Functional Anaerobic and Strength Training in Young Adults with Cerebral Palsy

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ABSTRACT

GILLETT, J. G., G. A. LICHTWARK, R. N. BOYD, and L. A. BARBER. Functional Anaerobic and Strength Training in Young Adults with Cerebral Palsy. *Med. Sci. Sports Exerc.*, Vol. 50, No. 8, pp. 1549–1557, 2018. **Purpose**: This study aimed to investigate the efficacy of a 12-wk combined functional anaerobic and strength training program on neuromuscular properties and functional capacity in young adults with spastic-type cerebral palsy. **Methods**: A total of 17 young adults (21 ± 4 yr, 9 males, Gross Motor Function Classification System I = 11 and II = 6) were randomized to 12 wk, 3 sessions per week, of high-intensity functional anaerobic and progressive resistance training of the lower limbs (n = 8), or a waitlist control group (n = 9). Pre- and posttraining plantarflexor and tibialis anterior muscle volumes and composition, passive and active plantarflexor muscle properties, and functional capacity outcomes were assessed. **Results**: The training group had higher values compared with the control group (adjusted mean difference) at 12 wk for the following: more- and less-impaired total plantarflexor and tibialis anterior muscle volumes, maximum isometric plantarflexion strength, muscle power sprint test peak power, agility shuttle time, composite functional strength score, and 6-min walk test distance. The change in total plantarflexor muscle volume was associated with the change in plantarflexor muscle strength. There were relationships between the change in plantarflexor muscle strength and the change in functional capacity outcomes (functional strength; 6-min walk test). **Conclusions**: Combined functional anaerobic and strength training increased muscle size, strength, and functional capacity in young adults with cerebral palsy. The addition of anaerobic training to progressive resistance training programs assists in the transfer to improved functional capacity.
Key Words: RESISTANCE TRAINING, HYPERTROPHY, FUNCTIONAL CAPACITY, MUSCLE STRENGTH

Absolute muscle size and rate of muscle growth are reduced in individuals with cerebral palsy (CP) (1–3). The gap between growth rates in typically developing (TD) individuals and those with CP also widens with age (2,3). This impaired muscle growth and adaptation has been described as a potential mechanism for the development of skeletal muscle deformity in children with CP (4). Muscle size is a major determinant of muscle strength. Reduced muscle size may therefore be a large contributor to the hallmark characteristics of muscle weakness (5) and reduced functional ability (6) seen in this population. Adolescents and young adults with CP also have reduced lower limb muscle volumes relative to total body mass compared with their TD counterparts (7). This normalized muscle mass deficit may lead to difficulties performing activities that require force and power generation from the lower limbs. The reduced muscle mass at a young age in individuals with CP has recently been compared with sarcopenia among older TD adults (8). This may lead to an accelerated decline in muscular strength reserve and diminished oxidative capacity of muscle tissue that has a detrimental effect on metabolic health.

Further musculotendinous adaptations such as reduced muscle quality (less force-generating contractile tissue relative to noncontractile tissue) (9) and increased joint and muscle fascicle stiffness (10) may also result in the inability of the muscle fascicles to reach lengths favorable for high force production. Importantly, muscle size and fascicle architecture, along with strength and power, have been shown to be responsive to progressive resistance training (PRT) in TD individuals (11–13).

Improvements in strength have been demonstrated for both TD and individuals with CP after PRT (13–17). Multiple studies have reported limited evidence for subsequent improvements in functional capacity and translation to improved physical activity performance in individuals with CP (15,17–19). The lack of strength transfer to functional capacity improvements in previous strength training studies may be due to a lack of specificity of training modes, insufficient training

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Submitted for publication November 2017.
Accepted for publication March 2018.

0195-9131/18/5008-1549/0
MEDICINE & SCIENCE IN SPORTS & EXERCISE®

DOI: 10.1249/MSS.0000000000001614

loads to illicit adaptation, lack of use of PRT guidelines, and confounding effects of multiple impairments in individuals with CP such as muscle weakness, stiffness, and altered motor control, which may all influence function (20,21).

The addition of functional training exercises to traditional PRT programs may lead to increased functional capacity according to the principle of specificity of training. Two well-designed studies have reported improvements in functional capacity after specific anaerobic training in children and adolescents with CP (22,23). Isolated resistance training does not train the skills or movements required to perform functional tasks, which may explain the incongruence between strength and functional adaptations after isolated resistance training interventions (15,18).

As most muscle-strengthening interventions in individuals with CP have focused on improving strength and mobility, the outcome measures have been predominantly gross motor and functional capacity measures without examining the muscle itself (17,24). Key morphological and architectural parameters, such as muscle size, have been extensively evaluated after PRT interventions in the TD population that provide a link between changes in muscle structure and functional outcomes such as increases in strength and power (12,25). Skeletal muscle hypertrophy in TD adults has been reported across a wide variety of resistance training interventions, age ranges, muscle groups, and sexes (26,27). Although the evidence is strong for positive muscle adaptation after PRT in TD individuals (27,28), a recent systematic review found only preliminary evidence for improved muscle morphology and architecture in children and adolescents with CP (14).

To the best of our knowledge, there have been no studies published in adults with CP that have measured muscle morphology, architecture, or muscle quality changes after resistance training interventions. The hypertrophic response to resistance training could be better understood by testing the efficacy of PRT interventions in more skeletally mature individuals with CP, alongside a control group measured at identical time points. It remains unknown whether muscle in skeletally mature individuals with CP can adapt similarly to TD muscle after PRT, and whether any morphological adaptations are related to strength and functional outcomes. Measuring muscle quality and muscle stiffness changes would also assist in understanding the structural mechanisms underpinning any functional capacity or strength improvements after training.

The purpose of this study was to test the efficacy of a high-intensity combined progressive resistance and anaerobic training intervention in individuals with CP 15–30 yr of age. We hypothesized that combined functional anaerobic and strength training would result in increased lower leg muscle volume, reduced muscle fascicle stiffness, and improvements in strength and functional capacity.

METHODS

A waitlist randomized controlled trial was conducted to test the efficacy of a 12-wk, 3 sessions per week, combined progressive resistance and functional anaerobic training program on lower limb neuromuscular properties and functional capacity compared with a waitlist control group.

