TITLE: Predictors of Treatment Response to Progressive Resistance Training for Adolescents With Cerebral Palsy

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AUTHORS:

Nicola Theis, PhD,[a*] Marika Noorkoiv, PhD,[b] Grace Lavelle, PhD,[b,d] and Jennifer Ryan, PhD [b,c]

AFFILIATIONS:

[a]*School of Sport and Exercise, University of Gloucestershire, Gloucestershire, UK*

[b]*College of Health and Life Sciences, Brunel University London, London*

[c]*Department of Public Health and Epidemiology, RCSI University of Medicine and Health Sciences, Dublin, Ireland*

[d]*Institute of Psychiatry, Psychology and Neuroscience, King's College London, London*

*Corresponding author

Dr Nicola Theis
School of Sport and Exercise,
University of Gloucestershire,
Longlevens, Gloucester, UK
GL2 9HW
ntheis@glos.ac.uk

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[H1]Abstract

Objective. The aim of the study was to examine the variability in plantar-flexor muscle strength changes after progressive resistance training for adolescents with cerebral palsy (CP) and to identify baseline variables associated with change in muscle strength.

Methods. Thirty-three adolescents with CP were randomized to a 10-week progressive resistance training program as part of a randomized controlled trial (STAR trial). The associations between muscle strength at 10 weeks (n = 30 adolescents) and 22 weeks (n = 28 adolescents) and biomechanical and neuromuscular baseline characteristics, motor function, and fidelity to the program were examined with multivariable linear regression.

Results. Changes in plantar-flexor muscle strength from baseline ranged from -47.7 to 192.3% at 10 weeks and -54.3 to 198.4% at 22 weeks. Muscle activation was the only variable associated with change in strength at 10 weeks and 22 weeks. A model containing peak muscle activity and baseline muscle strength explained 49.1% of the variation in change in muscle strength (R^2 = 0.491) at 10 weeks and 49.2% of the variation in change muscle strength at 22 weeks (R^2 = 0.492).

Conclusion. Assessing levels of muscle activation may be able to identify responders to a progressive resistance training program for adolescents with CP. These findings are a first step toward developing tools that can inform decision making in the clinical setting.

Impact. Due to the heterogenous nature of CP, it is challenging to assess the efficacy of strength training programs in individuals with CP and to understand the variability in outcomes among participants. This study provides a better understanding of the factors that predict response to an exercise program so that resistance training can be directed to those who will potentially benefit from it.

Lay Summary. There is wide variability in how well young people with CP respond to resistance training. If you are a young person with CP, your physical therapist can measure the amount of your gastrocnemius muscle activity to get an indication of how well you will respond.

[H1]Introduction

Cerebral palsy (CP) is a neurodevelopmental condition that begins in childhood, causing a multitude of symptoms including muscle weakness.[1] A predominant loss of strength is seen in the plantar-flexor muscles in many individuals with CP, compromising the ability to produce propulsive force during gait.[2] Resistance training for adolescents with CP is often advocated as a means of overcoming muscle weakness through a number of biomechanical and neuromuscular mechanisms.[3] However, the evidence for the use of resistance training to improve muscle strength and functional outcomes in this population remains equivocal.[4]

In the non-disabled population, the assumption of an exercise program is that the group average response represents the typical response for most individuals, when in fact, it is more common for individuals to show a wide range of responses to the same intervention.[5,6] Hubal et al[7] demonstrated that 12 weeks of resistance training in a sample of 585 men and women, resulted in large variations in muscle strength responses. Specifically, 31% showed increases of >25% in maximal strength compared to baseline, whilst 17% of participants had <5% change in strength. It was hypothesized that skill acquisition, hormonal responses or genetics could be responsible for this variability, although this remains inconclusive.

