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Research

Constraint-induced movement therapy improves upper limb activity and participation in hemiplegic cerebral palsy: a systematic review

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KEY WORDS

Cerebral palsy
Systematic review
Meta-analysis
Randomised controlled trials
Constraint-induced movement therapy

ABSTRACT

Questions: Does constraint-induced movement therapy improve activity and participation in children with hemiplegic cerebral palsy? Does it improve activity and participation more than the same dose of upper limb therapy without restraint? Is the effect of constraint-induced movement therapy related to the duration of intervention or the age of the children? **Design:** Systematic review of randomised trials with meta-analysis. **Participants:** Children with hemiplegic cerebral palsy with any level of motor disability. **Intervention:** The experimental group received constraint-induced movement therapy (defined as restraint of the less affected upper limb during supervised activity practice of the more affected upper limb). The control group received no intervention, sham intervention, or the same dose of upper limb therapy. **Outcome measures:** Measures of upper limb activity and participation were used in the analysis. **Results:** Constraint-induced movement therapy was more effective than no/sham intervention in terms of upper limb activity (SMD 0.63, 95% CI 0.20 to 1.06) and participation (SMD 1.21, 95% CI 0.41 to 2.02). However, constraint-induced movement therapy was no better than the same dose of upper limb therapy without restraint either in terms of upper limb activity (SMD 0.05, 95% CI –0.21 to 0.32) or participation (SMD –0.02, 95% CI –0.34 to 0.31). The effect of constraint-induced movement therapy was not related to the duration of intervention or the age of the children. **Conclusions:** This review suggests that constraint-induced movement therapy is more effective than no intervention, but no more effective than the same dose of upper limb practice without restraint. **Registration:** PROSPERO CRD42015024665. **[Chiu H-C, Ada L (2016) Constraint-induced movement therapy improves upper limb activity and participation in hemiplegic cerebral palsy: a systematic review. *Journal of Physiotherapy* 62: 130–137]**

Introduction

Cerebral palsy is a non-progressive neurological condition resulting in motor impairments that can change over time.[1] The impairments may originate directly from damage to an immature brain, or indirectly from compensatory movements or disuse during development.[1] Such impairments may result in activity limitations that require rehabilitation throughout life.[1] Among children with cerebral palsy, 29% have hemiplegia, that is, one side of the body is affected much more than the other, and the upper limb is typically more involved than the lower limb.[2] They may develop 'learned non-use' in their affected upper limb, because they tend to learn alternative strategies to manage daily tasks using the less affected limb.[3–5] Performance of tasks is often more efficient using the less affected upper limb, even if there is only mild impairment in the more affected limb.[3] Children with hemiplegic cerebral palsy usually have the intellectual capacity to attend regular schools, yet impaired upper limb function tends to restrict their participation in education and leisure, and impact their social image.

Therapists working with children with hemiplegic cerebral palsy encourage movement of the affected limb by repetitive practice of unilateral and bimanual activities. Constraint-induced movement therapy (CIMT) aims to overcome 'learned non-use' by intensive, targeted practice with the more affected limb during restraint of the less affected limb.[5] While restrained, only the affected upper limb can be used to carry out activities, forcing children to find solutions to their movement problems.[4,5]

There are four systematic reviews specifically examining the effect of CIMT in children with cerebral palsy or hemiplegia from other causes.[5–8] Two of the reviews included all published studies, regardless of design, and included low levels of evidence such as case studies.[5,8] The Cochrane review on this topic has not been updated since 2007 and includes only three randomised trials. These three trials were not pooled into a meta-analysis but the authors concluded that there was a trend towards a beneficial effect of CIMT.[7] The most recent review[6] to focus on CIMT reported a standardised effect size of 0.55 from the pooled estimate of 27 randomised trials of CIMT versus conventional therapy. One of the post-hoc analyses carried out was to divide the trials on the basis of the equivalence of dose of intervention. When CIMT was compared with a dose-equivalent intervention, the effect was much smaller (SMD 0.37) than the effect among trials without a dose-equivalent comparison group (SMD 0.84). These results give insight into the mechanism of CIMT. The effect of CIMT may be due to nothing more than the large amounts of practice that restraint of the less affected upper limb produces.

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In order to fully investigate the effect of CIMT on children with hemiplegic cerebral palsy, trials where CIMT is compared with no intervention need to be pooled separately from trials where CIMT is compared with the same dose of practice without restraint of the unaffected limb. The present systematic review therefore took this approach. In addition, this review examined outcomes at the level of activity and participation, because not only is the effect of CIMT on upper limb activity of interest, but also how improved activity might translate into the broader context of using the upper limb to participate at home, at school and in the community. This review also sought to determine whether the amount of benefit obtained from CIMT is associated with certain characteristics of the children or the CIMT.

Therefore, the research questions for this systematic review were:

1. Does CIMT improve activity and participation in children with hemiplegic cerebral palsy?
2. Does CIMT improve activity and participation more than the same dose of upper limb therapy without restraint?
3. Is the effect of CIMT related to the duration of intervention or the age of the child?

