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Predictive simulations identify potential neuromuscular contributors to idiopathic toe walking

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ABSTRACT

Background: Most cases of toe walking in children are idiopathic. We used pathology-specific neuromusculoskeletal predictive simulations to identify potential underlying neural and muscular mechanisms contributing to idiopathic toe walking.

Methods: A musculotendon contracture was added to the ankle plantarflexors of a generic musculoskeletal model to represent a pathology-specific contracture model, matching the reduced ankle dorsiflexion range-of-motion in a cohort of children with idiopathic toe walking. This model was employed in a forward dynamic simulation controlled by reflexes and supraspinal drive, governed by a multi-objective cost function to predict gait patterns with the contracture model. We validated the predicted gait using experimental gait data from children with idiopathic toe walking with ankle contracture, by calculating the root mean square errors averaged over all biomechanical variables.

Findings: A predictive simulation with the pathology-specific model with contracture approached experimental ITW data (root mean square error = 1.37SD). Gastrocnemius activation was doubled from typical gait simulations, but lacked a peak in early stance as present in electromyography. This synthesised idiopathic toe walking was more costly for all cost function criteria than typical gait simulation. Also, it employed a different neural control strategy, with increased length- and velocity-based reflex gains to the plantarflexors in early stance and swing than typical gait simulations.

Interpretation: The simulations provide insights into how a musculotendon contracture combined with altered neural control could contribute to idiopathic toe walking. Insights into these neuromuscular mechanisms could guide future computational and experimental studies to gain improved insight into the cause of idiopathic toe walking.

1. Introduction

Children often walk on their toes during the early stages of walking development (Sutherland et al., 1980), however, persistent toe walking beyond the age of three is considered pathological (O'Sullivan et al., 2019). Toe walking may be a symptom of an underlying condition (e.g., cerebral palsy, Charcot-Marie tooth disease, congenital talipes equinovarus), but in many cases the toe walking pattern is labelled

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idiopathic, without a clear underlying cause. Idiopathic toe walking (ITW) has been suggested to be a neurodevelopmental problem. Indeed, children with ITW display more neuropsychological problems than their typically developing (TD) peers (Engström et al., 2012) and show increased prevalence of several developmental delays (Shulman et al., 1997). Additionally, children with ITW score worse for various sensory tests than TD children (Williams et al., 2010, 2014).

Fortunately, ITW generally ceases over time without any need for intervention (Engström and Tedroff, 2018). However, those children who continue to toe walk during growth may develop a musculotendon contracture that progressively limits passive ankle joint dorsiflexion range-of-motion (Sobel et al., 1997; Solan et al., 2010). Older children with ITW who present with fixed ankle joint contracture commonly undergo orthopaedic surgery to lengthen the Achilles tendon (Kogan and Smith, 2001) or lengthen the muscle-tendon junction (Brierty et al., 2021) aiming to restore a typical gait pattern. Although these surgical interventions are effective in lengthening the muscle tendon unit with satisfactory restoration of gait biomechanics, it is an invasive procedure that can weaken muscles. Currently, it is unclear whether contracture is the only contributor to toe walking in older children who present with reduced dorsiflexion range of motion. Neurophysiological mechanisms could also contribute via altered neural control, but measurements of neural control and its underlying mechanisms have not been reported for children with ITW scheduled for a muscle or tendon lengthening surgery. Insights into how musculotendon contracture, and spinal and/or higher-level (i.e., supraspinal) neural control contribute to ITW could help to gain a better understanding of mechanisms involved in ITW development. Eventually, this may enable improved treatment or even prevent the need for surgery by being able to target these mechanisms.

Predictive, forward dynamic simulations of gait have a certain potential to unravel how musculotendon contracture and neural control could contribute to ITW. Such a physics based-framework can predict new gait patterns without the need for experimental data, enabling the opportunity to answer mechanistic 'what if'-questions. Cause-effect relationships can therefore be examined in a controlled setting. For example, predictive simulations have been applied to investigate the effects of plantarflexor weakness (Ong et al., 2019; Waterval et al., 2021) and contracture (Ong et al., 2019) on gait, with the latter finding that severe levels of plantarflexor contracture resulted in a simulated ITW. However, the level of contracture was not informed by ITW-specific musculotendon model parameters and the resultant gait pattern was not objectively compared to ITW patient data. Hence, it is still unclear whether simulations with a realistic pathology-specific contracture would predict ITW, and permit evaluation of other mechanisms that may be involved in ITW. Therefore, our study aimed to both (i) predict ITW with forward dynamic simulations, and (ii) evaluate the contribution of plantarflexor musculotendon contracture and neural control factors to ITW. It was hypothesised that

(1) Forward dynamic simulations that implement ITW-specific musculotendon model parameters would predict ITW kinematics and kinetics, and
(2) The primary contributor to the ITW pattern would be the modelled contracture without notable alterations in neural control.

2. Methods

2.1. Experimental ITW data

For validation of the predictive simulations, gait data were used from 17 children with ITW (Supplementary A) presenting with fixed ankle contracture. All children were scheduled for musculotendon lengthening surgery. Ethics approval for retrospective data was obtained from the Children's Health Queensland Human Research Ethics Committee (HREC/16/QRCH/107). For each subject, motion capture data was recorded using the Plug-In-Gait marker set (Vicon Motion Systems, Oxford, UK)(Davis et al., 1991; Kadaba et al., 1990) while subjects walked overground at their comfortable walking speed. Ground reaction forces (GRFs) were simultaneously recorded from three embedded force plates (AMTI, Watertown, MA, USA). Surface EMG (ZeroWire, Aurion, Milano, Italy) were recorded for the gastrocnemius medialis, tibialis anterior, medial hamstrings and rectus femoris.

