auditory metronome was set at the same cadence to cue the subject to maintain a consistent stepping rate. A practice trial on the treadmill followed by a 5-minute rest was performed prior to the test. During the test, the subjects wore a safety harness attached to an overhead gantry that was capable of supporting their weight if required, but it did not interfere with treadmill walking.

Kinematic data were collected using a three-dimensional motion analysis system (Charnwood Dynamics, Leicestershire, UK). Markers were applied bilaterally to: (1) the acromion; (2) a point midway between the anterior superior iliac spine (ASIS) and posterior superior iliac spine (PSIS); (3) a frame attached to the lateral aspect of the thigh proximal to the lateral condyle; (4) the fibular head; (5) the lateral malleolus; (6) the lateral heel; and (7) the base of the fifth metatarsal. All data were collected at a sampling rate of 200 Hz²⁶ and stored for offline analysis.

For every minute the subject remained walking on the treadmill, the following measures were taken:

- Kinematic data (over 15 seconds).
- Heart rate (Polar Electronics, Inc.).
- Perceived exertion as measured on the Borg perceived exertion scale.¹
- Pain on a 10-point visual rating scale.

The treadmill test was terminated when the subject reached 17 on the Borg scale, which corresponds to a perceived exertion of "very hard." Additionally, the test would have been stopped according to absolute and relative indications for terminating exercise tests as given by the American College of Cardiology/American Heart Association Task Force on Practice Guidelines,⁷ or if the pain scale exceeded 7 out of 10. Each control subject attempted to walk on the treadmill at the same speed, cadence, and duration as a matched CMT subject.

Session 2—At a follow-up session the effects of selectively fatiguing the hip flexors on walking endurance were tested. Subjects initially walked on the treadmill for 3 minutes at the same speed and cadence as the first session to obtain pre-fatigue kinematic data.

Hip Flexor Fatigue Protocol: Hip flexor MVC was first recorded as described previously (see Session 1 subsection). Subjects then performed alternating isometric contractions of the hip flexors to 50% of their MVC at a rate of 40 contractions/minute; visual feedback of the applied tension was provided. Measures of hip flexor MVC were taken every 2 minutes throughout the test. The test was terminated once the hip flexors had fatigued by 20%. Subjects were then immediately transferred to the treadmill and began a treadmill walking test identical to session 1 in terms of objective measures and criteria for termination. On immediate cessation of the treadmill test a repeat measurement of hip flexor MVC was taken.

Following both sessions, subjects were asked to rate any pain, dyspnea, and proximal and distal lower limb fatigue on a 10-point visual rating scale.

Analysis

Isometric strength and kinematic data were analyzed offline using customized programs (MatLab, version 14; The Mathworks, Natick, Massachusetts). MVC was defined as the difference between the peak and baseline force. Individual gait cycles and phases were identified from the motion of the heel and toe markers. Pre-swing was defined as the time between initial contact of the contralateral leg and toe off of the ipsilateral leg. Each gait cycle was normalized to 100%, and the average of three gait cycles taken.²⁵ Trunk and lower limb angles were calculated (Table 1). The primary analysis measured the following variables:

- Hip flexor and plantarflexor MVC.
- Peak hip flexion amplitude during the preswing and swing phase.
- Peak hip flexion velocity during the pre-swing and swing phase.

A secondary analysis further assessed changes in the kinematics at other joints:

- Peak sagittal ankle, knee, and hip amplitude and velocity during pre-swing.
- Peak sagittal ankle and knee amplitude and velocity during swing.
- Peak sagittal trunk flexion and peak-to-peak changes in coronal and horizontal trunk rotation.

Statistical Analysis

The response of CMT patients and the control group was compared using a repeated-measures general linear model (GLM). A factor of trial with two levels in session 1 (pre and post treadmill test) and three levels in session 2 (pre, post 1, and post 2) was included. A modified Bonferroni test was applied to account for multiple comparisons in the primary ($n = 6$) and secondary ($n = 19$) analyses.

