Accepted Manuscript

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PII: S0966-6362(18)31458-9
DOI: <https://doi.org/10.1016/j.gaitpost.2019.03.023>
Reference: GAIPOS 6744

To appear in: *Gait & Posture*

Received date: 23 August 2018
Revised date: 25 January 2019
Accepted date: 24 March 2019

Please cite this article as: Gillett JG, Lichtwark GA, Boyd RN, Carty CP, Barber LA, The effect of combined functional anaerobic and strength training on treadmill gait kinematics and kinetics in ambulatory young adults with cerebral palsy, *Gait and amp; Posture* (2019), <https://doi.org/10.1016/j.gaitpost.2019.03.023>

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Title: The effect of combined functional anaerobic and strength training on treadmill gait kinematics and kinetics in ambulatory young adults with cerebral palsy.

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Declarations of interests: None.

Highlights

- The FAST intervention resulted in no between-group differences in gait outcomes.
- Within-group improvement in peak positive ankle power in the intervention group.
- Discrepancy between treadmill-based and overground mobility outcomes post-training.

Introduction

Effective walking may be compromised in individuals with cerebral palsy (CP) due to both altered ability to coordinate muscle contractions, as well as adaptations in the musculoskeletal system that occur secondary to the brain lesion that causes CP. Secondary musculoskeletal adaptations include reduced leg muscle volumes [1], increased muscle and ankle joint stiffness [2], reduced muscle activation [3], muscle weakness [4], contracture [5], and bony deformity [6]. Combined with an already compromised motor control, these

adaptations commonly result in equinus [7], crouch [8], or other gait patterns depending on their relative contributions and whether the individual has unilateral or bilateral limb involvement.

Force contributions from the plantar flexor muscles are particularly important for body weight support during stance, and propulsion during push-off [9, 10]. In children with CP, the alterations to the plantar flexor muscle-tendon units (MTU) may therefore contribute to reduced ankle joint power generation [11, 12]. Normal gait in children with CP has been found to be robust to muscle weakness in isolation, due to the potential for a compensatory response of increased muscle activation [13]. Adults with CP, however, have compromised neural adaptability as the maximum activation capacity of their plantar flexors has been shown to be approximately 40% lower than typically developed (TD) individuals [14]. Increasing the strength of the plantar flexor muscles may therefore lessen the burden on the already reduced capacity of the neural system to maintain a more typical gait.

As individuals with CP develop with age, the plantar flexor muscle growth rate is reduced compared to aged matched TD peers [15], and the muscle size deficit increases relative to total body mass into adulthood [16], which may pose a further challenge for lower limb power generation during gait. The maximum isometric strength of the plantar flexor muscles have been recently shown to explain 61% of the variance in six-minute walk test (6MWT) performance in adults with CP [4]. In another experimental study on adults with CP, impaired gait function was associated with reduced rapid force generation of ankle muscles [17]. Taken together, these findings support the importance of muscular strength for maintaining mobility in this population, suggesting that interventions targeting neuromuscular properties of the ankle plantar flexors might be beneficial for improving gait function [18].

Despite these findings, and those from other cross-sectional studies reporting positive correlations between strength and mobility in individuals with CP [4, 19, 20], there is a paucity of evidence regarding the translation of strength improvements following resistance training to mobility-related measures such as walking performance [21-24]. One recent quasi-controlled study implemented a lower limb explosive progressive resistance training (PRT) program in adults with CP and reported increased rate of force development in ankle dorsiflexor muscles, as well as an increase in ankle dorsiflexion during walking [25]. There were no post-training differences found however, in functional capacity measures (6MWT; 10m walk test; timed up and down stairs test) between the training and control groups. Individuals with CP have difficulties with co-ordination and motor control, therefore, providing resistance training as an isolated intervention may not enhance motor learning or translate to improvements in walking ability [26].

