

Muscle strengthening is not effective in children and adolescents with cerebral palsy: a systematic review

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Question: Do strengthening interventions increase strength without increasing spasticity and improve activity, and is there any carryover after cessation in children and adolescents with cerebral palsy? **Design:** Systematic review with meta-analysis of randomised trials. **Participants:** Children with spastic cerebral palsy between school age and 20 years. **Intervention:** Strengthening interventions that involved repetitive, strong, or effortful muscle contractions and progressed as ability changed, such as biofeedback, electrical stimulation, and progressive resistance exercise. **Outcome measures:** Strength was measured as continuous measures of maximum voluntary force or torque production. Spasticity was measured as velocity-dependent resistance to passive stretch. Activity was measured as continuous measures, eg, 10-m Walk Test, or using scales eg, the Gross Motor Function Measure. **Results:** Six studies were identified and five had data that could be included in a meta-analysis. Strengthening interventions had no effect on strength (SMD 0.20, 95% CI -0.17 to 0.56), no effect on walking speed (MD 0.02 m/s, 95% CI -0.13 to 0.16), and had a small statistically-significant but not clinically-worthwhile effect on Gross Motor Function Measure (MD 2%, 95% CI 0 to 4). Only one study measured spasticity but did not report the between-group analysis. **Conclusion:** In children and adolescents with cerebral palsy who are walking, the current evidence suggests that strengthening interventions are neither effective nor worthwhile. [Scianni A, Butler JM, Ada L, Teixeira-Salmela LF (2009) **Muscle strengthening is not effective in children with cerebral palsy: a systematic review. Australian Journal of Physiotherapy 55: 81–87]**

Key words: Cerebral palsy, Physical therapy techniques, Rehabilitation, Review systematic, Meta-analysis, Randomised controlled trials, Muscle weakness, Children

Introduction

Muscle weakness is a common impairment in children with cerebral palsy (Brown et al 1991, Damiano et al 1995b, Wiley and Damiano 1998). Weakness has been attributed to incomplete recruitment or decreased motor unit discharge rates (Elder et al 2003, Rose and McGill 2005, Stackhouse et al 2005, Wiley and Damiano 1998), inappropriate coactivation of antagonist muscle groups (Elder et al 2003, Stackhouse et al 2005, Wiley and Damiano 1998), secondary myopathy (Friden and Lieber 2003, Lieber et al 2004, Rose et al 1994), and altered muscle physiology (Stackhouse et al 2005).

Correlation studies have demonstrated that muscle strength is related to activity in children with cerebral palsy. Ross and Engsborg (2007) reported a moderate correlation between strength and walking speed ($r = 0.61$) but little correlation between spasticity and walking speed ($r = 0.19$) in children with cerebral palsy who ambulate. Damiano et al (2001) also found moderate to high correlations between strength and activity limitations ($r = 0.70$ to 0.83).

Several uncontrolled trials have reported increases in strength after training in children with cerebral palsy and that increased strength can translate into improved activity (Blundell et al 2003, Damiano and Abel 1998, Eagleton et al 2004, MacPhail and Kramer 1995, Morton et al 2005). Likewise, two randomised trials have reported increases in 1 RM strength with training (Dodd et al 2003, Liao et al 2007) although with no clear carryover to activity. A recent systematic review (Mockford and Caulton 2008) concluded

that strength training was associated with moderate to large gains in both strength and activity. However, this review included uncontrolled trials, limiting the accuracy of the conclusions about the effect of strength training in children with cerebral palsy.

In order for strengthening interventions to be adopted widely, not only do they need to be effective but they also need to be worthwhile in terms of improvements in activity, and not harmful in terms of increasing spasticity. Therefore, the research questions of this systematic review were, in children and adolescents with cerebral palsy:

1. Can strength be increased, can it be increased without increasing spasticity, and does increased strength improve activity?
2. Are any gains maintained after intervention ceases?

In order to make recommendations based on the highest level of evidence, this review included only controlled trials of strengthening with participants randomised to receive a strengthening intervention versus placebo or no intervention. Strengthening was defined broadly as repetitive effortful contractions of any muscle and therefore could include electrical stimulation and biofeedback as well as progressive resistance exercise. Although strength training is usually considered to be progressive resistance exercise, it is important to consider different types of strengthening interventions because people with neurological conditions such as cerebral palsy may not have anti-gravity strength and therefore cannot undertake resisted exercise (Ada et al 2006).