Inverse kinematic and dynamic simulations were performed in OpenSim (version 4.0)(Seth et al., 2018). The gait2392 musculoskeletal model (Delp et al., 1990) was scaled to each subject's proportions according to a static T-pose trial. The subtalar and metatarsophalangeal joints were locked at zero degrees, as only a limited number of foot marker trajectories was measured. Inverse kinematic and dynamic tools were used to compute joint angles and moments during gait, using experimental marker trajectories and GRFs. Joint powers were calculated from these angles and moments using custom-written scripts in MATLAB 2016a (The MathWorks Inc., MA, USA). EMG data were filtered with a recursive second-order Butterworth bandpass filter between 30 and 300 Hz, full-wave rectified and subsequently low-pass filtered at 6 Hz. The EMG-linear envelopes were normalised by the highest value during each subject's gait trial. For each subject a left and right stride were used, except for one subject for whom no clear force plate strikes for the right leg were available, meaning that 33 strides remained. From these, time-normalised GRFs, joint angles, moments and powers, and muscle excitation patterns were ensemble averaged for use as comparative experimental data for children with ITW. For visualisation purposes, the muscle excitation amplitude was scaled to best match the simulation's average amplitude.

2.2. Pathology-specific musculoskeletal model

A pathology-specific model for ITW was created by implementing a plantarflexor contracture in a generic musculoskeletal model (based on Delp et al., 1990; described in detail in Veerkamp et al., 2021). Briefly, the base generic model had nine degrees of freedom in the sagittal plane only (i.e., pelvis-ground vertical and horizontal displacement, pelvic tilt, and left and right hip, knee, and ankle joints; the pelvis and trunk were merged). Nine musculotendon units were modelled in each leg (i.e., iliopsoas, gluteus, rectus femoris, vasti, bilateral hamstrings, biceps femoris short head, tibialis anterior, gastrocnemius, and soleus) using the Millard2013Equilibrium model with a compliant tendon (Millard et al., 2013).

The plantarflexor contracture was implemented by shifting the generic passive ankle moment-angle curves for the gastrocnemius and soleus by 20° with knee extended and flexed. The 20° value was chosen based on the average restriction in maximum passive dorsiflexion range-of-motion in the ITW cohort (Supplementary A). In the contracture model the plantarflexors' optimal fibre length and tendon slack length values were optimised to best represent these shifted curves, by minimising errors between the model's and the shifted curves using *fmincon* in Matlab (2016a; The MathWorks Inc., MA, USA). This resulted in an increased optimal fibre length of 0.097 m for gastrocnemius and 0.089 m for soleus (default: 0.060 and 0.050 m, respectively) and a reduced tendon slack length of 0.33 m for gastrocnemius and 0.20 m for soleus (default: 0.39 and 0.25 m). Combined, this led to musculotendon shortening of 0.023 m (5.1%) for gastrocnemius and of 0.011 m (3.7%) for soleus in the contracture model. The contracture parameters could not be validated against experimental data, but the finding of slightly increased fibre length and reduced tendon length agrees with experimental findings (Harkness-Armstrong et al., 2021a). Moreover, even when the contracture was modelled differently, by shortening either optimal fibre length or tendon slack length only, similar gait patterns were predicted (Supplementary D).

2.3. Predictive simulations of ITW

We used the open-source software SCONE (Geijtenbeek, 2019) with a previously developed predictive simulation framework that showed good agreement with typical gait (Veerkamp et al., 2021). Such a framework performs forward dynamic simulations, of which neural control is optimised by minimising a set cost function. Viscoelastic contact spheres were added on the heel and ball of each foot (Hunt and Crossley, 1975). The musculotendons units were activated by a reflex-based controller adapted from Geyer and Herr (2010) which we augmented with supraspinal drive consisting of reflex offsets and constant activation levels. The controller is fully described in Veerkamp et al. (2021). In the current study, the controller for the plantarflexors was expanded to include length- and velocity-based reflexes and supraspinal drive, instead of only force-based reflexes, to be a more complete and realistic representation of spindle inputs (Matthews, 1963; Matthews and Stein, 1969) and supraspinal structures. This controller expansion had negligible effects in predicting typical gait, but was considered necessary for a realistic evaluation of neural control (i.e., reflex gains and supraspinal drive) in ITW.

Reflex gains, supraspinal drive values, thresholds determining phases of the gait cycle, and the model's initial pose were design variables optimised by minimising a cost function. The cost function consisted of a hierarchical weighting of minimising cost of transport (Uchida et al., 2016), foot-ground impact, head stability, knee hyperextension, and muscle activation squared per meter travelled, as described in Veerkamp et al. (2021). A high plantarflexor fibre length penalty was also added to the cost function. This was motivated by our pilot simulations and the results from Ong et al. (2019), which revealed that during simulated walking the contracted plantarflexors favoured operation on the descending limb of their force-length curve. However, this may not be physiologically plausible, as shown for typical gait (Panizzolo et al., 2013; Rubenson et al., 2012), and for ITW (Veerkamp et al., 2022). Therefore, a penalty was applied when fibre lengths operated on the descending limb of the force-length curve, that is, when normalised fibre lengths above 1.05 were reached in the contracted plantarflexors. A relatively high weighting of 1000 was used, to ensure the plantarflexors operated on the ascending limb and plateau region of the force-length curve.