Method

Identification and selection of studies

Searches were conducted of Medline (1966 to June 2015), CINAHL (1982 to June 2015), PubMed (1966 to June 2015), Embase (1974 to June 2015), the Cochrane Library (1966 to June 2015), Web of Science (1945 to June 2015) and the Physiotherapy Evidence Database (PEDro) (to June 2015), without language restrictions using words related to *cerebral palsy* and *randomised controlled trials* and words related to *constraint-induced movement therapy* (such as constraint-induced movement therapy, forced and massed practice) (see Appendix 1 for full search strategy). Titles and abstracts were displayed and screened by one reviewer to identify relevant studies. Full-text copies of relevant studies were retrieved and their reference lists were screened. The methods of the retrieved papers were screened independently by two reviewers against the inclusion criteria: randomised or quasi-randomised trials; children or adolescents (< 18 years of age) with hemiplegic cerebral palsy; experimental intervention of CIMT; control intervention of no/sham intervention or same dose of upper limb therapy; and outcome measure(s) of activity or participation (Box 1).

Box 1. Inclusion criteria.

Design
- randomised or quasi-randomised trial

Participants
- children (ie, < 18 years old)
- hemiplegic cerebral palsy
- any level of disability

Intervention
- constraint-induced movement therapy (ie, restraint of the less affected limb) applied during supervised activity practice of the more affected upper limb

Outcome measures
- measures of activity or participation

Comparisons
- constraint-induced movement therapy vs no/sham intervention (sham defined as usual therapy ≤ 20% of time restrained)
- constraint-induced movement therapy vs same dose of upper limb therapy (defined as ≥ time restrained)

Assessment of characteristics of studies

Quality

The quality of included studies was assessed by extracting PEDro scores from the PEDro website. Each score on the PEDro website is generated by two accredited raters scoring the trial, with any discrepancies in rating resolved by a third accredited rater.

Participants

Studies involving participants of either gender, regardless of the level of initial disability, were included. The Manual Ability Classification System was used to quantify the severity of upper limb disability. The Manual Ability Classification System classifies how children with cerebral palsy use their hands to handle objects in daily activities, with I = minor limitations and V = severe limitations.[9] Age and Manual Ability Classification System level were recorded so that the similarity of participants between studies could be examined. If the Manual Ability Classification System level was not reported, reviewers classified the participants based on the available information.

Intervention

The experimental group had to have received CIMT (defined as restraint of the less affected upper limb during task practice of the more affected upper limb). To be eligible to answer the first study question, the control group had to receive no/sham intervention, defined as usual therapy ≤ 20% of the time that the experimental group spent restrained. To be eligible to answer the second study question, the control group received the same dose of upper limb therapy (unilateral or bilateral or both), defined as equal to or greater than the time that the experimental group spent restrained. Participants could be receiving other therapy as long as both groups received it. The frequency and duration of the intervention was recorded so that the similarity of intervention between studies could be examined.

Outcome measures

Measures that reflected upper limb activity and participation were used in the analysis. Upper limb activity was measured as what the child could do with their more affected limb. Therefore, measures using direct observation of unimanual performance of standardised upper limb tasks, such as Jebsen-Taylor Test of Hand Function, Nine-Hole Peg Test or Bruininks-Oseretsky Test of Motor Proficiency, Quality of Upper Extremity Skills Test or Melbourne Assessment of Unilateral Upper Limb Function, were used and reported as either level of difficulty or time taken. Upper limb participation was measured as what the child did in real life. Therefore, measures using direct observation or parent perception of bimanual real-life play, such as the Assisting Hand Assessment or Pediatric Motor Activity Log, were used and reported as level of difficulty.

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 and measures) and outcome data (ie, number of participants, mean (SD) activity and participation) were extracted. Authors of papers with missing data were contacted.

Most studies reported post-intervention scores immediately after intervention; therefore, these scores were used to obtain the pooled estimate of the effect of intervention. Since different measurement tools were used, the effect size was reported as Cohen's standardised mean difference (SMD, 95% CI). A random-effects model was used. The analyses were performed using MIX 2.0, which is a statistical add-in for performing meta-analysis in Excel.[10,11]

Simple linear regression was used to determine the association between the duration of CIMT and the effect of CIMT (on activity

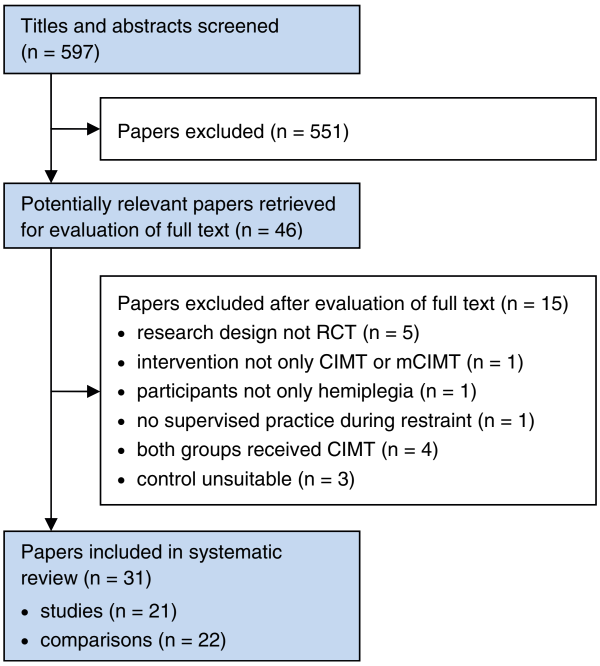

Figure 1. Flow of studies through the review.
RCT = randomised controlled trial, CIMT = constraint-induced movement therapy, mCIMT = modified constraint-induced movement therapy.

and participation) and as well as between age and the effect of CIMT (on activity and participation). Only the no/sham treatment-controlled studies were used in this analysis.

