



To what extent do the muscles and tendons influence metabolic cost and exercise tolerance in the hypermobile Ehlers-Danlos Syndrome and Hypermobility Spectrum Disorders?

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ABSTRACT

Background: Individuals with hypermobile Ehlers-Danlos Syndrome (hEDS) and Hypermobility Spectrum Disorders (HSD) often experience chronic pain, muscle fatigue, and exercise intolerance, potentially due to altered muscle-tendon mechanics. This study investigated the influence of Achilles tendon (AT) compliance and plantar flexor muscle function on the metabolic cost of walking in individuals with and without HSD/hEDS.

Methods: Eleven individuals with HSD/hEDS and 11 age- and sex-matched controls completed walking trials at, below, and above their preferred walking speed. Achilles tendon stiffness, medial gastrocnemius muscle shortening, AT energy storage, pain, and lower limb electromyographic activity were evaluated during stance phase. The energy cost of walking was also computed.

Findings: The hypermobile conditions were associated with significantly lower AT stiffness, higher energy cost of walking and increased pain. Muscle fascicle shortening, shortening velocity, muscle energy cost and mechanical efficiency were similar between groups. Greater muscle activation and antagonist coactivation were observed in HSD/hEDS, particularly during early stance, likely reflecting compensatory mechanisms for joint instability.

Interpretation: Elevated cost of walking in HSD/hEDS appears driven not by increased plantar flexor work, but by a redistribution of joint work to more proximal joints. These findings suggest that altered muscle-tendon properties and neuromuscular control strategies contribute to exercise intolerance and fatigue in the Hypermobility Spectrum Disorders and hypermobile Ehlers-Danlos Syndrome.

1. Introduction

The Ehlers-Danlos Syndromes (EDS) represent a group of 13 connective tissue disorders that are characterized by joint hypermobility, musculoskeletal manifestations, and multi-systemic co-morbidities. Hypermobile EDS (hEDS) is the most common EDS subtype and remains the only subtype without a confirmed genetic cause. Hypermobility

spectrum disorders (HSD) describe a collection of phenotypes related to joint hypermobility that do not meet the criteria for hEDS or another connective tissue disorder. The combined prevalence of HSD and hEDS is approximately 1 in 600 to 1 in 900 (Demmler et al., 2019). While the specific proteins impacted by HSD/hEDS remain unknown, collagen is hypothesized to be involved, either through abnormal synthesis or subsequent disruption, given the involvement of mutations related to

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Table 1
Participant characteristics.

	HSD/hEDS		CON	
Age (years)	33.2	± 14.0	32.6	± 14.1
Sex	n = 10 female; n = 1 male			
Height (cm)	169	± 6	166	± 10
Weight (kg)	70.6	± 11.0	67.4	± 14.6
PWS (m·s ⁻¹)	1.04	± 0.31	1.17	± 0.27
MVC PF Torque (Nm)	68.2	± 35.9	101.7	± 54.1*
AT moment arm (mm)	43.8	± 7.4	37.1	± 6.4*
AT stiffness (N·mm ⁻¹)	70.7	± 45.7	119.7	± 46.5*
Max AT force (N)	1680	± 1015	2655	± 1231*

Table 1. Participant Characteristics. Values are mean ± SD. MVC: Maximal voluntary contraction. PF: plantar flexion. AT: Achilles tendon.

* Significantly different between groups ($p < 0.05$).

forms of collagen implicated in other EDS subtypes (Malfait et al., 2017). The lower limb tendons may contain up to 80 % collagen, particularly collagen type I (Kannus, 2000), As such, any impairment in collagen

synthesis or structure may impair tendon mechanical properties. For example, females with hEDS show lower Achilles tendon (AT) stiffness compared to age- and sex-match controls (Rombaut et al., 2012a). Alterations to muscle-tendon function may contribute to the chronic pain, fatigue, and exercise intolerance experienced by many individuals with HSD/hEDS (Castori et al., 2017; Malfait et al., 2017), together or independent of increases in the energy cost of walking (E_{walk}).

Tendon mechanical properties coupled with muscle forces and inertial properties of the moving segment influence the amount and velocity of muscle shortening (Blazevich and Fletcher, 2023). If the tendons are too compliant, additional muscle shortening is required to stretch the tendon, elevating the metabolic cost (Lichtwark, Bougoulias, and Wilson, 2007). Conversely, more compliant tendons may store and return greater amounts of elastic strain energy for a given force, which could reduce the mechanical work of the muscle and reduce metabolic cost (Blazevich and Fletcher, 2023). In individuals with HSD/hEDS, the higher AT compliance may explain the elevated energy cost of walking (E_{walk}).

To compensate for reduced structural joint support in HSD/hEDS,

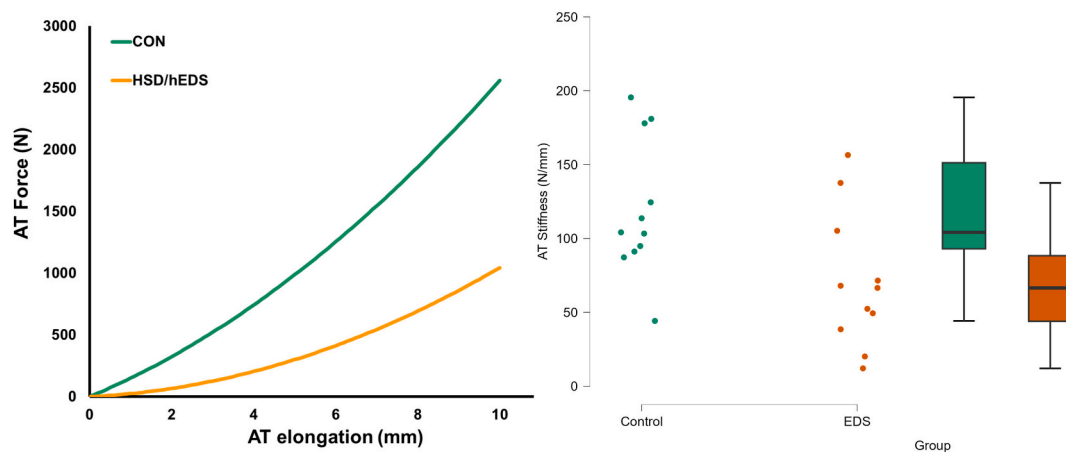


Fig. 1. Left. Exemplar Achilles tendon (AT) force vs. AT elongation in HSD/hEDS compared to CON participant. AT stiffness represents the linear portion of the force-elongation curve, from 50% to 100% maximal force, which was significantly lower in HSD/hEDS. Middle. Individual participant data and (right) boxplot. Bars represent the 25th and 75th percentile. AT stiffness was significantly lower in HSD/hEDS compared to CON ($p=0.021$). *Significantly different between groups.