The duration of each simulation was set to ten seconds and walking speed was free to vary above 0.2 m/s. There were no additional simulation constraints. A 24-core Intel Xeon CPU E5–2690 2.60GHz processor was used for the optimisations, which were performed using the genetic Covariance Matrix Adaptation Evolution Strategy (CMA-ES) (Hansen et al., 2003). For each scenario, six separate optimisations were performed with different random initial guesses to increase chances of finding an optimal solution. Optimisations stopped as soon as the cost averaged over the last 500 generations did not improve more than 0.01% per generation. From the six optimisations, the simulation with the lowest score for the cost function was selected for subsequent quantitative evaluation (scores ranged from 14.29 to 18.18). From this simulation, the first two gait cycles were excluded, and waveforms were time-normalised and averaged over all subsequent gait cycles, which were typically all very similar (Supplementary C).

We evaluated the effects of using the plantarflexor contracture model on the predicted gait. The design variables were optimised in two stages to increase the chances of obtaining a global minimum. The first stage used the generic model and its variables optimised to simulate typical gait. The first stage's optimised variables that produced the best solution were used as the initial guess in the second stage optimisation of the design variables for the contracture models.

The contracture model's plausibility in predicting ITW experimental data was assessed by root mean squares errors (RMSE) and coefficients of determination (R^2) between simulated and experimental ITW waveforms, which were calculated for lower limb joint angles, moments, and powers. For muscle excitations, only R^2 was calculated, since the experimental EMGs were not normalised to maximum voluntary contractions. The RMSE for each variable was divided by its average experimental standard deviation, which was calculated at each time point among subjects and then averaged over all time points. This allowed more fair comparisons between variables with different magnitudes. Both normalised RMSE and R^2 values were averaged for each category (angles, moments, powers and excitations), as well as over all categories to get a total RMSE and R^2. The RMSE and R^2 for the contracture simulation were compared to the RMSE and R^2 for the typical simulation that were calculated against typical experimental data. Additionally, cost function scores for each criterion and optimised neural control parameters (i.e., reflex gains and supraspinal drive) were compared against the typical gait simulation, to gain more insights into potential contributors to ITW.

3. Results

A predictive simulation with the contracture model resulted in a simulated ITW pattern (Figs. 1 and 2). The predicted gait showed increased ankle plantarflexion throughout the gait cycle, and a double bump of the ankle moment in stance. Notably, the predictive simulation showed increased gastrocnemius activation throughout stance and in late swing, but the activation peak in early stance was lower in relative magnitude to late stance compared to the experimental EMG from the ITW cohort (Fig. 3). Furthermore, the soleus showed increased activation in early stance, while being inactive during the rest of the gait cycle. The predicted gait approached ITW experimental data (RMSE:1.37SD; R^2:0.58) (Fig. 4). RMSE and R^2 were both lower than for typical gait (RMSE:2.46SD; R^2:0.69).

For the ITW simulation, each cost function criterion had higher values (i.e., increased cost) compared to typical gait (Table 1). Also, the optimised control strategy was different (Fig. 5). The most prominent differences were higher length- and velocity-based reflex gains in both plantarflexors during most gait phases, but mostly in early stance and swing, and decreased supraspinal drive to the soleus in all gait phases.

4. Discussion

We developed a pathology-specific musculoskeletal model with a plantarflexor contracture, representing children with ITW. Using this model in a predictive simulation framework, resulted in a simulation with a generally good match with ITW experimental gait data, confirming our first hypothesis that ITW could be simulated. Subsequent evaluation of the optimised model parameters revealed that the toe walking pattern was achieved by increasing length- and velocity-based reflex gains to the plantarflexors in early stance and swing, which is contrary to our second hypothesis that neural control would not be notably altered in the ITW simulation.

The ITW simulation provides insights into potential contributors to ITW. The individual cost was increased for each cost function criterion, hence, none of the initially considered cost function criteria would be a reason for preferring toe walking. However, the cost function in ITW may differ from typical gait, perhaps with additional criteria to incorporate feelings of discomfort or pain. For example, processing and/or control of the muscles' sensory inflow could be altered (Bartoletta et al., 2021; Chu et al., 2022; Montgomery and Gauger, 1978; Williams et al., 2010, 2014), preventing high fibre lengths to emerge through supraspinal control affecting reflex modulation. Length- and velocity-reflex gains were higher in the ITW simulation, suggesting that reflexes may be modulated differently than in typical gait, with a stronger plantarflexor stretch reflex through higher output from the muscle spindles.