Results

Flow of studies through the review

The search strategy identified 597 studies. After screening titles and abstracts, 46 full papers were retrieved. After being assessed against the inclusion criteria, 31 papers[12–42] of 21 studies[12,14–18,21–24,27,28,30,31,36–42] were included in the review (Figure 1; see Appendix 2 for excluded papers).

Characteristics of included studies

The 21 studies provided 22 comparisons that were relevant to this review because one study had three arms (reported in Fedrizzi et al 2013[24] and Facchin et al 2011[25]). Among the 22 comparisons, 15 investigated CIMT versus no/sham intervention[12,15–18,22–24,30,36–40,42] and seven investigated CIMT versus the same dose of upper limb therapy.[14,21,24,27,28,31,41] A summary of the studies is presented in Table 1.

Quality

The mean PEDro score of the papers was 5.8 (range 3 to 8) (Table 2). The majority of the papers: were randomised (100%), analysed the between-group difference (97%), reported point estimates and variability (87%), had similar groups at baseline (84%), reported $<$ 15% loss to follow-up (74%) and had blinded assessors (65%). The majority of studies did not conceal the allocation list (58%), carry out an intention-to-treat analysis (65%), nor blind participants or therapists (100%).

Participants

Participants were children and adolescents who were classified as having hemiplegic cerebral palsy, with the mean age across studies ranging from 2.4 to 10.2 years. Fourteen studies (63%) involved participants aged $<$ 4 years. Most of the studies investigated children classified as Manual Ability Classification System level I/II/III in the more affected limb (ie, able to handle objects without or with adaptive behaviour).

Intervention

The experimental group received CIMT with supervised upper limb practice (22 comparisons). The types of restraint included slings (seven studies), splints (four studies), gloves (eight studies), casts (two studies), and bandage (one study). Restraint was worn for 35 hours/week (range 2 to 84) for a duration of 5 weeks (range 2 to 10) in the comparisons with no/sham intervention and 23 hours/week (range 12 to 30) for a duration of 5 weeks (range 2 to 10) in the comparisons with the same dose of upper limb therapy. Supervised practice was undertaken for 50% of the time that the restraint was worn in the comparisons with no/sham intervention and 100% of the time that restraint was worn in the comparisons with the same dose of upper limb therapy. The control group received no/sham intervention (15 comparisons) or the same dose of upper limb therapy (seven comparisons). Sham intervention was a small amount (range 0.3 to 2.2 hours/week) of usual therapy, which was not necessarily specific to the upper limb and often not specified. The same dose of upper limb therapy usually involved bilateral training. Both groups received usual therapy in six comparisons.

Outcome measures

Measures of upper limb activity were reported in 19 studies. The measures chosen for the analysis of upper limb activity were: Jebsen-Taylor Test of Hand Function (four studies), Bruininks-Oseretsky Test of Motor Proficiency (one study), Quality of Upper Extremity Skills Test (six studies), Nine-Hole Peg Test (one study), Melbourne Assessment of Unilateral Upper Limb Function (three studies), Box and Block Test (two studies) and Pediatric Arm Function Test (two studies).

Measures of upper limb participation were reported in 12 studies. The measures chosen for the analysis of upper limb participation were: Assisting Hand Assessment (eight studies), Pediatric Motor Activity Log (three studies) and Caregiver Functional Use Survey (one study).

Effect of constraint-induced movement therapy versus no/sham intervention

Activity

The immediate effect of CIMT compared with no/sham intervention on activity was examined by pooling post-intervention data from 11 comparisons with a PEDro score of 5.5 and 302 participants, using a random-effects model. Four studies were unable to be included in the analysis because they had no appropriate measure of activity[13,22,40] or because of missing data.[38] CIMT increased activity (SMD 0.63, 95% CI 0.20 to 1.06) compared with no/sham intervention (Figure 2). See Figure 3 on the eAddenda for the detailed forest plot. There was substantial statistical heterogeneity (I^2 = 65%), indicating that the variation between the results of the trials was above the variation expected by chance. Sensitivity analyses revealed that the heterogeneity was not explained by the quality of the trials, assessor blinding, number or severity of participants.

Participation

The immediate effect of CIMT compared with no/sham intervention on participation was examined by pooling post-intervention data from eight comparisons with a PEDro score of 5.5 and 215 participants, using a random-effects model. Seven studies were unable to be included in the analysis because they had no appropriate measure of participation.[17,18,23,24,36,37,42] CIMT increased participation (SMD 1.21, 95% CI 0.41 to 2.02) compared with no/sham intervention (Figure 4). See Figure 5 on the eAddenda for the detailed forest plot. There was

Table 1
Characteristics of included studies (n = 21 studies across 31 papers, with 22 comparisons).