In individuals with CP, the response to strength training has also varied between studies. A 2017 Cochrane review concluded that resistance training may improve muscle strength in children, adolescents, and young adults in the short term (10 to 12 weeks) but there was limited high quality evidence to support this.[4] For example, Taylor[8] observed on average, a 27.1% increase in muscle strength after 12 weeks of resistance training (3 ×12 repetitions, twice weekly). This was similar to the 26.7% reported by Kara[9] (3 × 90 min sessions weekly). Scholtes[10] reported a lesser, but still statistically significant mean increase of 14% in knee extensor strength after 12 weeks (3 × 45 to 60 mins per week). Conversely, Maeland[11] reported, on average, a 4% increase after 8 weeks of progressive resistance training (4 × 12 to 15 repetitions, 3 days a week), which was not significant. It is evident in the majority of previous resistance training studies for children and adolescents with CP, that a large degree of variability in strength change exists.[8,9,11] However, it is difficult to determine whether this variability is a true response to resistance training in this population or whether these results are the product of methodological shortcomings.[4] Previous studies have employed resistance training protocols that are of an inadequate volume, intensity or duration[12] and utilize multi-joint exercises, where severe muscle weakness could be compensated for with stronger

muscles.[13,14] There is also a lack of high-quality research designs,[3] which may lead to further erroneous conclusions around the effects of progressive resistance training for children and adolescents with CP. The STAR trial implemented a robust, randomized controlled trial design to assess the effectiveness of progressive resistance training, on plantar-flexor muscle strength, following current guidelines for youth resistance training.[15] However, despite overcoming several shortcomings in previous studies, the authors found a group mean reduction in plantar-flexor strength of 5.9% and a high degree of variability in the response to resistance exercise[16].

It is challenging to assess the efficacy of strength training programs in individuals with CP and to understand the variability in outcomes between participants, due to the heterogenous nature of CP. A multitude of biomechanical and neuromuscular characteristics, as well as levels of motor function and fidelity to an exercise program may influence the response to a progressive resistance intervention.[1] Factors such as age, sex and physical activity have been shown to influence the response to strength training due to altered levels of anabolic hormones.[7] For those with CP, anatomical distribution, level of motor function and ankle joint range of motion might influence their ability to get into favorable positions to conduct the exercises and achieve maximal effort contractions.[17] Additionally, reduced muscle activation might make it difficult for those with CP to selectively activate the correct muscles and coupled with structural changes to the muscle-tendon unit, may impair the ability of the muscle to receive an adequate stimulus during resistance training exercises.[18] For example, reduced tendon stiffness has been shown to alter the force-length and force-velocity relationship of fascicles, reducing the force-producing capabilities and increasing the energy cost of movement. This could impair the muscle from receiving an adequate loading-stimulus and cause earlier levels of fatigue during the resistance exercises.[18] Finally, a dose-response relationship has been demonstrated between

resistance training and changes in strength, which might indicate those individuals with greater fidelity to the program would see the greatest benefit.[19]

A better understanding of the factors that predict response to resistance training is needed to direct interventions to those that will potentially benefit from it. The goals of this study were to (1) examine the variability in change in plantar-flexor muscle strength after progressive resistance strength training for adolescents/young adults with CP and (2) identify the variables associated with change in strength after progressive resistance training.

[H1]Methods

[H2]Participants

Sixty-four people with spastic cerebral palsy were recruited as part of the STAR trial, a multi-centre study to investigate the feasibility, acceptability and efficacy of strength training for adolescents with cerebral palsy.[3,16] The inclusion criteria were (1) adolescents with spastic CP aged 10 to 19 years, (2) the ability to walk independently with or without a mobility aid (ie, GMFCS levels I to III, as assessed by a physiotherapist) and (3) the ability to activate the ankle plantar-flexors, assessed using a modified version of the Selective Control Assessment of the Lower Extremity (SCALE).[20] Participants were randomly assigned to one of 2 groups (resistance-training or usual care control group) in a 1:1 ratio after completing baseline assessments.

Allocation was performed by an individual independent to the study according to a computer-generated random schedule in permuted blocks of two or four within Gross Motor Function Classification System (GMFCS) level strata. The allocation of participants to each group within each stratum was placed in sequentially numbered, opaque, sealed envelopes, so that

participants and researchers enrolling participants could not foresee assignment. All participants were instructed to continue their usual physiotherapy and activities.

