Minimization of metabolic cost of transport predicts changes in gait mechanics over a range of ankle-foot orthosis stiffnesses in individuals with bilateral plantar flexor weakness

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Abstract

Neuromuscular disorders often lead to ankle plantar flexor muscle weakness, which impairs ankle push-off power and forward propulsion during gait. To improve walking speed and reduce metabolic cost of transport (mCoT), patients with plantar flexor weakness are provided dorsal-leaf spring ankle-foot orthoses (AFOs). The mCoT during gait depends on the AFO stiffness where an optimal AFO stiffness exists that minimizes mCoT. The biomechanics of why and how there exists a unique optimal stiffness for individuals with plantar flexor weakness are not well understood. To help understand why, we hypothesized that gait adaptations can be predicted by mCoT minimization. To explain how, we hypothesized that the AFO would reduce the required support moment and, hence, metabolic costs from the ankle plantar flexor and knee extensor muscles during stance and reduce hip flexor metabolic cost to initiate swing.

To test these hypotheses, we generated neuromusculoskeletal simulations to represent gait of an individual with bilateral plantar flexor weakness wearing an AFO with varying stiffness. Predictions were predicated on the goal of minimizing mCoT at each stiffness level, and the motor patterns were determined via dynamic optimization. The simulation results were compared to experimental data from subjects with bilateral plantar flexor weakness walking with varying AFO-stiffness.

Our simulations demonstrated that minimization of mCoT predicts gait adaptations in response to varying AFO stiffness levels in individuals with bilateral plantar flexor weakness. Initial reductions in mCoT with increasing stiffness were attributed to reductions in quadriceps metabolic cost during midstance. Increases in mCoT above optimum stiffness were attributed to the increasing metabolic cost of both hip flexor and hamstrings muscles.

The insights gained from our simulations could inform clinicians on the prescription of personalized AFOs. With further model individualization, simulations based on mCoT minimization may sufficiently predict adaptations to an AFO in individuals with plantar flexor weakness.
Author Summary

Neuromuscular disorders like stroke, Charcot-Marie-Tooth disease, and poliomyelitis often lead to calf muscle weakness, which makes walking slower and more demanding. To improve walking speed and reduce energy demand, patients with calf muscle weakness are frequently provided ankle-foot orthoses (AFOs). The energy demand of walking is affected by the AFO’s stiffness and there is a stiffness that minimizes the energy demand for an individual with calf weakness. To uncover the optimal stiffness, we generated simulations of an individual with calf muscle weakness walking with an AFO over a range of stiffnesses. Stable walking patterns were generated that minimized the energy demand for a given stiffness. We found that the initial reductions in energy demand as stiffness increased, were attributed to reductions in quadriceps muscle energy. Increases in energy demand as stiffness increased above the optimum were attributed to the increased energetic cost of both hip flexor and hamstrings muscles. With further model individualization, we believe that simulations based on minimizing the energy demand of movement can sufficiently predict adaptations to an AFO. Simulations can enable the prescription of personalized AFOs for individuals with neuromuscular disorders that help them walk with sufficient speed and efficiency to keep up with their peers.
Introduction

The plantar flexor muscles, consisting of soleus and the gastrocnemius, are often weakened in persons with neuromuscular disorders, such as Charcot-Marie-Tooth disease and poliomyelitis [1][2]. Weakness of the plantar flexors results in an altered gait pattern, characterized by reduced push-off power, and excessive ankle dorsiflexion and knee flexion during stance [3][4]. These gait deviations lead to a lower walking speed [5] and an elevated metabolic cost of transport (mCoT) [6], which limits daily physical mobility [7]. Dorsal leaf spring (DLS) ankle-foot orthoses (AFOs) are often prescribed to provide mechanical support during stance, augment push-off, and hence to reduce mCoT. In a DLS-AFO, a leaf spring connects a footplate to a calf casing posterior of the ankle and passively restricts ankle dorsiflexion by producing an external plantarflexion moment when the ankle is dorsiflexed. As a spring, the AFO can store energy when moving into dorsiflexion and release this energy as the ankle moves towards plantarflexion, thereby providing additional positive work during push-off [8].