Method

Identification and selection of studies

Searches were conducted of MEDLINE (1966 to July 2008), CINAHL (1982 to July 2008), EMBASE (1974 to July 2008) and PEDro (to July 2008) databases, without language restrictions using words related to cerebral palsy and randomised, quasi-randomised, or controlled trials and words related to strengthening interventions such as electrical stimulation, biofeedback, and progressive resistance exercise (see Appendix 1 on the eAddenda for full search strategy). Titles and abstracts (where available) were displayed and screened by one reviewer to identify relevant studies. Full paper copies of relevant studies were retrieved and their reference lists were screened. The methods of the retrieved papers were extracted and reviewed independently by two reviewers using predetermined criteria (Box 1). Disagreements or ambiguous issues were resolved by consensus after discussion with a third reviewer. Therefore, during the review of the retrieved papers against the inclusion criteria, reviewers were blinded to authors, journal and outcomes.

Box 1. Inclusion criteria

Design

- Randomised, quasi-randomised, or controlled trial

Participants

- School age, ie, > 4 and < 20 years old
- Spastic cerebral palsy (any level of disability)
- No Botulinum Toxin A or surgery within last six months

Intervention

- One of the aims of intervention was to improve muscle strength, ie, strength was not measured to see if it was a by-product of the intervention
- Intervention (biofeedback, electrical stimulation, progressive resistance exercise) was repetitive, near maximal muscle contractions. Load progressed as participants' abilities changed
- Strengthening was at least half of the intervention

Outcome Measures

- Measure of muscle strength (maximum voluntary force production).

Comparisons

- Strengthening versus nothing/placebo
- Strengthening plus other therapy versus other therapy

Assessment of characteristics of studies

Quality: The quality of included studies was assessed by extracting PEDro scores from the Physiotherapy Evidence Database (Maher et al 2003). Rating of trials on this database is carried out by two independent trained raters and disagreements are resolved by a third rater. Where a study was not included on the database, it was assessed independently by two authors who had completed the PEDro Scale training tutorial on the Physiotherapy Evidence Database.

Participants: Studies involving participants of either gender, regardless of the level of initial disability, were included. Severity of disability was recorded, using the Gross Motor Function Classification System (Palisano et al 1997) if reported or the National Association of Sport for Cerebral Palsy (National Association of Sports for Cerebral

Palsy 2008), so that the similarity of participants between studies could be examined.

Intervention: The experimental intervention could be of any type but had to be of a dose that could be expected to improve strength, ie, it had to involve repetitive, strong or effortful muscle contractions, and it had to be stated or implied that the intervention was progressed as ability changed. Interventions were categorised as: (i) electrical stimulation (including triggered electrical stimulation); (ii) biofeedback (including EMG, force or position feedback); and (iii) progressive resistance exercise if the intervention consisted of movement against progressively increased resistance (including isokinetic, robotic, or repetition maximum resistance). Where the study involved more than two interventions, the experimental intervention was chosen as the one targeting the most muscles, while the control intervention was chosen as placebo over no intervention where the placebo was convincing.

Outcome measures: Continuous measures of muscle strength (eg, force, torque, work, EMG), spasticity (eg, hyperexcitability of the stretch reflex), and activity (eg, 10-m Walking Test, 9-Hole Peg Test) were used in the analysis where available. Otherwise, ordinal measures of strength (eg, Manual Muscle Test), spasticity (eg, Ashworth Scale) and activity (eg, Gross Motor Function Measure, activities of daily living) were used. When multiple measures were reported, the measure that reflected the body part to which the training was applied was used. When both limbs were trained, the most affected limb was used in the analysis.

Data analysis

Data were extracted from the included studies by one reviewer and cross checked by a second reviewer. Information about the method (ie, design, participants, intervention, measures) and outcome data (ie, number of participants and mean (SD) strength, spasticity and activity) was extracted.