[H2]Resistance training intervention

Participants were assessed at baseline, after 10 weeks of progressive resistance training and then again at 22 weeks (between 10 and 22 weeks all participants continued with usual care only). A comprehensive description is provided in the study protocol.[16] Briefly, adolescents in the resistance training program completed 10 supervised sessions carried out by a physiotherapist and 20 home sessions of resistance training over 10 weeks. Unilateral, straight-leg exercises, which targeted the plantar-flexors (predominantly gastrocnemius) were performed where possible. A standardized program was used to progress the intensity of the exercises, with resistance increasing from 12 repetition maximum to 6 repetition maximum and sets increasing from 4 to 8 over 10 weeks. During each supervised session, single-joint plantar-flexor exercises were prescribed based on individual strength capacities and included at least one of the following exercises each week depending on the adolescent's individual capacity: (1) seated straight knee calf press against resistance band (TheraBand, Hygenic Corporation), (2) seated straight knee calf press with a leg press machine, (3) standing calf raises against body weight with or without additional resistance and (4) standing calf raises in a hack squat machine.

Resistance was added to progress the training over the 10 weeks using free weights on a leg press or hack squat machine, weighted vests, ankle weights, or resistance band. Participants performed the exercise or a combination of exercises during the supervised session and home sessions to achieve the prescribed intensity for that week (eg, 4 sets at 12 repetition maximum in each session during week 1). Resistance was added incrementally at each supervised session

to ensure that the participant completed the prescribed number of repetitions at the supervised and home session to fatigue and was therefore exercising at the prescribed intensity.

[H2]Control Group

Those randomized to the control group, took part in usual care only. They were instructed to continue their usual physiotherapy and activities which was captured via a usual care checklist, developed from the results of a national survey of physiotherapists in the UK regarding usual care for adolescents with CP.

[H2]Primary outcome measure

Muscle strength was used as the primary outcome measure in this study from assessments conducted at baseline, at 10 weeks (immediately post-intervention), and at 22 weeks (follow-up).

[H3]Muscle strength

Plantar-flexor muscle strength was assessed on an isokinetic dynamometer (Cybex Norm, Lumex Corporation, Ronkonloma, NY, USA). Participants were secured in a seated position with the knee joint as close to full extension as possible and the foot secured to the footplate of the dynamometer with the ankle joint as close to 90° as possible. Each participant was required to push against the footplate producing a maximal voluntary isometric contraction manoeuvre for 5 s while plantar-flexor torque was recorded. To familiarize the participants with the equipment and the plantarflexion task, 3 to 5 submaximal isometric contractions were performed. These contractions also provided a task-specific warm-up to pre-condition the tendon and ensure consistency of load-deformation properties. After a mandatory 5 min rest period to minimise fatigue, participants performed three further contractions with maximal effort.

[H3]Baseline variables

Detailed methods for all baseline variables have been previously reported[16] but are briefly outlined here.

Gross motor function: Participants' gross motor function was assessed using dimensions D and E of the Gross Motor Function Measure (GMFM-66). Dimension D evaluates activities in standing. Dimension E evaluates activities in walking, running, and jumping. Participants' performance of dimensions D and E of the GMFM-66 was video recorded and scored by a physiotherapist blinded to group allocation. The scores recorded for each dimension were summed to create one variable. A higher score indicates better gross motor function (total possible score is 111).

Physical activity: Physical activity was measured using an accelerometer (30 Hz, Actigraph wGT3X) worn on the waist above the hip (on the least affected side in the case of significant asymmetry). Participants were asked to wear the accelerometer for 7 consecutive days at each assessment point. Data were exported in 15 s epochs using ActiLife software, Version 16.3.3 (ActiGraph, Pensacola, FL). Time spent in sedentary activity and moderate to vigorous activity (MVPA) was determined by classifying accelerometer counts according to cut-points validated in children and adolescents with CP.[21] Further detail on the identification of non-wear-time, criteria for valid wear-time, and classification of activity counts are provided in the full publication[16] (Appendix S2 online supporting information). Participants included in the analysis at 10 weeks wore the accelerometer for a median of 7 days (minimum 3 and maximum 7) and a mean of 735.4 (94.1) minutes per day. Participants included in the analysis at 22 weeks wore the accelerometer for a median of 7 days (minimum 3 and maximum 7) and a mean of 735.7 (97.5) minutes per day.