In individuals with plantar flexor weakness, the effects of an AFO on improving gait kinematics and kinetics and reducing mCoT have been shown to depend on the stiffness of the leaf spring [9][10][11]. Beginning at low and with increasing AFO stiffnesses, the mCoT first decreases, before increasing at higher stiffness levels, demonstrating a convex relation between AFO stiffness and mCoT with an optimum stiffness where mCoT is minimal [9][10]. As demonstrated in healthy individuals [12][13][14], minimizing mCoT is prioritized during gait. As such, it can be expected that patients with gait disorders prefer walking with the stiffness that minimizes their metabolic energy cost. In case of plantar flexor weakness, the initial reduction in mCoT is thought to be the result of normalizing ankle and knee angles and moments which requires adequate AFO stiffness [9][10]. Normalization of the ankle and knee biomechanics is hypothesized to lead to a decrease in the metabolic cost of the quadriceps muscles and thereby reduce mCoT [15]. The initial decrease in mCoT may be further explained by a reduction in the metabolic cost of the plantar flexors as the AFO replaces the biological ankle plantarflexion moment during stance [11][16][17]. However, at higher
stiffnesses, as the AFO restricts the ankle range of motion (RoM) [9][18][16], it limits active biological ankle power generation and energy storage and release [19][16] of the AFO during push-off [9][10]. The reduced ankle push-off work may result in higher energy losses at contralateral heel-strike and lead to compensatory hip flexion work to initiate the swing phase [16], which are potential causes for the increased mCoT at higher AFO stiffness levels. However, how each of these factors contribute to the relation between AFO stiffness and mCoT in people with plantar flexor weakness is unknown.

The aim of this study was to gain insights into why and how mCoT is affected by AFO stiffness variation in individuals with plantar flexor weakness by using predictive musculoskeletal simulations. First, based on the assumption that mCoT is a predictor for gait pattern changes in healthy individuals [14][12], we hypothesized that minimization of mCoT is a predictor of kinematic, kinetic, and mCoT changes to varying AFO stiffness in individuals with bilateral plantar flexor weakness. Second, we tested whether initial reductions in mCoT with increasing stiffness are explained by i) decreasing metabolic cost of the quadriceps as the knee moments are normalized, and ii) decreasing metabolic cost of the plantar flexors as the AFO replaces the ankle plantar-flexion moment during stance phase. Third, we hypothesized that increases in mCoT as stiffnesses exceed the optimum stiffness are caused by the increasing metabolic cost of hip flexor muscles to initiate the swing phase as total push-off power decreases.
Methods

We created a planar musculoskeletal model of an individual with bilateral plantar flexor weakness, similar to [20] using OpenSim [21][22], and implemented an AFO with varying stiffness. To generate predictive gait simulations, we employed a reflex-based neuromuscular controller and optimized the control parameters using dynamic optimization to minimize mCoT, and solved the optimization problem in SCONE [23][24][20]. Predictive simulation results were compared to experimental data of subjects with bilateral plantar flexor weakness walking with varying AFO stiffness [10].

Musculoskeletal model

Based on the model of Delp et al. [25][24], we created a model with 9 degrees of freedom (3 around the pelvis and 1 around the hip, knee and ankle of each leg), actuated by 9 Hill-type muscles per leg (tibialis anterior, soleus, gastrocnemius, vasti, rectus femoris, biceps femoris short head, biarticular hamstrings, iliopsoas, gluteus maximus) in OpenSim 3.3 [21][22]. We set the maximum isometric muscle strength of the soleus and gastrocnemius muscles of both legs to 40% of normal healthy values (i.e. 60% muscle weakness), to induce bilateral plantar flexor weakness. Additionally, we restricted the ability to activate the plantar flexor muscles to 50%, to take into account that the weakened muscles would completely fatigue if they would be maximally activated for 10-20% of the gait cycle [26][27][28]. We modified passive muscle and tendon parameters in the model to maintain similar passive muscle forces as in the healthy model [20][29]. We set the slow twitch fiber ratios according to Johnson et al.[30] and Garrett et al.[31], similarly to Ong et al.[24]. We scaled the model according to experimental marker data of one subject with bilateral plantar flexor weakness close to the group’s mean height (177 cm) and body mass (81 kg) from the experimental study [10].