The relationships between the clinical measures and the walking performance were analyzed using Spearman's rank correlation test. Clinical measures were compared using two-tailed unpaired t-tests. Non-parametric data were analyzed using the Mann–Whitney U-test. Significance was taken as $P < 0.05$ with the mean $\pm$ standard deviation reported unless indicated otherwise.

RESULTS

Group Differences

Eighteen patients with CMT disease (10 men, 8 women; age 37 ± 12.9 years, height 1.69 ± 0.7 m, weight 70.5 ± 12.2 kg) were compared with 14 healthy, matched controls (8 men, 6 women; age 34 ± 9.7 years, height 1.7 ± 0.5 m, weight 68.4 ± 10.3 kg). Four subjects in the CMT group wore ankle-foot orthoses (AFOs). One wore bilateral rigid AFOs, 2 wore less rigid bilateral ankle braces (Neoprene and silicon), and 1 wore an anti-inversion ankle brace on the left leg.

CMT subjects demonstrated differences in distal muscle strength, sensation, and range of motion compared with healthy subjects (Table 2). They also demonstrated greater levels of fatigue and lower scores for general health perception (Table 2).

Over 10 m, CMT patients walked significantly slower (CMT: 1.13 ± 0.1 m/s; controls: 1.59 ± 0.2 m/s) and with a reduced cadence (CMT: 108 ± 7.3 steps/minute; controls: 120 ± 10.7 steps/minute).

Session 1

Effect of Prolonged Walking: CMT patients walked for a mean time of 48 minutes. At the start of the treadmill test, the CMT patients reported their perceived exertion as level 9 on the Borg scale. Control subjects started at level 6.5. By the end of the treadmill test, those with CMT disease reported a median Borg level of 17. For the same walking speed and duration, controls reported a median Borg score of 8, which was significantly lower than that of CMT patients ($Z = -4.93$, $P < 0.0001$). In addition, heart rate, expressed as a percentage of the maximum predicted rate (defined as $220 - \text{age}$), was significantly higher in CMT patients ($t = 3.38$, $P = 0.002$) (Table 3).

Primary comparison

Isometric strength: At the end of the treadmill walking test both the CMT and control groups demonstrated a significant decrease in the MVC of the hip flexors (GLM: trial, $F = 33.76$, $P < 0.0001$). CMT patients decreased their MVC by 20% ($\pm 20\%$) compared with 14% ($\pm 7\%$) in control subjects (Fig. 1a). No changes were seen in grip strength, indicating that subjects' effort was the same before and after the treadmill test. Both groups increased plantarflexor MVC post walk but this difference was not significant (CMT: $9 \pm 30\%$; control: $6 \pm 11\%$).

The reduction in hip flexor MVC in the control subjects was unexpected. To investigate this further, 5 control subjects returned and repeated the treadmill walking test for the same amount of time as they had walked in the matched condition. On this occasion, they walked at their normal speed and cadence. Hip flexor MVC, recorded before and after treadmill walking, did not change significantly. In the original test walking at a matched speed, the difference in MVC with walking was significant for these 5 subjects ($t = 3.25$, $P = 0.03$).

Kinematics: Prolonged walking produced a significant reduction in hip flexion velocity during swing in the CMT group, whereas control subjects increased their hip flexion velocity (GLM: trial X group, $F = 9.31$, $P = 0.005$; post hoc t -tests: CMT, $t = -2.44$, $P = 0.03$; control, $t = 2.76$, $P = 0.02$; Fig. 1b, 2a) (Table 4). No other trial/group interactions were observed.

Secondary comparison: Peak knee flexion angle during the swing phase also changed by the end of the treadmill walking test. Control subjects significantly increased knee flexion,

whereas CMT subjects did not show a change (GLM: trial X group, $F = 7.50$, $P = 0.01$; post hoc t-test: control, $t = -2.8$, $P = 0.014$; Fig. 3a). There was a trend toward increased peak trunk flexion during pre-swing in the CMT group (GLM: trial X group, $F = 5.31$, $P = 0.03$; Fig. 3b) that was statistically non-significant after applying a modified Bonferroni correction. In addition, greater coronal trunk motion occurred in both groups (GLM: trial, $F = 8.59$, $P = 0.006$), with a significant increase apparent in the CMT group on post hoc testing ($t = -3.02$, $P = 0.008$; Fig. 3c).