Muscle-tendon mechanics: Achilles tendon stiffness and medial gastrocnemius muscle stiffness were estimated from force and length change data. Maximal isometric plantar-flexor torque measured on the isokinetic dynamometer (Cybex) was divided by Achilles tendon moment arm[22] (obtained using the tendon excursion method), to give an estimate of Achilles tendon force, for the purposes of calculating tendon stiffness. Plantar-flexor torque was also obtained during passive isolated ankle rotations in order to estimate medial gastrocnemius force for the purpose of calculating medial gastrocnemius stiffness.

The lengths of the medial gastrocnemius muscle and Achilles tendon were measured, using a combination of ultrasound (Echoblaster 128, Telemed, Vilnius, Lithuania) and the position of motion analysis (Motion Analysis, Santa Rosa, California, USA) markers on the medial epicondyle of the femur, the Achilles tendon insertion and on the ultrasound probe. Ultrasound images were manually digitized to identify the medial gastrocnemius muscle–tendon junction in each video frame (V.9, Vicon, Oxford, UK) and combined with coordinates from the ultrasound probe to give the position of the muscle–tendon junction in the global motion analysis coordinate system. Achilles tendon length was derived as the distance between the muscle-tendon junction and the calcaneus, and medial gastrocnemius muscle length was derived as the distance between the mid-point of the epicondyle markers and the muscle-tendon junction.

Achilles tendon stiffness was calculated as the change in Achilles tendon force (measured from maximal voluntary contraction maneuvers), divided by the corresponding change in Achilles tendon length in the linear portion of the force–length relationship. An estimate of medial gastrocnemius muscle stiffness was also derived from the data by dividing the medial

gastrocnemius force (measured from passive rotations maneuvers) by elongation of the medial gastrocnemius muscle.

Muscle activation of the gastrocnemius: Electrical activity of the lateral gastrocnemius (EMG) was recorded during treadmill walking. An EMG electrode (Trigno wireless system, Delsys Inc., Ltd., Boston, USA) was placed on the clean shaved skin, over the muscle belly and in the direction of underlying fibres, according to SENIAM guidelines**.** Data were synchronized with motion capture data and collected at a sampling frequency of 2000 Hz. The EMG signal was full wave rectified and a moving average was calculated with a time constant of 100 ms. Peak amplitude in mid-stance of gait was normalized to the average amplitude in a gait cycle and averaged over 6 cycles for each participant.

Gait kinematics: Reflective markers on the greater trochanters, medial and lateral femoral epicondyles, the medial and lateral malleoli, the heads of the first and fifth metatarsals were used to calculate ankle and knee range of motion angles during push-off. Marker coordinates were filtered with a 0-lag, fourth-order Butterworth filter with a cut-off frequency of 6 Hz. A visual 3D–linked model, was assigned to motion data. Joint angles were computed as the angles between the proximal and distal segment of the relevant joint. The line connecting the segments was calculated by finding the midpoint between medial and lateral markers. Specifically, ankle angle was measured as the angle between the line connecting the malleoli and the metatarsals (ie, foot segment), and the line connecting the malleoli and the epicondyles (ie, lower leg segment). Knee joint angle was measured as the angle between the line connecting the malleoli and the epicondyles (ie, lower leg segment), and the line connecting the epicondyles and the hip joint (ie, thigh segment).

Fidelity to the program: Attendance and compliance to the training intervention was monitored by the physiotherapist delivering the supervised sessions and through the home exercise diary. In addition to the diary, participants completed, physiotherapists also sought and recorded confirmation of home exercise sessions completed each week. Home fidelity to the program was expressed as a percentage of 20 possible home sessions and group fidelity was expressed as a percentage of 10 possible supervised group sessions.

[H2]Data analysis

A total of 33 participants were randomized to the intervention group to complete 10 weeks of resistance training. The variability in strength changes after 10 weeks of progressive resistance training and a follow up at 22 weeks was assessed by examining the mean change from baseline, standard deviation (SD) of the change from baseline, the range, the percentage of participants that increased or decreased from baseline, and the percentage of participants that increased by more than a minimal clinically important difference, calculated by halving the standard deviation of the change in strength.[23]

[H2]Statistical analysis

To investigate the baseline variables associated with strength changes after progressive resistance training, regression models were fitted to explore (1) the association between each individual baseline characteristic (independent variables) and absolute change in muscle strength at 10 weeks (ie, 10 week strength minus baseline strength), after adjusting for baseline strength and (2) the association between each individual baseline variable (independent variables) and absolute change in muscle strength at 22 weeks (ie, 22 week strength minus baseline strength), after adjusting for baseline strength.