Study	Design	Participants	Intervention: Experimental	Intervention: Control	Intervention: Both	Outcome measures
CIMT versus no/sham intervention						
Aarts et al 2010[12] Aarts et al 2011[13] Geerdink et al 2013[26]	RCT	n = 50 Mean age (range) = 2.9 yr (2.5 to 8) Classification = hemiplegia, MACS I to III	Restraint = sling 3 h/d x 3/wk x 6 wk (Total: 54 h) Super = 3 h/d x 3/wk x 6 wk+ Bimanual practice 3 h/d x 3/wk x 2 wk (Total: 72 h)	Usual therapy 1.5 h/wk x 8 wk (Total: 12 h)		• Activity: MAUULF (0 to 100) • Participation: AHA (0 to 100) • Timing = 0, 9, 26, 52 wk
Al-Oraibi et al 2011[15]	RCT	n = 14 Mean age (range) = 4.8 yr (1.8 to 9) Classification = hemiplegia, MACS[a] I to V	Restraint = glove 2 h/d x 6 or 7/wk x 8 wk (Total: 92 h) Super = 2 h/d x 6/wk x 8 wk (Total: 92 h)	Usual therapy 2 h/wk x 8 wk (Total: 16 h)		• Participation: AHA (0 to 100) • Timing = 0, 8 wk
Charles et al 2006[16]	RCT	n = 22 Mean age (range) = 6.7 yr (4 to 8) Classification = spastic hemiplegia, MACS[a] I to III	Restraint = sling 6 h/d x 5/wk x 2 wk (Total: 60 h) Super = 7 h/d x 5/wk x 2 wk (Total: 70 h)	No intervention		• Activity: JTTHF[b] (s) • Participation: CFUS-freq (0 to 5) • Timing = 0, 3 wk
Choudhary et al 2013[17]	RCT	n = 31 Mean age (range) = 5.1 yr (3 to 8) Classification = hemiplegia, MACS[a] I to III	Restraint = sling 3 h/d x 2-3/wk x 4 wk + 2 h/d x 4-5/wk x 4 wk (Total: 66 h) Super = 2 h/d x 2-3/wk x 4 wk (Total: 20 h)	No intervention	Usual therapy 0.3 h/d x 7/wk x 4 wk (Total: 8.5 h)	• Activity: QUEST-grasp (0 to 100) • Timing = 0, 4, 12 wk
De Brito Brandão et al 2010[18]	RCT	n = 16 Mean age (range) = 6 yr (4 to 8) Classification = spastic hemiplegia, MACS I to III	Restraint = sling 10 h/d x 5/wk x 2 wk (Total = 100 h) Super = 3 h/d x 5/wk x 2 wk+ bimanual practice 0.75 h/d x 3/wk x 1 wk (Total: 32 h)	Usual therapy 0.75 h/wk x 3 wk (Total = 2 h)		• Activity: JTTHF[b] (s) • Timing = –1, 3, 7 wk
Eliasson et al 2011[22]	Cross-over RCT	n = 25 Mean age (range) = 2.4 yr (1.5 to 5) Classification = hemiplegia, MACS[a] I to V	Restraint = glove 2 h/d x 7/wk x 8 wk (Total: 102 h) Super = 2 h/d x 7/wk x 8 wk (Total: 102 h)	No intervention	Usual therapy	• Participation: AHA (0 to 100) • Timing = 0, 8 wk
Eugster-Buesch et al 2012[23]	RCT	n = 23 Mean age (range) = 10.7 yr (6 to 16) Classification = hemiplegia, MACS[a] I to III	Restraint = splint 6 h/d x 7/wk x 2 wk (Total: 84 h) Super = 2 h/d x 7/wk x 2 wk (Total: 28 h)	No intervention	Usual therapy	• Activity: MAUULF (0 to 100) • Timing = 0, 2, 12, 52 wk
Fedrizzi et al 2013[24] Facchin et al 2011[25]	RCT	n = 48 Mean age (range) = 4.3 yr (2 to 8) Classification = hemiplegia, MACS[a] I to V	Restraint = glove 3 h/d x 7/wk x 10 wk (Total: 210 h) Super = 3 h/d x 7/wk x 10 wk (Total: 210 h)	Usual therapy 1-2/wk x 10 wk (Total: 15 h)		• Activity: QUEST-grasp (%) • Timing = 0, 10, 12, 26 wk
Rostami et al 2012[30]	RCT	n = 16 Mean age (range) = 8.2 yr (6 to 12) Classification = spastic hemiplegia, MACS[a] I to III	Restraint = splint 5 h/d x 7/wk x 4wk (Total: 140 h) Super = 1.5 h/d x 3/wk x 4 wk (Total: 18 h)	No intervention	Usual therapy 0.5 h/d x 2/wk x 4 wk (Total: 4 h)	• Activity: BOTMP-subtest 8 (0 to 9) • Participation: PMAL-quality (0 to 5) • Timing = 0, 4, 12 wk
Smania et al 2009[36]	Cross-over RCT	n = 10 Mean age (range) = 3.3 yr (1 to 9) Classification = hemiplegia, MACS[a] I to III	Restraint = glove 8 h/d x 7/wk x 5 wk (Total: 280 h) Super = 1 h/d x 2/wk x 5 wk (Total: 10 h)	Usual therapy 1 h/d x 2/wk x 5 wk (Total: 10 h)		• Activity: PAFT (0 to 120) • Timing = 0, 5 wk
Sung et al 2005[37]	RCT	n = 31 Mean age (range) = 3.1 yr (≤ 8) Classification = hemiplegia, MACS[a] I to III	Restraint = cast 12 h/d x 7/wk x 6 wk (Total: 500 h) Super = 0.5 h/d x 2/wk x 6 wk (Total: 6 h)	Usual therapy 0.5 h/d x 2/wk x 6 wk (Total: 6 h)		• Activity: BBT (blocks) • Timing = 0, 6 wk
Taub et al 2004[38] DeLuca et al 2006[20]	RCT	n = 18 Mean age (range) = 3.5 yr (0.5 to 8) Classification = hemiplegia, MACS[a] I to V	Restraint = cast 12 h/d x 7/wk x 3 wk (Total: 250 h) Super = 6 h/d x 7/wk x 3 wk (Total: 125 h)	Usual therapy 2.2 h/wk x 3 wk (Total = 7 h)		• Activity: QUEST (%) • Participation: PMAL-quality (0 to 5) • Timing = 0, 3 wk