The question remains which factor(s) originated ITW. Based on our findings, it could be argued that ITW is caused by a congenitally short Achilles tendon as suggested in early studies (Hall et al., 1967; Katz and Mubarak, 1984), and that the central nervous system adopts a control strategy with increased reflex gains to match the altered functional

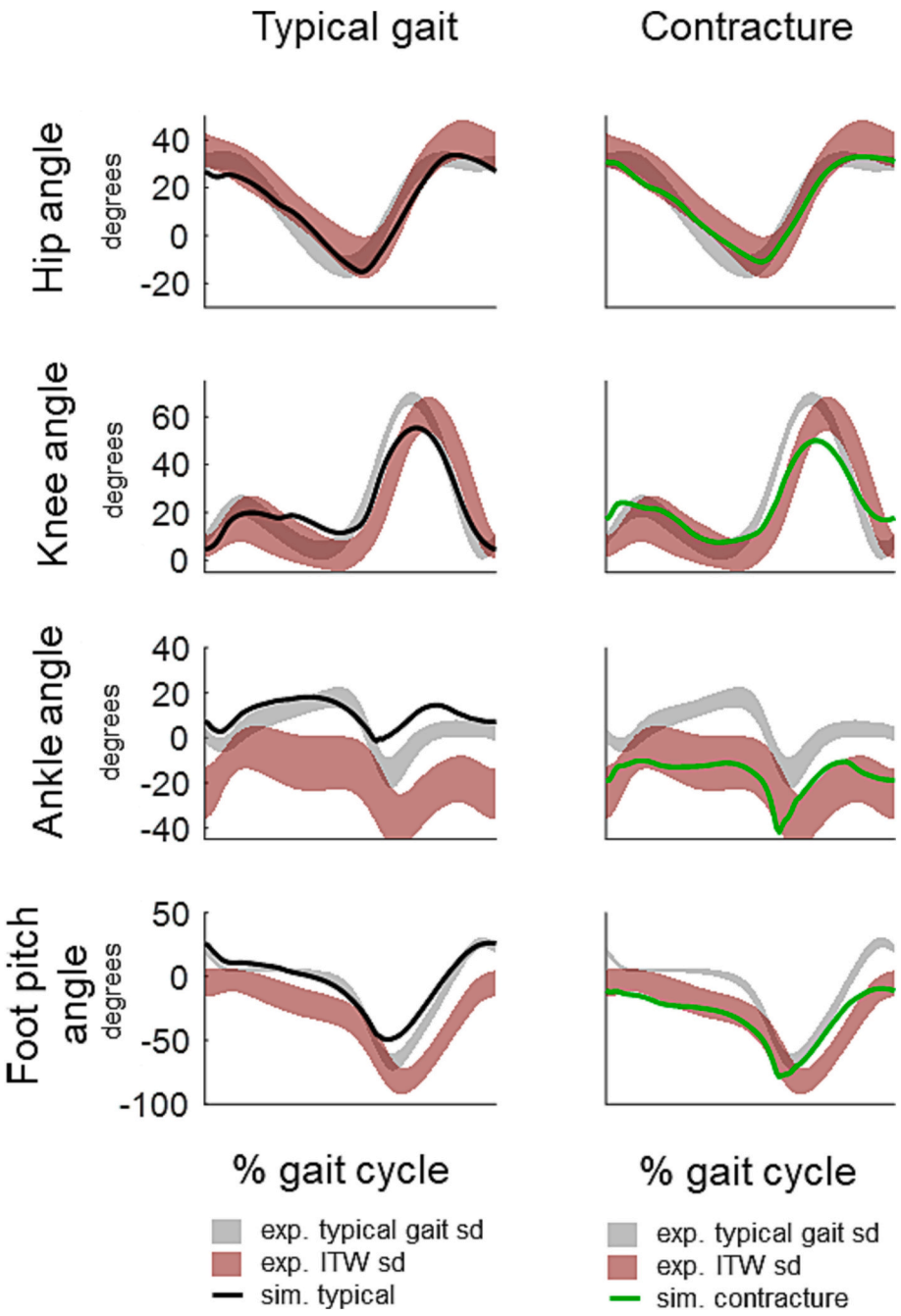

Fig. 1. Predicted kinematics for typical gait (left) and with the pathology-specific contracture model (right). Experimental kinematics display ±1 standard deviation from the mean. Comparative experimental data for typical gait was obtained as described in Veerkamp et al. (2021).

requirements, and possibly to prevent the plantarflexors operating at high fibre lengths, as described above. However, this may be fundamentally different from toe walking in young children who do not generally have contractures (Bartoletta et al., 2021; Ruzbarsky et al., 2016) and, when instructed, can readily walk with heel-toe gait (Ruzbarsky et al., 2016). Therefore, it is also likely that the preferred neural control strategy when learning to walk is altered in ITW, and that, in some children, the musculotendon unit adapts and develops a contracture over time.

To explore the plausibility of an altered neural control originating ITW, we imposed the optimised neural control from the simulation predicting ITW onto a typical, non-contracted musculoskeletal model to perform a forward dynamic simulation, and, indeed, a gait pattern with toe-landing emerged (Supplementary video), although unstable since the control strategy was not optimised for this model and optimisation would result in typical gait again. This suggests that the altered control strategy could precede, and possibly sustain, contracture development. Based on the facts that toe walking is common in human infants during typical development, and that different species employ toe-walking, it could be hypothesised that the altered control strategy is the result of delayed development of the neural control complexity (Dominici et al., 2011). The plausibility of this hypothesis is further strengthened by the lack of a clear activation peak in the gastrocnemius in early stance in the ITW simulation, whereas this peak was present in measured EMG. Thus, this peak could not be predicted by the current framework, but, instead, may be explained by a factor that was not modelled, such as the use of a limited number of synergies in ITW. Modelling a synergy-based controller could be used to further evaluate this hypothesis.