Participants. Participants were recruited across South East Queensland, Australia, from the Queensland Cerebral Palsy Register; Queensland Paediatric Rehabilitation Service; Cerebral Palsy League Queensland; Brisbane Paralympic Football Program; and expression of interest advertising from July 2015 to August 2017. Written informed consent (assent if 15–18 yr) was obtained from participants and a parent or guardian (if participant <18 yr). The study was approved by the Human Research Ethics Committees at The University of Queensland (2014000066); Children's Health Queensland Hospital and Health Service (HREC/15/QRCH/30); and the Cerebral Palsy League of Queensland (CPL-2016-001). This study was registered with the Australian New Zealand Clinical Trials Registry (ANZCTR: 12614001217695). Male and female participants were included who 1) were between 15 and 30 yr of age; 2) were diagnosed as unilateral or bilateral spastic type CP; 3) were able to walk independently; 4) were classified as levels I and II, using the Gross Motor Function Classification System (GMFCS) (29); and 5) had a maximum passive ankle dorsiflexion range of <5° (knee fully extended).

Design and procedure. After baseline assessments, participants were stratified according to age in either 15–18 or 18–30 yr bandwidths and sex. Once stratified, participants were then randomized into either the immediate intervention group or the waitlist control group using a computer-generated list of random numbers in concealed envelopes opened by nonstudy personnel. Participants assigned to the intervention group began training within 2 wk of the baseline assessments. The control group received no resistance or anaerobic training and was allowed to continue with usual daily activities. Both groups were reassessed within 3 d of completing the 12-wk intervention or control period. Data were collected in the Centre for Sensorimotor Performance at The University of Queensland, Australia, for both baseline and follow-up assessments. The intervention took place in a fully equipped tertiary institution gymnasium in Brisbane, Australia. Blinding for all measures was not possible as participants and trainers were aware of group allocation. Assessors were not blinded to group allocation. Adherence to the training program was recorded by the trainer at the end of each completed prescribed training session in participant training diaries. The full study protocol has been published (30).

Sample size. As no previous randomized trials have measured lower limb muscle volumes after resistance training in young adults with CP, pilot data from TD individuals were used to determine the sample size for this study. An 8-wk pilot study of our training program in 10 TD individuals revealed a mean medial gastrocnemius muscle volume difference of 11.5 mL posttraining with an SD of the difference between means of 14.0 mL. An estimated effect size of 0.85 calculated from this pilot data was used in an *a priori* power analysis determining that 16 experimental and 16 control subjects were required to confirm the null hypothesis with a power of 0.80 and an alpha level set at 0.05. To allow for an estimated 10% attrition rate during the intervention, 20 participants were required for each group.

Intervention. A detailed description of the content and progression of the training intervention has been published in the study protocol (30). Participants randomized to the training group undertook three training sessions per week, for 12 wk, totaling 36 sessions. The PRT component was performed first in each session, followed by the functional anaerobic exercises. Participants trained individually or in groups of no more than three, to allow strict supervision and adherence to the prescribed exercise and rest periods. The PRT component of each session consisted of five lower limb resistance exercise stations as follows: seated bent knee calf raise, leg press, seated straight knee calf press, seated tibialis anterior raise, and standing calf raise. The resistance training program was periodized, comprising multiple sets of between 6 and 12 repetitions. Training sets and repetitions progressed according to the training program every 4 wk, and training load was adjusted during any session based on participants completing the required number of sets and repetitions to task failure (30). The functional anaerobic training component consisted of two to three functional anaerobic exercises per session completed at maximal intensity that were adapted from a functional training study in children with CP, related to everyday activities such as stair climbing, bending, changing direction, and stepping over obstacles (22). The number of anaerobic exercises per session, repetitions performed, and work to rest ratio progressed every 4 wk (30).

Primary outcome. Full details of the outcome measures and instrumentation have been published in the study protocol (30). Muscle volumes were measured using magnetic resonance imaging pre- and postintervention. Axial plane scans of the lower leg were acquired using a Siemens 3.0 Tesla magnetic resonance imaging scanner (MAGNETOM Verio, Erlangen, Germany) with 2 × 6 channel body matrix array combined with a 24-channel spine coil. Two-point gradient echo Dixon images were acquired in 2D with repetition time/echo time = 970/13 ms, 140° flip angle, 4-mm slice thickness, 240 × 320 acquisition matrix, and 350 × 350 mm field of view. The borders of the individual muscles were manually segmented offline using Stradwin (version 4.2; Mechanical Engineering, Cambridge University, UK) reconstruction software, surface rendered, and then muscle volume (mL) calculations were performed using the measurement modules. This method has high test–retest reliability measuring medial gastrocnemius muscle volumes (intraclass correlation coefficient = 0.99) (31).

Secondary outcomes. Ankle and medial gastrocnemius fascicle active and passive mechanical properties were assessed during controlled movements using integrated dynamometry, surface electromyography, and B-mode ultrasound imaging (10). These outcomes were measured on the impaired limb in participants with unilateral CP, and the more-impaired limb in participants who had bilateral CP based on participant report. If the more impaired limb could not be determined, the right side was used. Two maximum voluntary isometric contractions (MVIC) of the plantarflexor muscles were performed at five angles corresponding to 5%, 25%, 50%, 75%, and 95% of the range between maximum plantarflexion and maximum dorsiflexion. The MVIC of the dorsiflexors was also performed at 50% of the participants' range of movement. The postintervention MVIC in each participant were performed at the same ankle angles used to test their MVIC at baseline. Absolute (N·m) and normalized (N·m·mL^{-1}, to plantarflexor and dorsiflexor volume) maximum torque across this range was used for subsequent analysis. Changes in muscle fascicle length and pennation angle with changes in joint angle or during contraction were assessed using ultrasound imaging and a semiautomated tracking algorithm (32–34).

Fascicle slack length was defined as the measured fascicle length (mm) from a slow passive ankle rotation (10°·s^{-1}) at an ankle joint plantarflexion torque of 1 N·m in all participants. Fascicle stiffness was calculated by fitting an exponential function to the muscle fascicle versus joint torque curve for three successive passive ankle rotations. The stiffness value is the coefficient obtained from the resultant exponential fit. Ankle slack angle (°) and ankle joint stiffness were calculated using the same procedure, fitting an exponential equation to the ankle angle versus joint torque curve. A higher exponential coefficient corresponds to stiffer muscle fascicles or ankle joint.