To investigate which variables best predicted change in muscle strength at 10 and 22 weeks, we included variables that were individually associated with muscle strength at 10 weeks ($P < .10$) together in a multivariable regression model, while also adjusting for baseline strength. This was then repeated for strength at 22 weeks. Assumptions of linear regression, namely a linear association between independent and dependent variables, homoscedasticity, and normally distributed errors, were explored using scatter plots, Q-Q plots, and histograms. All analyses were performed in Stata version 15.0 (StataCorp LLC, College Station, TX, USA).

[H1]Results

Of the 33 participants that were randomly assigned to the exercise group, 3 were not included in the analysis at 10 weeks and 5 were not included at 22 weeks due to incomplete strength testing at 10 and/or 22 weeks. Descriptive statistics for the participants at 10 and 22 weeks are reported in Tables 1 and 2.

[H2]Variability in plantar-flexor muscle strength

Mean (SD) strength at baseline was 30.5 (18.1) Nm, which increased to 36.5 (18.4) Nm after 10 weeks of progressive resistance training, resulting in a 34.3% increase but with a high degree of variability (SD = 62.0%; range = -47.7 to 192.3%) (Fig. 1). Additionally, 68% of the participants showed an increase in strength from baseline, with 40% achieving a minimal clinically important difference of 7.4 Nm.

When followed up at 22 weeks, mean (SD) strength had decreased to 34.8 (15.9) Nm resulting in an average 33.5% increase in strength from baseline (SD = 67.1%; range = -54.3 to 198.4%) (Fig. 1) with 61% showing an increase in strength from baseline. Thirty-six percent of participants who showed an increase above the minimal clinically important difference of 7.4

Nm. The maximum response to the intervention was an increase in strength of 192.3% at 10 weeks and 198.4% at 22 weeks. However, a decrease of -47.7% and -54.3% at 10 and 22 weeks, respectively, were also observed.

[H2]Associations with change in plantar-flexor muscle strength at 10 weeks and 22 weeks

Associations between baseline characteristics and change in plantar-flexor muscle strength at 10 weeks and 22 weeks are shown in Tables 1 and 2, respectively. Peak muscle activity during walking at baseline was the only variable associated with strength at 10 weeks (P = .001). A 1 mV increase in peak muscle activity was associated with an average increase of 6.93 Nm in muscle strength between baseline and 10 weeks. Baseline muscle strength explained 7.6% of the variation in change in muscle strength between baseline and 10 weeks. Baseline strength alone explained 7.6% of the variation in change in muscle strength at 10 weeks, whilst peak muscle activity and baseline muscle strength explained 49.1% of the variation in change in muscle strength (R^2 = 0.491, P < .001). There were no other associations between baseline characteristics and change in strength at 10 weeks.

Peak muscle activity (P = .005), GMFM D&E (P = .016), GMFCS (P = .022), sex (P = .082), sedentary time (%) (P = .054) and home fidelity to the program (P = .012) were independently associated with change in plantar-flexor muscle strength at 22 weeks. A 1 mV increase in peak muscle activity during walking was associated with an average increase of 5.84 Nm in muscle strength between baseline and 22 weeks. A one-point increase on the GMFM D&E scale was associated with a 0.22 Nm increase in muscle strength between baseline and 22 weeks. Similarly, a 1% increase in fidelity to the home program was

associated with a 0.25 Nm increase in muscle strength between baseline and 22 weeks. Finally, a 1% decrease in sedentary time resulted in a 0.51% increase in muscle strength.

For change in strength at 22 weeks, sex, peak muscle activity, sedentary time (%), GMFM D&E and fidelity to the home program were entered into a model together with baseline strength, as they were associated with change in strength at $P < .10$. GMFCS was not entered into the multivariable model to reduce the number of variables in the model and avoid collinearity because GMFCS and GMFM are closely related. Together, these variables explained 63.2% of the variation in change in muscle strength at 22 weeks ($R^2 = 0.632$, $P = .001$) with peak muscle activity during walking (coefficient 4.49, 95% CI = 0.04 to 8.94, $P = .048$) being the only independent predictor of muscle strength at 22 weeks. In a model containing only peak muscle activity, and baseline strength, 49.2% of the variation in change muscle strength at 22 weeks was explained ($R^2 = 0.492$, $P < .001$). Baseline strength alone explained 30.2% of the variation in change in muscle strength at 22 weeks.