The addition of functional training exercises to appropriately designed, targeted resistance training of the lower limbs may lead to greater improvements in mobility due to the specificity of the training modes. We have previously published a combined functional anaerobic and strength training (FAST) protocol designed to improve lower limb muscle properties and functional capacity in adolescents and young adults with CP [27]. Participants in the 12-week FAST intervention group increased lower limb muscle size, isometric strength and functional capacity (6MWT; agility; muscle power sprint test) compared to the control group after training [28]. It remains unknown whether muscle morphological or functional capacity improvements were related to any changes in overall gait quality or individual gait parameters. Alterations in gait kinematics or kinetics after targeted plantar flexor and dorsiflexor training could be a mechanism for the improvements in functional capacity

previously reported, such as an increased distance walked on the 6MWT [29]. Gait scores and kinematic profiles are also of clinical interest and have been used as a measure of the effectiveness of resistance training interventions in young adults with CP [21].

Therefore, the purpose of this study was to evaluate the secondary effects of the FAST intervention [27] on gait kinematics and kinetics in individuals with CP aged 15 – 30 years. We hypothesised that combined functional anaerobic and strength training would result in increased ankle dorsiflexion at foot contact and during stance, improved gait profile scores, and increased ankle power during late stance, compared to a control group receiving no training.

Methods

A waitlist randomized controlled trial was conducted to test the efficacy of a 12-week, 3 sessions per week, combined progressive resistance and functional anaerobic training program on lower limb gait kinematics and kinetics compared to a waitlist control group. This study presents secondary gait outcome data from a published trial [27, 28].

Participants

Male and female participants aged 15 – 30 years were recruited who had a diagnosis of unilateral or bilateral spastic type CP; able to walk independently; and classified as level I or II, using the Gross Motor Function Classification System (GMFCS) [29]. Written informed consent (assent if 15-18 years) was obtained from all participants and the study was approved by institutional ethics committees (UQHREC 2014000066; HREC/15/QRCH/30; CPL-2016-001).

Design and setting

Participants were stratified according to age in either 15-18 years or 18-30 years band widths, and sex, following the baseline measures. Once stratified, participants were then randomized into either the immediate intervention group or waitlist control group using a computer-generated list of random numbers in concealed envelopes opened by non-study personnel. The control group received no prescribed training and were allowed to continue with usual daily activities. The training intervention took place at a tertiary institution gymnasium, and commenced within 2 weeks of randomisation to the intervention group. Both groups were reassessed within 3 days of completing the 12-week intervention or control period. A training diary was completed for all participants to monitor adherence and session performance.

Intervention

A detailed description of the acute program variables and exercises performed in the FAST intervention can be found in the published study protocol [27]. Briefly, participants randomized to the intervention group undertook three supervised training sessions per week, for 12-weeks. Each session comprised PRT and functional anaerobic exercises. The PRT component was performed first in each session, followed by the functional anaerobic exercises. The PRT specifically targeted the plantar flexor muscles and tibialis anterior, comprising the following exercises: seated bent knee calf raise, leg press, seated straight knee calf press, seated tibialis anterior raise, and standing calf raise. The PRT was periodized, comprising multiple sets of between 6 – 12 repetitions. The number of sets and set structure progressed every four weeks and training load could be adjusted during any session. Two or three (depending on training period) functional anaerobic exercises were performed per session, completed at maximal intensity lasting between 20 and 30 seconds per bout. These exercises were related to everyday activities such as stair climbing, bending, changing

direction and stepping over obstacles [30]. The number of anaerobic exercises per session; repetitions performed; and work to rest ratio progressed every 4 weeks [27].

Gait analysis protocol

Participants walked at a self-selected walking speed in enclosed footwear on a force instrumented, tandem (fore-aft split belt) treadmill (AMTI, USA) while three-dimensional (3D) kinematics and kinetics were simultaneously acquired. Participants self-selected walking pace was determined for both baseline and follow-up assessments by increasing or decreasing the treadmill belt speed at 0.2 km.hr⁻¹ increments each 30 – 60s until they reported the speed that was most comfortable. A minimum of ten strides were collected for each individual, with the average of all available complete strides used in the analysis for each participant. All discrete measurements were made on the impaired leg in individuals with unilateral CP, and on the most impaired leg in individuals with bilateral CP. Full details of the outcome measures and instrumentation have been published in the study protocol [27].