Table 1 (*Continued*)

Study	Design	Participants	Intervention			Outcome measures
			Experimental	Control	Both	
Taub et al 2011[39]	RCT	n = 20 Mean age (range) = 3.7 yr (2 to 6) Classification = hemiplegia, MACS[a] I to V	Restraint = splint 12 h/d x 5/wk x 3 wk (Total: 90 h) Super = 6 h/d x 5/wk x 3 wk (Total: 90 h)	No intervention	Usual therapy 1.5 hr/wk x 3 wk (Total: 4.5 h)	• Activity: PAFT (0 to 64) • Participation: PMAL-quality (0 to 5) • Timing = 0, 3 wk
Wallen et al 2011[40]	RCT	n = 50 Mean age (range) = 3.1 yr (1.5 to 8) Classification = spastic hemiplegia, MACS I to IV	Restraint = glove 2 h/d x 7/wk x 8 wk (Total: 112 h) Super = 2 h/d x 7/wk x 8 wk (Total: 112 h)	Usual therapy 0.3 h x 7/wk x 8 wk (Total: 17 h)		• Participation: AHA (0 to 100) • Timing = 0, 10, 26 wk
Yu et al 2012[42]	RCT	n = 20 Mean age (range) = 9.4 yr (9 to 10) Classification = hemiplegia, MACS[a] I to III	Restraint = sling 1 h/d x 2/wk x 10 wk (Total: 20 h) Super = 1 h/d x 2/wk x 10 wk (Total: 20 h)	No intervention	Usual therapy 0.5 h/d x 2/wk x 10 wk (Total: 10 h)	• Activity: BBT (blocks) • Timing = 0, 10 wk
CIMT versus same dose of upper limb therapy						
Abd el-Kafy et al 2014[14]	RCT	n = 27 Mean age (range) = 6.1 yr (4 to 8) Classification = spastic hemiplegia, MACS II to IV	Restraint = sling 6 h/d x 5/wk x 4 wk (Total: 120 h) Super = 6 h/d x 5/wk x 4 wk (Total: 120 h)	Bimanual practice 6 h/d x 5/wk x 4 wk (Total: 120 h)		• Activity: QUEST (%) • Timing = 0, 4, 12 wk
Deppe et al 2013[21]	RCT	n = 29 Mean age (range) = 6.3 yr (3.3 to 12) Classification = hemiplegia, MACS I to III	Restraint = bandage 4 h/d x 5/wk x 3 wk (Total: 60 h) Super = 4 h/d x 5/wk x 3 wk + bimanual practice 4 h/d x 5/wk x 1 wk (Total: 80 h)	Bimanual practice 4 h/d x 5/wk x 4 wk (Total: 80 h)		• Activity: MAUULF (0 to 122) • Participation: AHA (22 to 88) • Timing = 0, 4 wk
Fedrizzi et al 2013[24] Facchin et al 2011[25]	RCT	n = 48 Mean age (range) = 4 yr (2 to 8) Classification = hemiplegia, MACS[a] I to V	Restraint = glove 3 h/d x 7/wk x 10 wk (Total: 210 h) Super = 3 h/d x 3/wk x 10 wk (Total: 210 h)	Bimanual practice 3 h/d x 7/wk x 10 wk (Total: 210 h)		• Activity: QUEST-grasp (%) • Timing = 0, 10, 26 wk
Gelkop et al 2015[27]	Cross-over RCT	n = 12 Mean age (range) = 4.3 yr (1.5 to 7) Classification = spastic hemiplegia, MACS I to III	Restraint = glove 2 h/d x 6/wk x 8 wk (Total: 96 h) Super = 2 h/d x 6/wk x 8 wk (Total: 96 h)	Bimanual practice 2 hx 6/wk x 8 wk (Total: 96 h)		• Activity: QUEST-grasp (%) • Participation: AHA (0 to 100) • Timing = 0, 8 wk
Gordon et al 2011[28] De Brito Brandao et al 2012[19] Hung et al 2011[29]	RCT	n = 42 Mean age (range) = 6.3 yr (3.5 to 10) Classification = hemiplegia, MACS I to III	Restraint = sling 6 h/d x 5/wk x 3 wk (Total: 90 h) Super = 6 h/d x 5/wk x 3 wk (Total: 90 h)	Bimanual practice 6 h/d x 5/wk x 3 wk (Total: 90 h)		• Activity: JTTHF[b] (s) • Participation: AHA (logits) • Timing = 0, 3 wk
Sakzewski et al 2011a[31] Sakzewski et al 2011b[32] Sakzewski et al 2011c[33] Sakzewski et al 2011d[34] Sakzewski et al 2012[35]	RCT	n = 63 Mean age (range) = 10.2 yr (5 to 16) Classification = spastic hemiplegia, MACS I to III	Restraint = glove 6 h/d x 5/wk x 2 wk (Total: 60 h) Super = 6 h/d 5/wk x 2 wk (Total: 60 h)	Bimanual practice 6 h/d x 10 days (Total: 60 h)		• Activity: JTTHF[b] (s) • Participation: AHA (0 to 100) • Timing = 0, 3 wk
Xu et al 2012[41]	RCT	n = 45 Mean age (range) = 4.6 yr (2 to 14) Classification = hemiplegia, MACS[a] I to III	Restraint = splint 3 h/d x 5/wk x 2 wk (Total: 30 h) Super = 4 h/d x 5/wk x 2 wk (Total: 40 h)	Bimanual practice 3 h/d x 5/wk x 2 wk (Total: 30 h)		• Activity: 9-HPT[b] (s) • Timing = 0, 2 wk