To model the forces between the ground and the foot, we used a compliant Hunt-Crossley contact model [32]. We placed one contact sphere at the heel and one at the toe of each foot (Fig 1). We set the force parameters (stiffness, dissipation and friction) according to Veerkamp et al.[33], and modelled
the knee ligaments using a rotational spring (2 Nm/deg) and damper (0.2 Nm/deg/s) around the knee
joint if the knee angles were outside the 5-120 deg flexion range [20].

We modelled each AFO as two rigid parts, including a calf casing and a footplate with their
experimental mass (calf casing: 0.2 kg, footplate and shoe: 0.5 kg) [10]. We attached the AFO parts
rigidly to the tibia and calcaneus, respectively (Fig 1). We modelled the stiffness of the AFO as two
linear torsional springs for ankle dorsiflexion and for plantarflexion. In order to match experimental
movement of the ankle within the AFO, the AFO did not deliver a moment in the neutral angle range,
i.e. between 4.5 deg plantarflexion and 2 deg dorsiflexion. In DLS-AFOs, this small range depends on
the material and manufactured geometry of the AFO, and its fit on the subject’s leg. The neutral angle
range was defined from the ankle angle range during swing phase of the subject because in swing
phase the AFO exerts only small moments on the ankle joint [34].

Fig 1. Musculoskeletal model of an individual with bilateral plantar flexor weakness equipped with
AFOs. The stiffness (range 0 − 7 Nm/deg) of the dorsal leaf spring is modelled in OpenSim as a torsional
spring between the calf-casing and footplate of each AFO (black). Contact between the foot and the ground
are modelled by forces generated by compliant contact spheres (cyan).

Simulation framework

We used SCONE (v1.6.0), a simulation, control, and dynamic optimization framework [23], to
simulate gait of 10 seconds in duration. The muscle activations were generated by a reflex-based gait
controller [35][24], whose parameters were optimized by minimizing the specified objective function
using the Covariance Matrix Adaptation evolutionary strategy (CMA-ES) [36][20][24][37].

The objective function (J) was comprised of desired high-level tasks during gait, where minimization
of mCoT ($J_{mCoT}$) was the primary measure. The following measures were included in the objective
function to be minimized:

$J_{mCoT}$ was the mCoT measure, which aggregated the total muscle metabolic cost divided by the
distance travelled. We computed the metabolic cost of each individual muscle, according to the
muscle metabolic model by Uchida et al. [38].
P_{Gait} was a penalty on the deviations of the simulation from gait at a specified minimum velocity of 1.22 m/s, to match experimental data without falling down [10].

We added P_{DOFLimAnkle} and P_{DOFLimKnee} penalties to keep the ankle angle and passive knee forces within physiological limits. We gave penalties, when the ankle angle was outside of the \([-60, 60]\) deg range and when the absolute coordinate limit moment acting on the knee joint was larger than 5 Nm [20].

P_{FGImpact} was a penalty composed of the sum of the absolute ground reaction force derivative over the simulation divided by the distance travelled, which was included to penalize high loading rates at impact.

P_{HeadStab} was a penalty for excessive head accelerations calculated as the sum of the absolute head accelerations normalized by distance travelled [39][40].

The weights associated to these high-level tasks were \(w_{mCoT}=1.5\), \(w_{Gait}=10^9\), \(w_{DOFLimAnkle}=0.1\), \(w_{DOFLimKnee}=0.01\), \(w_{FGImpact}=0.05\), \(w_{HeadStab}=0.1\). We chose the weights based on a previous study [20], but adapted with a higher emphasis on \(J_{mCoT}\) to test the hypothesis that energy cost minimization can predict gait changes with AFO stiffness.

We ran the simulations for stiffness levels between 0 and 7 Nm/degree, with steps of 1 Nm/degree.

We ran 5 optimizations in parallel with different random seeds in each round. Each optimization was terminated when the average reduction of the cost function score in the last 200 generations was smaller than 0.01 %. As initial guess, we used a controller with parameters resulting in healthy gait [20]. We set the initial step size (\(\sigma\)), as the initial standard deviation of the parameters, to 0.05 [41].