Factors Affecting Walking Endurance: No significant correlations were observed between total walking time on the treadmill and strength, sensory impairment, and cardiorespiratory measures. Significant correlations were found between walking time and a number of measures, which included fatigue severity as measured by the FSS ($r = -0.68$, $P = 0.002$), sections of the SF-36 relating to physical functioning ($r = 0.71$, $P = 0.002$), role limitations due to physical problems ($r = 0.65$, $P = 0.006$), and energy and fatigue ($r = 0.52$, $P = 0.037$). There were no significant correlations between the change in primary outcome variables and walking duration.

CMT group patients were asked what factors caused them to stop walking during the treadmill test. Sixty-seven percent of subjects reported that they stopped the test due to fatigue of the legs and a deterioration of their gait pattern, whereas 22% stopped due to pain and 11% due to breathlessness. Visual analog scores taken after the treadmill walking test showed proximal fatigue was the most highly rated symptom with 50% of subjects scoring over 5 out of 10.

Session 2—Of the original 18 CMT subjects, 16 returned for the hip flexor fatigue test. One subject dropped out of the study, and another was unable to continue due to a newly diagnosed cardiac condition.

Hip Flexor Fatigue Test: During the hip flexor fatigue test, the left and right sides did not fatigue at the same rate, with the left side fatiguing more quickly in the majority of subjects (percentage decrease: left 19.5%, right 10.2%). In keeping with the larger percentage drop in MVC on the left side, the kinematic changes were more marked on the left and will be reported on separately.

General Gait Comparison: Following the hip flexor fatigue task, CMT patients walked on the treadmill for a mean of 26 minutes. This was significantly less than the mean time of 48 minutes in session 1 ($t = 2.077$, $P = 0.047$). The median perceived exertion at the start of the walking test was at level 11 on the Borg scale and increased to 17 by the end of the test.

Primary Kinematic Comparison: Peak hip flexor velocity during swing significantly decreased on the left side immediately after the hip flexor fatigue test (GLM: trials, $F = 6.92$, $P = 0.003$; post hoc: pre test vs. post test 1, $t = -2.18$, $P = 0.046$) (Table 4). No further change was seen after the treadmill test, and no change was observed with the right hip (GLM: $F = 0.97$, $P = 0.38$).

Secondary Kinematic Comparison: Increased trunk flexion during pre-swing was observed following the hip flexor fatigue test but did not change further after the treadmill test (GLM: $F = 4.96$, $P = 0.01$; post hoc: pre vs. post 1, $t = 4.34$, $P = 0.0006$). In contrast, the total range of coronal trunk motion did not change after the fatigue test but did increase with the treadmill test (GLM: $F = 9.70$, $P = 0.0006$; post hoc: post 1 vs. post 2, $t = 2.79$, $P = 0.01$).

DISCUSSION

The results of this study indicate that there is increased effort in those with CMT disease when they perform the same walking test as controls. This leads to fatigue of the hip flexor muscles with an accompanying reduction in hip flexor velocity. Fatiguing the hip flexors specifically also reduced hip flexor velocity and reduced the amount of time subjects walked. The inference of these and other findings will be explored further.

Group Differences

As expected, CMT patients showed greater weakness and sensory loss distally compared with healthy control subjects. The FSS and SF-36 revealed findings consistent with previous literature. The increased fatigue reported in this study reflects findings by Kalkman et al.⁹ and Vinci et al.,²³ who also reported poor general health perception as measured by the SF-36.

