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# Adaptive ankle exoskeleton gait training demonstrates acute neuromuscular and spatiotemporal benefits for individuals with cerebral palsy: A pilot study

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ABSTRACT

*Background:* Gait abnormalities from neuromuscular conditions like cerebral palsy (CP) limit mobility and negatively affect quality of life. Increasing walking speed and stride length are essential clinical goals in the treatment of gait disorders from CP. *Research question.* How does over-ground gait training with an untethered ankle exoskeleton providing adaptive assistance affect mobility-related spatiotemporal outcomes and lower-extremity muscle activity in people with CP?
*Methods:* A diverse cohort of individuals with CP ($n = 6$, age 9–31, Gross Motor Function Classification System Level I – III) completed four over-ground training sessions ($98 \pm 17$ min of assisted walking) and received pre- and post-training assessments. On both assessments, participants walked over-ground with and without the exoskeleton while we recorded spatiotemporal outcomes and muscle activity. We used two-tailed paired t-tests to compare all parameters pre- and post-training, and between assisted and unassisted conditions.
*Results:* Following training, walking speed increased 0.24 m/s ($p = 0.006$) and stride length increased 0.17 m ($p = 0.013$) during unassisted walking, while walking speed increased 0.28 m/s ($p = 0.023$) and stride length increased 0.15 m ($p = 0.002$) during exoskeleton-assisted walking. Exoskeleton training improved stride-to-stride repeatability of soleus and vastus lateralis muscle activation by up to 51 % ($p \leq 0.046$), while the amount of integrated stance-phase muscle activity was similar across visits and conditions. Relative to baseline, post-training walking with the exoskeleton resulted in a soleus activity pattern that was 39 % more similar to the typical pattern from unimpaired individuals ($p < 0.001$).
*Significance:* This study demonstrates acute spatiotemporal and neuromuscular benefits from over-ground training with adaptive ankle exoskeleton assistance, and provides rationale for completion of a longer randomized controlled training protocol.

## 1. Introduction

Cerebral palsy (CP) results from insult to the developing brain and is the most prevalent cause of child-onset physical disability [1]. Most people with CP have diminished neuromuscular control of movement and inefficient gait patterns that limit physical activity and negatively affect quality of life [2]. Increasing walking speed and stride length are essential clinical goals in the treatment of gait disorders from CP [3]. Clinical gait interventions often employ task specificity, an essential part of improving motor function [4]; task-specific gait training [5] has achieved greater success than strength training and passive stretching in improving gait function [6–8]. Most gait training protocols for individuals with CP have involved using a treadmill in conjunction with a system that either partially supports body weight or moves legs in a specific trajectory [8–14].

Wearable assistive devices hold promise for improving walking ability for healthy individuals and people suffering from neuromuscular impairment [15,16]. Stemming from the critical role of the ankle joint in efficient walking [17,18], researchers have developed robotic ankle devices to enhance ankle function and walking economy by providing external plantar-flexor torque [19–22]; nearly all studies have focused on treadmill walking. We previously developed an ankle exoskeleton to target one of the most common deficits in CP — ankle plantar-flexor weakness [23], which contributes to insufficient ankle power

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generation [24], a crouched walking posture [25], and reduced walking speed and stride length [26]. Designed to be used following surgical interventions to treat deformities affecting the ankle, like equinus [27], we previously observed improved total positive ankle power, lower-extremity posture, and walking economy during assisted treadmill walking [28,29]. These prior findings, coupled with the potential for over-ground interventions to offer improved access and similar or greater improvements in walking outcomes [14], suggest that over-ground gait training with an untethered ankle exoskeleton may provide the unique opportunity to reinforce improved walking mechanics.

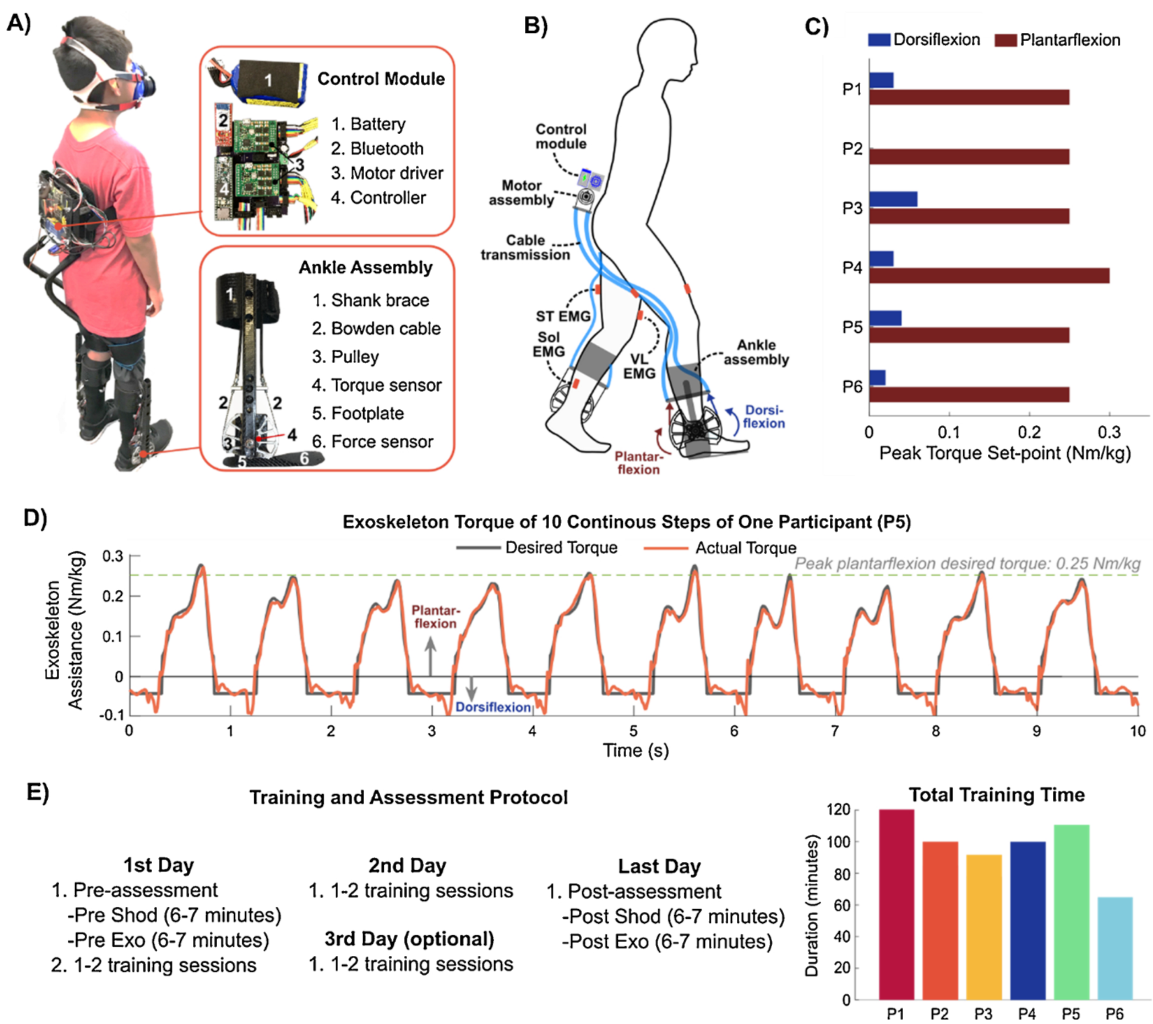
The purpose of this pilot study was to determine how repeated over-ground walking with personalized ankle plantar- and dorsi-flexor assistance affects spatiotemporal gait parameters and lower-extremity muscle activity in individuals with CP. Our primary hypothesis was that walking speed and stride length would increase following exoskeleton-assisted over-ground gait training, and that these measures would be greater during walking with vs. without assistance. We also hypothesized that training with the exoskeleton would cause muscle activity patterns to become more regular (i.e., reduce inefficient variability) and increase the similarity of the soleus firing pattern relative to that of unimpaired individuals. To test these hypotheses, we recruited six participants with CP to complete walking assessments before and after four over-ground training sessions with a powered ankle exoskeleton.