To check the robustness of our results, we ran multiple optimizations in sequence. We used the best results of an optimization to initialize the next optimization with the same model (same AFO stiffness setting) and the same initial step size, similar to Song et al. [37] and Ong et al. [41]. Since the trend of the results was not changing qualitatively between the first and second round of optimizations, we performed only two rounds of optimizations. We considered the results of the second round as the final results.
Comparison with experimental data

To test whether mCoT is a good predictor of the gait changes with varying AFO stiffness, we compared our predictive simulations with experimental gait and mCoT data of 24 bilateral weakness subjects walking with 5 different AFO stiffness configurations (2.8, 3.5, 4.3, 5.3, 6.6 Nm/deg) [10]. In this experimental study, the mean mCoT (in J/kg/m) was evaluated from a 6-min comfortable walk test with simultaneous gas-analysis over the last three minutes of the test. The study assessed gait kinematics, kinetics and ground reaction forces with a 3D gait analysis on a 10-meter walkway using the PlugInGait marker model [42]. Based on these measurements, clinically important gait features for the evaluation of AFOs, e.g. the peak ankle dorsiflexion angle, ankle power, knee angle, knee moment and AFO-generated power, were calculated using a custom-made script in MATLAB® R2015b (MathWorks Inc.).

To calculate the joint moments from the predictive simulations, we processed the simulation results with the Analysis Tool in OpenSim. Based on the joint angles and moments, we calculated the joint powers (Fig 2). To calculate negative and positive joint work over the whole gait cycle and separate gait phases we used trapezoidal numerical integration of the joint power. We divided the gait cycle into gait phases according to the definitions of Whittle [43]. These gait phases were: loading response, midstance, push-off comprising of terminal stance and preswing, and swing. In order to assess the source of the mCoT in detail, we calculated the simulated muscle metabolic energy cost [38] over whole gait cycles, and different gait phases, for all 9 muscles. We normalized the metabolic cost by body mass, mean walking speed and simulation duration to get the total metabolic cost over a gait cycle in J/kg/m. We used a custom-made script in MATLAB® R2020b (MathWorks Inc.) for all calculations.

To compare simulation-based outcome measures to experimental observations, we calculated the effect of 1 additional Nm/degree in stiffness for both the simulations and experimental data using a linear fit across the stiffness levels for the following key gait features: peak ankle dorsiflexion angles, peak total-, biological- and AFO ankle joint moments and powers, peak knee extension angles and...
peak knee joint moments (between 35-50% of gait cycle) [10]. We assessed the goodness of fit of the curve by its coefficient of determination value (Rsq), calculated in MATLAB® R2020b (MathWorks Inc.) [44]. To assess the similarity between the simulated and experimentally obtained slopes, we expressed the difference in slope in standard deviation of the experimental slope based on the 24 patients.
Results

Our predictive gait simulations took 20.46 hours on average to complete on an AMD Ryzen 9 3950X (16 CPUs – 32 virtual cores with hyperthreading, 3.5 GHz base) computer on 10 parallel threads. The primary objective of mCoT minimization contributed to about 90% of the final optimization scores in all simulations. In the final simulations, $P_{\text{Gait}}$ and $P_{\text{DoFLimAnkle}}$ were optimized to zero and did not contribute to the objective score. An overview of the simulated joint angles, moments and powers for varying AFO stiffness levels are presented in Fig 2.

Comparison of simulated and experimental results

The predicted slopes of peak total, biological and AFO-provided ankle joint moment and power, peak ankle dorsiflexion angle, peak knee extension angle and peak internal knee flexion moment were all within 1.2 standard deviations (SD) of the experimental data. The highest slope difference was found for peak total ankle moment and peak AFO moment, where a larger effect of additional stiffness was predicted by the simulations than found in experimental data. Peak total ankle moment was approximately constant in the experiments but showed an increasing trend in the simulations (Fig 2, Fig 3 and S1 Table).