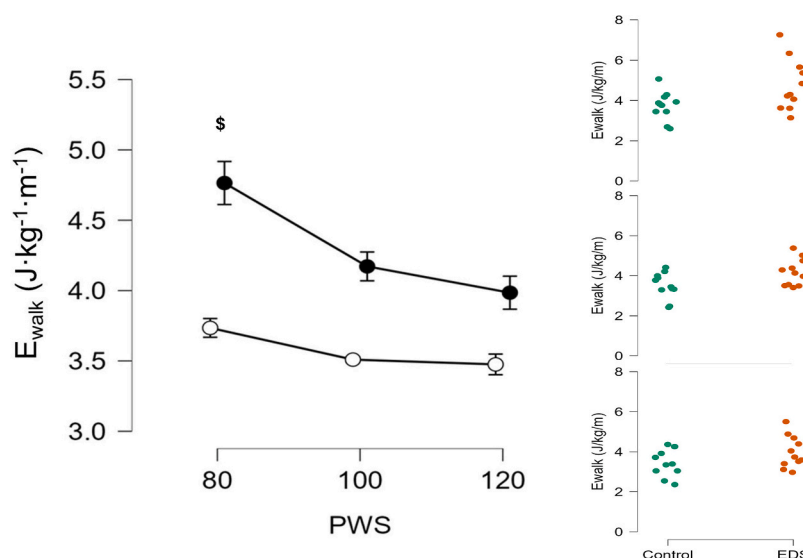


Fig. 2. Left. Energy cost of walking (E_{walk}) at speeds above and below preferred walking speed (PWS) in CON (○) and HSD/hEDS (●). Values are mean±standard error of the mean (SEM). Right. Individual participant data and boxplots for the three different walking speeds (top to bottom; 80 to 120% PWS). Bars represent the 25th and 75th percentile. E_{walk} was significantly higher in HSD/hEDS compared to CON ($p=0.037$). §Significantly higher E_{walk} compared to the other speeds in HSD/hEDS only. *Significantly different between groups.

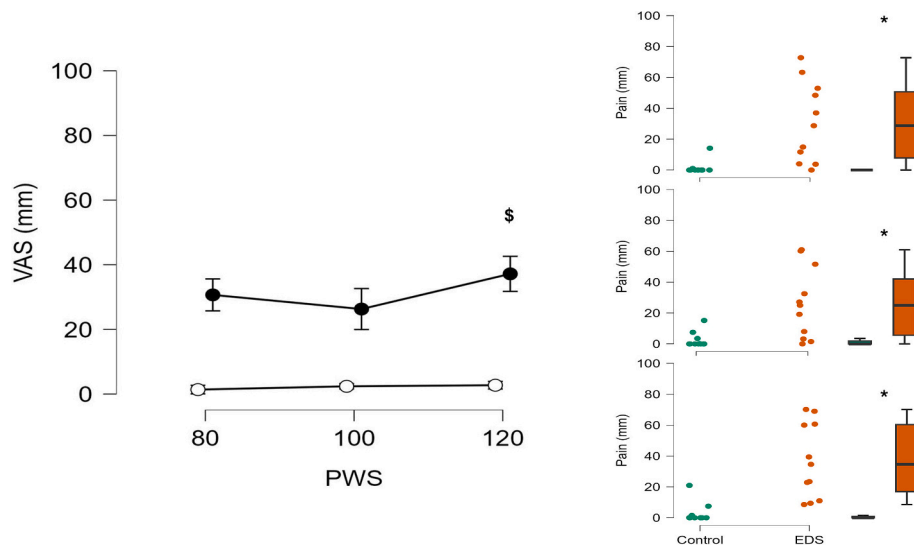


Fig. 3. Pain assessed from a 100 mm visual analog scale across walking speeds in CON (○) and HSD/hEDS (●). Values are mean \pm standard error of the mean (SEM). **Right.** Individual participant data and boxplot for the three different walking speeds (top to bottom; 80 to 120% PWS). Bars represent the 25th and 75th percentile. Pain was significantly higher in HSD/hEDS (mean difference: 29.2 ± 7.2 mm, $p < 0.001$) compared to CON. §significantly higher pain compared to the other speeds in HSD/hEDS only. *Significantly different between groups.

muscle contractions actively stiffen the joint, improving stability but also elevating the cost of activation (Cashaback and Cluff, 2015). This activation likely precipitates the increased metabolic demand of walking and exacerbates the symptoms of pain and fatigue commonly reported by this population. How muscle activation presents in HSD/hEDS during locomotion remains to be evaluated.

Despite growing interest in muscle-tendon dynamics during locomotion, limited evidence exists surrounding the interaction between increased AT compliance (and the potential to store and return a greater elastic strain energy), muscle activation and muscle length change in explaining E_{walk} in HSD/hEDS. Therefore, the primary objective of this study was to evaluate muscle-tendon dynamics during walking in people with and without HSD/hEDS. Our primary hypothesis was that E_{walk} would be higher in HSD/hEDS due to higher AT compliance and a higher cost of activation to stabilize lower limb joints. Our secondary hypothesis was that elevated E_{walk} would, under specific conditions (e.g., faster walking speed), be associated with higher reported pain during walking.

2. Methods

2.1. Participants

Twenty-two participants participated in the study. Individuals with HSD/hEDS were recruited from a tertiary physiatry clinic focused on the musculoskeletal consequences of HSD/hEDS. Participants aged 18–50 were included if they were previously diagnosed with hEDS ($n = 10$) or met the criteria for generalized joint HSD (G-HSD) ($n = 1$) as outlined by (Castori et al., 2017). Sex and age-matched participants without HSD/hEDS ($n = 11$, 10 females) with no prior cardiovascular, neurological, musculoskeletal, or connective tissue disorders were recruited from two local universities and served as controls (CON). Participant characteristics are presented in Table 1. Participants in both groups had to self-report being capable of walking for a minimum of 30 min continuously to participate in the experimental protocol. Individuals were excluded from participating if they: were previously diagnosed with any major confounding medical conditions (e.g., rheumatoid arthritis, type 1 diabetes); were taking any medications that could impact their ability to complete the exercise testing; had a history of smoking; or had a positive response to the Physical Activity Readiness Questionnaire (Shephard, 1988). This study was approved by the Mount Royal University Human Research Ethics Board (HREB ID #102279) and all participants provided

voluntary informed written consent to participate.

2.2. Experimental protocol

Participants visited the laboratory on a single occasion. Initially participants lay prone on an isokinetic dynamometer (System 3, Biodex Medical Systems Inc., Shirley, NY, USA) with the right knee fully extended. The shank and right foot were affixed to the dynamometer foot plate using Velcro straps to ensure the ankle joint was aligned with the center of rotation of the dynamometer. The ankle was secured at 90° (the angle of the foot in relation to the long axis of the shank). Two 12.5 MHz linear array B-mode ultrasound probes (65 mm, LV8-4L65S-3, MicrUS EXT-1H, Teleded, Vilnius, Lithuania) were secured to the lower limb using elastic tensor bandages. One probe was placed over the musculotendinous junction (MTJ), while the second probe was placed over the medial gastrocnemius (MG) muscle belly for MG fascicle assessment. Ultrasound images were recorded at 39 Hz. Participants then actively rotated their ankle from maximal plantar flexion to maximal dorsiflexion to determine each participant's unique ankle range of motion (ROM). The ankle was then passively rotated at $0.1745 \text{ rad}\cdot\text{s}^{-1}$ through the participant's voluntary ROM to estimate AT moment arm (AT_{MA}) using the tendon excursion method, accounting for passive forces (Fletcher and MacIntosh, 2018).