Fatigue in the Hip Flexors

When the CMT patients walked until they reached a “very hard” level of perceived exertion, there was a concomitant reduction of their hip flexor MVC. This change could have been due to peripheral muscular fatigue but it could also have been due to reduced motivation. The grip strength measure, however, was unchanged by the prolonged treadmill walking. This suggests that subjects had not lost the motivation to exert maximal forces. Unexpectedly, the control subjects also showed a reduction on hip flexor MVC test after walking on the treadmill. The control subjects reported that the slower walking speed they adopted in order to match the CMT group felt very unnatural, and they perceived changes had occurred in their gait pattern. Alterations in the gait pattern may have meant that hip flexor activity was more prolonged and/or of a higher amplitude than normal, resulting in a degree of fatigue in that muscle. The 5 subjects who were recalled to perform the treadmill task at a self-selected pace did not show the same drop in hip flexor MVC. This indicates that the slow pace was indeed a factor. Despite this, although the control subjects demonstrated decreased hip flexor MVC after the original walking test, they only reported level 8 on the Borg scale as compared with a level of 17 for CMT patients. This indicated that the drop in hip flexor strength did not appreciably increase the perceived walking effort in the control subjects, and they would have been able to continue walking considerably longer than the CMT group.

After the treadmill test in session 1, the hip flexor MVC dropped by a mean of 20% in CMT patients and a similar percentage drop was induced in the left leg by the fatigue test in session 2. Similar kinematic changes were seen in session 1 with prolonged walking and in session 2 immediately after specific fatigue of the left hip flexors. In particular, there was a reduction in the velocity of hip flexion in both sessions. This suggests that these kinematic changes with prolonged walking may be a direct consequence of hip flexor fatigue. Interestingly, the right side that only fatigued by 10% in session 2 did not show these changes, suggesting that hip flexor strength has to fall below a threshold value before kinematic changes occur.

The subjects' impressions that proximal leg fatigue was the reason for cessation of the treadmill test in session 1 and for the faster time to walking cessation in session 2, further supports the idea that prolonged walking is limited by fatigue in the hip flexor muscles. Such fatigue would affect the ability to swing the leg forward and make walking more effortful. The hip flexor muscles are thought to work synergistically with gastrocnemius to accelerate the limb from pre-swing into swing phase.^{18,27} The control subjects did not show a reduction in hip velocity, possibly because the intact gastrocnemius assisted the

acceleration of the limb. Studies that model the effects of different muscles during walking have suggested that the plantarflexor muscles may compensate for weakness in proximal muscles.⁸ Therefore, it is possible that, in healthy subjects, distal compensation prevented a reduction in velocity of hip flexion. Therefore, if the plantarflexors are weak, as in CMT disease, the hip flexors may not have the synergistic assistance from gastrocnemius, and will thus fatigue prematurely. In 4 subjects, weakness in the plantarflexors could have been further compounded by wearing AFOs that restricted ankle motion.

A change in hip flexor MVC and velocity with prolonged walking may not necessarily reflect a compensation for weakness in the plantarflexor muscles. Don et al. (2007) found an increase in the hip flexion angular impulse during late stance and hip flexor angle during the swing phase in CMT patients.²⁸ This was most marked in those who had weakness in the ankle dorsiflexors in the absence of ankle plantarflexor weakness. This suggests that a change in the timing and/or amplitude of hip flexor activity may be a compensation for poor foot clearance. However, regardless of the underlying cause of any compensatory activity in the hip flexors the results of the present study suggest that fatigue in the hip flexor muscles can limit prolonged walking.

One assumption needs to be considered, however. This study looked at prolonged walking on a treadmill and not over-ground walking. In healthy subjects, gait kinematics and kinetics have been found to be similar,²¹ but this has not been explored in peripheral neuropathy. There is a possibility that if the differences in walking pattern differ greatly in CMT patients, then the results of this study cannot be extrapolated to over-ground walking. Testing walking on the treadmill, however, was necessary in this study to maintain consistency of speed and ensure safety, as the person fatigued with the fixed harness.

Secondary Compensations

A trend toward increased trunk flexion was seen in CMT patients following the treadmill test (session 1) and after the hip flexor fatigue test (session 2). It is possible that the increase in trunk flexion is a secondary compensation that is employed when the hip strategy fails through fatigue. Alternatively, it could be argued that increased trunk flexion results from trunk and limb fatigue or a generalized feeling of fatigue as the subject reaches a Borg score of 17. Results from session 2 refute this, as the increase in trunk flexion was seen immediately following the selective hip fatigue test when the Borg score was 11. If we assume that the increased hip flexion primarily assists limb progression, then it is possible that trunk flexion has a similar action and is brought into play when the hip flexors start to fatigue. This is supported by studies of trunk motion during walking, which have suggested that a “trunk leading” strategy is a way of using the heavy trunk segment to direct movement of the lower body by pulling the leg into the swing phase.¹³ Due to the increased motion of the heavy trunk segment, this strategy may be more costly and less efficient than the hip flexor strategy, which could explain why the walking time was almost halved in session 2. An increase in coronal trunk motion was observed after treadmill walking in both sessions, but did not occur immediately after the hip flexor fatigue test in session 2. An increase in coronal motion may therefore be a consequence of fatigue of other muscle groups and unrelated to changes in hip strength.