Fig 3. Peaks of relevant joint and AFO powers, moments and angles during the stance phase. AFO stiffness was varied from 1 – 7 Nm/deg. The results of simulation with fitted lines are shown in green, and mean experimental outcomes of all patients in blue. As experimental data the mean and SD (blue shading) of the individual fitted lines were used.
Simulated AFO effects on mCoT and muscle metabolic consumption

The mCoT showed a clear minimum with increasing stiffness in both the simulated and individual experimental results (Fig 4). The simulations presented a strong quadratic trend, Rsq = 0.836, while the average experimental results showed a less pronounced quadratic trend, Rsq = 0.634, due to large inter-subject variability (Fig 4).

Fig 4. The mCoT in simulation and individual experiments wearing an AFO with varying stiffness. The individual experiments included the condition without an AFO and wearing shoes for 21 subjects. A quadratic curve was fitted to the data points for each subject dataset and the minimum of the fitted curve was taken for each subject as their individual minimum mCoT value which is happening at their individual optimal stiffness. The mCoT values of the subjects were shifted by their minimum mCoT value and the AFO stiffness values were shifted by the subject’s optimal stiffness value. The shifted individual experimental subject data is shown in different shades of grey. One quadratic curve was fitted to all shifted experimental subject data (dotted line), the goodness of fit is indicated by the Rsq number on the plot (Rsq = 0.634). The same was done for the simulation results (solid line, Rsq = 0.836). Both the experimental (EXP – shaded dots) and simulation data (SIM – open circles) show quadratic trends (Rsq > 0.63).

The largest change in metabolic cost of individual muscles was found in the vasti, which also showed a quadratic trend (Rsq = 0.928). In contrast, the metabolic cost of the hamstrings and iliopsoas increased continuously. Both the soleus and gastrocnemius metabolic cost did not change substantially with increasing AFO stiffness (Fig 5 and S2 Table). Gluteus maximus, tibialis anterior, rectus femoris and biceps femoris short head muscles did not show any change with increasing AFO stiffness (S2 Table).

Fig 5. The mCoT, and total metabolic cost of the top 5 muscle contributors in simulations. Total metabolic cost was taken during one whole gait cycle as AFO stiffness was varied from 0 – 7 Nm/deg. Quadratic curves were fitted to the data-points and the Rsq values represent the goodness-of-fit of the curves.
Joint work and muscle metabolic consumption per gait phase

Total knee joint work did not differ with increasing AFO stiffness during the loading response, while vasti metabolic cost decreased and hamstrings metabolic cost increased, especially above 3 Nm/degree. In midstance, positive knee joint work decreased, negative knee joint work increased and vasti metabolic cost decreased, while hamstrings metabolic cost did not show a clear trend with increasing AFO stiffness. (Fig 6, S3 and S4 Table).

Fig 6. Knee joint work, vasti and hamstrings metabolic cost during loading response, midstance, and push-off. AFO stiffness was varied from 0-7 Nm/deg. Knee joint work was portioned into positive and negative work and these were totalled and reported for each phase of gait.

During loading response, negative biological ankle work decreased with increasing AFO stiffness, while no effect of stiffness on AFO work was found. Similarly, no effect on the metabolic cost of the soleus or gastrocnemius was found with increasing stiffness. In midstance, negative biological ankle joint work decreased and negative AFO work increased with increasing stiffness. Soleus metabolic cost increased slightly until 5 Nm/deg AFO stiffness. During push-off, biological ankle work, AFO work, and soleus metabolic cost increased until 3 Nm/deg, At higher stiffnesses, biological ankle work generation and soleus metabolic cost decreased again (Fig 7, S3 and S4 Table).

Fig 7. Biological ankle and AFO work, gastrocnemius and soleus metabolic cost during loading response, midstance, and push-off. AFO stiffness was varied from 0-7 Nm/deg, Biological ankle joint and AFO work was portioned into positive and negative work and these were totalled and reported for each phase of gait.

During loading response, negative hip joint work decreased and hamstrings metabolic cost increased with increasing stiffness. In early midstance, positive hip joint work increased, and in late midstance, negative hip joint work and iliopsoas metabolic cost increased with increasing AFO stiffness (Fig 8, S3 and S4 Table).