2.3. Achilles tendon stiffness

The right AT stiffness was assessed using the same dynamometer and ultrasonography described above, with the ultrasound probe positioned over the MTJ and secured with elastic bandages to minimize movement. Participants performed three isometric ramp maximal voluntary contractions (MVC) of the right plantar flexors lasting 5 s each with 90 s of rest between trials. External joint moment during ramp contraction was sampled at 100 Hz. The trial eliciting the highest peak plantar flexion moment was used for analysis. AT force was calculated by dividing the net ankle external joint moment by the estimated AT_{MA} . AT force (F)-elongation (d_L) data were fit to a second order polynomial regression using the equation:

$$F = Ad_L^2 + Bd_L$$

where A and B are constants. AT stiffness was defined as the slope of the

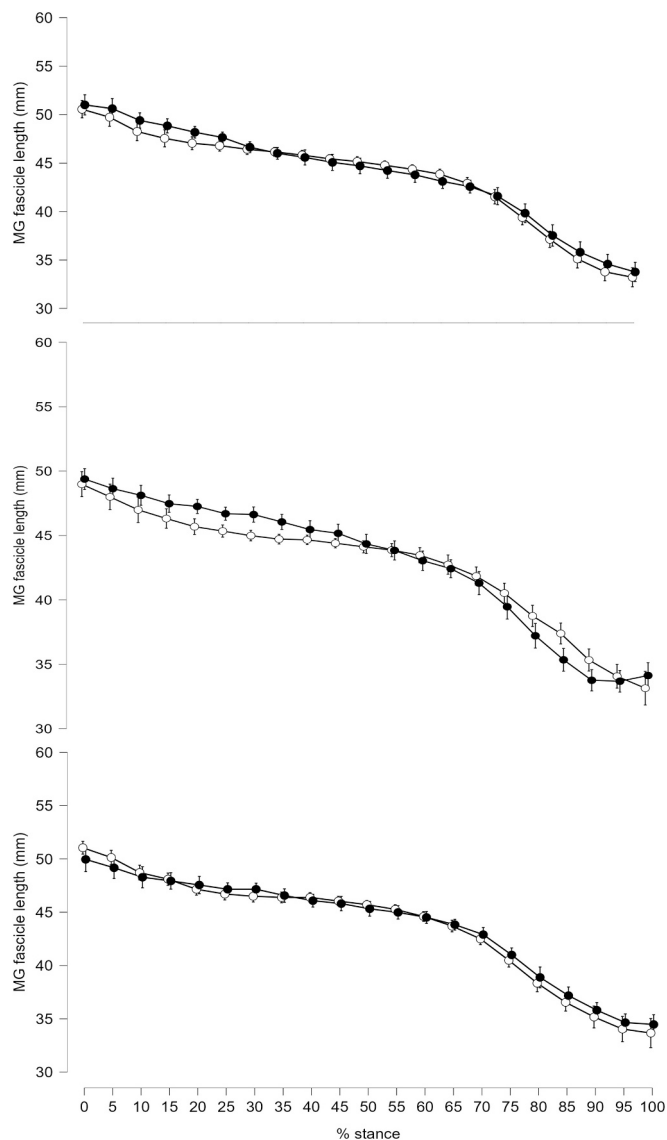


Fig. 4. Fascicle length \times %stance across speeds. **Top-Middle-Bottom:** 80-100-120% PWS, respectively in CON (\circ) and HSD/hEDS (\bullet) Values are mean \pm standard error of the mean (SEM). Fascicle shortening velocity was similar between groups across speeds ($p=0.556$).

fitted F-d_L equation between 50 and 100 % of maximum isometric plantar flexion force (Fletcher, Esau, and MacIntosh, 2010; Fletcher and MacIntosh, 2015).

2.4. Energy cost of walking

Participants then walked for 10-min at varying speeds on a motorized treadmill (Woodway Pro, Woodway USA, Waukesha, WA) with no gradient to identify their preferred walking speed (PWS) according to Dal, Erdogan, Resitoglu, and Beydagi (2010). Participants began walking at a slow speed. The speed was then progressively increased at 30 s intervals until the participant perceived the speed to be too fast. At that point the speed was decreased until participants were satisfied with that walking speed. Once a unique PWS was identified, participants completed three 6-min walking trials, with two minutes of quiet standing or sitting recovery between each trial. The trials were performed at 80, 100, and 120 % PWS in a randomized order. Immediately after each walking trial, participants were provided with a 100 mm visual analog scale (VAS) to rate their perceived pain during the trial. In

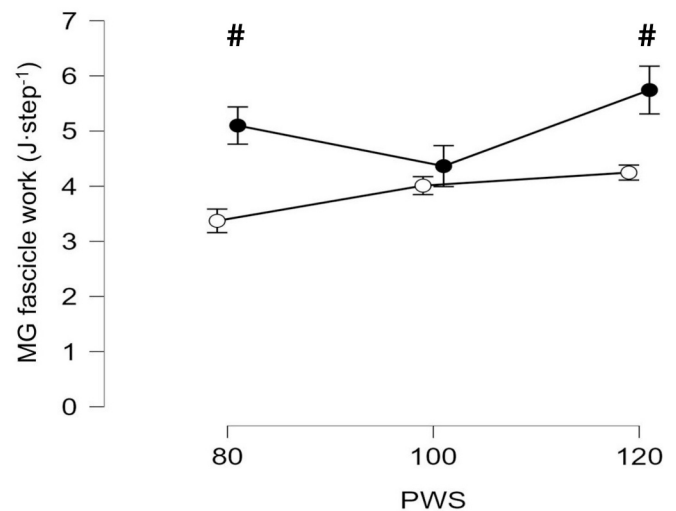


Fig. 5. Medial gastrocnemius (MG) fascicle positive mechanical work at 80-100-120% PWS, respectively in CON (\circ) and HSD/hEDS (\bullet). Values are mean \pm standard error of the mean (SEM). #significantly higher muscle work compared to PWS in CON only.

the final two minutes of walking at each speed, expired VO_2 and VCO_2 were measured using a metabolic cart (Quark CPET, Cosmed, Rome, Italy). The metabolic cart was calibrated using room air and a gas mixture of known composition (5 % CO_2 and 16 % O_2) prior to each testing session. The turbine and flow sensor were manually calibrated with a 3 L syringe. Expired gases were collected through the metabolic mask for the entire duration of each trial. A steady state VO_2 (defined as a change of <200 mL/min for any 10s period) was achieved for all participants during the last two minutes of each trial.

The energy cost of walking (E_{walk}) was calculated from the average steady-state VO_2 and VCO_2 at each speed according to Péronnet and Massicotte (1991), and expressed as a relative energy cost per unit distance ($\text{J}\cdot\text{kg}^{-1}\cdot\text{m}^{-1}$):

$$E_{\text{walk}} (\text{J}\cdot\text{kg}^{-1}\cdot\text{m}^{-1}) = 16.89\dot{V}\text{O}_2 + 4.84\dot{V}\text{CO}_2 \times \text{BM}^{-1} \times s^{-1} \times 1000$$

where VO_2 and VCO_2 are in $\text{L}\cdot\text{s}^{-1}$, BM is body mass (in kg), s is speed (in $\text{m}\cdot\text{s}^{-1}$) and $1000 \text{ J}\cdot\text{kJ}^{-1}$.

2.5. Muscle fascicle length change

The MTJ and MG muscle fascicle of the right leg were visualized throughout each trial from ultrasonography described above. The MTJ displacement was considered as lengthening and shortening of the AT. MTJ displacement and MG fascicle lengths were measured using *ImageJ* (NIH, Bethesda, USA) from the ultrasound images during stance phase. From the measured fascicle and AT length change, both tendon and MG velocity, mechanical work and power were calculated at each 5 % of stance for the duration of stance and averaged over ten consecutive stance phases at each speed. Sagittal plane ankle angles were recorded from videography (Ziqian, N5 1080p Webcam, 50 Hz) and measured throughout stance using *Tracker* (v.6.0.8, Open-Source Physics, Compadre.org/osp). AT length change due to ankle joint rotation (in mm) was calculated from ankle joint angle change and the measured AT_{MA} length, a derivation of the equation used to calculate AT_{MA} from the tendon excursion method (Baxter and Piazza, 2018; Fletcher and MacIntosh, 2018). Instantaneous tendon length was estimated by subtracting the measured MTJ excursion and AT length due to ankle rotation.