All studies reported pre- and post-intervention scores; therefore, post-intervention scores were used to obtain the pooled estimate of the effect of intervention. When the same methods of measurement were used, the size of the effect was reported as weighted mean difference (95% CI). When different methods were used, the effect size was reported as Cohen's standardised mean difference (95% CI). In both cases, a random effects model was used. Post-hoc analysis of subgroups (eg, upper-limb versus lower-limb training, different durations of intervention, and different interventions) were done when there was clinical heterogeneity. The analyses were performed using MIX^a (Bax et al 2006, Bax et al 2008). When data were not able to be included in the pooled analysis, the outcome of the between-groups analysis was reported.

Results

Flow of studies through the review

The search strategy identified 1880 studies. After screening titles and abstracts, 57 full papers were retrieved. After being assessed against the inclusion criteria, five randomised trials (Dodd et al 2003, Engsborg et al 2006, Kerr et al 2006, Liao et al 2007, van der Linden et al 2003) and one quasi-randomised trial (McCubbin and Shasby 1985) were included in the review. See Figure 1 for details of the flow of studies throughout the review. See Table 1 for a summary of the excluded papers (see eAddenda for Table 1).

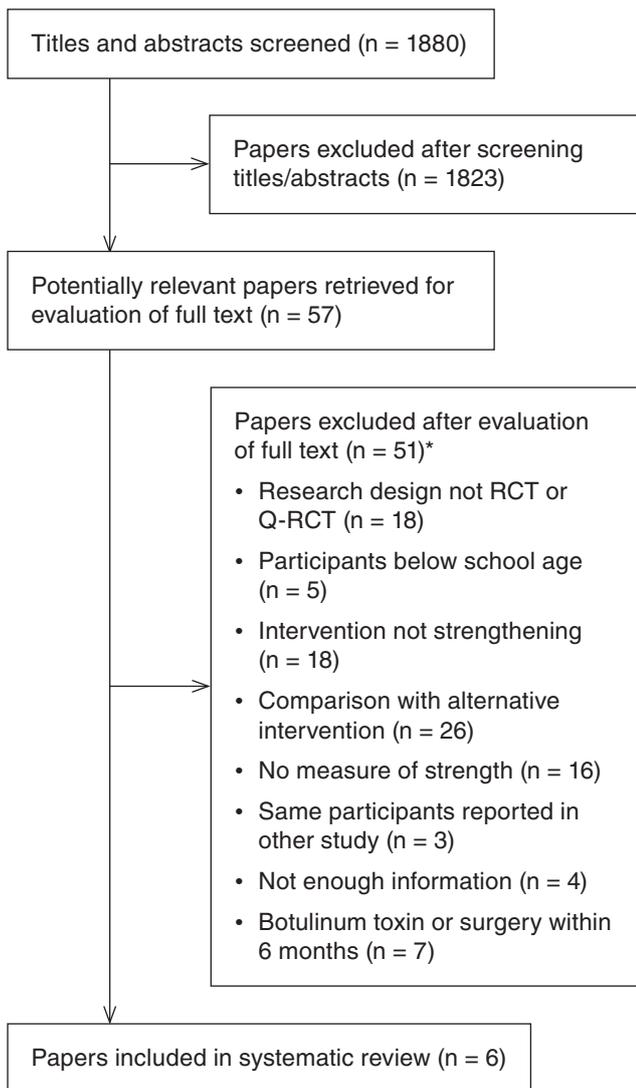


Figure 1. Identification and selection of studies. *Papers may have been excluded for failing to meet more than one inclusion criteria.

Characteristics of included studies

Five studies investigated lower limb strengthening and one study investigated upper limb strengthening. The quality of included studies is displayed in Table 2 and a summary of the studies is presented in Table 3.

Quality: The median PEDro score of the studies was 5.5. Randomisation was carried out in 83% of studies, concealed allocation in 33%, assessor blinding in 50%, and intention-to-treat analysis in 67%. Half the studies (50%) reported more than 15% loss to follow-up. No studies blinded participants or therapists, which is difficult or near-impossible with these interventions.

Participants: The mean age ranged from 7 to 15 years; 52% of participants were boys and 48% girls. The participants in the five studies examining lower limb strengthening were all independent walkers either with or without aids; 70% were classified as Level 1 or 2 (independent walkers) and 30% were Level 3 (independent walkers with an aid) on the Gross Motor Function Classification System (Palisano et al 1997). The participants in the study examining upper limb strengthening were classified using the National Association of Sport for Cerebral Palsy system (National Association of Sports for Cerebral Palsy 2008); 57% were classified in the

Table 2. PEDro scores for included studies (n = 6).