Fig 8. Hip joint work, iliopsoas and hamstrings metabolic cost during loading response, midstance, and push-off. AFO stiffness is varied from 0-7 Nm/deg. Hip joint work was portioned into positive and negative work and these were totalled and reported for each phase of gait.
Discussion

The aim of this study was to gain insights into why and how motor pattern adaptations in people with bilateral plantar flexor weakness result in an optimal AFO stiffness to minimize mCoT. As hypothesized, our results showed that minimization of mCoT predicts most of the kinematic, kinetic, and mCoT changes due to varying AFO stiffness in this population. Initial reductions in mCoT with increasing stiffness were attributed to reductions in quadriceps metabolic cost, as hypothesized, but in contrast to our hypothesis, plantar flexor metabolic cost did not decrease. Increases in mCoT above the optimum AFO stiffness were attributed to the increasing metabolic cost of both hip flexor muscles and hamstrings muscles.

The mCoT appears to be a good predictor of gait changes in individuals with bilateral plantar flexor weakness wearing AFOs with varying stiffness. Our forward simulations predicted changes in lower extremity kinematics and kinetics due to AFO stiffness variations within 1.2 SD of the experimentally observed changes. Although mCoT was not the only factor within our objective function, it had by far the largest contribution as it was responsible for 90% of the final objective function values. These findings support the claims that humans tend to minimize mCoT when walking as previously demonstrated in healthy subjects [12][13][14] and in simulations of patients walking without assistive devices [45].

Differences between simulated and experimental data were found in the knee joint angle and moment curves (Fig 2). Although the effects of varying AFO stiffness on specific gait features at midstance were predicted reasonably well, in early stance the knee angle and moment became more extended with increasing AFO stiffness (Fig 2 and 3). This effect is likely explained by the fact that more extended knees in early stance are linked to decreased mCoT [46][47][48]. The human likely minimizes or is subjected to other factors, such as muscle fatigue and loading rate [49][50][33], which may cause the knee flexion in loading response instead of the metabolically more efficient straight knee. Although loading rates were penalized in our simulations, loading rates still increased up to
twice as much as found in healthy subjects as AFO stiffness increased (S1 Fig), which could increase the risk of lower limb stress fractures [51][52].

The convex mCoT trend with respect to AFO stiffness can be explained by the metabolic cost changes in the quadriceps (vasti), hip flexor (iliopsoas) and hamstrings muscles. This parabolic trend was also present in the individual experimental data [10] (Fig 4). As hypothesized, initial reductions in mCoT starting at low and with increasing AFO stiffness were due to a decrease in the metabolic cost of the quadriceps (vasti) muscles (Fig 5). From low to medium AFO stiffnesses, the knee angle and moment normalized, reducing the metabolic cost of the vasti [46][48]. At higher stiffness levels, the knee became increasingly extended, which minimized mCoT but might cause knee pain in real life [51][52]. Contradicting our hypothesis and experimental data in healthy subjects [53], metabolic cost of the plantar flexor muscles did not decrease with increasing AFO stiffness. As muscle activation and metabolic cost changes are related factors, our simulation result was also contrary to the findings of Harper et al. [18] who found reductions in medial gastrocnemius muscle activation with increasing AFO stiffness in lower limb salvage patients [18]. We likely did not observe reductions in plantar flexor metabolic cost, because the low muscle strength in the model resulted in proportionally low muscle mass, which reduces the muscle’s contribution to metabolic cost [29], and hence, even without an AFO the plantar flexors did not contribute substantially to mCoT.

In agreement with our hypothesis, increases in mCoT above the optimum stiffness were partly due to increases in the metabolic cost of the hip flexor (iliopsoas) muscles. Iliopsoas metabolic cost increased at the end of midstance before the start of push-off, potentially as a pre-activation to help initiate the swing phase. Increased hip work was also shown in an experimental study in patients with chronic stroke or multiple sclerosis where 0.5-5.4 Nm/deg AFO stiffnesses were tested [16]. Additionally, an increase in metabolic cost of the hamstrings muscles added to the increase in mCoT above the optimum stiffness. This metabolic cost increase can be seen during early stance where slightly more extended hip joint angles, larger hip extension moments (Fig 2) and decreasing negative hip joint work (Fig 8) can also be observed as AFO stiffness increases. At high stiffness levels, the hip
is more extended at initial contact, and hip flexion is reduced during loading response that further contributes to the increased knee joint loading rates at high stiffness.