Table 2
Total muscle energy cost, mechanical efficiency and AT energy storage during stance.

	HSD/hEDS			CON		
	80	100	120	80	100	120
Stance time duration (ms)	976 ± 188	891 ± 181	781 ± 143	851 ± 111	765 ± 100	695 ± 85
Mechanical efficiency (%)	26.6 ± 7.8	26.4 ± 10.4	24.8 ± 10.1	32.4 ± 11.3	29.1 ± 13.5	32.2 ± 11.1
Muscle energy cost (J·step ⁻¹)	12.9 ± 6.2	15.8 ± 7.1	18.2 ± 8.1	16.7 ± 7.4	17.8 ± 9.2	18.6 ± 7.0
AT energy storage (J·step ⁻¹)	7.1 ± 6.8	10.9 ± 11.2	11.9 ± 10.3	9.2 ± 5.2	10.4 ± 9.3	8.8 ± 7.4
Muscle:mechanical energy ratio	4.2 ± 3.8	4.2 ± 5.4	4.9 ± 8.7	2.0 ± 2.0	2.2 ± 1.2	3.1 ± 2.2

* main effect of speed ($p < 0.05$). %main effect of group ($p < 0.05$). Data shown are mean ± SD.

2.6. Kinematic and kinetics

Vertical ground reaction forces of the right foot were measured using a force insole placed in the participant's own shoe (Loadsol, Novel.de, St Paul MN USA) at 100 Hz for the same ten consecutive steps during each walking trial. Data were saved to a smart device (iPad mini-4, Apple Inc. Cupertino CA) for subsequent analysis. Plantar flexion moment during stance was calculated according to [Hullfish and Baxter \(2020\)](#). The force insole contained three distinct force-sensing regions (forefoot, midfoot, heel) used to measure the corresponding force applied orthogonal to the insole. The geometric centres of pressure corresponding with each force-sensing zone were measured using digital calipers (Mastercraft Tool Co, Earth City, MO) to the nearest 0.02 mm. The sagittal plane plantar flexion moment was calculated from the sum of each zone's moment arm relative to the ankle joint center and the applied force in the region ([Hullfish and Baxter, 2020](#)). From these computed ankle joint moments, instantaneous ankle joint mechanical power was calculated as the product of net plantar flexion moment and ankle joint angular velocity ([Farris and Sawicki, 2012](#)). Instantaneous ankle joint power during stance was expressed relative to body mass ($W \cdot kg^{-1}$).

AT force was determined by dividing the calculated plantar flexion moment by the measured AT_{MA} , which when appropriately accounting for passive forces, does not change as a function of ankle angle ([Fletcher and MacIntosh, 2018](#)). To calculate MG force, the MG physiological cross-sectional area relative to all ankle plantar flexors (0.1746, ([Fukunaga et al., 1992](#)) was divided by the cosine of the measured pennation angle of the MG muscle fascicles. Mechanical work performed by the MG was calculated as the integral of fascicle force and length change during stance. Fascicle shortening was considered positive mechanical muscle fascicle work ([Jinha and Herzog, 2024](#)). AT strain energy storage was calculated by integrating AT force over AT elongation during stance. This enabled quantification of the AT energy storage during the measured tendon lengthening and AT energy return during tendon shortening exclusive to stance phase ([Kharazi, Bohm, Theodorakis, Mersmann, and Arampatzis, 2021](#)).

2.7. Electromyography

Four wireless electromyography (EMG) sensors (Delsys Trigno, Natick Massachusetts, USA) were affixed to the participants' right lower leg, along the presumed fascicle angle according to SENIAM guidelines ([Stegeman and Hermens, 2007](#)), using double-sided stickers. The EMG sensors were placed on the lateral gastrocnemius (LG), soleus (SOL), tibialis anterior (TA), and fibularis longus (FL). EMG signals from each muscle were collected at 2048 Hz for the same 10 consecutive stance phases. The signals were filtered through a 4th-order Butterworth filter (high- and low- pass filter of 20 and 450 Hz, respectively). EMG amplitude was calculated as the root mean square (RMS) from the raw filtered EMG signal using a 125 ms window length with a 62.5 ms window overlap. The RMS was interpreted as the level of muscle activation during stance. The mean RMS was calculated across three distinct periods of stance according to [Schmitz, Silder, Heiderscheidt, Mahoney, and Thelen \(2009\)](#). These distinct stance periods included: loading (from 0 to 10 % of the entire gait cycle), midstance (from 10 to 30 % of the entire gait cycle) and terminal stance (from 30 to 60 % of the entire gait cycle). The mean RMS across each period of stance was then normalized to the mean RMS across the entire stance phase for subsequent interpretation.

2.8. Muscle energy cost

The MG energy cost during stance was determined from the estimated number of half-sarcomeres in series, the estimated number of parallel crossbridges required to generate the measured MG force, and the estimated number of crossbridge cycles necessary to accommodate the measured MG fascicle shortening ([Bennett, Machado, and Fletcher,](#)