Study	Random allocation	Concealed allocation	Groups similar at baseline	Participant blinding	Therapist blinding	Assessor blinding	< 15% dropouts	Intention-to-treat analysis	Between-group difference reported	Point estimate and variability reported	Total (0 to 10)
Dodd et al (2003)	Y	Y	N	N	N	Y	Y	Y	Y	Y	7
Engsberg et al (2006)	Y	N	N	N	N	N	N	N	Y	Y	3
Kerr et al (2006)	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Liao et al (2007)	Y	N	Y	N	N	Y	N	N	Y	Y	5
McCubbin & Shasby (1985)	Y	N	Y	N	N	N	N	N	Y	Y	4
Van der Linden et al (2003)	Y	N	Y	N	N	Y	Y	N	Y	Y	6

PEDro scores from <http://www.pedro.org.au>

Table 3. Summary of included studies (n = 6).

Study	Design	Participants	Intervention*	Outcome measures
Dodd et al (2003)	RCT	n = 21 Age (yr) = 13.1 (SD 3.1) Gender = 10 M, 11 F Classification = spastic diplegia, GMFCS Level I: 7, II: 5, III: 9	Exp = PRE of ankle PF, knee E, hip E 3 x 10 RM x 3/wk x 6 wk Con = no intervention	Muscle strength = summed peak force of ankle PF, knee E, hip E (kg) Activity = GMFM D (standing) and E (walking, running and jumping) (%), walking speed (m/min) Follow up = 0, 6, 18 wk
Engsberg et al (2006)	RCT	n = 12 Age (yr) = 9.9 (SD 3.5) Gender = 3 M, 9 F Classification = spastic diplegia, GMFCS Level I: 4, II: 5, III: 2	Exp = PRE of ankle PF + DF 6 x 10 (\geq 80% 1 RM) x 3/wk x 12 wk Con = no intervention	Muscle strength = peak torque PF+DF (Nm/kg) Spasticity = velocity-dependent resistance to passive PF stretch (J/[°/s]) Activity = GMFM E (%) Follow up = 0, 12 wk
Kerr et al (2006)	RCT	n = 60 Age (yr) = 11.0 (SD 3.5) Gender = 38 M, 22 F Classification = diplegia: 55, quadriplegia: 1, dystonia: 1, ataxia: 1, non-classifiable: 2 Independent walkers: without aid: 34; with crutches/stick: 8; with posterior walker: 18	Exp = ES of knee E 60 min (**) x 5 /wk x 16 wk Con = placebo: no stimulation delivered through electrodes 480 min x 5/wk x 16 wk Both = usual PT	Muscle strength = peak torque knee E (Nm) Activity = GMFM total score (%) Follow up = 0, 16, 22 wk
Liao et al (2007)	RCT	n = 20 Age (yr) = 7.4 Gender = 12 M, 8 F Classification = mild spastic diplegia, GMFCS Level I: 10, II: 10	Exp = loaded STS 10 x (20% 1 RM) + repeatedly until fatigue (50% 1RM) + 10 x (20% 1 RM) x 3/wk x 6 wk Con = no intervention Both = usual PT	Muscle strength = max knee E force (kg) Activity = GMFM D and E (%), walking speed (m/min) Follow up = 0, 6 wk
McCubbin & Shasby (1985)	Q-RCT	n = 30 Age (yr) = (10–20) Gender = Not reported Classification = NASCP Level 1–4: 13; 4–8: 17	Exp = PRE of elbow E 3 x 10 (isokinetic exercise, maximal speed, maximal resistance) x 3/wk x 6 wk Con = no intervention	Muscle strength = peak torque elbow E (ft-lbs) Follow up = 0, 3, 6 wk
Van der Linden et al (2003)	RCT	n = 22 Age (yr) = 8.3 Gender = 7 M, 15 F Classification = diplegia: 14, quadriplegia: 1, hemiplegia: 7, all independent walkers	Exp = ES of hip E 60 min (**) x 6/wk x 8 wk Con = no intervention Both = usual PT	Muscle strength = peak force of hip E (N/kg) Activity = GMFM E (%), walking speed (m/s) Follow up = 0, 8 wk