Data collection and processing

Three-dimensional motion capture data was collected at 200 Hz using an 8-camera motion capture system (Qualisys, Sweden). Thirty-two reflective markers (12 mm) were attached to specific anatomical locations on the pelvis (anterior and posterior superior iliac spines), thigh (greater trochanter, 3-marker cluster), knee (medial and lateral femoral condyles), shank (3-marker cluster), ankle (medial and lateral malleoli) and foot (first metatarsal head, fifth metatarsal head, calcaneus), and used to calculate ankle, knee and hip joint angles.

Ground reaction forces (GRF) were collected at 2000 Hz from the front and rear force plates mounted beneath the treadmill, synchronised to the marker trajectory data. Marker trajectory

and GRF data were filtered with a bidirectional second-order low-pass Butterworth digital filter with a 15 Hz cut-off frequency. A modified Gait2392 model [31] was scaled using marker locations from a static calibration trial for each participant, in conjunction with standard scaling procedures using OpenSim software (v3.2) [32]. Joint angles and moments were computed using inverse kinematics and dynamics analyses in OpenSim [32].

Instantaneous joint powers for the ankle, knee, and hip were calculated by multiplying the net joint moments by joint velocities. Joint moments and powers were normalised to each individual's body weight.

Primary outcomes specified a-priori in the study protocol were walking speed (m.s^{-1}), stride length (m), and maximum ankle dorsiflexion at foot contact and during the stance phase. The gait profile score (GPS) ($^{\circ}$) [33] was calculated to assess overall gait quality before and after the intervention. Each individual gait variable score that made up the GPS was calculated as the root mean square (RMS) difference between the median of all available gait cycles from the CP participants, and that of a reference group of ten TD young adults (aged 24 ± 4 years; height 178.8 ± 6.6 cm; weight 80.3 ± 12.0 kg) collected using an identical protocol and instrumentation. A minimum change in GPS of 1.6° was used to determine a meaningful change in gait [34]. Other secondary outcomes included peak positive ankle power in late stance (W.kg^{-1}), peak positive hip power in late stance (W.kg^{-1}), and the ratio of peak ankle to peak hip power during late stance. Custom Matlab (The Mathworks, USA) scripts were written to perform all analyses following the inverse dynamics procedures.

Data analysis

Primary outcome measures were compared between the intervention and control groups at 12-weeks using general linear models with group allocation serving as the main effect within

the model. Covariates in the regression models were baseline values, age, and sex. Alpha was set at 0.05 for primary analyses. Within-group analysis was performed on the secondary outcome measures using paired t-tests. All available data was included in the analysis using the intention to treat principle. The carry forward method was not applied for the specific variables where data was missing to avoid introducing bias to the analysis with a small sample size [35]. Statistical analysis was conducted using SPSS (v.24, IBM Corporation, USA).

Results

A flow diagram of study recruitment, allocation and follow-up is reported according to CONSORT guidelines in Figure 1.

<insert Figure 1 about here>

There were missing data at follow-up for two participants in the control group (one relocated during the control period; one did not complete assessment within specified timeframe).

There was missing data from two participants in the intervention group (valid kinetic data could not be obtained for one participant due an inability to walk on the treadmill appropriately; missing pre-training data for one participant due to technical data collection issues). This resulted in a total sample size of seven intervention and seven control participants for kinematic analysis, and six intervention and seven control participants for kinetic data analysis. The personal demographics and characteristics at baseline are presented in Table 1.

<insert Table 1 about here>

Details of training adherence and adverse events for the intervention have been reported elsewhere [28]. Participants randomised to the intervention group completed 95% of all training sessions over the 12-week period. Total training time was 38.9 hours, made up of 28.5 hours of PRT and 10.5 hours of functional anaerobic training. There were two separate instances of minor musculoskeletal pain reported during the intervention. In both cases, training was modified by reducing the loads lifted until pain had ceased and then progressing with the established protocol after this time.