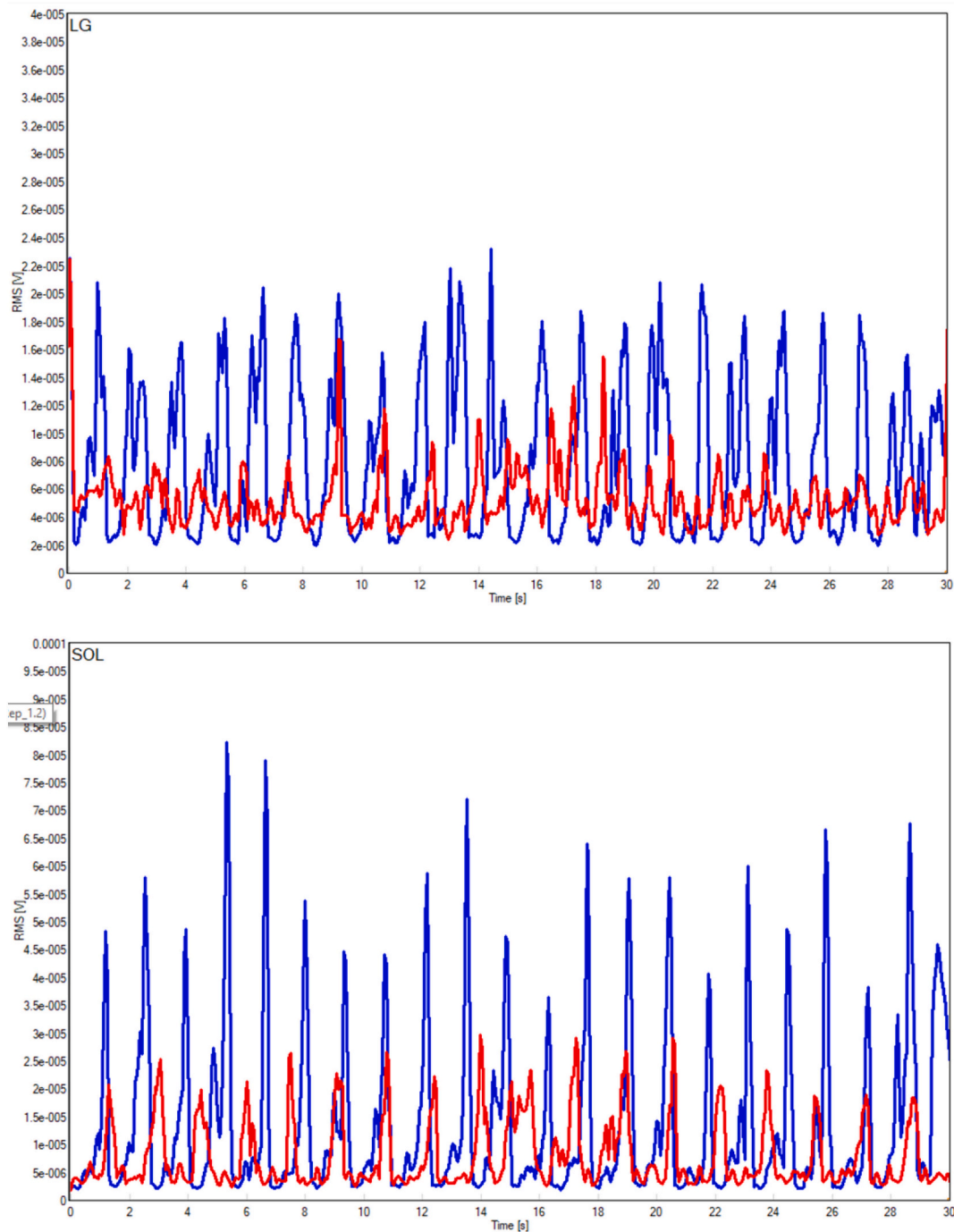


Fig. 6. Exemplar filtered EMG RMS during walking at PWS for HSD/hEDS (blue) and CON (red). LG (**top**) and SOL (**bottom**) are shown for both an HSD/hEDS participant and their age- and sex-matched control during 30s of steady-state walking at PWS.

2023; Fletcher and MacIntosh, 2015). The estimated number of in-series sarcomeres was estimated from resting fascicle length, measured using ultrasonography, and assuming an optimal sarcomere length at peak isometric force of $2.6 \mu\text{m}$ (Herzog and Ter Keurs, 1988). The estimated number of in-parallel crossbridges was calculated from the MG force divided by the estimated force per crossbridge. The force per crossbridge decreases with an increasing shortening velocity from a crossbridge force of 3 pN (Linari, Piazzesi, and Lombardi, 2009) under near-isometric conditions to 0 pN at maximal shortening velocity, based on the linear sarcomere force-velocity relationship (De Tombe and Ter Keurs, 1990). Sarcomere shortening velocity (V) was derived from the instantaneously measured fascicle shortening velocity throughout

stance and scaled to maximal shortening velocity (V_{max}). The maximal fascicle shortening velocity was assumed to be $10.6 \text{ fascicle lengths}\cdot\text{s}^{-1}$, assuming maximal shortening velocities of Type I and Type II muscle fibers of $4.4 \text{ fascicle lengths}\cdot\text{s}^{-1}$ and $16.8 \text{ fascicle lengths}\cdot\text{s}^{-1}$, respectively, at physiological temperatures (Bohm, Mersmann, Santuz, and Arampatzis, 2021) with the assumption that the MG consisted of 50 % Type I fibers (Edgerton, Smith, and Simpson, 1975).

2.9. Statistical analysis

Statistical analyses were selected to align with the study design and hypotheses, with independent t -tests used for between-group

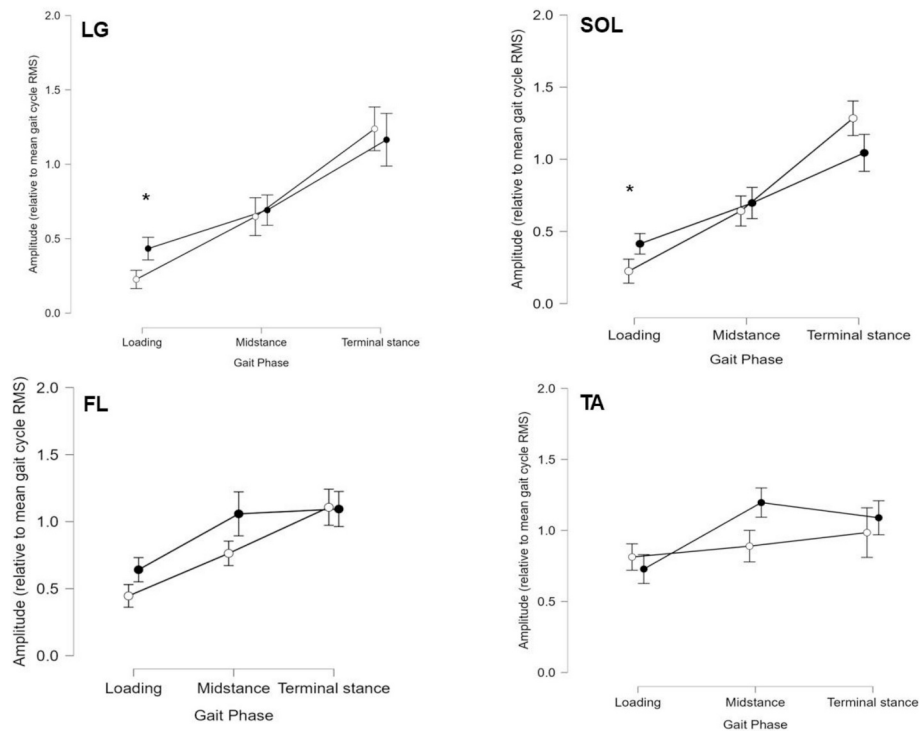


Fig. 7. Magnitude of lower limb muscle activation during the stance phase at 100% PWS in CON (○) and HSD/hEDS (●). Values are mean±standard error of the mean (SEM) relative to the mean EMG amplitude across the entire gait cycle. LG: lateral gastrocnemius, SOL: soleus, FL: fibularis longus, TA: tibialis anterior. *Significantly different ($p < 0.05$), HSD/hEDS vs. CON. Across speeds, both SOL ($p = 0.04$) and LG ($p = 0.014$) activation were higher during loading in HSD/hEDS compared to CON.