* Only the groups related to the current study objectives. ** maximum tolerable muscle contraction elicited. GMFCS = Gross Motor Function Classification System, GMFM = Gross Motor Function Measure, NASCP = National Association of Sport for Cerebral Palsy, RCT = randomised controlled trial, Q-RCT = Quasi-randomised controlled trial, M/F = Male/Female, RM = repetition maximum, PRE = progressive resistance exercise, ES = electrical stimulation, PT = physiotherapy, STS = sit to stand, Exp = experimental group, Con = control group, E = extensors, DF = dorsiflexors, PF = plantarflexors

mild half of the scale, while 43% were in the severe half of the scale.

Intervention: Strengthening interventions included electrical stimulation (two studies) and progressive resistance exercise (four studies) but there were no studies of biofeedback. In the electrical stimulation studies, a maximum tolerable contraction was produced by electrical stimulation for 60 minutes/day over 8 or 16 weeks, 5 or 6 days/week. In the progressive resistance exercise studies, strength training was carried out over 6–12 weeks, 3 days/week. Intensity was high (~ 80–100% x 1 RM) with low repetitions (~3 sets x 10) in three studies and medium (20–50% x 1 RM) with large repetitions (20–30 minutes until fatigue) in one study.

The control intervention was no intervention for five studies and placebo for one study.

Outcome measures: Strength was reported as continuous measures of maximum voluntary force or torque production in all studies. Spasticity, measured with the velocity-dependent resistance to passive stretch test, was reported in only one study. Activity was measured in the five studies examining lower limb strengthening using the Gross Motor Function Measure, either as a total score (one study) or using the dimensions of standing and walking, running and/or jumping. Three of these studies also measured walking speed using the 10-m Walking Test. The study examining upper limb strengthening did not measure activity.

Effect of strengthening interventions

Strength: Because there was no between-study statistical heterogeneity for this outcome (heterogeneity < 1,2 (Higgins and Thompson 2002), $I^2 < 30\%$), the immediate effect of strengthening interventions on strength was examined by pooling post-intervention data from five studies (Dodd et al 2003, Kerr et al 2006, Liao et al 2007, McCubbin and Shasby 1985, van der Linden et al 2003). Strengthening interventions increased strength by 0.20 (95% CI -0.17 to 0.56) compared with placebo or no intervention (Figure 2, see also Figure 3 on the eAddenda for detailed forest plot). One study was unable to be included in the pooled analysis (Engsberg et al 2006) because the intervention group had only two participants, and therefore SD could not be calculated. This study did not report a between-group analysis for strength. The retention of strength was examined by pooling post-intervention data from two studies (Dodd et al 2003, Kerr et al 2006). Six to 12 weeks after the cessation of intervention, the effect size was 0.05 (95% CI -0.47 to 0.58) compared with placebo or no intervention (Figure 4, see also Figure 5 on the eAddenda for detailed forest plot).

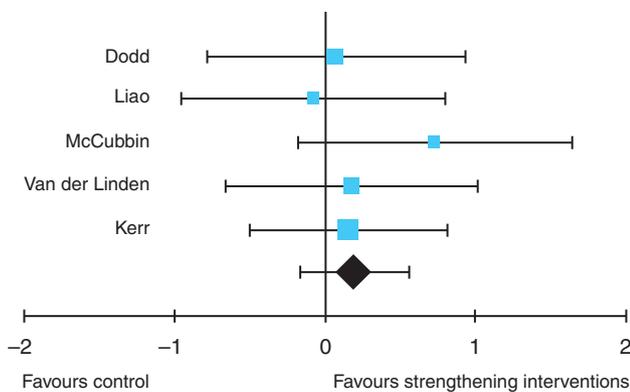


Figure 2. SMD (95% CI) of effect of strengthening interventions immediately after 6 to 16 weeks of training on strength by pooling data from 5 studies (n = 119).