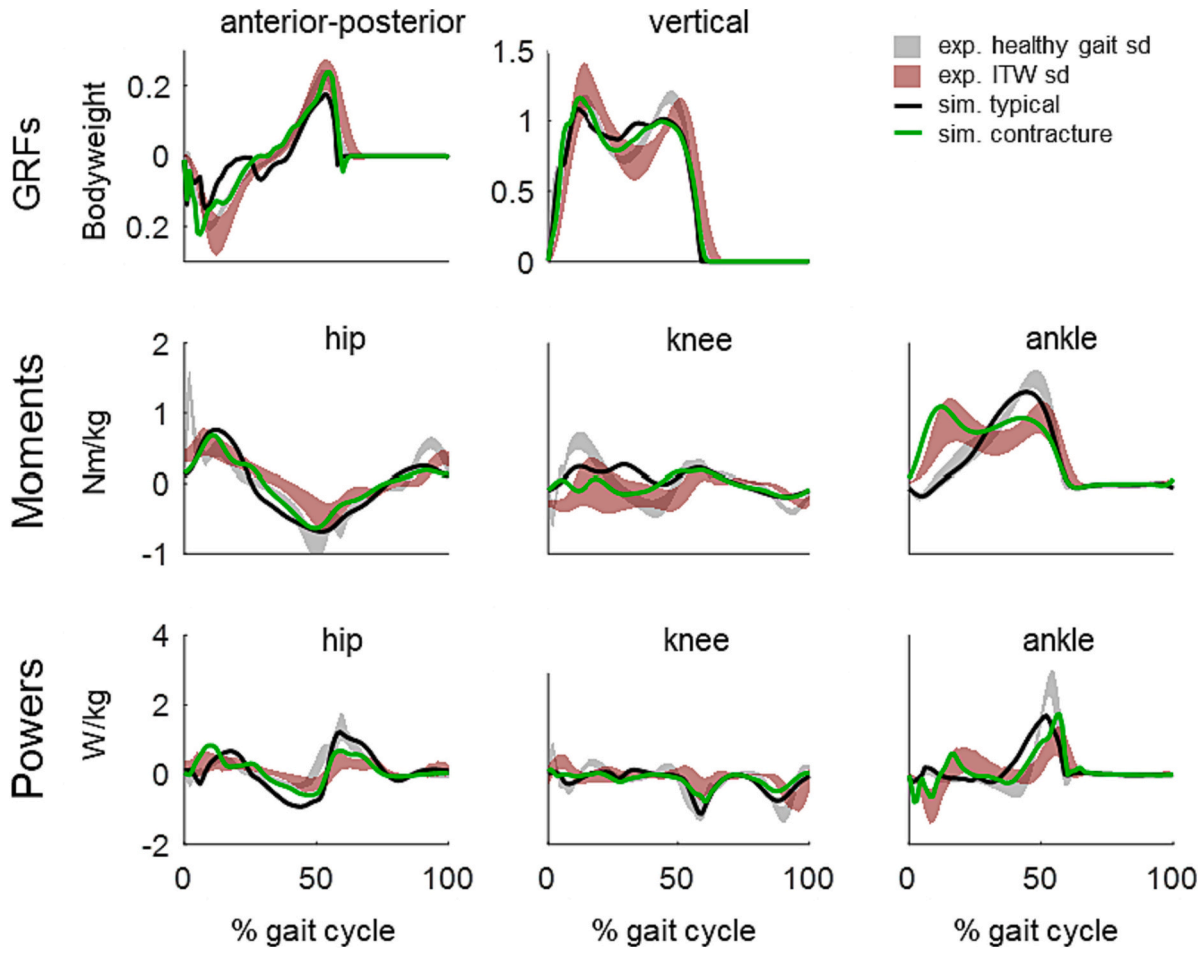

Fig. 2. The predicted kinetics by the typical simulation and the simulation with the pathology-specific contracture model, compared against experimental data for typical gait and ITW. Comparative experimental data for typical gait was obtained as described in Veerkamp et al. (2021).

Nevertheless, to be able to find the root cause of ITW, longitudinal experimental cohort studies would be needed, following neurophysiological and musculoskeletal development combining passive ankle range-of-motion, EMG and ultrasound measurements, starting at the point a child starts walking. Given the methodological difficulties that come with this, a first step could be to compare the control strategy in ITW to the control strategy of TD children voluntarily walking on their toes. This could help gain further insights into whether an atypical control indeed originates ITW.

We added a penalty to the existing framework (Veerkamp et al., 2021, 2022) to prevent the plantorflexors from operating at unphysiologically high fibre lengths, i.e., on the descending limb of the force-length curve. Without this penalty, the model preferenced a typical gait pattern while operating with high fibre lengths (Supplementary E). This was presumably to enable efficient force production by exploiting the passive parallel elastic component of force-length relationship of the contractile element in the muscle model. Perhaps, this is what happens in children with CP with abnormally stretched sarcomeres (Lieber and Fridén, 2019). A large contribution from passive forces with a modelled plantarflexor contracture in isolation was also found in previous predictive simulation (Ong et al., 2019) and inverse simulation (Fox et al., 2018) studies. However, walking at such high fibre lengths may not be realistic, as shown for typical gait (Panizzolo et al., 2013; Rubenson et al., 2012), and also for ITW (Veerkamp et al., 2022). Therefore, prevention of high fibre lengths needs to be incorporated into current simulation approaches of ITW, to produce valid, physiologically plausible simulations with contracture models. However, the exact regulating mechanism in vivo remains unclear. Therefore, we do not know if the modelled penalty is directly or indirectly reflecting the physiology. We can only speculate that fibre length operating ranges are "sensed" and regulated by the central nervous system through pathways that are outside of what was modelled explicitly. Subconscious motor control mediated in regions of the brain (e.g., thalamus, cerebellum) receives projections that include muscle spindle type II afferents (i.e., that have muscle length receptors)(Kröger and Watkins, 2021), as well as type III and type IV afferents, which may each, or all, be involved in sensing and using various mechanical (e.g., fibre length) and/or metabolic objectives when governing muscle function at different fibre lengths (Mense, 1996). However, further research is needed to find the underlying regulating mechanisms.