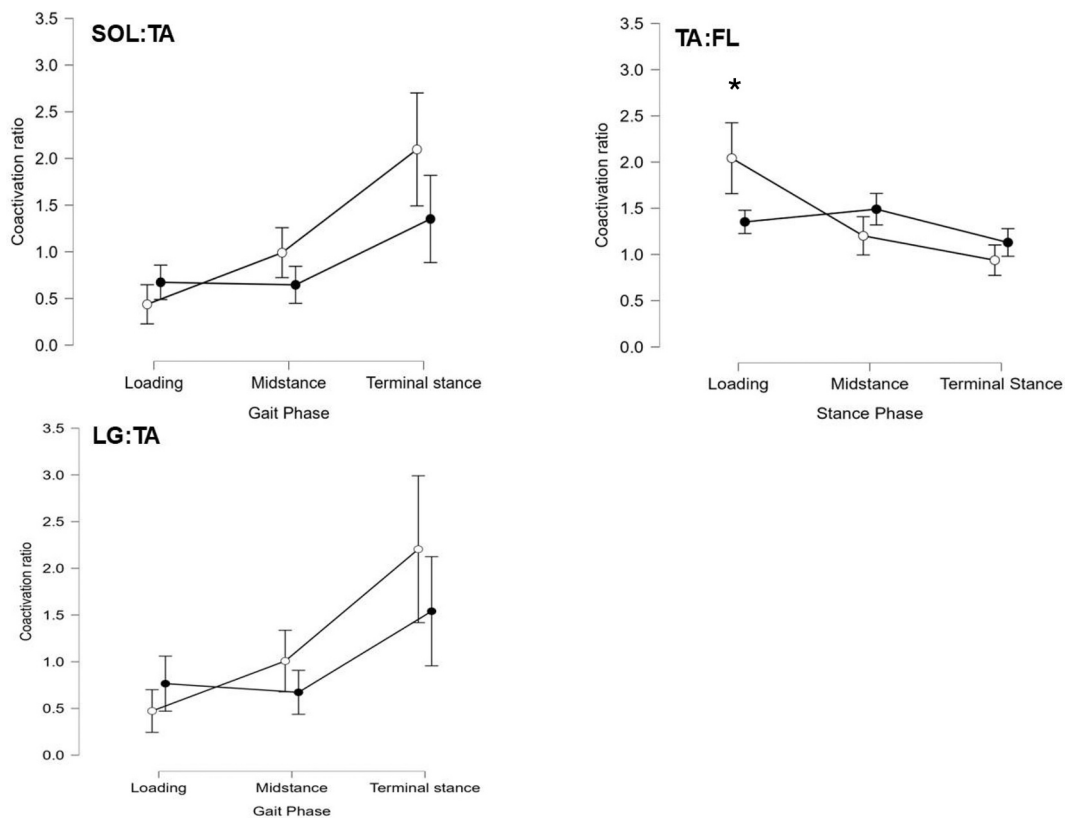


Fig. 8. Lower limb agonist-antagonist muscle coactivation ratio during the stance phase at PWS in CON (○) and HSD/hEDS (●). Values are mean±standard error of the mean (SEM). LG: lateral gastrocnemius, SOL: soleus, TA: tibialis anterior. Loading was associated with a lower TA:FL coactivation ratio in HSD/hEDS compared to controls ($p = 0.012$). *Significantly different ($p < 0.05$), HSD/hEDS vs. CON.

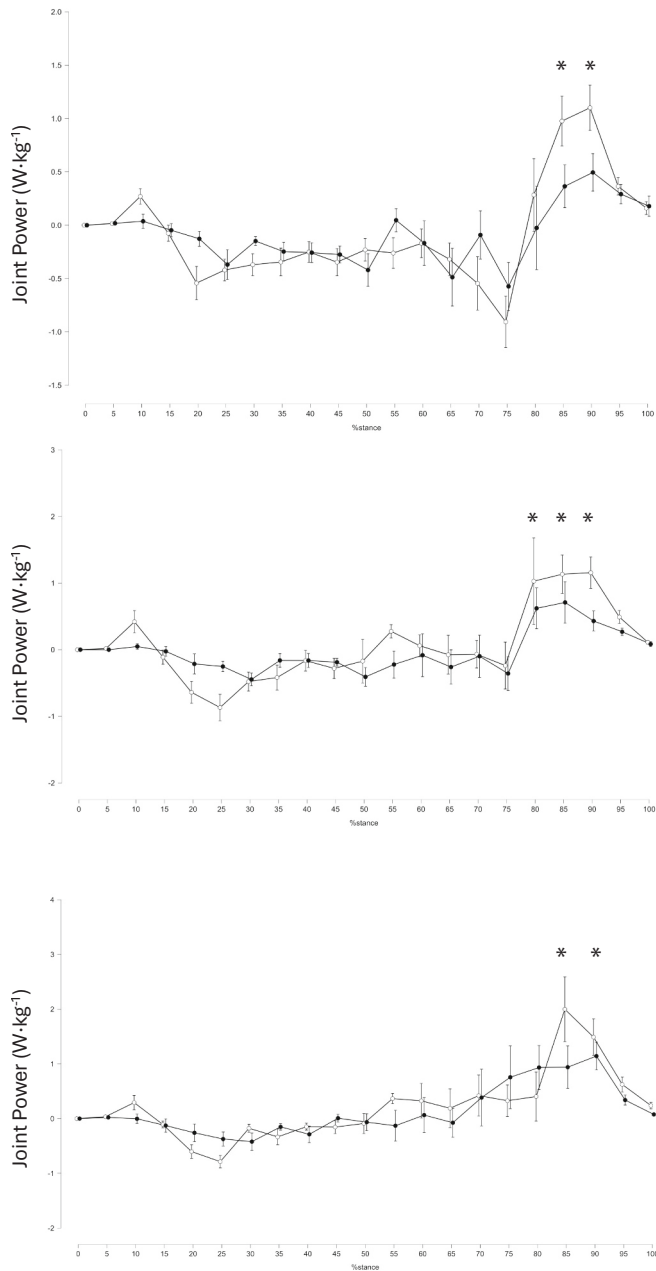


Fig. 9. Relative instantaneous ankle joint power during the stance phase of walking at 80% (top), 100% (middle) and 120% of PWS (bottom) in CON (○) and HSD/hEDS (●). Values are mean ± standard error of the mean (SEM). *Significant group differences ($p < 0.05$).

comparisons and mixed-model ANOVAs applied to evaluate group \times condition effects. Values are presented as mean \pm standard deviation (SD), unless otherwise specified. Statistical analyses were performed using JASP (JASP Team, 2024. Version 0.19.1). Normality and equality of variance for all dependent variables were assessed using Shapiro-Wilk and Mauchly's test of sphericity, respectively. Student's independent sample t-tests were used to determine between-group differences (HSD/hEDS and controls). A two-way (group \times speed) mixed analysis of variance (ANOVA) was used to test for differences in VAS across speeds and groups. When the assumption of sphericity was violated, a Greenhouse-Geisser correction was performed to correct for the Type I error rate. Muscle-tendon dynamics were evaluated at every 5 % of stance using a two-way mixed ANOVA (group \times %stance). Holm's post hoc tests were used to detect significant differences between groups during stance

when there was no significant interaction, but a significant main effect of group was found. Effect sizes were considered according to either Cohen (2013) where $d \geq 0.20$, $d \geq 0.50$ and $d \geq 0.80$ were considered small, medium and large effect sizes, respectively or eta-squared (η^2) for mixed-ANOVA ($\eta^2 \geq 0.01$, $\eta^2 \geq 0.06$ and $\eta^2 \geq 0.14$ for small, medium and large effects, respectively (Cohen, 1988). The a priori level of statistical significance was set at $p < 0.05$.

3. Results

Participant characteristics are presented in Table 1. An exemplar force-elongation curve, from which AT stiffness was calculated for each participant, is shown in Fig. 1. AT stiffness was significantly lower ($p = 0.021$) and AT_{MA} significantly longer in HSD/hEDS compared to CON ($p = 0.036$). Age, height, weight, PWS, and ankle range of motion were similar between groups ($p > 0.292$). Maximal plantarflexion moment ($p = 0.10$, $d = 0.73$) was similar and maximal AT force significantly lower in HSD/hEDS compared to CON ($p = 0.048$, $d = 0.964$).

E_{walk} was significantly higher in HSD/hEDS compared to CON ($p = 0.037$, Fig. 2). E_{walk} was significantly higher at 80 % PWS compared to both 100 % and 120 % PWS in HSD/hEDS ($p < 0.034$) whereas E_{walk} was similar across speeds in CON ($p = 0.99$).

Pain was significantly higher in HSD/hEDS (mean difference (MD): 29.2 ± 7.2 mm, $p < 0.001$) compared to CON (Fig. 3). Pain was significantly higher at 120 % PWS (37 ± 24.2 mm) compared to 80 % PWS (30.7 ± 25.8 mm, $p = 0.041$) and PWS (26.3 ± 22.9 mm, $p = 0.011$) in HSD/hEDS. In the control group, pain was similar across all walking speeds (range: 1.4 ± 4.2 mm at 80 % PWS to 2.7 ± 6.4 mm at 120 % PWS, $p = 0.99$).