## 2. Methods

### 2.1. Exoskeleton and control

We used a previously-developed untethered bilateral ankle exoskeleton for this study [28]. The mechanical components of the system included a motor assembly, carbon fiber footplates and shank braces, and an ankle pulley mounted in-line with the ankle joint. The electrical control module consisting of a 910 mA h battery, printed circuit board with micro-controller, motor drivers, and Bluetooth module (Fig. 1A).

A proportional joint-moment control scheme, developed to account for stride-to-stride variability [30], provided plantar-flexor assistance proportional to the real-time biological ankle joint moment. We estimated the instantaneous biological ankle moment using force sensors placed under the forefoot. A torque set-point (e.g., 0.25 Nm/kg) was used to specify the nominal peak torque provided during steady-state walking. Plantar-flexor torque was prescribed as a fixed percentage (i.e., proportional) to the real-time estimated ankle moment during the



stance phase. During swing phase, the controller provided a small amount of dorsi-flexor assistance for participants that exhibited toe-drag, or no assistance (zero torque) for the other participants.

### 2.2. Participants and study protocol

Six people with CP between 9–31 years old and with Gross Motor Function Classification System (GMFCS) level of I – III participated in the study (Table 1), which was approved by the Northern Arizona University (NAU) Institutional Review Board. Participants over 18 years old read and signed an informed consent document. For each minor, we obtained verbal assent and informed written consent from a parent. Inclusion criteria included a diagnosis with unilateral or bilateral spastic CP, the ability to walk over-ground for 6 min with or without a walking aid, at least 20° of passive ankle plantarflexion range of motion, no knee extension or ankle dorsiflexion contractures greater than 15°, and the ability to understand and follow instructions. Subjects were excluded if they had orthopedic surgery within the prior 6 months or any medical conditions that would affect their safe participation.

Participants completed pre- and post-training assessments and four sessions of over-ground exoskeleton-assisted gait training across three or four visits at NAU's Human Performance Laboratory. The first visit included the pre-training assessment and the first training session(s), while the last visit included only the post-training assessment. Visits took place on consecutive days. Participants that completed three visits received two training sessions on the first day and two on the second day, while participants that completed four visits received one training session on the first day, and 1–2 sessions on the 2nd and 3rd days, respectively. Each training session consisted of roughly two 10-minute bouts of walking around a 61-meter oval track. Training time varied depending on walking ability (Fig. 1E), and there was no significant relationship between training duration and change in step length ($R2 = 0.151$, $p = 0.446$) or change in velocity ($R2 = 0.191$, $p = 0.386$). During the assessments, each subject completed over-ground trials while (1) walking wearing their own shoes and orthoses if prescribed by a physician (Shod), and (2) while walking with the exoskeleton as it provided plantar-flexor assistance (Exo). The nominal magnitude of plantar-flexor torque, either 0.25 or 0.30 Nm/kg, which was based on the previously-established optimal range [28], remained the same for each participant's pre-post comparison. Due to the adaptive nature of the exoskeleton controller, the peak torque provided to the user varied stride-to-stride based on stride-to-stride variation in the estimated biological ankle moment (Fig. 1D).

The baseline Shod condition took place before the Exo condition on the pre-training assessment, while condition order was randomized during the post-training assessment (Supplemental Table 1). Participants were instructed to walk at their preferred speed for all training and assessment trials.

**Table 1**
Participant characteristics.

| Participant | Sex | Age (yrs) | Height (m) | Mass (kg) | GMFCS Level | Gait Type |
|---|---|---|---|---|---|---|
| P1 | M | 9 | 1.37 | 30.4 | I | Mild ankle PF dysfunction and bilateral crouch |
| P2 | M | 31 | 1.70 | 53.7 | II | Moderate ankle PF dysfunction and bilateral crouch |
| P3 | F | 23 | 1.47 | 46.0 | III | Severe ankle PF dysfunction and bilateral crouch gait |
| P4 | M | 10 | 1.39 | 36.8 | I | Mild ankle PF dysfunction and bilateral crouch gait |
| P5 | M | 9 | 1.26 | 23.8 | III | Severe ankle PF dysfunction and asymmetric crouch gait* |
| P6 | M | 13 | 1.51 | 43.5 | I | Mild ankle PF dysfunction and bilateral crouch |

### 2.3. Experimental data

We recorded lap time, step count, and muscle activity data for each trial. Gait cycle states (e.g., stance and swing phases) were recorded wirelessly from the exoskeleton at 100 Hz. Electromyography (EMG) data from the soleus, vastus lateralis, and semitendinosus were collected bilaterally at 1926 Hz using a wireless electrode system (Trigno, Delsys, Natick, MA). A trigger synchronized EMG and exoskeleton data at the start of each trial.