[H1]Discussion

A large degree of variability in change in strength is evident in the majority of previous resistance training studies for children and adolescents with CP.[8,9,11,16] However, it is difficult to determine whether this variability is a true response to resistance training in this population or whether these results are the product of methodological shortcomings.[4] In order to understand this variability and to create a more efficient and effective model of care for those with CP, it is critical to provide the right service users the therapies and interventions that have the most effective outcomes. Therefore, the first purpose of the study was to examine the variability in change in plantar-flexor muscle strength after 10 weeks of progressive resistance training for individuals with CP. The second purpose was to identify the baseline variables

associated with change in strength at 10 weeks, immediately after the cessation of the intervention, and at the 22-week follow-up. We observed a wide variation in change in strength at both time points, with some participants showing exceptionally large increases in muscle strength and others showing declines in muscle strength. We found that baseline muscle strength and gastrocnemius peak muscle activation during walking was a significant predictor of change in strength at 10 weeks and 22 weeks.

Using baseline data to predict who may respond more favourably to an intervention can assist clinicians in directing service users to the most effective treatment, potentially saving time, and concomitantly reducing healthcare costs. The models developed in the current study show that the use of baseline measures and participant characteristics can successfully predict 49.1% to 63.2% of the variance in strength to a progressive resistance training program. While we are not aware of previous research studies examining the ability of baseline characteristics to predict change in strength after progressive resistance training in CP, studies have demonstrated successful prediction models in other populations. For example, predictor variables such as age, pain, duration of symptoms, and gait speed were used to achieve 65% classification accuracy for determining responders to a physical therapy intervention with hip osteoarthritis.[24] Thus, the results of the current study suggest that objective baseline variables may provide a robust method for identifying young people with CP who may benefit from a progressive resistance program.

The finding that gastrocnemius peak muscle activation during walking and baseline plantar-flexor muscle strength, were the only significant predictors of change in muscle strength at both time points is an important finding. Interestingly, muscle activity was a stronger predictor of change in strength, than baseline muscle strength at 10 weeks, but at 22 weeks, baseline muscle strength was a larger predictor. This suggests differing mechanisms of strength gains

between the 2 time points, which may be consistent with previous studies in non-CP populations. For example, in the first 4 to 6 weeks of resistance training, adaptations have been shown to be neurological in nature,[25] causing early strength gains by adaptations to the nervous system. This is consistent with the results here, that higher baseline muscle activity may influence these neurological strength gains at 10 weeks but not 22 weeks. In children with spastic CP, muscle activation tends to occur in a variety of patterns and magnitudes in comparison to the typical patterns displayed by children without disability.[26] This impairment in motor control might affect the ability to voluntarily and efficiently recruit muscles to perform desired actions, which may limit the neural drive reaching the muscle and explain why individuals with low muscle activation in the gastrocnemius do not respond as well to progressive plantar-flexor resistance training. In this study, those individuals with the greatest levels of activation were likely to see improvements in muscle strength with progressive resistance training, therefore suggesting that higher peak muscle activity may be the most effective measure to determine a subset of individuals who will respond best to a progressive resistance intervention. It should be noted that gastrocnemius muscle activity in this study was measured during walking and not during the plantarflexion exercises themselves, which may alter the activation pattern observed here.

Conversely, at 22 weeks, baseline strength explained most of the change in strength. After 10 weeks, any continued change in strength may have been due to factors, such as hormone levels and nutrition, whereby those who started off with low levels of muscle strength were unable to significantly increase their plantar-flexor muscle strength further, whilst those with already higher baseline strength, may have had better hormone responses or nutrition to continue gaining strength. This is also an important finding, because although gastrocnemius muscle activity was an important predictor at 10 weeks, these findings suggest that baseline muscle

strength might be more important to predict longer term strength gains and would also be an easier clinical measure to assess than muscle activity, prior to individuals starting an intervention.