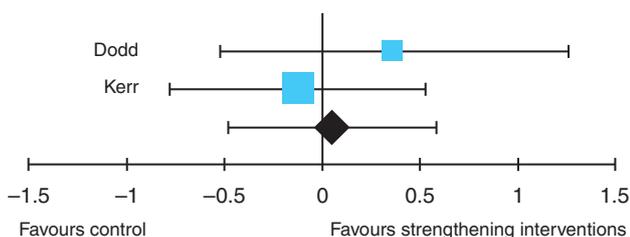


Figure 4. SMD (95% CI) of effect of strengthening interventions 6 to 12 weeks after cessation of training on strength by pooling data from 2 studies (n = 56).

Spasticity: The study that measured spasticity immediately after intervention (Engsberg et al 2006) did not report the between-group analysis.

Activity: Because there was no between-study statistical heterogeneity for this outcome (heterogeneity < 1,2 (Higgins and Thompson 2002), $I^2 < 30\%$), the immediate effect of strengthening interventions on activity was examined by pooling post-intervention data from four studies (Dodd et al 2003, Kerr et al 2006, Liao et al 2007, van der Linden et al 2003). Strengthening interventions increased

the Gross Motor Function Measure score by 2% (95% CI 0 to 4) (Figure 6, see also Figure 7 on the eAddenda for detailed forest plot) and walking speed by 0.02 m/s (95% CI -0.13 to 0.16) (Figure 8, see also Figure 9 on the eAddenda for detailed forest plot) compared with control. One study was unable to be included in the pooled analysis (Engsberg et al 2006) because the intervention group had only two participants, and therefore SD could not be calculated. This study did not report a between-group analysis for strength. The retention of activity was examined by pooling post-intervention data from two studies (Dodd et al 2003, Kerr et al 2006). Six to 12 weeks after the cessation of intervention, the Gross Motor Function Measure score was still increased by 2% (95% CI -4 to 7) compared with placebo or no intervention (Figure 10, see also Figure 11 on the eAddenda for detailed forest plot).

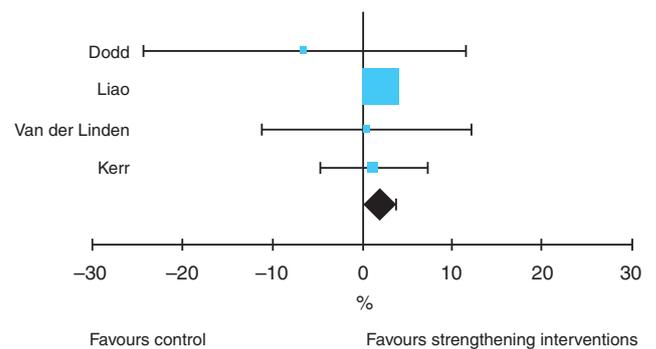


Figure 6. MD (95% CI) of effect of strengthening interventions immediately after 6 to 16 weeks of training on Gross Motor Function Measure score by pooling data from four studies (n = 99).

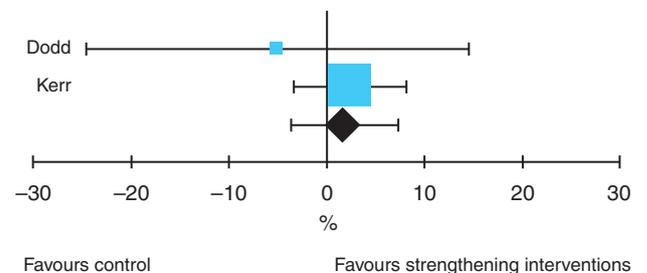


Figure 8. MD (95% CI) of effect of strengthening interventions 6 to 12 weeks after cessation of training on Gross Motor Function Measure score by pooling data from two studies (n = 56).

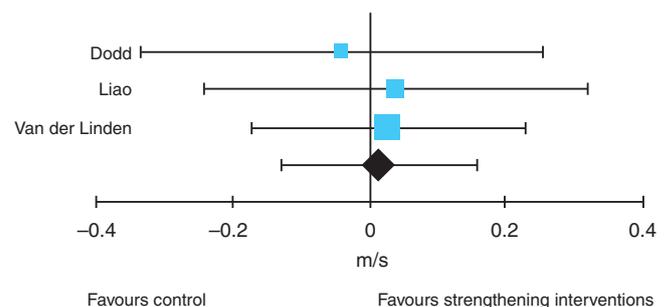


Figure 10. MD (95% CI) of effect of strengthening interventions immediately after 6 weeks of training on walking speed by pooling data from three studies (n = 63).