### 2.4. Data analysis

Walking assessments were between six-to-seven minutes in duration. We analyzed spatiotemporal and EMG data over the first full lap that occurred after five minutes of walking, allowing for five minutes of familiarization prior to each assessment period. Stride length was calculated by dividing the length of track by the number of strides completed in the lap. Cadence was determined by dividing the lap time by the number of strides. EMG data were band-pass-filtered between 15 and 380 Hz, rectified, and low-pass-filtered at 7 Hz to create a linear envelope [31]. The filtered EMG from the analyzed lap were divided into gait cycles and normalized to percent gait cycle. Outlier gait cycles, identified using an interquartile range approach, were removed from analysis to minimize the influence of miss-steps or stumbles [32]. We calculated the variance ratio, which reflects the repeatability of muscle activity, using the following equation [33]:

$$VR = \frac{\sum_i \sum_j \left(EMG_{ij} - EMG_j\right)^2 / m(n-1)}{\sum_i \sum_j \left(EMG_{ij} - EMG\right)^2 / (mn-1)}$$

where $i = 1 \ldots m$ is the number of gait cycles, $j = 1 \ldots n$ is the time points within each gait cycle, $EMG_{ij}$ is the EMG of gait cycle i at time point j, $EMG_j$ is the mean EMG at time point j across all gait cycles, and *EMG* is the mean EMG across all gait cycles and time points. Variance ratio ranges from 0 to 1, with larger values indicating higher stride-to-stride variability. For comparing the amount of muscle activity across visits, we normalized the filtered EMG data for all conditions by the peak EMG value of the pre-training Shod condition [34]. The area under the average EMG curve (integrated EMG, iEMG) was calculated for the stance phase as an indication of muscle work [35]. We calculated the cross-correlation coefficient between filtered soleus EMG patterns from our participants and from unimpaired individuals walking over-ground at 1.25 m/s [36]. Variance ratio, iEMG, and cross-correlation coefficient were averaged across limbs.

### 2.5. Statistical analysis

To test our *a priori* hypotheses that walking with powered assistance and multi-day gait training would improve spatiotemporal and muscle activity outcomes, we used paired two-tailed t-tests to compare between conditions (Exo vs. Shod) within each evaluation visit (pre-/post-training), and across evaluation visits (pre- vs. post-training) within to pre-intervention baseline performance. We used linear regression to assess the relationships between stride length and walking speed, between cadence and walking speed, and between variance ratio and walking speed. Statistical significance was set at $p < 0.05$ for all tests.

## 3. Results

### 3.1. Spatiotemporal outcomes

All participants walked faster and with longer strides post-training. For the Shod condition, walking speed increased 0.24 m/s ($p = 0.006$) and stride length increased 0.17 m ($p = 0.013$). For the Exo condition, walking speed increased 0.28 m/s ($p = 0.023$) and stride length increased 0.15 m ($p = 0.002$). Post-training, walking speed and stride length were 6.28 % ($p = 0.045$) and 3.69 % ($p = 0.022$) greater, respectively, for the Exo compared to the Shod condition. Walking speed and stride length increased 0.32 m/s ($p = 0.007$) and 0.22 m ($p = 0.013$), respectively, during Exo walking post-training vs. Shod walking pre-training. Walking cadence was not significantly different pre- vs. post-training or between conditions (Fig. 2).

### 3.2. Muscle activity

Variance ratio was significantly lower, indicating higher stride-to-stride repeatability, post-training compared to pre-training for soleus and vastus lateralis. The soleus had the greatest decrease in variability post-training: 51 % for Shod walking ($p = 0.017$) and 48 % for Exo walking ($p = 0.017$). Vastus lateralis variability decreased 24 % for Shod walking ($p = 0.046$) and 23 % for Exo walking ($p = 0.023$) post- vs. pre-training. There was no significant difference in variance ratio between conditions for either assessment (Fig. 3).

Integrated muscle activation during stance phase was similar for all muscles pre- and post-training, and between Shod and Exo conditions. The cross-correlation coefficient between the soleus activity pattern of our cohort and that of unimpaired individuals increased during exoskeleton walking post-training ($p = 0.018$). The cross-correlation coefficient increased 39 % from the pre-training Shod condition to post-training Exo condition ($p < 0.001$) (Fig. 4).

### 3.3. Relationships between stride length, cadence, variance ratio, and walking speed

There was a significant relationship between stride length and walking speed: participants took longer strides while walking at a faster speed ($R^2 = 0.92$, $p < 0.001$). Cadence accounted for 57 % of the variance in walking speed ($R^2 = 0.57$, $p < 0.001$). There was a significant relationship between the variance ratio averaged across the lower extremity and walking speed ($R^2 = 0.81$, $p < 0.001$; Shod only: $R^2 = 0.90$, $p < 0.001$; Exo only: $R^2 = 0.72$, $p < 0.001$); lower variance ratio was associated with faster walking speed (Fig. 5).

## 4. Discussion

We confirm our hypothesis that over-ground exoskeleton-assisted gait training would improve walking speed and stride length, and that these outcomes would be enhanced while using the device. We partially confirm our hypothesis that the intervention would reduce stride-to-stride variability of muscle activity during walking: the soleus and vastus lateralis muscles had more uniform activity patterns, yet the semitendinosus remained unchanged. We also partially confirm our hypothesis of improved soleus activation pattern; an improvement was observed during assisted walking (Exo) following training but not during unassisted (Shod) walking.

Over-ground gait training with ankle exoskeleton assistance resulted in a significant improvement in gait function, even when walking without the device. All of our participants walked faster and took longer steps after training. On average, height-normalized stride length increased from 0.74 to 0.86 m/m, and height-normalized walking speed increased from 0.68 to 0.85 (m/s)/m in our cohort, improvements which were within the typical ranges reported for individuals without impairment walking in a straight line (0.8–1 m/m and 0.78 – 0.86 (m/s)/m, respectively) (Fig. 2) [37,38].