**Limitations and future work**

To test our hypotheses, we used a simplified, planar musculoskeletal model where medio-lateral stabilization was excluded, which could explain why our mCoT results were ∼10% lower [54] than in the experiments. With suboptimal AFO settings, the out-of-plane compensation, such as trunk motions, are known to be more extreme [55], hence the sensitivity of the mCoT trend to AFO stiffness could be higher in reality than in our simulations.

In the experimental study that was used for comparison, only AFOs with a stiffness in the range of 2.8-6.6 Nm/deg were tested. Hence, we were unable to verify the validity of our prediction with low stiffness levels.

In the future, simulations might be used to predict the individual optimal AFO properties, for which improving our understanding of the underlying mechanisms in this study was an essential first step. To be able to accurately predict adaptations to an AFO at the level of an individual, out-of-plane degrees of freedom and muscle actions should be investigated to understand the affects out-of-plane compensations. Furthermore, sensitivity analyses should be performed to evaluate the effect of patient and device characteristics, such as body weight, muscle weakness and muscle spasticity, and the neutral angle range of the AFO, have on the optimal AFO stiffness. With individualized models, our forward simulations could help predict the individual adaptations of patients to an AFO and improve the prescription of AFO settings.

**Conclusion**

We showed that adaptations in gait mechanics due to varying AFO stiffness, in individuals with bilateral plantar flexor weakness, can be predicted by minimization of mCoT. Our simulation results demonstrate the convex relation between mCoT and AFO stiffness, and are able to explain this shape by decreases in quadriceps metabolic cost in midstance, and increases in metabolic cost of the
hamstrings during loading response and iliopsoas in mid-to-late stance as AFO stiffness increases above the optimal. In the future, mCoT minimization may enable predictions for individualized gait adaptations to an AFO for people with bilateral plantar flexor weakness and facilitate optimal AFO prescriptions. The musculoskeletal models (in OpenSim, https://simtk.org/projects/opensim) and code, which were used to execute the gait optimization (in SCONE, https://simtk.org/projects/scone), and our complete simulation results are provided at https://simtk.org/projects/afo-predictions.

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Supporting information

S1 Fig. Peak loading rate (GRF derivative) in loading response across 0-7 Nm/deg stiffnesses (BW: body weight). The found peak loading rate values are more than twice as high as the loading rate on healthy subjects during walking at 1.3 m/s [51], but lower than the loading rate on healthy subjects during running at 3.7 m/s [56].

S1 Table. Slope of relevant joint kinematics, kinetics and powers during the stance phase of gait. AFO stiffness was varied from 1 – 7 Nm/deg. From left to right: slope of the line fitted to the forward simulation result, mean of the slope of the lines fitted to the bilaterally affected patients’ results, standard deviation (SD) of the slope of the lines fitted to the bilaterally affected patients’ result, difference between the simulation slopes and the mean of the experimental slopes divided by the standard deviation of the experimental slopes.

S2 Table. Mean metabolic cost for the whole model and for each muscle group of the model. Data taken during a whole gait cycle as AFO stiffness was varied from 0 – 7 Nm/deg.

S3 Table. Positive and negative mechanical joint work calculated with integration for each gait phase. AFO stiffness was varied from 0 – 7 Nm/deg.

S4 Table. Metabolic cost of transport of each muscle group calculated with integration for each gait phase. AFO stiffness was varied from 0 – 7 Nm/deg.
Fig 4
Fig 5

- Total mCoT (J/kg/m) with Rsq=0.836
- Vasti metabolic cost (J/kg/m) with Rsq=0.928
- Gastrocnemius metabolic cost (J/kg/m) with Rsq=0.214
- Soleus metabolic cost (J/kg/m) with Rsq=0.781
- Iliopsoas metabolic cost (J/kg/m) with Rsq=0.524
- Hamstrings metabolic cost (J/kg/m) with Rsq=0.77

AFO stiffness (Nm/deg)
Fig 6
Fig 7