At all walking speeds, MG fascicles shortened continuously throughout stance ($p < 0.001$, Fig. 4). Fascicle shortening velocity was also similar between groups across speeds ($p = 0.556$). Although not statistically significant ($p = 0.08$), peak AT force during stance was 8.3 ± 7.3 %, 9.0 ± 8.4 % and 9.9 ± 9.1 % higher in HSD/hEDS compared to CON, demonstrating a medium ($d = 0.427$) to large ($d = 0.511$) effect size from 80 to 120 % PWS, respectively. In CON, fascicle work was significantly higher at 80 % and 120 % PWS compared to PWS ($p = 0.016$; $d = 0.604$) whereas MG fascicle work was similar across speeds in HSD/hEDS ($p > 0.174$, $d < 0.104$, Fig. 5).

Stance time decreased as a function of %PWS ($p < 0.001$) and was significantly longer at all speeds in HSD/hEDS compared to CON ($p = 0.023$, $d = 0.802$, Table 2). Muscle energy cost increased with speed in both groups ($p = 0.024$), with faster walking speeds associated with higher muscle energy costs. However, muscle energy cost was similar between groups ($p = 0.488$, $\eta^2 = 0.019$). Muscle mechanical efficiency was similar across speeds in both HSD/hEDS (25.9 ± 9.2 %) and CON (30.8 ± 11.7 %). No significant group differences were observed ($p = 0.247$, $\eta^2 = 0.01$). There were also no group differences in AT strain energy storage ($p = 0.88$, $\eta^2 < 0.0001$, Table 2). At all speeds, the ratio of muscle energy cost to AT energy storage during stance was greater than 1.0 ($p < 0.001$), suggesting a higher muscle metabolic cost to store AT mechanical energy. This ratio was similar between groups ($p = 0.27$, $\eta^2 = 0.05$).

An exemplar 30 s filtered SOL and MG EMG RMS signal during walking at PWS is shown for both an HSD/hEDS participant and their age- and sex-matched control (Fig. 6). Across speeds, both SOL ($p = 0.04$) and LG ($p = 0.014$) activation were higher during loading in HSD/hEDS compared to CON (Fig. 7). Muscle activation for both TA ($p = 0.271$) and FL ($p = 0.349$) was similar between groups. There were no between-group differences in muscle co-activation during stance for either SOL:TA ($p = 0.151$) or LG:TA ($p = 0.207$). A significant group \times stance phase interaction on TA:FL coactivation was demonstrated, with loading associated with a lower coactivation ratio in HSD/hEDS compared to controls ($p = 0.012$). These data are shown in Fig. 8. The calculated agonist-antagonist ratio was not equal for CON (test for equality: $p < 0.05$ for both SOL:TA and LG:TA) whereas it was in HSD/

Table 3
Summary of main statistical outcomes.

Outcome Variable	Statistical Test	Comparison / Factor (s)	p-value	Effect Size	Direction / Interpretation
Achilles tendon stiffness	Independent t-test	HSD/hEDS vs. CON	0.021	$d = 1.07$	↓ in HSD/hEDS
AT moment arm length	Independent t-test	HSD/hEDS vs. CON	0.036	$d = 0.96$	↑ in HSD/hEDS
Max plantarflexion moment	Independent t-test	HSD/hEDS vs. CON	0.102	$d = 0.73$	↓ in HSD/hEDS
Max AT force	Independent t-test	HSD/hEDS vs. CON	0.048	$d = 0.96$	↓ in HSD/hEDS
Energy cost of walking	Two-way mixed ANOVA	Group main effect	0.034	$\eta^2 = 0.17$	↑ in HSD/hEDS
Pain	Two-way mixed ANOVA	Group main effect	<0.001	$\eta^2 = 0.42$	↑ in HSD/hEDS; ↑ with speed
MG fascicle shortening velocity	Two-way mixed ANOVA	Group main effect	0.556	$\eta^2 < 0.001$	n.s.
MG fascicle work	Two-way mixed ANOVA	Speed main effect	0.016	$d = 0.60$	↑ at 80 % and 120 % PWS in CON
Stance time	Two-way mixed ANOVA	Group main effect	0.023	$d = 0.80$	↑ in HSD/hEDS
Muscle energy cost	Two-way mixed ANOVA	Group main effect	0.488	$\eta^2 = 0.02$	↑ with speed only ($p = 0.024$)
Mechanical efficiency	Two-way mixed ANOVA	Group main effect	0.247	$\eta^2 = 0.06$	n.s.
AT strain energy storage	Two-way mixed ANOVA	Group main effect	0.880	$\eta^2 < 0.001$	n.s.
SOL activation (loading phase)	Two-way mixed ANOVA	Group main effect	0.040	$d = 0.48$	↑ in HSD/hEDS
LG activation (loading phase)	Two-way mixed ANOVA	Group main effect	0.014	$d = 0.43$	↑ in HSD/hEDS
TA & FL activation	Two-way mixed ANOVA	Group main effect	>0.271	$\eta^2 < 0.02$	n.s.
SOL:TA coactivation	Two-way mixed ANOVA	Group main effect	0.135	$\eta^2 = 0.05$	n.s.
LG:TA coactivation	Two-way mixed ANOVA	Group main effect	0.207	$\eta^2 = 0.03$	n.s.
TA:FL coactivation	Two-way mixed ANOVA	Group × %stance	0.041	$\eta^2 = 0.09$	↓ in HSD/hEDS in loading
Instantaneous ankle mechanical power (late stance)	Two-way mixed ANOVA, post-hoc	Group × %stance	<0.05	$d = 1.22$	↓ in HSD/hEDS (85–95 % stance)

Abbreviations: d : Cohen's d ; η^2 : eta-squared; PWS: preferred walking speed; n.s.: non-significant. Arrows indicate direction of difference in HSD/hEDS relative to CON.

Table 4
Key findings and clinical relevance.

Energy Cost of Walking (E_{walk})	Finding: E_{walk} significantly higher in HSD/hEDS ($p = 0.037$); E_{walk} at 80 % PWS ($p < 0.034$). Clinical Relevance: The higher E_{walk} confirms greater energetic demands of walking in HSD/hEDS. While tendon compliance could contribute to this elevated cost, our data suggest that redistribution of joint work to the hip and knee is a more plausible mechanism.
Pain	Finding: Pain significantly higher in HSD/hEDS vs. controls ($p < 0.001$); Increases with speed in HSD/hEDS ($p < 0.041$). Clinical Relevance: Pain increased, particularly at faster speeds, consistent with increased muscle activation and coactivation needed for stability in HSD/hEDS. This suggests that compensatory neuromuscular strategies, rather than tendon mechanics alone, contribute to pain and reduced walking tolerance.
Achilles Tendon Mechanics	Finding: AT stiffness significantly lower ($p = 0.021$) and AT moment arm significantly longer ($p = 0.036$) in HSD/hEDS. Clinical Relevance: Although compliant tendons may theoretically increase muscle work and metabolic cost, we did not observe significantly higher fascicle work or muscle metabolic cost. Thus, altered tendon mechanics alone are unlikely to explain the elevated E_{walk} , pointing instead to joint power redistribution and compensatory activation.
Muscle Activation	Finding: SOL and LG activation higher in HSD/hEDS during loading (SOL $p = 0.04$; LG $p = 0.014$). Clinical Relevance: Greater plantarflexor activation likely reflects compensatory stiffening to stabilize hypermobile joints. While this increases metabolic demand, it also provides critical joint stability, helping explain both the higher E_{walk} and higher pain ratings observed.
Ankle Joint Power	Finding: Instantaneous ankle joint mechanical power significantly lower in HSD/hEDS during late stance ($p < 0.05$). Clinical Relevance: Lower ankle power output supports the interpretation that positive mechanical work is redistributed to proximal joints. This less efficient gait strategy increases energetic cost and parallels adaptations observed in aging populations.