Taking longer steps requires increasing swing-limb advancement and stance-limb extension. Our prior research demonstrated that individuals with CP increased stance limb extension across the lower extremity by 14° during treadmill walking with this ankle exoskeleton [30]. Here, the exoskeleton likely elicited similar improvements in over-ground walking posture, while repeated training may have reinforced the behavior to the point where it transferred to walking without the device. The increase in walking speed following training was achieved primarily through longer strides instead of a faster cadence, a clinical goal in the treatment of gait pathology for individuals with neuromuscular impairment [3]. Furthermore, the stride length-walking speed relationship was similar to a prior report of unimpaired young adults [39] (Fig. 5A).

Walking with the exoskeleton improved spatiotemporal outcomes compared to walking without the device on the final assessment. Ankle plantar-flexor power is a strong predictor of step length [40]. At the level of assistance assessed in this study, muscle activity was not significantly different between conditions. Therefore, there appears to have been an additive effect whereby the exoskeleton assistance combined with the underlying biological contribution to elicit improved gait mechanics, but only once users were acclimated to assistance. We theorize that users need 30–60 minutes to feel comfortable walking with the exoskeleton and get the muscles to work in synergy with assistance, which is supported by the reduction in stride-to-stride muscle variability across assessments and the inverse relationship between muscle variance ratio and walking speed (Fig. 5C).

After training over-ground with the ankle exoskeleton, stride-to-

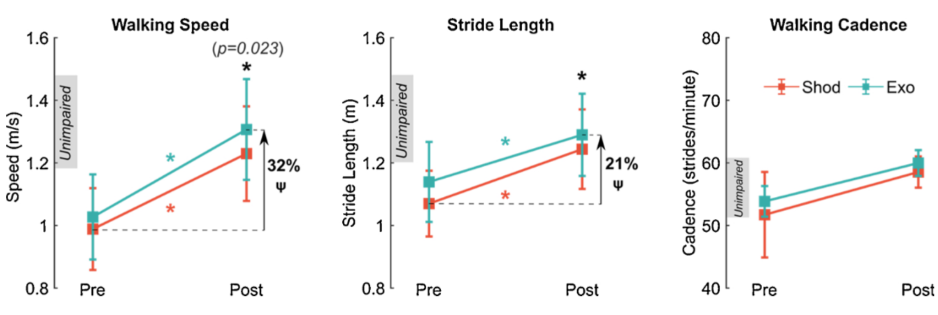



**Fig. 2.** Walking speed, stride length and cadence pre- and post-training for each condition. Over-ground exoskeleton-assisted gait training improved walking speed and stride length. Speed and stride length were greater during the post-training Exo vs. post-training Shod walking. Neither training nor assistance statistically affected walking cadence. * indicates a significant difference between conditions within the same visit or between visits of the same condition. Ψ indicates a significant difference between pre-training Shod and post-training Exo conditions. Error bars indicate