Intramuscular fat content of the medial gastrocnemius muscle was calculated from two-point gradient echo Dixon magnetic resonance images (9) in a subsample of participants (n = 6 intervention; n = 3 control). Erroneous Dixon image acquisition due to technical issues with the implemented protocol resulted in unusable data in eight participants. The ratios of the water and the fat signal intensities within the regions of interest along the midquartile of the muscle were used to quantify average intramuscular fat using the following equation:

$$A_f = \sum_{i=1}^{n} \left(\frac{I_f}{I_f + I_w} \right) \times 100, \qquad [1]$$

where A_f is the average percentage fat, I_f is the pixel intensity in fat-saturated images, and I_w is the pixel intensity in water-saturated images.

The muscle power sprint test was used to estimate anaerobic power output (35). Participants completed six 15-m runs as quickly as possible with 10-s rest between sprints. An individual's ability to change direction rapidly without losing balance was assessed using the 10 × 5-m sprint test (35). Participants performed ten 5-m sprints continuously between two sets of cones. A 30-s repetition maximum test was used as a functional strength assessment involving components of balance, speed, coordination, endurance, and muscular strength (36). Participants completed as many repetitions as possible in 30 s of the following exercises: 1) lateral step-up, 2) sit-to-stand, and 3) stand from half-kneel. The total number of repetitions performed in 30 s for each exercise was summed and used in the analysis. The 6-min walk test was used to assess the maximum distance participants could walk during a 6-min period on a 30-m, indoor, flat, nonslippery track. A timed stairs test assessed the time taken for participants to ascend and descend a five-step set of stairs as quickly as possible (without running). The clinimetric properties of these outcome measures are reported in the full study protocol (30). Other secondary outcome measures were collected (30); however, these are not reported in this article as they do not contribute to the specific study aims and hypotheses. Assessments made at 12-wk postintervention are not reported in this study.

Statistical analysis. Continuous data were examined with the Shapiro–Wilk test for normality. General linear models were used to compare the differences between groups for primary and secondary outcome variables at 12 wk, with group allocation (waitlist, 0; intervention, 1; serving as the main effect within the model). Baseline values, age, and sex were used as covariates in the regression models. Assumptions of the model were met, including homoscedasticity and linearity, and residuals were found to be normal. Data are given as mean (SD), and alpha was set at 0.05 for primary analyses. Results are presented as between-group differences

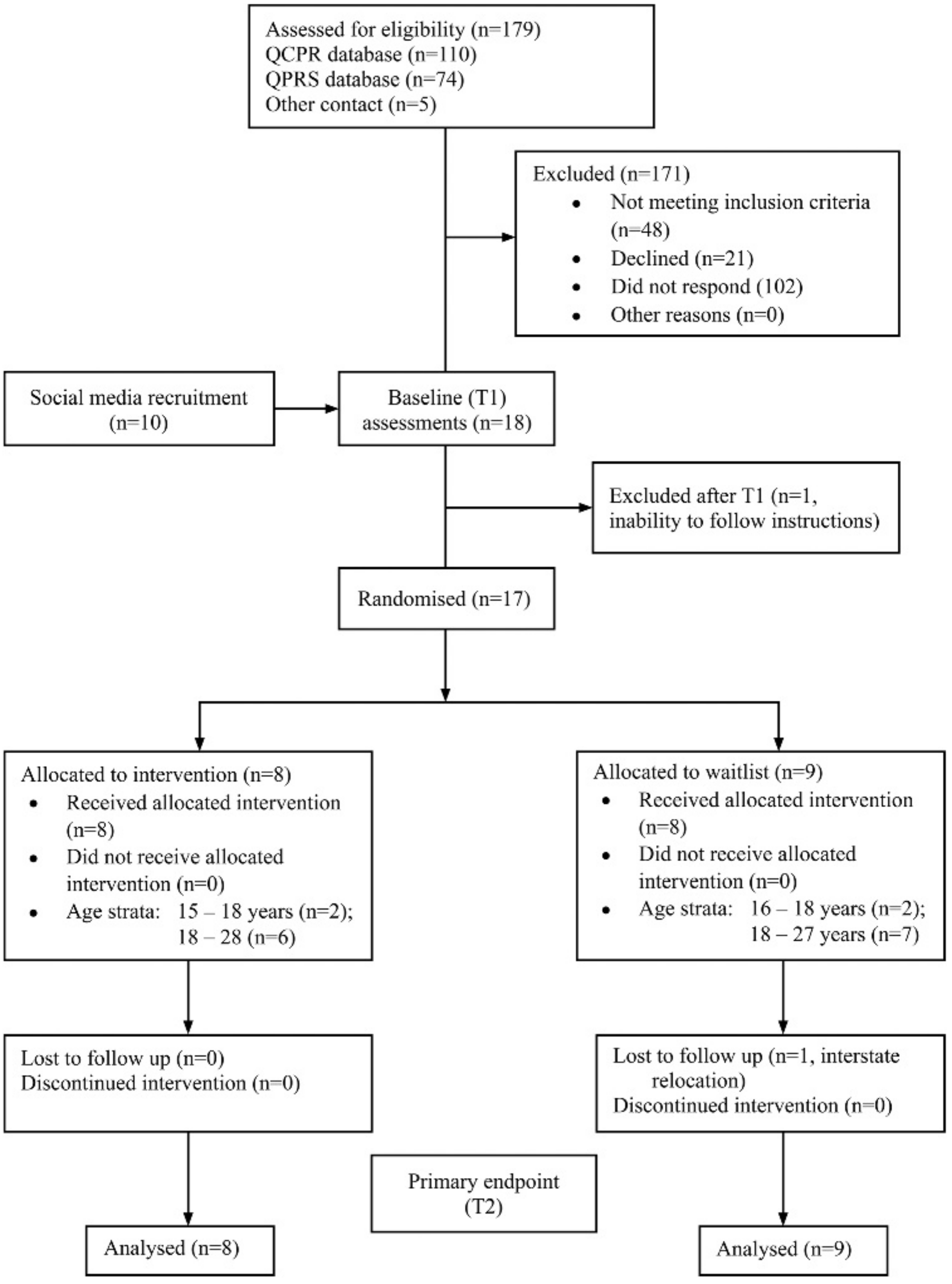

FIGURE 1—CONSORT study flow diagram. QCPR, Queensland Cerebral Palsy Register; QPRS, Queensland Paediatric Rehabilitation Service.

with 95% confidence intervals. The relationships between changes in muscle volume, strength, and functional capacity outcomes were assessed using linear regression. Data analysis was performed using SPSS (version 24; IBM Corporation, Armonk, NY). Analyses were conducted on the basis of intention to treat. Missing values were imputed as last observation carried forward.