4.1. Assumptions and limitations

In this study, it was assumed that a 2D framework would be sufficient since ITW is a condition that predominantly manifests in sagittal plane gait deviations. However, compensations in other planes will have been missed, which is a limitation of the framework, but we expect these to be relatively minor compared to differences in observed in the sagittal plane. Development of a 3D framework would be an essential step, but is only feasible when computational times can be reduced (currently 14 h). Also, the controller that was used is a relatively simple representation of human walking, revealed in the relatively poor match between simulated and experimental muscle excitations. Such a poor match is common in both inverse and predictive simulations, and emphasises the need for model and cost function personalisation for improving modelling accuracy. The control scheme and the use of a relatively

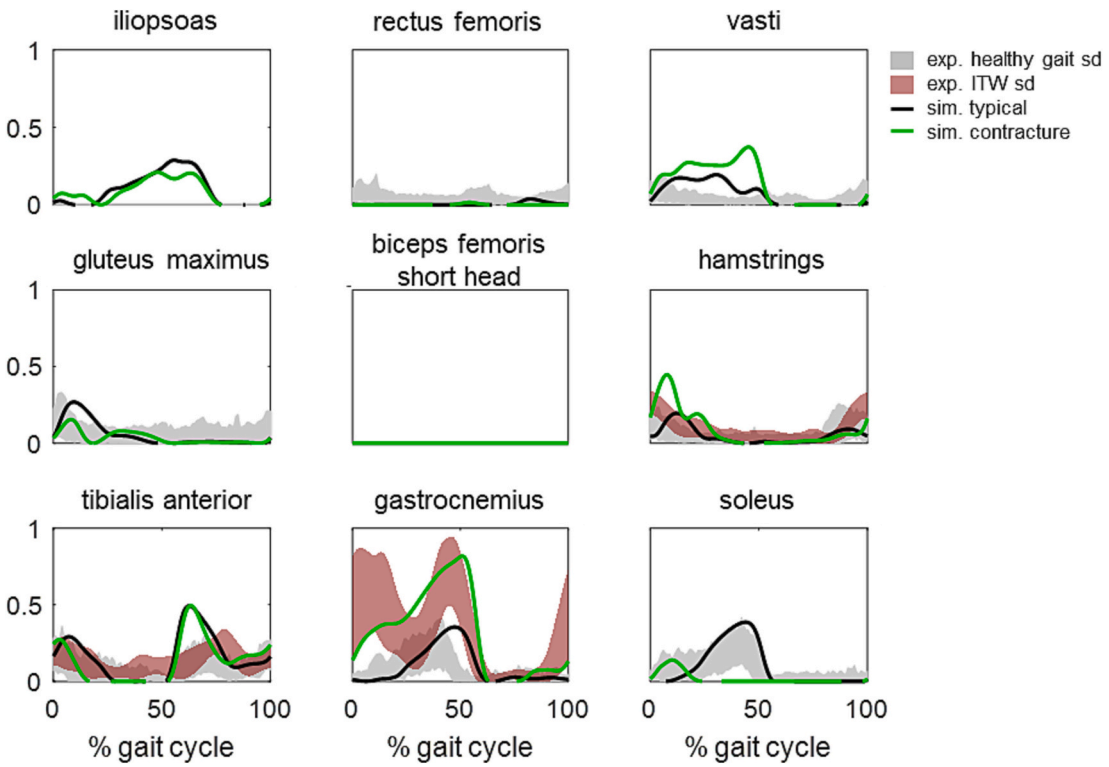

Fig. 3. Predicted, simulated muscle excitations from the typical simulation and the simulation with the pathology-specific contracture model, compared to normative EMG data. For ITW, EMG was only available for the rectus femoris, hamstrings, tibialis anterior, and gastrocnemius. The magnitude of the ITW EMG was scaled such that its average matched the average of the excitations of the contracture simulation to facilitate waveform pattern comparison. Please note that the rectus femoris EMG waveform has such a low amplitude that it is not visible.