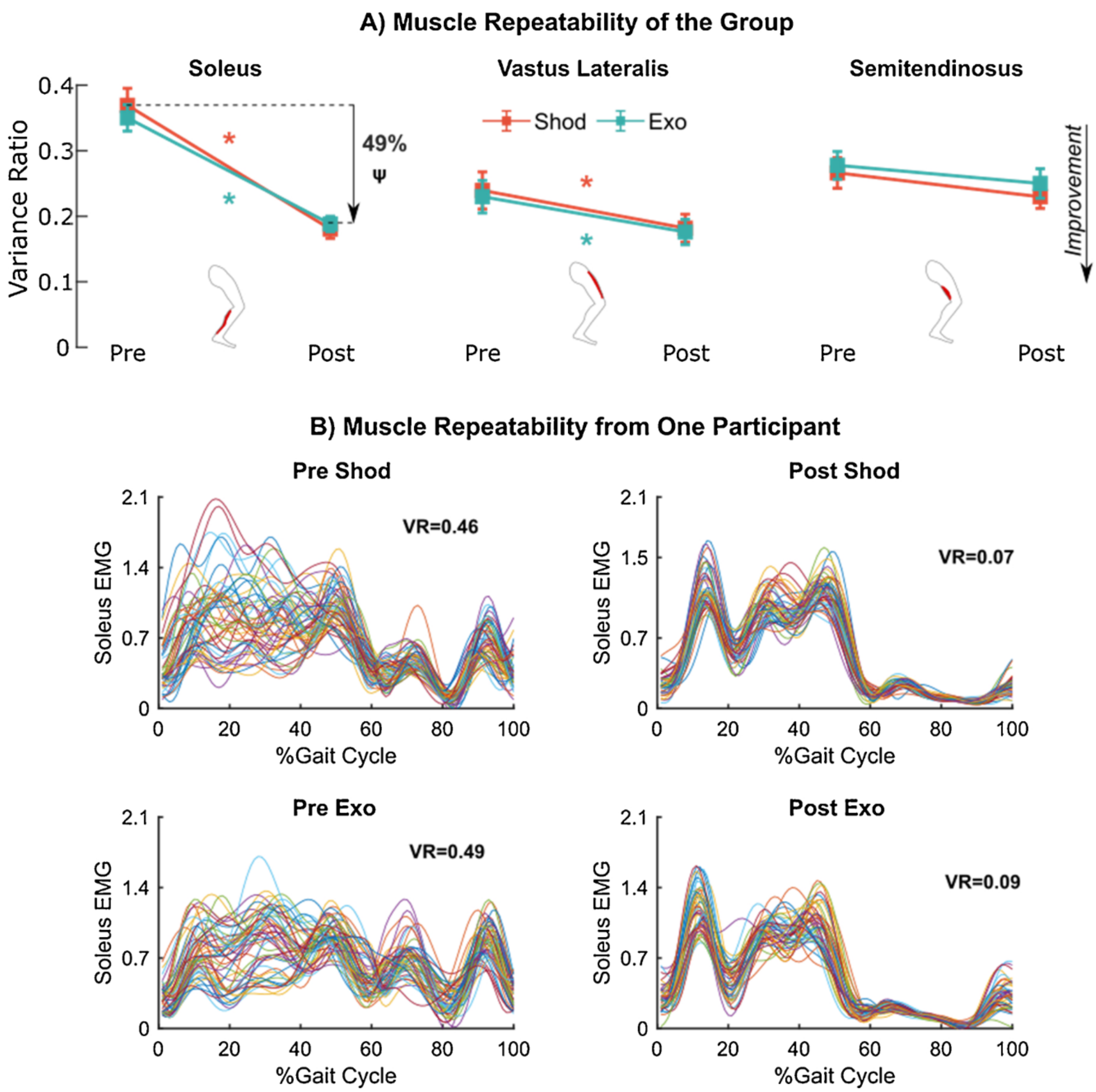



**Fig. 3.** A) Variance ratio (VR) for soleus, vastus lateralis, and semitendinosus pre- and post-training for the Shod and Exo conditions. Training improved the uniformity of muscle activity for all muscles except the semitendinosus. * indicates a significant difference between the first and last visits for Shod (red) or Exo (green). Ψ indicates a significant difference between pre-training Shod and post-training Exo conditions. Error bars indicate standard error of the mean. B) Normalized soleus EMG during the Shod and Exo walking conditions pre- and post-training for a representative participant (P2). Each color indicates one gait cycle.

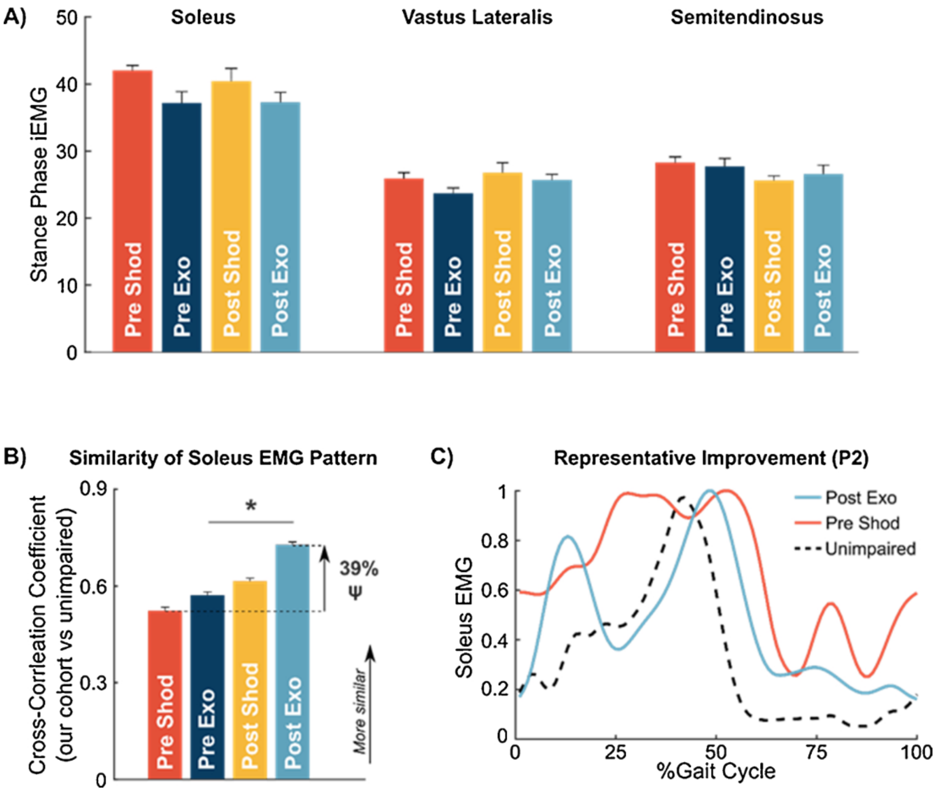



**Fig. 4.** A) Stance phase integrated EMG (iEMG) of the soleus, vastus lateralis, and semitendinosus pre- and post-training for the Exo and Shod conditions. B) Coefficient of cross-correlation between the soleus activity pattern of our cohort and that of unimpaired individuals walking over-ground at 1.25 m/s [36]. Post-training, soleus activation pattern during walking with the device increased in similarity to that of unimpaired individuals. C) Normalized soleus EMG from a representative participant (P2) for pre-training Shod (red line) and post-training Exo (teal line) conditions; normative data from the average unimpaired pattern are also shown (dashed black line). * indicates a significant difference between visits within the same condition. Ψ indicates a significant difference between pre-training Shod and post-training Exo conditions. Error bars indicate standard error of the mean.

stride variability was significantly reduced during both assisted and unassisted walking. The greatest improvement occurred in the ankle plantar-flexors, where stride-to-stride repeatability nearly doubled. We anticipate that plantar-flexor assistance primarily influenced motor control of the lower-extremity extensor muscles by providing a repeatable proprioceptive cue for muscles used to support and propel the body. This may explain our finding of unchanged variance ratio for the knee flexors muscles. Reduced variability during acclimated walking with assistance is consistent with a prior knee-exoskeleton study, where individuals with CP had increased repeatability of knee extensor (vastus lateralis) activity following 30–65 minutes of training. However, the same study reported greater variation in muscle activity when walking with non-adaptive assistance compared to without the device [33]. In contrast, muscle variability was similar between walking with vs. without the device on either assessment in our cohort, which may be attributed to the adaptive control strategy [30].

Acclimated walking with the exoskeleton resulted in a significant improvement in the soleus activation pattern compared to the pattern exhibited by unimpaired individuals (Fig. 4). People with CP often activate the soleus early in the stance phase and have a lower peak during push-off – a suggested contributor to the flexed posture and insufficient propulsion in this patient population [34]. In contrast, the typical soleus EMG pattern during walking by unimpaired individuals is cone-shaped with only one peak in the late stance [18]. Before training, all participants had a bimodal pattern of soleus activity during stance. After training, three participants (P2, P4, and P6) showed a more prominent peak in late stance during unassisted and assisted walking (Supplemental Fig. 1). The adaptive exoskeleton controller may have been acting as a mechanical cue to the nervous system to help trigger the structured walking protocol. Future research should also quantify the anticipated improvements in lower-extremity kinematics and kinetics following over-ground ankle exoskeleton gait training. When considering a suitable cohort for these futures studies, impaired cognitive or verbal communication ability do not appear to preclude benefiting from ankle exoskeleton training so long as a trusted guardian is present during the initial acclimation period. This study demonstrated that the device can be used safely for individuals who have at least 20° of passive ankle plantarflexion range of motion and have no knee extension or ankle dorsiflexion contractures greater than 15°. We cannot recommend using the device for patients with contractures, spasticity, or dystonia that do not meet these inclusion criteria, or individuals with ataxia who are unable to ambulate safely with a walker. We observed a potential trend towards greater improvement for our participants with GMFCS level I compared to level II and III. For example, walking speed increased by 42 % on average for those with GMFCS level I, compared to 11 % and 16 % for levels II and III, respectively. Overall, training with this exoskeleton benefited users with a wide range of age and walking ability.