hEDS. Functionally, in HSD/hEDS at 80 % PWS, the mean activation for the agonist muscle (SOL or LG) was similar to that of the antagonist (TA). The agonist-antagonist ratio was greater than 1.0 for both HSD/hEDS and CON at all other walking speeds ($p = 0.33$ for 100 % PWS and $p = 0.119$ at 120 % PWS), indicating higher activation of the plantarflexor agonists (SOL or LG, respectively) compared to the dorsiflexor antagonist (TA). TA:FL coactivation ratios were not significantly different between groups ($p = 0.17$).

Instantaneous mechanical joint power increased with walking speed ($p < 0.001$) and was significantly lower in HSD/hEDS compared to CON ($p < 0.05$, Fig. 9). Specifically, instantaneous positive ankle power was significantly lower in HSD/hEDS compared to CON during late stance (from 85 % to 95 % of the stance phase, $p < 0.05$). Table 3 summarizes the primary outcomes of the study alongside their clinical relevance, highlighting the most important findings for interpretation and application in HSD/hEDS management. (See Table 4.)

4. Discussion

This study set out to evaluate the impact of altered muscle and tendon mechanical properties on the energy cost of walking in people with and without common joint hypermobility conditions. A lower AT stiffness and weaker plantar flexor strength was confirmed in people living with HSD/hEDS, supporting previous literature. (Alsiri, Al-Obaidi, Asbeutah, Almandeel, and Palmer, 2019; Rombaut et al., 2012b). In this investigation we observed a higher energy cost of gait and higher pain levers in people with HSD/hEDS. The elevated E_{walk} in HSD/hEDS supports the notion that increased tendon compliance requires additional muscle work for a given muscle-tendon unit length change. The additional muscle work would incur a greater metabolic cost as the muscle must actively shorten more against a more compliant tendon. Despite this notion, we could not demonstrate a significantly higher muscle metabolic cost or mechanical work in HSD/hEDS, suggesting factors other than these must contribute to the higher E_{walk} .

While we hypothesized that a lower AT stiffness would also result in greater fascicle shortening in individuals with HSD/hEDS, this hypothesis was not supported by our empirical data showing similar muscle fascicle shortening and shortening velocity during walking compared to individuals without HSD/hEDS. We speculated, therefore, that fascicle lengths were similar between groups because of lower ankle joint mechanical power in HSD/hEDS. Stenroth, Sipilä, Finni, and Cronin (2017)

showed similar MG fascicle lengths in young vs. older adults during walking at their preferred walking speeds. To support this hypothesis, we found a lower instantaneous ankle joint power in HSD/hEDS during the propulsive phase of stance. As a result, these individuals would have had to redistribute positive mechanical joint work to more proximal joints, such as at the knee and/or the hip, to walk at similar gait speeds, similar to what is seen in aging gait (Devita and Hortobagyi, 2000; Franz, 2016). The speculation is that mechanical joint work is redistributed more proximally because of reduced muscle strength and/or power of the ankle plantarflexors, which appears to also be the case in HSD/hEDS. Performing mechanical work at more proximal joints is thought to elevate E_{walk} because muscles crossing the knee and hip have relatively longer fascicle lengths and shorter in-series tendons (Sawicki, Lewis, and Ferris, 2009). Activating longer muscle fascicles at the knee and/or hip compared to activating short fascicles of the plantarflexors increases the muscle energy cost because each sarcomere in series must be engaged, consuming a greater volume of ATP. Further, short in-series tendons also contribute to an elevated E_{walk} because less energy is stored for a given level of strain in a short tendon (Blazevich and Fletcher, 2023).

As noted by Krupenevich, Beck, Sawicki, and Franz (2022), ankle mechanical power output is not solely generated by the plantarflexor muscles alone. Positive mechanical ankle power is generated by a combination of muscle and tendon mechanical power output, which when stretched, can return a portion of the stored mechanical energy contributing to mechanical power amplification of the muscle-tendon unit (Blazevich and Fletcher, 2023). For a given AT force developed during stance, a more compliant tendon will store more elastic strain energy. This mechanism was not fully utilized by HSD/hEDS individuals: despite a higher AT compliance, AT energy storage was similar between hEDS/HSD and CON.

Together, we posit that E_{walk} was higher in HSD/hEDS because of greater mechanical joint work performed at the knee and the hip compared to CON who could walk with a relatively greater positive ankle joint work. The latter would reduce E_{walk} because of the morphological properties of the plantarflexor muscle-tendon unit: short, pennate fascicles, and a long Achilles tendon.

Lower limb muscle activation may also explain an elevated E_{walk} in HSD/hEDS. A low E_{walk} is associated with a finely tuned pattern of activation vs. deactivation of agonist and antagonist muscles during specific phases of the gait cycle. Any increase in the level of agonist-antagonist coactivation will increase the metabolic cost due to the increase cost of muscle activation (Moore, Jones, and Dixon, 2014). In addition, a higher level of coactivation for the same level of muscle activation (and likely muscle force) would reduce net mechanical ankle joint work, further requiring additional mechanical work to be performed at presumably less efficient knee and hip joints (Sawicki, Lewis, and Ferris, 2009).

An elevated E_{walk} might also be attributed to increased pain and fatigue seen in HSD/hEDS (Krahe, Adams, and Nicholson, 2018), particularly at higher walking speeds, where higher coactivations are required to increase joint stability. The increased cost of muscle activation observed in HSD/hEDS may both be reflected in the observed higher pain levels and the elevated muscle activations seen during stance. Greater muscle activation would require additional metabolic energy to increase joint stability in HSD/hEDS (Ball et al., 2024), a compensatory mechanism to maintain joint stability in the face of joint hypermobility but one which likely increases metabolic cost and contributes to higher muscle fatigue and pain. While absolute AT force during stance was similar between groups ($p = 0.08$, small effect size), individuals with HSD/hEDS walked at a higher *relative* force compared to CON. This may have also contributed to the self-reported fatigue.

4.1. Limitations

While we aimed to match individuals with hypermobile conditions

with otherwise healthy peers based on age and sex, we did not match for activity levels. Thus, many of the similarities in walking mechanics and energetics may have stemmed from our sample of HSD/hEDS individuals being relatively younger and more active. The lack of meaningful reductions in preferred walking speed in HSD/hEDS further support this notion.

5. Conclusions

In this investigation, people with HSD/hEDS showed a significantly higher energy cost of walking and lower muscle strength. These differences were accompanied by significantly higher ratings of pain and higher muscle coactivation during stance following walking at, above and below their preferred walking speed. Lower muscle weakness, and higher muscle activation likely contributes to higher fatigability in individuals with HSD/hEDS.

Disclosure statement

The authors report there are no competing interests to declare.

CRediT authorship contribution statement

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Jared R Fletcher reports financial support was provided by The Ehlers-Danlos Society. Jared R Fletcher reports financial support was provided by Natural Sciences and Engineering Research Council of Canada. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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