[a] MACS level estimated by reviewers.
[b] Experimental and control scores reversed for analysis because a smaller score denotes better performance.
AHA = Assisting Hand Assessment, BBT = Box and Block Test, BOTMP = Bruininks-Oseretsky Test of Motor Proficiency, CFUS freq = Caregiver Functional Use Survey, JTFHT = Jebsen-Taylor Test of Hand Function, MACS = Manual Ability Classification System, MAUULF = Melbourne Assessment of Unilateral Upper Limb Function, PAFT = Pediatric Arm Function Test, PMAL = Pediatric Motor Activity Log, QUEST = Quality of Upper Extremity Skills Test, RCT = randomised controlled trial, Super = supervised practice, 9-HPT = Nine Hole Peg Test.

substantial statistical heterogeneity ($I^2 = 84\%$), indicating that the variation between the results of the trials was above the variation expected by chance. Sensitivity analyses revealed that the heterogeneity was not explained by the quality of the trials, assessor blinding or the number or severity of participants.

Effect of constraint-induced movement therapy versus same dose of upper limb therapy

Activity

The immediate effect of CIMT compared with the same dose of upper limb therapy on activity was examined by pooling data after

Table 2
PEDro scores for included papers (n = 31).

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)
Aarts et al 2010[12]	Y	N	Y	N	N	Y	Y	N	Y	Y	6
Aarts et al 2011[13]	Y	N	Y	N	N	Y	Y	N	Y	Y	6
Abd el-Kafy et al 2014[14]	Y	N	Y	N	N	Y	Y	N	Y	N	5
Al-Oraibi et al 2011[15]	Y	N	N	N	N	Y	N	N	Y	Y	4
Charles et al 2006[16]	Y	N	Y	N	N	Y	N	N	Y	Y	5
Choudhary et al 2013[17]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
De Brito Brandão et al 2010[18]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
De Brito Brandão et al 2012[19]	Y	Y	Y	N	N	N	Y	N	Y	Y	6
De Luca et al 2006[20]	Y	N	N	N	N	Y	Y	N	Y	N	4
Deppe et al 2013[21]	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Eliasson et al 2011[22]	Y	N	N	N	N	Y	N	N	Y	Y	4
Eugster-Buesch et al 2012[23]	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Fedrizzi et al 2013[24]	Y	N	Y	N	N	N	Y	N	Y	N	4
Facchin et al 2011[25]	Y	N	Y	N	N	N	Y	N	Y	N	4
Geerdink et al 2013[26]	Y	N	Y	N	N	N	Y	Y	Y	Y	6
Gelkop et al 2015[27]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Gordon et al 2011[28]	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Hung et al 2011[29]	Y	N	N	N	N	Y	Y	N	Y	Y	5
Rostami et al 2012[30]	Y	N	Y	N	N	Y	Y	Y	Y	Y	7
Sakzewski et al 2011a[31]	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Sakzewski et al 2011b[32]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Sakzewski et al 2011c[33]	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Sakzewski et al 2011d[34]	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Sakzewski et al 2012[35]	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Smania et al 2009[36]	Y	N	N	N	N	Y	N	N	Y	Y	4
Sung et al 2005[37]	Y	N	Y	N	N	N	N	N	Y	Y	4
Taub et al 2004[38]	Y	N	Y	N	N	Y	N	N	Y	Y	5
Taub et al 2011[39]	Y	N	Y	N	N	N	Y	N	Y	Y	5
Wallen et al 2011[40]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Xu et al 2012[41]	Y	N	Y	N	N	Y	N	N	Y	Y	5
Yu et al 2012[42]	Y	N	Y	N	N	N	N	N	N	Y	3