This study had several limitations. An unavoidable experimental limitation was that we assessed muscle activity across visits; those results should be interpreted with caution. To minimize the influence of differences in electrode placement and skin-electrode conductivity across visits, we measured and marked electrode locations and followed the same preparation procedure (i.e., shaving and alcohol swab cleaning). We sought to maximize the potential benefits of ankle exoskeleton gait training, and therefore customized a small amount of swing-phase dorsi-flexor assistance for each participant; the amount remained consistent across training and assessments. A limitation of this design was that we were unable to isolate the individual contributions of

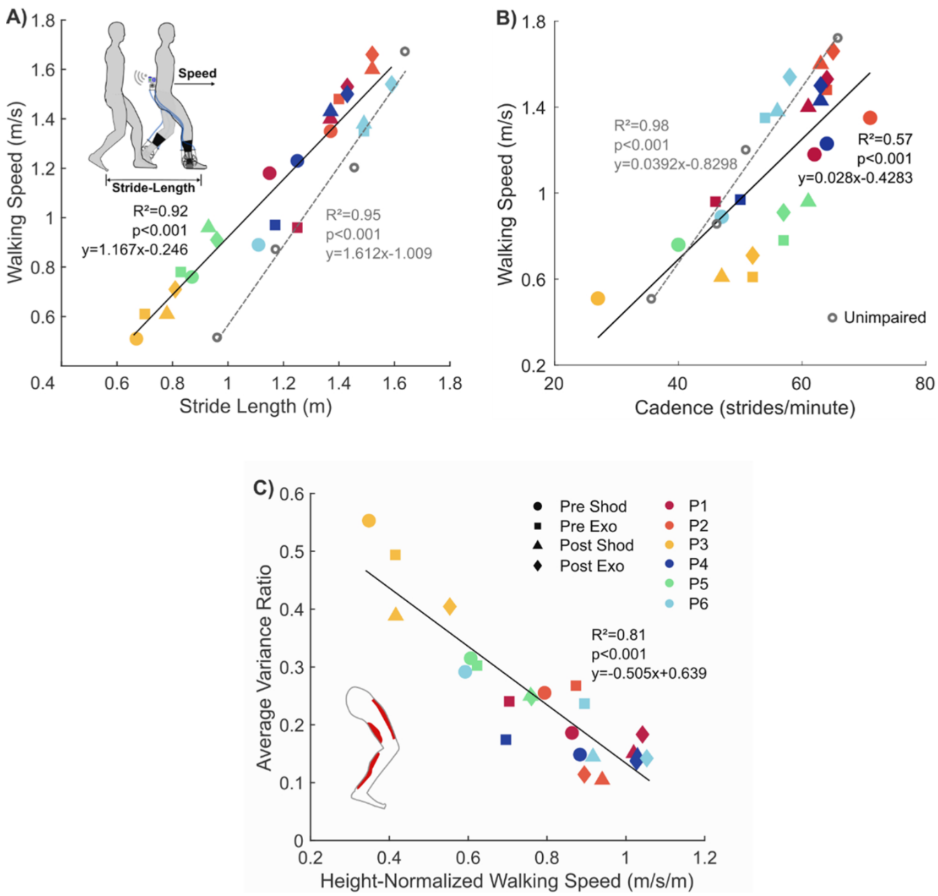



**Fig. 5.** Relationship between A) walking speed and stride length and B) walking speed and cadence of our cohort (black solid line) and, for reference, the relationships reported for unimpaired young adults (gray dotted line) [39]. C) Relationship between height-normalized walking speed and muscle variance ratio (combined average of the soleus, vastus lateralis, and semitendinosus) across both assessments (pre- and post-training) and both conditions (Shod and Exo). Stride length and cadence explained 92 % and 57 % of the variance in walking speed, respectively. Average variance ratio explained 81 % of the variance in normalized walking speed, and lower muscle variance ratio corresponded to faster walking speed. Each color represents a participant, and each shape indicates a condition (Shod/Exo) within each visit (pre-/post-training).

Lastly, our study was implemented on an oval track because continuous over-ground gait training in a perfectly straight path is not feasible. While minimal, the gradual turning required by the oval path cannot be eliminated as a confounding factor on our outcome measures.

In summary, over-ground gait training using an untethered ankle exoskeleton was effective in improving spatiotemporal outcomes in a diverse cohort of individuals with CP. Following training, we observed improved ankle plantar-flexor activation patterns while walking with the exoskeleton, and a favorable increase in stride-to-stride repeatability of the ankle plantar-flexor and knee extensor muscles during walking both with and without the device. These results suggest that individuals with CP can quickly benefit from structured over-ground gait training with powered assistance. This study provides a strong rationale for completing a longer, randomized controlled trial of wearable ankle exoskeleton for children and young adults with neuromuscular disorders.

## 5. Research ethics and patient consent

This study was approved by the Northern Arizona University (NAU) Institutional Review Board under protocol # 986744. Participants over 18 years old read and signed an informed consent document. For each minor, we obtained verbal assent and informed written consent from one of their parents.

available from the corresponding author on reasonable request. The exoskeleton code, CAD files, and Bill of Materials is publicly available here: http://biomech.nau.edu/index.php/resources/

## CRediT authorship contribution statement

**Ying Fang:** Formal analysis, Investigation, Methodology, Visualization, Writing - original draft, Writing - review & editing. **Greg Orekhov:** Investigation, Methodology, Writing - review & editing. **Zachary F. Lerner:** Conceptualization, Investigation, Methodology, Funding acquisition, Supervision, Writing - review & editing.