Our results shown here suggest that baseline muscle strength and gastrocnemius muscle activity might be important modifiable predictors to assess not just who will respond favourably, but how we can make individuals respond more favourably. Baseline strength is made up of a multitude of factors including not only muscle activity, but muscle size, increased stiffness and perhaps even hormonal and dietary factors which have scarcely been researched. Thus, research must firstly determine the cause of such weakness before baseline strength could be modified to help those individuals respond more favourably to a resistance training intervention. Muscle activity has been shown to be a modifiable variable through interventions such as neuromuscular electrical stimulation, which has been shown to improve muscle activation patterns after 8 weeks of repeated stimulation to the vastus lateralis in locomotive syndrome patients,[27] and combined with constraint-induced movement therapy, has also been shown to improve muscle recruitment and coordination in children with hemiplegic cerebral palsy.[28] The addition of neuromuscular stimulation to a resistance training program or as a preliminary intervention before the commencement of resistance training may improve the strength outcomes for those with low baseline muscle activity.

Overall, these findings provide an important step in determining the basis for exercise interventions. Whilst many therapies may be offered on the basis of age, physical activity and gross motor function, these findings suggest that these are not the most important variables in predicting the outcome to strength training. The response to strength training appears to be more complex and may be influenced to a greater extent by baseline muscle strength and peak

muscle activity. Although the current study provides new insights into predicting the response to progressive resistance training in children and young adults with CP, it remains a preliminary investigation with known limitations. First, the identified predictors may be prognostic factors that are not specific to this treatment. In other words, although the predictors were clinically interpretable as being associated with a progressive resistance training program, given the current design and selection bias, we cannot rule out that these factors may simply relate to high responders in general and as such, these individuals would respond well to other treatment interventions not just progressive resistance training. Second, there are a relatively low number of participants involved in the investigation and as such, there is risk of that the lack of associations observations are due to a lack of statistical power. Regardless of the number of participants, additional testing on an independent sample is required to determine its true predictive capability. Therefore, it is our hope that the findings presented in this study can be a first step towards developing tools that can use baseline variables to inform decision-making about progressive resistance training in the clinical setting.

[H1]Author Contributions

Concept/idea/research design: N. Theis, G. Lavelle, J.M. Ryan

Writing: N. Theis, J.M. Ryan

Data collection: N. Theis, M. Noorkoiv, G. Lavelle, J.M. Ryan

Data analysis: N. Theis, M. Noorkoiv, J.M. Ryan

Project management: G. Lavelle, J.M. Ryan

Providing participants: G. Lavelle

Providing facilities / equipment: G. Lavelle

Providing institutional liaisons: N. Theis

Clerical / secretarial support: G. Lavelle

Consultation (including review of manuscript before submitting): N. Theis, G. Lavelle

[H1]Ethics Approval

This study was approved by the Institutional Review Board, Brunel University, and National Health Service Ethics. All parents/guardians signed an informed consent document.

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[H1]Disclosures

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

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Table 1. Results From Regression Models Examining the Association Between Absolute Change in Muscle Strength Between Baseline and 10 Weeks and Baseline Characteristics (n = 30 unless stated otherwise)

Characteristic	**Mean (SD) or Frequency**	***P***	**Coefficient (95% CI)[a]**	
Age, y	13.4 (2.7)		-0.54 (-2.08–1.01)	.483
Mass	48.0 (15.8)		-0.03 (-0.29–0.24)	.833
Sex				
Male	19		Ref	
Female	11		4.15 (-4.61–12.90)	.340
Distribution				
Unilateral	12		Ref	
Bilateral	18		-0.01 (-9.06–9.04)	.998