Discussion

This systematic review suggests that strengthening interventions do not increase strength or improve activity in cerebral palsy. Furthermore, while they do not appear to increase spasticity, there is insufficient evidence to be conclusive. This is the first systematic review to pool data from randomised trials of strengthening interventions in children and adolescents with cerebral palsy. Given that 8 was the likely maximum PEDro score achievable because it was not usually possible to blind the therapist or the participants, the mean PEDro score of 5.5 for the studies included in this review represents moderate quality, suggesting that the findings are credible.

The small, non-significant increase in strength found in this review may be because strengthening interventions were not of sufficient duration and/or intensity. Strength gains of 30–50% are typically observed in untrained youth following 8 to 12 weeks of training (Faigenbaum 2007). The average duration of strengthening in this review was 8 weeks. Although one study investigated 16 weeks of strengthening (Kerr et al 2006), their results were similar (0.16, 95% CI –0.50 to 0.81) to the 6 to 8 weeks of strengthening investigated in the other studies (0.21, 95% CI –0.22 to 0.65).

Furthermore, although strengthening interventions were progressive, they were not administered consistently at the intensity recommended by the American College of Sports Medicine (American College of Sports Medicine 2002). For example, Liao et al (2007) investigated a program of standing up from a chair with a load of 20–50% of 1 RM when the American College of Sports Medicine guidelines suggest a load of 60–70% of 1 RM for novices. In addition, the two studies investigating electrical stimulation (Kerr et al 2006, van der Linden et al 2003) concluded that, although on average a clearly visible isometric contraction was achieved, the intensity of the stimulation may not have been sufficient to achieve substantial strength gains.

Post-hoc analyses indicate that type of intervention (progressive resistance exercise and electrical stimulation) or the part of the body to which the intervention was applied (upper and lower limb) make little difference to the size of the effect. Progressive resistance exercise in three studies (61 participants) produced an effect size of 0.23 (95% CI –0.28 to 0.73) whereas electrical stimulation in two studies (58 participants) produced a similar effect size of 0.17 (95% CI –0.35 to 0.68). Four studies of lower limb strengthening (99 participants) produced an effect size of 0.10 (95% CI –0.30 to 0.49), whereas one study of upper limb strengthening (20 participants) produced an effect size of 0.72 (95% CI –0.18 to 1.62). While strengthening of the upper limb produced the only clinically-significant effect size, it was not statistically significant (with wide CI) and was the result of only one study.

Only one study in this review measured spasticity (Engsberg et al 2006). Although the between-group difference was not reported, spasticity decreased in the strength group. This agrees with previous uncontrolled studies of strength training in children with cerebral palsy that reported no increase in spasticity (Damiano et al 1995a, Fowler et al 2001). Taken together, these findings suggest that strength training is not harmful.

Strengthening interventions were accompanied by statistically-significant but not clinically-worthwhile improvements in activity (2% in Gross Motor Function Measure score and 0.02 m/s of walking speed). Given that there was no increase in strength, this is perhaps not surprising. Furthermore, this small increase in activity could be the result of the high level of activity of the participants. In the studies that investigated lower limb muscle strengthening, all the participants could walk. Buchner et al (1996) reported a non-linear relationship between leg strength and walking speed. The authors suggest small changes in physiological capacity may produce relatively large effects on performance in severe disability, while large changes in capacity have little or no effect on daily activity in mild disability. It is therefore possible that increases in strength would not affect walking speed in the population of this review who were walking. Ada et al (2006) reported similar results for people after stroke where the effect of strengthening on activity in participants who had antigravity strength was small.

In children and adolescents with cerebral palsy who are walking, the current evidence suggests that strengthening interventions are neither effective nor worthwhile, but are probably not harmful. Future studies investigating muscle strengthening at high intensities in children and adolescents with cerebral palsy with lower levels of activity may be useful to guide clinical practice. ■

Footnotes: ^aMIX – Meta-analysis made easy. <http://www.mix-for-meta-analysis.info/>

eAddenda: Appendix 1, Table 1, Figures 3, 5, 7, 9, 11 at AJP.physiotherapy.asn.au.

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