## Declaration of Competing Interest

ZFL is a named inventor on pending utility patent applications that describe the exoskeleton design and controller utilized in the study. ZFL is a co-founder of a company seeking to commercialize the device. The other authors declare no conflict of interest.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.gaitpost.2020.11.005.

## References


[1] P. Rosenbaum, N. Paneth, A. Leviton, M. Goldstein, M. Bax, A report: the definition and classification of cerebral palsy April 2006, Dev. Med. Child Neurol. 49 (2007) 8–14, https://doi.org/10.1111/j.1469-8749.2007.tb12610.x.

[2] J.L. Benner, S.R. Hilberink, T. Veenis, H.J. Stam, W.M. van der Slot, M. E. Roebroeck, Long-term deterioration of perceived health and functioning in adults with cerebral palsy, Arch. Phys. Med. Rehabil. 98 (2017) 2196–2205, https://doi.org/10.1016/j.apmr.2017.03.013, e1.

[3] F.N. Todd, L.W. Lamoreux, S.R. Skinner, M.E. Johanson, R. St Helen, S.A. Moran, R. K. Ashley, Variations in the gait of normal children. A graph applicable to the documentation of abnormalities, J. Bone Jt. Surg. 71 (1989) 196–204, https://doi.org/10.2106/00004623-198971020-00005.

[4] H. Barbeau, Locomotor training in neurorehabilitation: emerging rehabilitation concepts, Neurorehabil. Neural Repair 17 (2003) 3–11, https://doi.org/10.1177/0888439002250442.

[5] I. Carvalho, S.M. Pinto, V. D. das, J.L. Chagas, T. Praxedes dos Santos, L.A. Batista de Sousa Oliveira, Robotic gait training for individuals with cerebral palsy: a systematic review and meta-analysis, Arch. Phys. Med. Rehabil. 98 (2017) 2332–2344, https://doi.org/10.1016/j.apmr.2017.06.018.

[6] A.J. Dallmeijer, E.A. Rameckers, H. Houdijk, S. de Groot, V.A. Scholtes, J. G. Becher, Isometric muscle strength and mobility capacity in children with cerebral palsy, Disabil. Rehabil. 39 (2017) 135–142, https://doi.org/10.3109/09638288.2015.1095950.

[7] M.N. Eek, R. Tranberg, R. Zügner, K. Alkema, E. Beckung, Muscle strength training to improve gait function in children with cerebral palsy, Dev. Med. Child Neurol. 50 (2008) 759–764, https://doi.org/10.1111/j.1469-8749.2008.03045.x.

[8] N.G. Moreau, A.W. Bodkin, K. Bjornson, A. Hobbs, M. Soileau, K. Lahasky, Effectiveness of rehabilitation interventions to improve gait speed in children with cerebral palsy: systematic review and meta-analysis, Phys. Ther. (2016), https://doi.org/10.2522/ptj.20150401.

[9] N. Smania, P. Bonetti, M. Gandolfi, A. Cosentino, A. Waldner, S. Hesse, C. Werner, G. Bisoffi, C. Geroin, D. Munari, Improved gait after repetitive locomotor training in children with cerebral palsy, Am. J. Phys. Med. Rehabil. 90 (2011) 137–149, https://doi.org/10.1097/PHM.0b013e318201741e.

[10] M. Druzbicki, W. Rusek, S. Snela, J. Dudek, M. Szczepanik, E. Zak, J. Durmala, A. Czernuszenko, M. Bonikowski, G. Sobota, Functional effects of robotic-assisted locomotor treadmill therapy in children with cerebral palsy, J. Rehabil. Med. (2013), https://doi.org/10.2340/16501977-1114.

[11] K.J. Dodd, S. Foley, Partial body-weight-supported treadmill training can improve walking in children with cerebral palsy: a clinical controlled trial, Dev. Med. Child Neurol. (2007), https://doi.org/10.1111/j.1469-8749.2007.00101.x.

[12] T.E. Johnston, K.E. Watson, S.A. Ross, P.E. Gates, J.P. Gaughan, R.T. Lauer, C. A. Tucker, J.R. Engsberg, Effects of a supported speed treadmill training exercise program on impairment and function for children with cerebral palsy, Dev. Med. Child Neurol. (2011), https://doi.org/10.1111/j.1469-8749.2011.03990.x.

[13] T. Jung, Y. Kim, L.E. Kelly, M.F. Abel, Biomechanical and perceived differences between overground and treadmill walking in children with cerebral palsy, Gait Posture (2016), https://doi.org/10.1016/j.gaitpost.2015.12.004.

[14] K.L. Willoughby, K.J. Dodd, N. Shields, S. Foley, Efficacy of partial body weight-supported treadmill training compared with overground walking practice for children with cerebral palsy: a randomized controlled trial, Arch. Phys. Med. Rehabil. (2010), https://doi.org/10.1016/j.apmr.2009.10.029.

[15] A. Esquenazi, M. Talaty, A. Jayaraman, Powered exoskeletons for walking assistance in persons with central nervous system injuries: a narrative review, PM&R 9 (2017) 46–62, https://doi.org/10.1016/j.pmrj.2016.07.534.

[16] L. Miller, A. Zimmermann, W. Herbert, Clinical effectiveness and safety of powered exoskeleton-assisted walking in patients with spinal cord injury: systematic review with meta-analysis, Med. Devices Evid. Res. 9 (2016) 455–466, https://doi.org/10.2147/MDER.S103102.

[17] G.S. Sawicki, D.P. Ferris, Mechanics and energetics of level walking with powered ankle exoskeletons, J. Exp. Biol. 211 (2008) 1402–1413, https://doi.org/10.1242/jeb.009241.

[18] S.H. Collins, M.B. Wiggin, G.S. Sawicki, Reducing the energy cost of human walking using an unpowered exoskeleton, Nature 522 (2015) 212–215, https://doi.org/10.1038/nature14288.

[19] L.N. Awad, J. Bae, K. O'Donnell, S.M.M. De Rossi, K. Hendron, L.H. Sloot, P. Kudzia, S. Allen, K.G. Holt, T.D. Ellis, C.J. Walsh, A soft robotic exosuit improves walking in patients after stroke, Sci. Transl. Med. (2017), https://doi.org/10.1126/scitranslmed.aai9084.