GMFCS			
I	13	Ref	
II	12	-5.80 (-15.64–4.05)	.237
III	5	-4.69 (-19.18–9.80)	.512
GMFM D&E	86.2 (33.9)	0.02 (-0.13–0.17)	.760
Sedentary time (%) (n = 28)	67.5 (11.6)	-0.26 (-0.63–0.13)	.183
MVPA (n = 28)	53.1 (25.4)	0.01 (-0.18–0.20)	.919
Achilles tendon CSA (cm^2) (n = 26)	0.42 (0.08)	47.18 (-13.82–108.18)	.123
Tendon stiffness ($Nm \cdot mm^{-1}$) (n = 28)	155.2 (106.5)	-0.01 (-0.06–0.04)	.593
Muscle stiffness ($Nm \cdot m^{-1}$) (n = 27)	2.24 (2.21)	-0.46 (-2.49–1.58)	.648
Peak muscle activity (mV)	1.39 (1.03)	6.93 (3.90–9.96)	<.001
Ankle angle at push-off (°) (n = 24)	-28.86 (13.4)	-0.163 (-0.49–0.16)	.314
Knee angle at push-off (°) (n = 24)	2.85 (9.6)	-0.98 (-0.58–0.39)	.679
Fidelity to the program (%)			
Home	72.7 (22.3)	-0.03 (-0.23–0.16)	.717
Group	81.3 (15.3)	-0.08 (-0.35–0.19)	.558

[a]All associations adjusted for baseline strength. CI = confidence interval; CSA = cross-sectional analysis; GMFCS = Gross Motor Function Classification System; GMFM D&E = Gross Motor Function Measure dimension D and E; MVPA = moderate to vigorous activity; NNcost = nondimensional cost; Ref = reference; SD = standard deviation; y = year.

Table 2. Results From Regression Models Examining the Association Between Absolute Change in Muscle Strength Between Baseline and 22 Weeks and Baseline Characteristics (n = 28 unless stated otherwise)

Characteristic	**Mean (SD) or Frequency**	**Coefficient (95% CI)[a]**	***P***
Age (y)	13.5 (2.6)	-1.03 (-2.96–0.90)	.284
Mass	48.4 (14.8)	-0.09 (-0.44–0.25)	.581

Sex			
Male	17	Ref	
Female	11	9.22 (-1.27–19.71)	.082
Distribution			
Unilateral	12	Ref	
Bilateral	16	-0.41 (-11.22–10.40)	.938
GMFCS			
I	13	Ref	
II	11	-4.42 (-15.63–6.80)	.424
III	4	-19.99 (-36.82–-3.16)	.022
GMFM D&E	88.6 (31.1)	0.22 (0.04–0.39)	.016
Sedentary time (%) (n = 27)	67.5 (10.0)	-0.51 (-1.02–0.01)	.054
MVPA (n = 27)	54.4 (23.8)	0.12 (-0.12–0.73)	.317
Achilles tendon CSA (cm^2) (n = 24)	0.42 (0.08)	23.88 (-55.58–103.33)	.539
Tendon stiffness ($Nm \cdot mm^{-1}$) (n = 26)	155.0 (109.3)	0.01 (-0.05–0.07)	.673
Muscle stiffness ($Nm \cdot m^{-1}$) (n = 25)	2.26 (2.29)	-0.18 (-2.32–1.96)	.862
Peak muscle activity (mV)	1.50 (1.11)	5.84 (1.91–9.77)	.005
Ankle angle at push-off (°) (n = 23)	-28.9 (13.7)	0.004 (-0.37–0.38)	.983
Knee angle at push-off (°) (n = 23)	2.65 (9.7)	0.084 (-0.68–0.51)	.769
Fidelity to the program (%)			
Home	74.3 (23.0)	0.25 (0.05 – 0.45)	.018
Group	83.6 (13.9)	0.22 (-0.13 to 0.58)	.207

[a]All associations adjusted for baseline strength. CI = confidence interval; CSA = cross-sectional analysis; GMFCS = Gross Motor Function Classification System; GMFM D&E = Gross Motor Function Measure dimension D and E; MVPA = moderate to vigorous activity; NNcost = nondimensional cost; Ref = reference; SD = standard deviation; y = year.

FIGURE CAPTION:

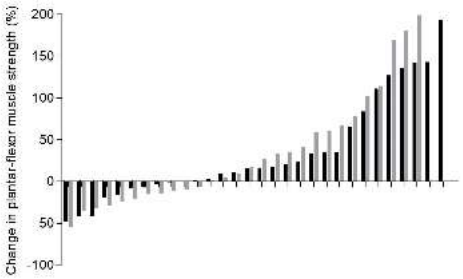

Figure 1. Individual responses to progressive resistance training after 10 weeks (black) and 22 weeks (grey). Data are expressed as percentage change in plantar-flexor muscle strength from baseline (10 weeks is n = 30) (22 weeks is n = 28).