Representative baseline and follow-up ankle angle, moment and power data for one subject with unilateral involvement (GMFCS level I) compared to the TD group average are shown in Figure 3. Unadjusted baseline and 12-week follow-up data are presented in Table 2. At 12-weeks, there were no difference between the intervention and control groups in walking speed (mean difference 0.05 m.s^{-1} , 95% CI $-0.03 - 1.24$), stride length (mean difference 0.02m , 95% CI $-0.13 - 1.71$), ankle angle at foot contact (0.26° , 95% CI $-4.468 - 5.20$), and maximum ankle angle during stance (0.30° , 95% CI $-6.96 - 7.57$). There were also no differences between groups for secondary outcomes including GPS (1.09° , 95% $-0.65 - 2.84$), peak ankle power during late stance (0.47 W.Kg^{-1} , 95% CI $-0.01 - 0.96$), peak hip power during late stance (0.17 W.Kg^{-1} , 95% CI $-0.02 - 0.35$), and the ratio of peak ankle to hip power during late stance (-0.14 , 95% CI $-1.27 - 0.98$).

<insert Figure 2 about here>

<insert Table 2 about here>

Within-group analyses revealed an increase in peak ankle power generation during late stance in the intervention group after training (post-pre difference $0.31 \pm 0.28 \text{ W.Kg}^{-1}$, $p=0.043$).

There was no difference after training in peak hip power generation during late stance, which caused a concurrent increase in the ratio of ankle to hip power generation within the intervention group (post – pre difference 0.43 ± 0.37 , $p=0.034$). Individual baseline and follow-up kinetic data for participants randomised to the intervention group are shown in Figure 3.

<insert Figure 3 about here>

Discussion

This study examined the effect of a 12-week combined functional anaerobic and strength training intervention on treadmill gait kinematics and kinetics at self-selected walking speed in young adults with CP. Our hypotheses that the intervention group would have increased ankle dorsiflexion at foot contact and during stance, increased ankle power during late stance, and an improved GPS following training compared to a control group receiving no training were not supported. There were no changes in participants' preferred treadmill walking speed or stride length after training.

The FAST intervention, a combination of PRT and anaerobic exercises, was designed to address the muscle size, muscle weakness, and anaerobic capacity deficits, without any specific treadmill gait training. The training program incorporated maximum effort anaerobic exercises (running, agility and stair climbing exercises) that we believe led to improvements in overground measures of functional capacity (6MWT, agility, muscle power sprint test) [28]. The training stimulus was successful at addressing the primary training goals but may not have been sufficient or specific enough to change treadmill gait kinematics or kinetics at

preferred walking speed [36]. If improving treadmill gait kinematics is the primary training goal, then specific gait training may be more effective at improving those outcomes [37].

The lack of change in ankle kinematics and GPS after training compared to the control group is consistent with findings by Taylor et al. [21], who reported no change in GPS or preferred walking speed following a well-designed PRT intervention targeting individual lower limb strength deficits in adolescents and young adults with CP. Our FAST intervention specifically trained the distal lower limb muscles, including the tibialis anterior [28], that may have been expected to translate to improved ankle dorsiflexor function, however, there was no improvement in ankle kinematics during walking. The finding that GPS did not change following training is an important result to show that individuals with CP can perform high intensity anaerobic training and heavy PRT without a deterioration in their gait.

In contrast to our findings, Kirk et al. [25] reported increased ankle dorsiflexion during toe lift, at foot contact, and during stance following explosive PRT in adults with CP. The increased rate of force development of the ankle dorsiflexor muscles reported following the 12-week training program could account for the improved ankle joint kinematics during gait [25]. The main difference between Kirk et al.'s [25] PRT intervention design compared to our study and that of Taylor et al. [21], was that participants were required to lift with "full intentional acceleration" (explosive) during the concentric phase of each repetition.

Participants in our FAST training intervention were required to lift explosively for the final four weeks of the program, however this may have been insufficient training volume to induce adaptations similar to those reported by Kirk et al [25].

The improved ankle joint kinematics following explosive PRT reported by Kirk et al. [25], did not, however, translate to any improvements in overground functional capacity measures. The mechanisms for improving functional capacity may therefore be multiple in origin, and not related to discrete changes in preferred-speed walking kinematics or kinetics. The FAST intervention did improve overground 6MWT performance in the training group compared to the control group [28], and hence while treadmill gait kinematics did not differ between groups after training in our study, overground walking capacity did.

Participants' walking speeds on the treadmill were approximately 45% slower than their average walking speeds during the overground baseline 6MWT [28], and approximately 30% slower than previously reported preferred walking speeds on a treadmill in typically developing young adults [38]. Walking at slower speeds requires less ankle power generation during late stance, and may be achieved with no change in gait kinematics [39]. Strength improvements in the plantar flexors may therefore not be reflected at slower walking speeds where ankle power generation requirements are less, suggesting that the evaluation of a range of walking speeds around typical may be useful in future studies.