Factors Limiting Walking

The changes in hip kinematics and strength may indicate that fatigue of a compensatory hip flexor strategy limits walking. However, no correlation was seen between the drop in hip flexor MVC and the time spent walking on the treadmill. Regression analysis indicated that additional nonphysical factors may impact on walking time. Subjects’ perception of fatigue and physical limitation in particular did appear to have a significant influence on walking

endurance in CMT patients. Both the FSS and SF-36 are multidimensional scales that reflect more than peripheral muscle fatigue. Chronic fatigue that occurs independent of peripheral muscle fatigue has been reported in other long-term conditions such as multiple sclerosis and chronic demyelinating polyneuropathy.^{2,20} Increased central activation failure, as measured by superimposed electrical stimulation during an MVC, has been reported in a cohort of patients with CMT disease.²² The central activation failure correlated positively with reported fatigue severity, thus supporting the assumption that fatigue reported by CMT patients is due to central factors rather than peripheral muscle fatigue. It is likely that the limitations to walking endurance are therefore due to a number of factors that vary between individuals.

Clinical Implications

A reduction in hip flexor strength and an alteration in hip kinematics is seen following prolonged walking in those with CMT disease. In order to prolong functional walking distances, training the proximal muscles, perhaps specifically the hip flexors, may enable CMT patients to compensate for distal weakness for longer periods. In view of the link between walking endurance and fatigue severity, approaches that have been shown to influence fatigue in other chronic conditions could also be tested in clinical trials in patients with CMT disease, such as trials of exercise training and drug therapy.^{11,14}

In conclusion, this study suggests that the hip flexor muscles fatigue during prolonged walking due to their role in compensating for distal weakness. This appears to limit walking duration, although other factors, such as self-reported fatigue, are also influential. Future intervention studies should address the specific issue of hip flexor endurance but also the impact of more general fatigue.

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FIGURE 1.

Significant changes in primary outcome measures. (A) Hip flexor MVC measures before and after the treadmill walk test. Error bars indicate standard error of the mean (*significant differences pre and post walk test). (B) Hip flexor velocity at the start and end of the treadmill walk test. Error bars are the standard error of the mean. PwCMT, people with CMT; Controls, control subjects (*significant differences pre and post walk test).

FIGURE 2.

(A) Knee flexor angle, (B) trunk flexion angle, and (C) peak-to-peak trunk coronal angle at the start and end of the treadmill walk test. Error bars indicate standard error of the mean. PwCMT, people with CMT; Controls, control subjects (*significant differences pre and post walk test).

FIGURE 3.

(A) Session 1 grand average of sagittal hip angular velocity for people with CMT (PwCMT) and control subjects. Solid lines are pre walk test and dashed lines are post walk test. (B) Session 2 grand average of sagittal hip angular velocity for PwCMT. Solid lines: pre walk test; dashed lines: post hip flexor fatigue test; dotted lines: post treadmill walking test.