RESULTS

Study recruitment, allocation, and follow-up are reported according to CONSORT guidelines in Figure 1. Participants who proceeded to baseline assessments were adolescents and young adults (n = 18) with spastic-type CP (8 unilateral; 9 males; mean ± SD age = 20.7 ± 4.1 yr; age range, 15–28 yr). One participant was excluded during the baseline assessments because of an inability to follow instructions resulting in a total sample size of 17 participants who progressed to the intervention phase. The personal demographics and characteristics at baseline are presented in Table 1. In the intervention group, eight participants started training and were assessed at 12 wk (100% retention); in the waitlist control group, eight participants were assessed at 12 wk (88% retention), with one participant lost to follow-up because of relocation. Sensitivity analysis was performed by removing the one control participant with missing follow-up data from the postintervention analysis to determine whether their removal changed any of the results. The removal of their data did not influence the mean difference or statistical significance for any outcome measure.

On average, participants completed 33.7 (out of 36, 95% adherence) training sessions over the 12-wk period. The mean total dose of the 12-wk training intervention was 38.9 h, comprising 28.5 h of PRT (73%) and 10.5 h of functional anaerobic training (27%). There were two instances of minor musculoskeletal pain recorded during the intervention. One participant reported lateral ankle pain during the last 2 wk of the training period that did not require medical treatment. The other participant reported lower back and knee pain during the last 2 wk of the intervention, which was treated by their physician. In both instances, training continued; however, individual exercises were modified by reducing the resistance training load and progressing once pain had ceased.

TABLE 1. Participant demographics and baseline characteristics.

Characteristics	Intervention Group (n = 8)	Control Group (n = 9)
Age at enrolment, yr:month	20:6 (4:8)	21:8 (4:3)
Sex, M/F	4/4	5/4
Height, cm	163.3 (15.7)	170.3 (7.3)
Weight, kg	67.7 (17.0)	68.4 (13.9)
Lower limb involvement, n (%)		
Unilateral	5 (62.5)	3 (33.3)
Bilateral	3 (37.5)	6 (66.7)
GMFCS, n (%)		
Level I	6 (75)	5 (55.6)
Level II	2 (25)	4 (44.4)
Previous lower limb surgery, n (%)[a]		
Yes	4 (50)	3 (33.3)

Data are presented as mean (SD).
[a]Surgery types: muscle–tendon lengthening (n = 7), osteotomy (n = 2).
M, male; F, female.

Unadjusted baseline and 12-wk follow-up data are presented in Table 2. Adjusted mean differences between groups at 12 wk are presented in Table 3. At 12 wk, plantarflexor and tibialis anterior muscle volumes of the more- and less-impaired limbs were significantly greater in the training group than the control group. The proportion of medial gastrocnemius intramuscular fat content was not significantly different for the usable data in the intervention group (n = 6) compared with the control group (n = 3) at 12 wk. There were no statistical differences in passive muscle or ankle joint properties between the training and the control groups at 12 wk.

Absolute and normalized maximum isometric plantarflexor strength was greater in the training group than the control group at 12 wk (Table 3). Peak anaerobic power, functional strength, agility, and walking distance were greater in the intervention group compared with the control group at 12 wk (Table 3).

The change in total plantarflexor muscle volume was associated with the change in isometric plantarflexor strength (R^2 = 0.47, P = 0.002). There were relationships between the change in isometric plantarflexor strength and changes in composite functional strength score (R^2 = 0.32, P = 0.018) and the 6-min walk test distance (R^2 = 0.28, P = 0.028).

DISCUSSION

A randomized controlled trial of a 12-wk combined progressive resistance and functional anaerobic training program in young adults with CP demonstrated a significant increase in plantarflexor and tibialis anterior muscle volumes, along with a concurrent increase in strength and functional capacity. To our knowledge, this is the first study to report increases in muscle size after PRT in young adults with CP that were significantly related to functional capacity and muscle strength improvements. These findings support the importance of appropriate exercise intervention design to improve neuromuscular impairments and functional capacity in individuals with CP (22,23).

The magnitude of hypertrophy shown within the training group (7.5%–9.6% across plantarflexor muscles) was of a similar magnitude to lower limb muscle hypertrophy in TD adults that has been reported after PRT (12,27). The hypertrophy seen in this study is less, however, than the previously reported muscle volume increases of 23%–24% in the medial and lateral gastrocnemii after targeted plantarflexor strength training in children with CP (19). The large amount of hypertrophy reported in a pre- and postintervention study by McNee et al. (19) may be explained by lower baseline muscle volumes from their younger sample (age range, 6–16 yr), as well as natural muscle growth over the 10-wk intervention period, resulting in a larger absolute increase in muscle size than that reported in this study.

The external training stimulus is responsible for promoting the complex postexercise physiological cascade, shifting

TABLE 2. Outcomes at baseline (T1) and follow-up (T2) assessments (immediately after intervention) for muscle morphology and architecture, maximum isometric strength, and functional capacity measures by group allocation.