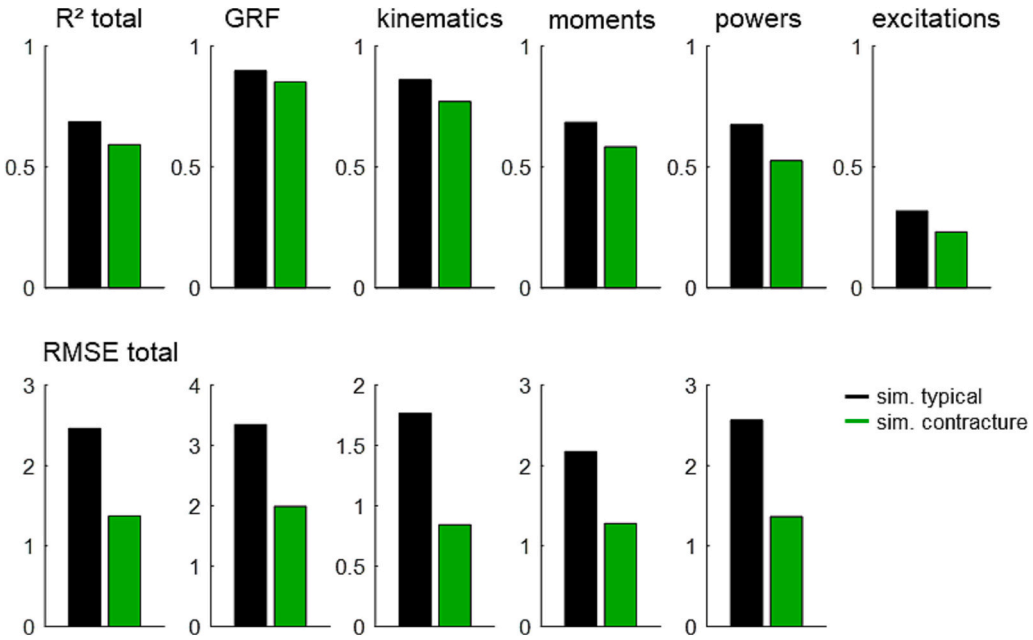

Fig. 4. Match with experimental data for the predictive simulations of typical gait (compared to typical experimental data) and the simulation with pathology-specific contracture (compared to ITW experimental data). Comparisons were quantified by the coefficient of determination (R^2) and root mean square errors (RMSE) for different biomechanical categories, as well as averaged over all categories (total).

simple model could play a role in the uneven excitation magnitude distribution between the gastrocnemius and soleus in the ITW simulation, which is unlikely to be realistic. However, this could not be confirmed, as no soleus EMG was measured. An existing dataset was used, in which EMG was measured for only four muscles in the children with ITW. To our knowledge, an extensive EMG dataset has not been previously published for children with ITW. Therefore, the limited validation of the simulated neural control prescribes some caution on conclusions regarding the neural control in ITW. Nevertheless, the soleus activation peak in early stance displayed by our model has also been

Table 1
Weighted scores for all cost function criteria in the typical gait simulation and the simulation with the pathology-specific contracture model.

	Typical gait	Contracture
Cost of Transport	6.42	8.52
Muscle Activation Squared	0.29	0.63
Head Acceleration	2.32	2.97
Foot-Ground Impact	1.44	1.95
Knee Extension	0.056	0.050
Fibre length		0.16
Total score	**10.53**	**14.29**

observed in adults that voluntarily toe walked (Kuska et al., 2020; Lorentzen et al., 2018). A further limitation is that intrinsic foot muscles were not modelled, which might have impacted the simulation given their role in human locomotion (Farris et al., 2019). The metatarsal phalangeal joint was locked, but since the frontal contact sphere was placed underneath this joint, the foot could still rotate around the ball of the foot while walking. Even though adding this joint is possible when interested in toe kinematics (Waterval et al., 2023), we could not have validated predicted toe kinematics with the experimental data. The data was recorded with the Plug-in-Gait marker model, which defines the foot as a single segment with locked subtalar and metatarsal phalangeal joints. It cannot account for foot deformities, although children with ITW generally do not present with foot deformities or mid-foot break (Brierty et al., 2021). Furthermore, for some outcomes the differences between the simulations were smaller than between the experimental data. This may be related to the typical simulation not being a perfect prediction of typical gait experimental data. However, the changes are generally in the right direction, which we consider to be a valuable indicator of a valid model response to the contracture. Another assumption was that the previously developed framework for typical gait used an adult-size model and could be used to represent gait of children that ITW. However, we would not assume scaling the model would affect the results substantially, since it was used to predict gait on a group level. Analysis on pathology-specific group level is common in predictive simulations due to computational demands and for straightforward validation (Ong et al., 2019; Veerkamp et al., 2021; Waterval et al., 2021). However, such group level analysis is not able to account for the heterogeneity within the population. Indeed, kinematic and kinetic standard deviations for ITW were somewhat larger than for typical gait. Further validation of patient-specific predictive simulations would be required to enable within-population analysis. Nevertheless, patient-specific modelling adds more challenges regarding scaling and personalisation, and, thus, pathology-specific analyses do provide a more comprehensible first step in simulation validation that is not affected by uncertainties in inter-subject variations. Also, it was assumed that the gastrocnemius and soleus were altered in a similar way in ITW, whereas, for example, ultrasound measures have only been confirmed for the gastrocnemius (Harkness-Armstrong et al., 2021a; Harkness-Armstrong et al., 2021b). However, since the average maximum dorsiflexion angle limitation was similar with the knee flexed as with the knee extended, we would not expect any substantial differences between the muscles. Additionally, it needs to be emphasised that our results cannot be generalised to all children with ITW. The children with ITW that were included in this study all were scheduled for tendon lengthening surgery because of contracture. However, not all children with ITW will develop such contracture (Caserta et al., 2022) and require this intervention.