[20] J. Zhang, P. Fiers, K.A. Witte, R.W. Jackson, K.L. Poggensee, C.G. Atkeson, S. H. Collins, Human-in-the-loop optimization of exoskeleton assistance during walking, Science (80) (2017), https://doi.org/10.1126/science.aal5054.

[21] K.Z. Takahashi, M.D. Lewek, G.S. Sawicki, A neuromechanics-based powered ankle exoskeleton to assist walking post-stroke: a feasibility study, J. Neuroeng. Rehabil. 12 (2015) 23, https://doi.org/10.1186/s12984-015-0015-7.

[22] J.R. Koller, C.D. Remy, D.P. Ferris, Biomechanics and energetics of walking in powered ankle exoskeletons using myoelectric control versus mechanically intrinsic control, J. Neuroeng. Rehabil. (2018), https://doi.org/10.1186/s12984-018-0379-6.

[23] G.G. Handsfield, C.H. Meyer, M.F. Abel, S.S. Blemker, Heterogeneity of muscle sizes in the lower limbs of children with cerebral palsy, Muscle Nerve 53 (2016) 933–945, https://doi.org/10.1002/mus.24972.

[24] J. Riad, Y. Haglund-Akerlind, F. Miller, Power generation in children with spastic hemiplegic cerebral palsy, Gait Posture (2008), https://doi.org/10.1016/j.gaitpost.2007.08.010.

[25] C.F. Ong, T. Geijtenbeek, J.L. Hicks, S.L. Delp, Predicting gait adaptations due to ankle plantarflexor muscle weakness and contracture using physics-based musculoskeletal simulations, PLoS Comput. Biol. (2019), https://doi.org/10.1371/journal.pcbi.1006993.

[26] M. Pirpiris, A.J. Wilkinson, J. Rodda, T.C. Nguyen, R.J. Baker, G.R. Nattrass, H. K. Graham, Walking speed in children and young adults with neuromuscular disease: comparison between two assessment methods, J. Pediatr. Orthop. 23 (2003) 302–307, https://doi.org/10.1097/01241398-200305000-00006.

[27] T.A.L. Wren, S. Rethlefsen, R.M. Kay, Prevalence of specific gait abnormalities in children with cerebral palsy: Influence of cerebral palsy subtype, age, and previous surgery, J. Pediatr. Orthop. (2005), https://doi.org/10.1097/00004694-200501000-00018.

[28] Z.F. Lerner, G.M. Gasparri, M.O. Bair, J.L. Lawson, J. Luque, T.A. Harvey, A. T. Lerner, An untethered ankle exoskeleton improves walking economy in a pilot study of individuals with cerebral palsy, IEEE Trans. Neural Syst. Rehabil. Eng. 26 (2018) 1985–1993, https://doi.org/10.1109/TNSRE.2018.2870756.

[29] Z.F. Lerner, T.A. Harvey, J.L. Lawson, A battery-powered ankle exoskeleton improves gait mechanics in a feasibility study of individuals with cerebral palsy, Ann. Biomed. Eng. 47 (2019) 1345–1356, https://doi.org/10.1007/s10439-019-02237-w.

[30] G.M. Gasparri, J. Luque, Z.F. Lerner, Proportional joint-moment control for instantaneously adaptive ankle exoskeleton assistance, IEEE Trans. Neural Syst. Rehabil. Eng. 27 (2019) 751–759, https://doi.org/10.1109/TNSRE.2019.2905979.

[31] Z.F. Lerner, D.L. Damiano, T.C. Bulea, A robotic exoskeleton to treat crouch gait from cerebral palsy: initial kinematic and neuromuscular evaluation, 2016 38th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc., IEEE (2016) 2214–2217, https://doi.org/10.1109/EMBC.2016.7591169.

[32] S. Walfish, A review of statistical outlier methods, Pharm. Technol (2006) 1–5. https://pdfs.semanticscholar.org/0469/f92dbce67ec4444d094e818eeebaaed3d8d5.pdf.

[33] T.C. Bulea, Z.F. Lerner, D.L. Damiano, Repeatability of EMG activity during exoskeleton assisted walking in children with cerebral palsy: implications for real time adaptable control, 2018 40th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc., IEEE (2018) 2801–2804, https://doi.org/10.1109/EMBC.2018.8512799.

[34] J. Kang, D. Martelli, V. Vashista, I. Martinez-Hernandez, H. Kim, S.K. Agrawal, Robot-driven downward pelvic pull to improve crouch gait in children with cerebral palsy, IEEE Trans. Autom. Sci. Eng. 2 (2017), https://doi.org/10.1126/scirobotics.aan2634 eaan2634.

[35] S. Bouisset, F. Goubel, Integrated electromyographical activity and muscle work, J. Appl. Physiol. 35 (1973) 695–702, https://doi.org/10.1152/jappl.1973.35.5.695.

[36] A.L. Hof, H. Elzinga, W. Grimmius, J.P.K. Halbertsma, Speed dependence of averaged EMG profiles in walking, Gait Posture 16 (2002) 78–86, https://doi.org/10.1016/S0966-6362(01)00206-5.

[37] C.J. Kim, S.M. Son, Comparison of spatiotemporal gait parameters between children with normal development and children with diplegic cerebral palsy, J. Phys. Ther. Sci. 26 (2014) 1317–1319, https://doi.org/10.1589/jpts.26.1317.

[38] H. Stolze, J. Kuhtz-Buschbeck, C. Mondwurf, A. Boczek-Funcke, K. Jöhnk, G. Deuschl, M. Illert, Gait analysis during treadmill and overground locomotion in children and adults, Electroencephalogr. Clin. Neurophysiol. Mot. Control. 105 (1997) 490–497, https://doi.org/10.1016/S0924-980X(97)00055-6.

[39] M.D. Latt, H.B. Menz, V.S. Fung, S.R. Lord, Walking speed, cadence and step length are selected to optimize the stability of head and pelvis accelerations, Exp. Brain Res. (2008), https://doi.org/10.1007/s00221-007-1094-x.

[40] J.O. JudgeRoy, B. Davis, S. Ounpuu, Step length reductions in advanced age: the role of ankle and hip kinetics, J. Gerontol. Ser. A Biol. Sci. Med. Sci. 51A (1996) M303–M312, https://doi.org/10.1093/gerona/51A.6.M303.