	T1 (Baseline), Mean (SD)		T2 (12 wk) Mean (SD)	
Outcomes	Intervention (n = 8)	Control (n = 9)	Intervention (n = 8)	Control (n = 9)
Muscle volume (mL)				
More impaired limb				
MG	115.50 (48.85)	145.12 (53.75)	125.54 (58.49)	140.63 (47.50)
LG	62.81 (19.07)	87.93 (29.49)	69.60 (28.75)	83.94 (27.85)
SOL	248.37 (151.73)	313.37 (76.99)	263.39 (165.11)	306.47 (73.54)
Total PF (summed MG, LG, SOL)	425.91 (205.76)	545.71 (150.33)	458.53 (227.86)	531.04 (136.50)
TA	56.20 (21.51)	70.43 (19.74)	60.84 (25.38)	69.72 (22.81)
Less impaired limb				
MG	161.77 (79.91)	172.41 (59.38)	179.70 (93.18)	168.84 (56.27)
LG	80.56 (39.24)	92.94 (31.24)	90.53 (43.99)	89.38 (27.91)
SOL	286.25 (121.32)	342.84 (78.50)	309.92 (146.43)	336.45 (77.05)
Total PF (summed MG, LG, SOL)	528.58 (229.95)	608.27 (102.94)	580.15 (274.14)	594.67 (151.71)
TA	76.66 (35.53)	88.18 (29.94)	80.60 (35.96)	86.76 (29.12)
More impaired limb MG intramuscular fat (%)[a]	19.02 (12.51)	21.96 (12.97)	18.52 (13.72)	23.85 (8.18)
Less impaired limb MG intramuscular fat (%)[a]	18.45 (12.83)	20.87 (11.63)	17.84 (12.39)	21.83 (8.66)
Passive fascicle stiffness (k)	0.56 (0.44)	0.42 (0.19)	0.44 (0.15)	0.35 (0.16)
Passive ankle stiffness (k)	0.09 (0.02)	0.08 (0.02)	0.08 (0.01)	0.08 (0.01)
Ankle slack angle (PF degrees)	16.30 (11.97)	22.47 (11.21)	22.79 (6.95)	21.34 (11.24)
Fascicle slack length (mm)	45.83 (7.05)	51.23 (6.64)	46.50 (10.12)	48.47 (6.36)
Isometric strength (N·m)				
PF	67.39 (32.42)	90.51 (26.41)	84.32 (26.28)	80.90 (33.10)
DF	9.28 (4.47)	13.69 (7.73)	11.56 (4.61)	12.76 (6.93)
Normalized isometric strength (N·m·mL^{-1})				
PF	0.17 (0.01)	0.17 (0.03)	0.20 (0.05)	0.16 (0.05)
DF	0.18 (0.10)	0.19 (0.10)	0.21 (0.12)	0.19 (0.09)
Ankle angle at maximum isometric PF strength (°)	−17.38 (5.60)	−16.11 (5.49)	−17.38 (5.60)	−16.11 (5.49)
Ankle angle at maximum isometric DF strength (°)	10.06 (4.50)	8.67 (10.44)	10.06 (4.50)	8.67 (10.44)
Power				
Peak MPST (W)	304.07 (289.53)	389.19 (268.55)	330.08 (289.26)	381.08 (260.70)
Mean MPST (W)	242.43 (221.59)	344.41 (240.93)	272.29 (231.92)	340.23 (241.32)
Agility				
10 × 5 m shuttle (s)	28.86 (10.93)	24.77 (8.98)	25.00 (8.08)	24.42 (8.92)
Functional strength				
30sRM total score (repetitions)	69.00 (37.99)	83.78 (34.35)	103.63 (40.97)	86.44 (37.30)
Timed stairs				
Time up-stairs (s)	4.38 (2.13)	3.24 (0.43)	3.30 (0.85)	3.10 (0.41)
Time down-stairs (s)	5.48 (4.50)	2.99 (0.56)	3.88 (2.72)	2.86 (0.61)
Walking ability				
6-MWT distance (m)	500.35 (145.09)	543.46 (139.90)	530.91 (124.67)	521.41 (133.36)

[a]Usable data for intervention group (n = 6), control group (n = 3).

MG, medial gastrocnemius; MPST, muscle power sprint test; LG, lateral gastrocnemius; SOL, soleus; total PF, summed muscle volume of medial gastrocnemius, lateral gastrocnemius, and soleus; TA, tibialis anterior; Functional strength, summed score of 30 s repetition maximum for lateral step-up, lunge, and sit-to-stand; 6-MWT, 6-min walk test; 30sRM, 30-s repetition maximum; negative ankle angle represents dorsiflexion.

muscle protein balance to favor synthesis over degradation, which ultimately leads to a hypertrophic response (increased contractile tissue size) (37,38). Skeletal muscle hypertrophy has been proposed as the primary mechanism underpinning the growth of contractile tissue volume after PRT in humans (28). Achieving recruitment of the greatest number of available muscle fibers and exposing them to the exercise stimulus seem to be important for attaining skeletal muscle hypertrophy in TD individuals (26). In the present study, there was more hypertrophy in the plantarflexors of the less-impaired limb compared with more-impaired limb. Designing appropriate PRT parameters in individuals with CP may therefore be imperative when targeting specific muscles, where range of movement may be reduced affecting the amount and range of tension that can be developed in the muscles. Individuals classified at lower GMFCS levels (III–V), with a greater muscle contracture, reduced range of motion, bony deformity, or reduced motor control may not be able to recruit a large enough number of muscle fibers, as well as expose the recruited muscle fibers to the exercise stimulus (loaded controlled contraction) to initiate a hypertrophic response. The conventional dynamic PRT implemented in this study, in high functioning individuals with CP (GMFCS levels I–II), followed prescribed guidelines set down by international strength and conditioning associations that have produced significant skeletal muscle hypertrophy in TD individuals (26).

The upregulation of satellite cell activity has been proposed as a key mechanism underpinning skeletal muscle growth during development (39). There is conjecture in the literature as to whether satellite cell addition is required for skeletal muscle hypertrophy (40). Recent evidence suggests that children with CP muscle contracture (GMFCS levels II–V) have a reduced number of satellite cells (41). Reduced satellite cell number has therefore been proposed to account for the reduced muscle growth in individuals with CP, as well as a diminished ability to strengthen these muscles (39). In addition, there is evidence of competing signaling pathways of muscle hypertrophy from altered transcriptional profiles analyzed using muscle biopsies from wrist muscles in six

TABLE 3. Difference between intervention and control groups immediately after intervention (T2) for primary and secondary outcome measures adjusted for baseline values, age, and sex.