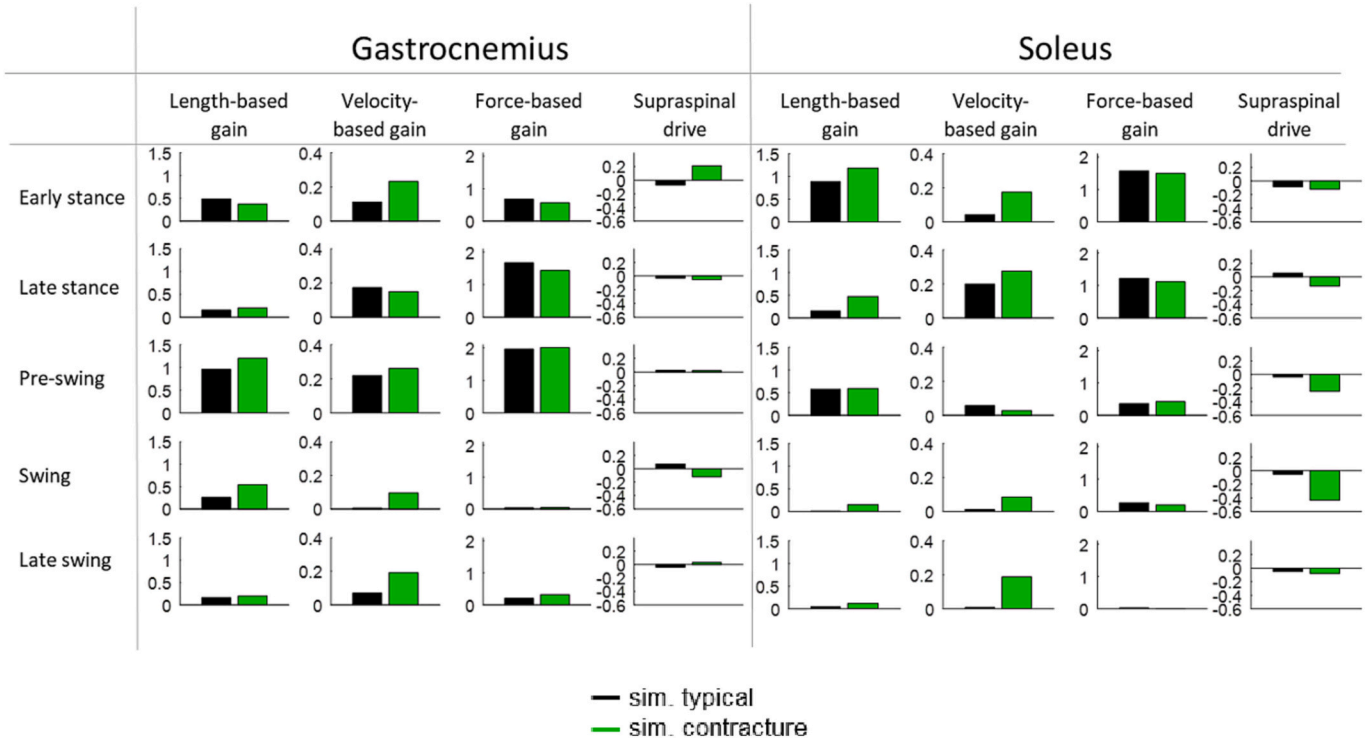

Fig. 5. Optimised design variables (reflex gains and supraspinal drive) for the gastrocnemius and soleus for each of the phases of the gait cycle in simulated typical gait and the simulation with the pathology-specific contracture model.
Gait phases are defined by optimised thresholds:

- Early stance: Ground reaction force greater than threshold
- Late stance: Sagittal distance stance foot
- Pre-swing: Contralateral foot enters early stance
- Swing: Ground reaction lower than threshold
- Late swing: Sagittal distance swing foot

4.2. Implications and future studies

Our simulations provide insights into how neuromuscular factors could contribute to ITW. With a method that can mechanistically simulate ITW, the next steps are threefold. First, the developed method can be used to run computational trials by implementing and testing different types of treatment for this condition. Second, the developed pathology-specific framework may be further evolved to perform patient-specific analyses for finding adequate personalised treatment. Specifically, the framework could be used to investigate the interaction effects of contracture with other impairments like weakness and spasticity (Veerkamp et al., 2023; Waterval et al., 2021), which are not straightforward but important for clinical interpretation. Third, the simulations provide rationale to define sensible hypotheses to direct experimental studies. For example, future studies could explore treatment targeting the neural control strategy in ITW before contracture development, for example by using biofeedback training such as applied previously in cerebral palsy (Flux et al., 2023), where feedback on plantarflexor EMG improved peak ankle push off power. Combining such training with treatment to prevent musculotendon contracture, for instance by using ankle-high, stiff-soled shoes, could help to promote a heel-toe walking gait. This strategy could possibly also prevent development of foot deformity that can result from long-term toe walking, further reducing the need for surgery.

5. Conclusion

The current study has shown how simulation experiments can complement experimental studies in evaluating the contributors to pathological gait. Forward dynamic simulations with a pathology-specific contracture model were able to closely predict ITW experimental data, and this provided insights into neuromuscular contributions to ITW. An altered neural control strategy may contribute to ITW, providing rationale for future computational and experimental studies to gain more insights into the original cause of and optimal treatment for ITW.

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Declaration of Competing Interest

None.

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