To the best of our knowledge, this is the first study to report gait kinetics in young adults with CP following a resistance training intervention. There were no between-group differences in late stance ankle power, hip power, or ankle to hip power ratio after 12-weeks of training. There was, however, a within-group increase in ankle power during late stance in the intervention group. Of the available kinetic data, four participants who were GMFCS Level I showed increases in their ankle push-off power following training, whereas the two participants who were GMFCS Level II, who both had bilateral involvement, showed minimal change post-training (Figure 3). There may have been differential adaptations to the

FAST intervention based on the severity of motor impairment and limb involvement, however, subgroup analysis in this study was not plausible due to low participant numbers. Future investigations with larger sample sizes are required to answer these important differential adaptation questions. In three out of four participants who increased ankle power during late stance, there was a compensatory reduction in hip power generation in late stance. This trade-off between the ankle and hip joints has been shown to occur in TD individuals when asked to voluntarily increase ankle push-off [40], as well as following a plantar flexor training program in a pilot study of three young children with CP [41], indicating that this trade-off relationship between the two joints may occur after targeted resistance training.

Limitations

The sample of young adults with CP in this study were of a high functional classification (GMFCS Level I-II). The results are therefore not generalizable across the spectrum of CP impairment levels. Improvements in functional capacity outcomes measured in the same sample have been reported in our previous study [29] indicating that controlled gait analysis may not detect meaningful differences in functional capacity for individuals already of a high functional level. Within the study sample, there was a mix of bilateral and unilateral limb impairments, as well as different treatments and therapies reported during childhood. These factors increased the heterogeneity of the sample and may have different effects on ankle, knee, and hip kinematics as well as how the individual adapted to the FAST intervention. A major strength of this study design was the use of a control group to overcome many limitations of uncontrolled cohort studies. The target sample size was not met however, despite an extensive recruitment strategy being implemented over two years and so this study may be underpowered to detect differences in gait outcomes between groups. Further

research using larger sample sizes to examine gait outcomes following this type of training in young adults with CP is required to validate the results.

Conclusion

The combined FAST program did not lead to objective improvements in treadmill gait kinematics or kinetics at a preferred walking speed in the intervention group compared to control participants. We hypothesise that the FAST intervention was not task-specific to treadmill walking at a preferred speed. The discrepancy in treadmill gait outcomes and improvements in overground functional capacity [28] requires further exploration and suggests that treadmill-based gait outcomes at preferred walking speed may not be related to measures of overground functional capacity in young adults with CP.

Conflict of interest statement: All authors declare there are no conflicts of interest associated with the production of this manuscript.

Acknowledgements

We gratefully acknowledge the support of Miss Shari O'Brien for technical assistance during data collection. Thank you to the Queensland Cerebral Palsy Register and Queensland Paediatric Rehabilitation Service for their assistance in participant recruitment. This research was supported by Merchant Charitable Foundation via the Children's Hospital Foundation (Donation ID 10415); Cerebral Palsy International [grant number R-810-13]; Cerebral Palsy Alliance [grant number CDG213]; National Health and Medical Research Council of Australia [grant numbers 1075642, 1070623, 1105038]; and Australian Rotary Health / Rotary Club of St Ives.

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Figure Captions

Figure 1. CONSORT study flow diagram. Abbreviations: QCPR, Queensland Cerebral Palsy Register; QPRS, Queensland Paediatric Rehabilitation Service.

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Figure 2. Representative data from one CP participant (unilateral involvement, GMFCS Level I) before (dashed black line) and after (solid black line) the intervention compared to the TD group average $\pm$ 1SD (grey shaded area).

Figure 3. Individual baseline and follow-up data points from individuals randomised to the intervention group for peak ankle power during late stance (A), peak hip power during late stance (B), and the ratio of peak ankle to peak hip power during late stance (C).

Abbreviations: B, bilateral involvement; GMFCS, Gross Motor Function Classification System; U, unilateral involvement.