Outcome Measure	Mean Difference (95% CI)		P
Muscle volume (mL)			
More impaired limb MG	13.21	(0.96 to 25.45)	0.037
More impaired limb LG	12.96	(2.48 to 23.49)	0.020
More impaired limb SOL	25.50	(13.66 to 37.34)	0.001
More impaired limb total PF	48.77	(22.54 to 75.01)	0.002
More impaired limb TA	7.76	(3.19 to 12.33)	0.003
Less impaired limb MG	20.46	(9.04 to 31.89)	0.002
Less impaired limb LG	12.98	(1.67 to 24.28)	0.028
Less impaired limb SOL	36.44	(13.96 to 58.93)	0.004
Less impaired limb total PF	69.89	(29.28 to 110.51)	0.003
Less impaired limb TA	5.12	(0.67 to 9.57)	0.028
Intramuscular fat (%)[a]			
More-impaired limb MG	−2.31	(−10.30 to 5.69)	0.468
Less-impaired limb MG	−1.97	(−8.13 to 4.18)	0.424
Passive properties			
Passive fascicle stiffness (k)	0.07	(−0.08 to 0.22)	0.336
Passive ankle stiffness (k)	−0.01	(−0.02 to 0.01)	0.653
Fascicle slack length (mm)	3.17	(−2.67 to 9.00)	0.260
Ankle slack angle (°)	−4.71	(−14.24 to 4.82)	0.303
Strength and functional capacity			
Isometric PF strength (N·m)	22.47	(3.36 to 41.57)	0.025
Isometric DF strength (N·m)	2.53	(−0.44 to 5.51)	0.088
Normalized isometric PF strength (N·m·mL^{-1})	0.05	(0.01 to 0.09)	0.031
Normalized isometric DF strength (N·m·mL^{-1})	0.03	(−0.03 to 0.09)	0.266
Functional strength (total repetitions)	32.64	(21.72 to 43.55)	<0.001
MPST peak power (W)	31.25	(4.49 to 58.01)	0.026
MPST mean power (W)	34.85	(−5.63 to 75.33)	0.085
10 × 5 m Agility Shuttle (s)	−2.83	(−5.02 to -0.64)	0.016
6-MWT (m)	47.65	(16.16 to 79.14)	0.006
Timed up-stairs (s)	−0.25	(−0.62 to 0.12)	0.167
Timed down-stairs (s)	−0.44	(−1.20 to 0.32)	0.229

[a]Usable data for intervention group (n = 6), control group (n = 3).
CI, confidence interval; MG, medial gastrocnemius; LG, lateral gastrocnemius; SOL, soleus; total PF, summed muscle volume of medial gastrocnemius, lateral gastrocnemius and soleus; TA, tibialis anterior; Functional strength, summed score of 30 s repetition maximum for lateral step-up, lunge, and sit-to-stand; 6-MWT, 6-min walk test; MPST, muscle power sprint test; DF, dorsiflexion; negative time (s) indicates an improvement.

children with CP with severe contracture (42). The heterogeneous presentation of CP poses the question as to whether a reduction in satellite cell activity and altered myogenic signaling pathways occurs in all muscles of individuals with the disorder, who may be of varying functional classification (GMFCS levels I–V), or only in the most severely affected muscles (muscular contracture). The measurement of cellular mechanisms was beyond the scope of this study, making it difficult to know whether skeletal muscle hypertrophy and muscle strengthening were mediated by an increase in satellite cell activity, or via other mechanisms. Further research is needed to determine the cellular mechanisms for muscle adaptation after training interventions in individuals with CP.

Intramuscular fat content did not change after training. An increase in contractile tissue after training may therefore have been accompanied by concurrent increases in noncontractile tissue resulting in similar muscle compartment tissue composition at 12 wk. An absolute increase in contractile tissue, however, would still have a positive effect on the force-generating capacity of the muscle. Any increase in noncontractile tissue that may have occurred did not result in stiffer muscle fascicles, as the passive medial gastrocnemius muscle fascicle stiffness did not increase after training. This finding must be interpreted with caution due to the limited number of Dixon images that could be used in the analysis.

Maximum isometric plantarflexion strength increased after training within the training group by 25%. Furthermore, the change in total plantarflexor muscle volume was significantly associated with the change in plantarflexion strength (R^2 = 0.47), indicating a positive relationship exists between plantarflexor muscle hypertrophy and strength in people with CP. When plantarflexion strength was normalized to total plantarflexor muscle volume, there was still a significant difference between groups at 12 wk, suggesting that the strength increase of the training group was not explained by morphological changes alone. A plausible explanation for this is the neural changes that occur alongside muscular adaptation after PRT leading to improved motor learning and control (43). Similar increases in strength (27%) have been reported in young adults with CP (GMFCS levels II–III) after a robustly designed lower limb PRT intervention (15).

The young adults in the training group showed improvements from baseline to 12 wk in anaerobic capacity (peak power, 8.3%), functional strength (30-s repetition maximum test, 50.2%), agility (13.4%), and walking capacity (6-min walk test, 6.1%). In this study, functional anaerobic exercises were conducted based on a previous 8-month functional training program in younger individuals with CP (age 7–18 yr), which showed improvements in anaerobic capacity (25%) and functional strength (20%–23%) (22). A recent functional power training study performed in even younger children with CP (age 4–10 yr), used similar exercises with the addition of external load, and found 83% improvement in anaerobic capacity measured using the muscle power sprint test (23). The functional anaerobic training in our study made up less than 30% of the total training program volume, which may explain the reduced gains in anaerobic capacity, but greater functional strength improvements seen in our group of young adults with CP compared with previous studies (22,23). The participants in our study were also of greater mean age compared with previous interventions, and of high functional classification (GMFCS level I = 11; level II = 6), potentially reducing the capacity for improvement in functional tasks due to their higher pretraining level.

The improved walking capacity on the 6-min walk test in the training group after training compared with the control group (MD 47.65 m) is similar to the proposed improvement (50 m) required to be of clinical and functional importance to adults with CP (44). This finding provides evidence of a beneficial transfer to a functional capacity task that was not specifically trained. An increased rate of force development in the dorsiflexors, as well as greater range of ankle joint movement during gait, has been reported previously after PRT in adults with CP, supporting the notion that PRT of the lower extremity muscles can improve gait outcomes in this population (45).

The change in plantarflexion strength in young adults with CP in this study was significantly associated with changes in their functional strength test score (R^2 = 0.32) and 6-min walk test distance (R^2 = 0.28). This finding indicates that an increase in plantarflexion strength underpinned a significant proportion of the improvement in functional capacity outcomes. This finding supports recent evidence that muscle strength is an important predictor of lower limb functional capacity tasks in adults with CP (6). A further explanation of the improvements in functional capacity measures was the specificity of our training program. The functional anaerobic training included activities such as step-ups, shuttle running, stair climbing, and agility drills that were designed to improve anaerobic capacity in a context related to everyday activities. Part of the improvements in functional capacity outcomes were likely due to performing training tasks that closely resembled the outcome measures.