Y = yes, N = no, PEDro = Physiotherapy Evidence Database.
PEDro scores extracted from website www.pedro.org.au

intervention from five comparisons with a PEDro score of 6.8 and 218 participants, using a random-effects model. Two studies were unable to be included in the analysis because they had no post-intervention data[41] or missing data.[14] CIMT did not increase activity (SMD 0.05, 95% CI –0.21 to 0.32, I^2 = 0%) compared with the same dose of upper limb therapy (Figure 6). See Figure 7 on the eAddenda for the detailed forest plot.

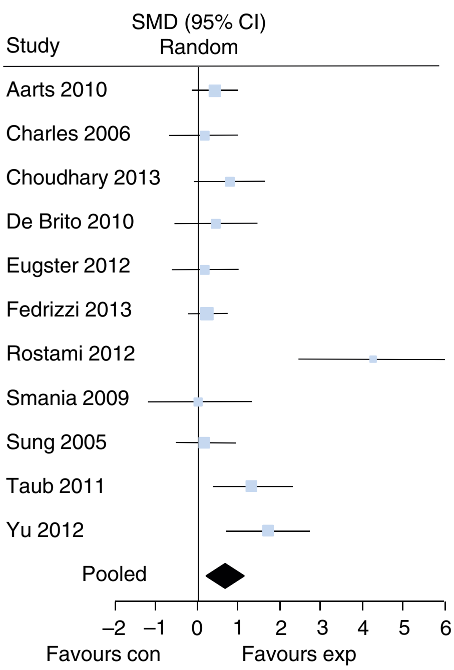

Figure 2. SMD (95% CI) of effect of constraint-induced movement therapy compared with no/sham intervention on upper limb activity immediately after intervention by pooling data from 11 trials (n = 302) using a random-effects model (I^2 = 65%).

Participation

The immediate effect of CIMT compared with the same dose of upper limb therapy on participation was examined by pooling data after intervention from four comparisons with a PEDro score of 7.5 and 146 participants, using a random-effect model. Three studies were unable to be included in the analysis because they had no appropriate participation measure.[14,24,41] CIMT did not increase participation (SMD –0.02, 95% CI –0.34 to 0.31, I^2 = 0%) compared with the same dose of upper limb therapy (Figure 8). See Figure 9 on the eAddenda for the detailed forest plot.

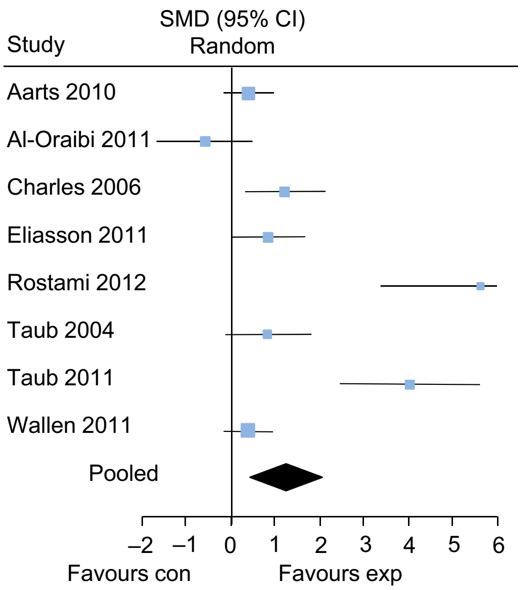

Figure 4. SMD (95% CI) of effect of constraint-induced movement therapy with no intervention on upper limb participation immediately after intervention by pooling data from eight trials (n = 215) using a random-effects model (I^2 = 84%).

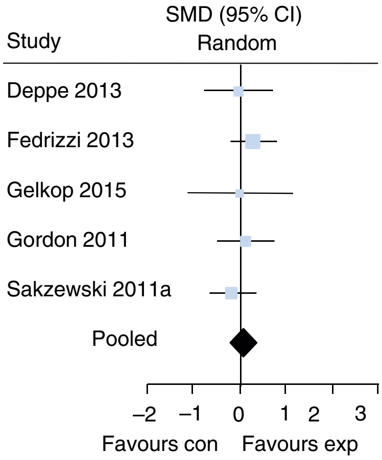

Figure 6. SMD (95% CI) of effect of constraint-induced movement therapy with same dose of upper limb therapy on upper limb activity immediately after intervention by pooling data from five trials (n = 218) using a random-effect model (I^2 = 0%).