A. Peak ankle power (late stance)

B. Peak hip power (late stance)

C. Ankle to hip power ratio (late stance)

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Table 1. Participant demographics and characteristics at baseline.

Characteristics	Intervention group (n= 7)	Control group (n= 9)
Age at enrolment, y:mo	21y3mo $\pm$ 4y8mo	21y8mo $\pm$ 4y3mo
Sex: M/F	3/4	5/4
Height, cm	162.16 $\pm$ 16.18	170.3 $\pm$ 7.3
Weight, kg	67.7 $\pm$ 17.0	68.4 $\pm$ 13.9
Lower limb involvement, n (%)		
Unilateral	4 (57)	3 (33)
Bilateral	3 (43)	6 (67)
GMFCS, n (%)		
Level I	5 (71)	5 (56)
Level II	2 (29)	4 (44)
Previous lower limb surgery, ^a n (%)		
Yes	3 (43)	3 (33)

Data are mean $\pm$ SD. M, male; F, female; GMFCS, Gross Motor Function Classification System; ^a Surgery types: muscle-tendon lengthening (n=6), osteotomy (n=2).

Table 2. Outcomes at baseline (T1) and follow-up (T2) assessments (immediately following intervention) by group allocation; difference within groups; and difference between groups adjusted for age, sex and baseline values.

Outcome measure	T1 (baseline) mean $\pm$ SD		T2 (12-weeks) mean $\pm$ SD		Within-group difference, mean $\pm$ SD				Between-group difference, mean (95% CI)		
	Int (n=7)	Con (n=9)	Int (n=7)	Con (n=7)	Int T2-T1	<i>p</i>	Con T2-T1	<i>P</i>	Int T2 – Con T2	<i>p</i>	
Walking speed (m.s ⁻¹)	0.79 $\pm$ 0.35	0.80 $\pm$ 0.22	0.80 $\pm$ 0.22	0.83 $\pm$ 0.21	0.06 $\pm$ 0.07	0.063	0.03 $\pm$ 0.04	0.134	0.05		(-0.03 – 1.24) 0.22 9
Stride length (m)	1.03 $\pm$ 0.33	1.03 $\pm$ 0.30	1.03 $\pm$ 0.22	1.04 $\pm$ 0.22	0.00 $\pm$ 0.17	0.931	0.01 $\pm$ 0.06	0.675	0.02		(-0.13 – 1.71) 0.73 9
Ankle angle at foot contact (PF, deg)	-6.05 $\pm$ 6.64	-7.04 $\pm$ 3.51	-7.05 $\pm$ 3.51	-7.91 $\pm$ 5.44	-0.63 $\pm$ 4.06	0.694	-0.87 $\pm$ 4.00	0.586	0.26		(-4.68 – 5.20) 0.90 8

Maximum ankle angle during stance (DF, deg)	7.28 ± 3.04	9.17 ± 2.96	8.30 ± 2.96	9.07 ± 6.04	1.02 ± 5.00	0.609	-0.10 ± 5.10	0.959	0.30	$(-6.96 - 7.57)$	0.927
GPS (deg)	9.61 ± 3.99	6.76 ± 2.06	10.51 ± 4.16	6.74 ± 1.76	0.90 ± 1.35	0.129	-0.02 ± 0.88	0.965	1.09	$(-0.65 - 2.84)$	0.190
Peak ankle power during late stance (W.Kg ⁻¹)	1.12 ± 0.81	1.23 ± 0.79	1.43 ± 0.88	1.05 ± 0.48	0.31 ± 0.28	0.043	-0.18 ± 0.46	0.336	0.47	$(-0.01 - 0.96)$	0.055
Peak hip power during late stance (W.Kg ⁻¹)	0.82 ± 0.44	0.70 ± 0.54	0.76 ± 0.31	0.53 ± 0.28	-0.06 ± 0.21	0.522	-0.17 ± 0.29	0.155	0.17	$(-0.02 - 0.35)$	0.071

Ankle to

hip power	1.29 ± 0.28	2.00 ± 0.57	1.72 ± 0.55	2.09 ± 0.47	0.43 ± 0.37	0.034	0.09 ± 0.76	0.775	-0.14	(-1.27 – 0.77 0.98)	4
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Con, control group; Int, intervention group.