Limitations. A potential limitation was that we were unable to definitively separate the contribution of PRT and anaerobic training components to the changes in outcome measures. The PRT component, however, made up more than 70% of the total training volume, so it was the likely contributor to the muscle hypertrophy and strength improvements of the lower leg muscles in this study. The target sample size was not met despite an extensive recruitment strategy being implemented over 2 yr. The recruitment strategy used local CP register databases, targeted mail-outs, social media advertising, and rehabilitation hospitals. The study was constrained by a single-site for the intervention, which limited our recruitment to participants within geographical locations able to access the training facility. The study also had a limited timeframe for completion resulting in recruitment being halted before the targeted sample size being reached. Despite the smaller sample size, this intervention was feasible in high functioning young adults with CP and found differences in muscle volumes, strength, and functional capacity between groups at 12 wk. Additional limitations include the imbalance between groups in terms of lower limb involvement and GMFCS level and the lack of assessor blinding for outcome measures. Future research is required with larger sample sizes in adults with CP, across wider functional classification levels, to further investigate the neuromuscular responses to PRT in this population.

Implications. From a clinical perspective, functional strength and measures of functional capacity improved after training, which provides strong evidence for the inclusion of functional anaerobic exercises in PRT interventions for individuals with CP. This type of training is relatively inexpensive, accessible in the community, and provides a potential avenue to address the muscle size deficit seen in adolescents and young adults with CP.

The authors acknowledge the expertise and support of Queensland X-Ray, Coorparoo, Brisbane, Australia, for assistance with magnetic resonance image data collection and processing techniques. They are grateful to the Queensland Cerebral Palsy Register and Queensland Paediatric Rehabilitation Service for their assistance in participant recruitment. This research was supported by the Merchant Charitable Foundation via the Children's Hospital Foundation (Donation ID 10415), the Cerebral Palsy International (grant no. R-810-13), the Cerebral Palsy Alliance (grant no. CDG213), the National Health and Medical Research Council of Australia (grant nos. 1075642, 1070623, and 1105038), and the Australian Rotary Health/Rotary Club of St Ives.

All authors have read and approved the final manuscript. The authors declare no conflicts of interest. The results of the present study do not constitute endorsement by the American College of Sports Medicine. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

REFERENCES

1. Noble JJ, Fry NR, Lewis AP, Keevil SF, Gough M, Shortland AP. Lower limb muscle volumes in bilateral spastic cerebral palsy. *Brain Dev*. 2014;36(4):294–300.
2. Herskind A, Ritterband-Rosenbaum A, Willerslev-Olsen M, et al. Muscle growth is reduced in 15-month-old children with cerebral palsy. *Dev Med Child Neurol*. 2016;58(5):485–91.
3. Barber LA, Read F, Lovatt Stern J, Lichtwark G, Boyd RN. Medial gastrocnemius muscle volume in ambulant children with unilateral and bilateral cerebral palsy aged 2 to 9 years. *Dev Med Child Neurol*. 2016;58(11):1146–52.
4. Gough M, Shortland AP. Could muscle deformity in children with spastic cerebral palsy be related to an impairment of muscle growth and altered adaptation? *Dev Med Child Neurol*. 2012;54(6):495–9.
5. Wiley ME, Damiano DL. Lower-extremity strength profiles in spastic cerebral palsy. *Dev Med Child Neurol*. 1998;40(2):100–7.
6. Gillett JG, Lichtwark GA, Boyd RN, Barber LA. Functional capacity in adults with cerebral palsy: lower limb muscle strength matters. *Arch Phys Med Rehabil*. 2018;99(5):900–6.
7. Noble JJ, Chruscikowski E, Fry NR, Lewis AP, Gough M, Shortland AP. The relationship between lower limb muscle volume and body mass in ambulant individuals with bilateral cerebral palsy. *BMC Neurol*. 2017;17(1):223.
8. Verschuren O, Smorenburg ARP, Luiking Y, Bell K, Barber L, Peterson MD. Determinants of muscle preservation in individuals with cerebral palsy across the lifespan: a narrative review of the literature. *J Cachexia Sarcopenia Muscle*. 2018;9(3):453–64.
9. Noble JJ, Charles-Edwards GD, Keevil SF, Lewis AP, Gough M, Shortland AP. Intramuscular fat in ambulant young adults with bilateral spastic cerebral palsy. *BMC Musculoskelet Disord*. 2014; 15(1):236–43.
10. Barber L, Barrett R, Lichtwark G. Passive muscle mechanical properties of the medial gastrocnemius in young adults with spastic cerebral palsy. *J Biomech*. 2011;44(3):2496–500.
11. Schoenfeld BJ, Ogborn D, Krieger JW. Effects of resistance training frequency on measures of muscle hypertrophy: a systematic review and meta-analysis. *Sports Med*. 2016;46(11):1689–97.
12. Franchi MV, Atherton PJ, Reeves ND, et al. Architectural, functional and molecular responses to concentric and eccentric loading in human skeletal muscle. *Acta Physiol (Oxf)*. 2014;210(3): 642–54.
13. Abe T, DeHoyos VD, Pollock LM, Garzarella L. Time course for strength and muscle thickness changes following upper and lower body resistance training in men and women. *Eur J Appl Physiol*. 2000;81(3):174–80.
14. Gillett JG, Boyd RN, Carty CP, Barber LA. The impact of strength training on skeletal muscle morphology and architecture in children and adolescents with spastic cerebral palsy: a systematic review. *Res Dev Disabil*. 2016;56:183–96.