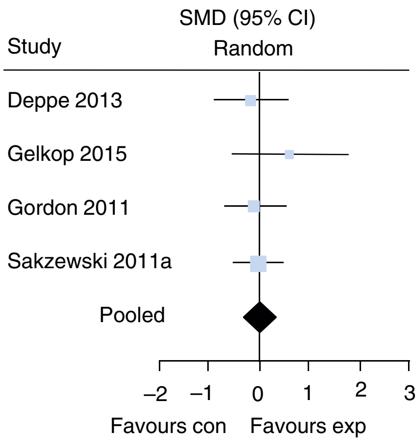

Figure 8. SMD (95% CI) of effect of constraint-induced movement therapy with same dose of upper limb therapy on upper limb participation immediately after intervention by pooling data from four trials (n = 146) using a random-effects model (I^2 = 0%).

Relation between the effect and duration of constraint-induced movement therapy and age for activity and participation

There was no significant relation between duration of CIMT (total duration of CIMT) and effect of CIMT on activity (r = –0.25, p = 0.46) or participation (r = –0.10, p = 0.81). Neither was there a significant relation between age and effect of CIMT on activity (r = 0.37, p = 0.26) or participation (r = 0.58, p = 0.13).

Discussion

This systematic review found that CIMT had a beneficial effect compared with no/sham intervention for children with hemiplegic cerebral palsy. Furthermore, the effect was beneficial in terms of both activity and participation, suggesting that the improved upper limb activity carried over into what the children actually did in real life with their upper limb. On the other hand, when CIMT was compared with the same dose of upper limb therapy, there was little effect on activity or participation. Neither duration of CIMT nor age influenced the size of the effect of CIMT.

This review was based on randomised trials of reasonable to good quality. Given that 8 was the likely maximum PEDro score achievable, because it is not possible to blind the therapists or participants during complex interventions such as CIMT, the mean PEDro score of 5.8 for the papers included in this review suggested that the findings were reasonably credible. Although CIMT was effective, it was no more effective than the same dose of upper limb therapy without restraint. This suggests that the mechanism of the effect is the dose of practice undertaken, rather than the type of practice (ie, CIMT). In the studies where CIMT was compared with no/sham intervention, children in the CIMT group were restrained for an average of 5 hours/day and they spent just over 50% of this period engaged in supervised practice. In the studies where CIMT was compared with the same dose of upper limb practice without restraint, children in the CIMT group were restrained for an average of 4 hours/day and they spent 100% of this period engaged in supervised practice, sometimes carrying out extra unrestrained practice.

The findings from this review are supported by the findings of the only other systematic review to specifically examine CIMT where a meta-analysis was performed.[5] In this previous review, when all studies were pooled, CIMT provided a moderate beneficial effect of 0.55. When only the studies of CIMT against a non-equivalent dose intervention were analysed, the estimated effect size was 0.84, which was similar to our estimated effect size of 0.63 for activity and 1.21 for participation. On the other hand, when only the studies of CIMT against an equivalent dose of practice were analysed, the estimated effect size was 0.37, which is larger than our estimated effect size of 0.05 for activity and –0.02 for participation. This may be because Chen et al[5] included seven studies in their analysis that were not considered dose equivalent by our definition.[12,13,26,36,40,43,44] Since the control groups in these studies received less practice than the CIMT groups, this may explain why the effect that Chen et al found was larger than in our review. In a general review, Sazewski et al[45] also came to the conclusion that the mechanism of the effect was the dose of practice undertaken, rather than the type of practice.

There were some limitations to this review. First, there were some missing data, so not all the included studies are represented in the final pooled estimate, although this only amounts to 15% of the total data. Second, although a large number of studies were represented, most were of a small sample size. On average, there were 33 participants per study included in the meta-analyses, leaving the review vulnerable to small trial bias. Third, there were high levels of statistical heterogeneity ($I^2 > 60\%$) in the analyses of CIMT against no/sham intervention, and the source of this heterogeneity was not obvious.

This review generates several implications for clinical practice with children with hemiplegic cerebral palsy. CIMT is an effective way to improve upper limb function at the activity level and this can be expected to carry over into participation in real life. Given that the same dose of practice without restraint is likely to result in the same outcome, it seems that as long as large amounts of practice are carried out, regardless of whether that is with restraint (unimanual) or without restraint (bimanual and unimanual), improvement will occur. In the studies of CIMT against no/sham intervention, children were supervised to practise using their upper limb for an average of 2.5 hours a day, with a further 2.5 hours of restraint forcing more practice. Ultimately, the way in which practice is achieved may be best chosen by a combination of the child and the parents, as well as the therapists. For example, it may be easier to 'force' practice over long periods of time at home using CIMT than practising without restraint under the supervision of parents.

What is already known on this topic: Children with hemiplegia due to cerebral palsy may have impairments due to damage to an immature brain, indirectly from compensatory movements or from learned disuse. Such impairments may result in limitations in activity requiring rehabilitation throughout life.
What this study adds: Constraint-induced movement therapy is an effective way to improve upper limb function, but as long as large amounts of practice are carried out, regardless of whether that is achieved with or without restraint, this benefit can be expected.

eAddenda: Figures 3, 5, 7 and 9; Appendices 1 and 2, can found at: doi:10.1016/j.jphys.2016.05.013

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