Table 1

Definition of joint angles measured for two-dimensional kinematic analysis

	First vector	Second Vector
Sagittal trunk angle	Acromion-to-ASIS markers in XZ plane	Z-axis
Sagittal hip angle	Acromion-to-ASIS markers	Upper-to-lower femoral markers
Sagittal knee angle	Upper-to-lower femoral markers	Fibular head-to-malleolar markers
Sagittal ankle angle	Fibular head-to-malleolar markers	Heel-to-toe markers
Coronal trunk angle	Left-to-right acromial markers in the YZ plane	Y-axis
Coronal pelvic angle	Left-to-right ASIS marker motion in the YZ plane	Y-axis
Horizontal trunk angle	Left-to-right acromial markers in the XY plane	X-axis
Horizontal pelvic angle	Left-to-right ASIS markers in the XY plane	X-axis

Table 2

Clinical measures in patients with CMT disease and control subjects

	CMT	Control
Resting heart rate (bpm)	74 ± 9	65 ± 13
Blood pressure		
Systolic (mm Hg)	123 ± 9	128 ± 16
Diastolic (mm Hg)	78 ± 10	78 ± 9
Lung function		
FEV1 (liters)	3.2 ± 0.7	3.5 ± 1.0
FVC (liters)	3.9 ± 0.9	4.3 ± 1.0
PEF (liters/min)	394 ± 115	464.5 ± 163
MVC (Nm/kg)		
Hip flexors (seated with 50° hip flexion)	1.13 ± 0.42	1.32 ± 0.38
Hip extensors (seated with 50° hip flexion)	0.65 ± 0.33	1.09 ± 0.68
Knee extensors (seated with 90° knee flexion)	1.53 ± 0.68	2.06 ± 0.64
Plantarflexors (seated with ankle in plantigrade)	0.63 ± 0.57 *	1.21 ± 0.58
Dorsiflexors (supine 10° ankle plantarflexion)	0.10 ± 0.08 *	0.39 ± 0.17
Sensation		
Light pressure	5 ± 2.9 * (of 10)	10 ± 0 (of 10)
Vibration	AT: 6.1 ± 6.1 *	AT: 0.6 ± 0.7
Maleolus	DT: 4.9 ± 5.2 *	DT: 1.1 ± 1.1
Threshold (μm)	AT: 8.4 ± 8.5 *	AT: 0.4 ± 0.3
Great toe	DT: 6.0 ± 6.3 *	DT: 0.2 ± 0.2
Fatigue Severity Scale	38.2 ± 14.9 *	16.9 ± 6.6
Short Form-36 total	998.2 ± 1034.0 *	3227.9 ± 183.3
Physical function	59.7 ± 24.3 *	97.5 ± 4.0
Role limitation (physical)	43.8 ± 47.0 *	100 ± 0
Role limitation (emotional)	68.9 ± 46.2	94.4 ± 19.2
Energy/fatigue	51.3 ± 21.3 *	72.5 ± 14.7
Emotional well-being	78.7 ± 15.3	85 ± 11.1
Social functioning	68.0 ± 28.1 *	92.1 ± 16.1
Pain	66.1 ± 26.6 *	96.7 ± 4.9
General health	61.6 ± 21.3 *	83.8 ± 11.7

Data expressed as mean ± standard deviation.

* P < 0.05 for CMT vs. control comparison.

Table 3

Average walk time, change in Borg scale, and heart rate expressed as a percentage of maximum predicted value ($220 - \text{age}$) on cessation of walk test.

	CMT group	Control group
Mean walk time (minutes)	48.3 $\pm$ 40.5	44.0 $\pm$ 40.8
Median Borg scale (start)	9	6.5
Median Borg scale (finish)	17 *	8
% of maximum heart rate (finish)	60.0 $\pm$ 10.7 *	57.8 $\pm$ 11.1

Data expressed as mean $\pm$ standard deviation.

* $P < 0.05$ for CMT vs. control comparison.

Table 4

Changes in primary and secondary kinematic variables following selective fatigue of hip flexors.

	Pre HF fatigue test	Post HF fatigue test	Post treadmill test
Average peak left hip flexion velocity at swing (degrees/s)	164.15 ± 38.96	147.38 ± 30.82 *	141.08 ± 32.63
Peak trunk flexion angle at pre-swing (degrees)	9.08 ± 6.45	11.26 ± 5.82 *	12.50 ± 4.43
Peak-to-peak coronal trunk (degrees)	4.94 ± 5.17	5.59 ± 5.55	6.59 ± 6.13 [†]

Data expressed as mean ± standard deviation.

* Significant difference between pre HF fatigue and post HF fatigue test.

[†] Significant difference between post HF fatigue test and post walking test.