15. Taylor NF, Dodd KJ, Baker RJ, Willoughby K, Thomason P, Graham HK. Progressive resistance training and mobility-related function in young people with cerebral palsy: a randomized controlled trial. *Dev Med Child Neurol*. 2013;55(9):806–12.
16. Damiano DL, Vaughan CL, Abel MF. Muscle response to heavy resistance exercise in children with spastic cerebral palsy. *Dev Med Child Neurol*. 1995;37(8):731–9.
17. Ross SM, MacDonald M, Bigouette JP. Effects of strength training on mobility in adults with cerebral palsy: a systematic review. *Disabil Health J*. 2016;9(3):375–84.
18. Scianni A, Butler JM, Ada L, Teixeira-Salmela LF. Muscle strengthening is not effective in children and adolescents with cerebral palsy: a systematic review. *Aust J Physiother*. 2009;55(2):81–7.
19. McNee AE, Gough M, Morrissey MC, Shortland AP. Increases in muscle volume after plantarflexor strength training in children with spastic cerebral palsy. *Dev Med Child Neurol*. 2009;51(6):429–35.
20. Verschuren O, Ada L, Maltais DB, Gorter JW, Scianni A, Ketelaar M. Muscle strengthening in children and adolescents with spastic cerebral palsy: considerations for future resistance training protocols. *Phys Ther*. 2011;91(7):1130–9.
21. Ryan JM, Cassidy EE, Noorduyn SG, O'Connell NE. Exercise interventions for cerebral palsy. *Cochrane Database Syst Rev*. 2017; 6:Cd011660.
22. Verschuren O, Ketelaar M, Gorter JW, Helders PJ, Uiterwaal CS, Takken T. Exercise training program in children and adolescents with cerebral palsy: a randomized controlled trial. *Arch Pediatr Adolesc Med*. 2007;161(11):1075–81.
23. van Vulpen LF, de Groot S, Rameckers E, Becher JG, Dallmeijer AJ. Improved walking capacity and muscle strength after functional power-training in young children with cerebral palsy. *Neurorehabil Neural Repair*. 2017;31(9):827–41.
24. Park EY, Kim WH. Meta-analysis of the effect of strengthening interventions in individuals with cerebral palsy. *Res Dev Disabil*. 2014;35(2):239–49.
25. Ferri A, Scaglioni G, Pousson M, Capodaglio P, Van Hoecke J, Narici MV. Strength and power changes of the human plantar flexors and knee extensors in response to resistance training in old age. *Acta Physiol Scand*. 2003;177(1):69–78.
26. Wernbom M, Augustsson J, Thomeé R. The influence of frequency, intensity, volume and mode of strength training on whole muscle cross-sectional area in humans. *Sports Med*. 2007;37(3):225–64.
27. Schoenfeld BJ, Ogborn D, Krieger JW. Dose–response relationship between weekly resistance training volume and increases in muscle mass: a systematic review and meta-analysis. *J Sports Sci*. 2017;35(11):1073–82.
28. Schoenfeld BJ. The mechanisms of muscle hypertrophy and their application to resistance training. *J Strength Cond Res*. 2010; 24(10):2857–72.
29. Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. *Dev Med Child Neurol*. 1997;39(4):214–23.
30. Gillett JG, Lichtwark GA, Boyd RN, Barber LA. FAST CP: protocol of a randomised controlled trial of the efficacy of a 12-week combined Functional Anaerobic and Strength Training programme on muscle properties and mechanical gait deficiencies in adolescents and young adults with spastic-type cerebral palsy. *BMJ Open*. 2015;5(6):e008059.
31. Barber L, Barrett R, Lichtwark G. Validation of a freehand 3D ultrasound system for morphological measures of the medial gastrocnemius muscle. *J Biomech*. 2009;42(9):1313–9.
32. Gillett JG, Barrett RS, Lichtwark GA. Reliability and accuracy of an automated tracking algorithm to measure controlled passive and active muscle fascicle length changes from ultrasound. *Comput Methods Biomech Biomed Engin*. 2013;16(6):678–87.
33. Cronin NJ, Carty CP, Barrett RS, Lichtwark G. Automatic tracking of medial gastrocnemius fascicle length during human locomotion. *J Appl Physiol (1985)*. 2011;111(5):1491–6.
34. Farris DJ, Lichtwark GA. UltraTrack: software for semi-automated tracking of muscle fascicles in sequences of B-mode ultrasound images. *Comput Methods Programs Biomed*. 2016;128:111–8.
35. Verschuren O, Takken T, Ketelaar M, Gorter JW, Helders PJ. Reliability for running tests for measuring agility and anaerobic muscle power in children and adolescents with cerebral palsy. *Pediatr Phys Ther*. 2007;19(2):108–15.
36. Verschuren O, Ketelaar M, Takken T, Van Brussel M, Helders PJ, Gorter JW. Reliability of hand-held dynamometry and functional strength tests for the lower extremity in children with Cerebral Palsy. *Disabil Rehabil*. 2008;30(18):1358–66.
37. Glass DJ. Skeletal muscle hypertrophy and atrophy signaling pathways. *Int J Biochem Cell Biol*. 2005;37(10):1974–84.
38. Schoenfeld BJ. Postexercise hypertrophic adaptations: a reexamination of the hormone hypothesis and its applicability to resistance training program design. *J Strength Cond Res*. 2013;27(6):1720–30.
39. Dayanidhi S, Lieber RL. Skeletal muscle satellite cells: mediators of muscle growth during development and implications for developmental disorders. *Muscle Nerve*. 2014;50(5):723–32.
40. O'Connor RS, Pavlath GK, McCarthy JJ, Esser KA. Last word on Point:Counterpoint: satellite cell addition is/is not obligatory for skeletal muscle hypertrophy. *J Appl Physiol (1985)*. 2007; 103(3):1107.
41. Smith LR, Chambers HG, Lieber RL. Reduced satellite cell population may lead to contractures in children with cerebral palsy. *Dev Med Child Neurol*. 2013;55(3):264–70.
42. Smith LR, Pontén E, Hedström Y, et al. Novel transcriptional profile in wrist muscles from cerebral palsy patients. *BMC Med Genomics*. 2009;2:44.
43. Moritani T, Devries H. Neural factors versus hypertrophy in the time course of muscle strength gain. *Am J Phys Med*. 1979;58(3): 115–30.
44. Maeland S, Jahnsen R, Opheim A, Froslie KF, Moe-Nilssen R, Stanghelle JK. No effect on gait function of progressive resistance exercise in adults with cerebral palsy: a single-blind randomized controlled trial. *Adv Physiol Educ*. 2009;11(4):227–33.
45. Kirk H, Geertsen SS, Lorentzen J, Krarup KB, Bandholm T, Nielsen JB. Explosive resistance training increases rate of force development in ankle dorsiflexors and gait function in adults with cerebral palsy. *J Strength Cond Res*. 2016;30(10):2749–60.