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The State of the Evidence for Intensive Upper Limb Therapy Approaches for Children With Unilateral Cerebral Palsy

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Abstract

Children with unilateral cerebral palsy experience difficulties with unimanual and bimanual upper limb function, impacting independence in daily life. Targeted upper limb therapies such as constraint-induced movement therapy, bimanual training, and combined approaches have emerged in the last decade. This article reviews the scientific rationale underpinning these treatments and current evidence to improve upper limb outcomes and goal attainment. Intensive models of therapy achieved modest to strong effects to improve upper limb function compared to usual care. Dose-matched comparisons of bimanual and unimanual training demonstrated similar gains in upper limb outcomes. The optimum timing, dose and impact of repeat episodes of intensive upper limb therapies require further investigation. Characteristics of children who achieve clinically meaningful outcomes remain unclear. Key components of intervention include collaborative goal setting with families and intensive repetitive, incrementally challenging, task practice. Choice of treatment approach should be governed by child/family goals and preferences, individual, and contextual factors.

Keywords

constraint-induced movement therapy, hand arm–intensive bimanual training, hemiplegia, efficacy, review

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In all aspects of daily life, we perform activities that require the use of 2 hands. Children with unilateral cerebral palsy, at all ages, who experience reduced function in 1 hand will continuously experience problems with day-to-day occupational performance, impacting broader participation in life situations.[1] These children are usually integrated in society making them more likely to compare themselves with their typically developing peers. Children with unilateral cerebral palsy have various degree of decreased upper limb function, from slight clumsiness to almost no ability to use the hand. Weakness and sensation are commonly impaired which is closely related to severity of hand function.[2,3]

Traditional neurodevelopmental models of treatment have focused on reducing tone and normalizing upper limb movement patterns, thereby reducing functional limitations.[4] Evidence for these approaches to ameliorate upper limb activity limitations is weak.[5] In recent years, there has been a greater focus on improving coordination between hands and use of the impaired upper limb as a helping hand or support. Advances in understanding motor learning has framed intervention to focus on the persons' self-initiated voluntary movements and problem solving in daily activities, recognizing the importance of repetition of activities at the "just right challenge" to yield sustained ability in new tasks.[6] This represents a theoretical shift from targeting impairments at a Body Structure and Function Level of the International Classification of Functioning, Disability and Health to activity level change.

Constraint-induced movement therapy and intensive bimanual training are 2 contemporary motor learning–based approaches directly focusing on upper limb function in children with unilateral cerebral palsy. The theoretical foundations of constraint-induced movement therapy can be traced back nearly a century with behavioral studies of monkeys with pyramidal tract lesions inducing

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hemiplegia, whereby it was suggested that the motor impairments were largely due to disuse of the paretic upper limb.[7,8] Recovery of function was observed after immobilization of the contralateral upper limb. A similar phenomenon was observed in experimentally induced unilaterally deafferented monkeys by Taub and colleagues.[9] Taub established the "learned non-use" hypothesis, whereby deafferentation led to inactivity and created disincentive to use the limb.[10] These results led to a testable hypothesis in humans. Following a case study more than 30 years ago,[11] Wolf and colleagues[12] were the first to study the application of this "forced use" approach in human adults following stroke. Subsequently, a more active approach combined structured practice utilizing shaping to the restraint, which was termed "constraint-induced movement therapy."[13,14] One of the first multisite physical rehabilitation randomized control trials, the EXCITE trial,[15] and subsequent Cochrane review,[16] have since shown constraint-induced movement therapy to result in significant and lasting improvements of upper limb function in a portion of adults with hemiparetic stroke.

The signature form of constraint-induced movement therapy developed for adults is an intensive physical intervention that, in its original form, is not child-friendly and is potentially invasive. Specifically, it requires restraining the less impaired upper limb 90% of waking hours for 14 consecutive days, with 6 hours of intensive programming for 10 of 14 days. During this time, the impaired upper limb is used in activities characterized by 2 types of practice: repetitive task practice and shaping.[17] Both types of practice involve adult-oriented, monotonous tasks (eg, screwing/unscrewing bolts, adult-appropriate functional tasks) that would unlikely hold a child's interest for long. Adult constraint-induced movement therapy is focused on overcoming "learned non-use." Children likely have "developmental non-use," whereby they can be asked to use their limbs unimanually for the first time. This increases focus on their impairments, and the likely high rate of initial failures at performing these tasks may cause frustration and potentially affect self-esteem. Unlike adults with stroke, young children may not be motivated to improve function. Finally, using a restraint outside structured practice (ie, forced use) could result in additional frustration and result in increased family burden and safety concerns. Thus, procedures associated with constraint-induced movement therapy in adults may not be appropriate for children.

The use of physical restraints of the less affected upper limb had previously been described in children with unilateral cerebral palsy,[18,19] and the first formalized proof of principle case study of constraint-induced movement therapy was reported more than a dozen years ago.[20] In this application, a cotton sling (rather than a cast, often used in adults) was used to restrain the less-impaired upper limb 6 hours/d for 10 days, with training administered by a physical therapist in the home environment. Subsequently, pediatric constraint-induced movement therapy has been applied in day camp settings to maximize efficient delivery, social participation, modeling, and enjoyment[21-26] or used home-based models whereby younger children were engaged in preschool settings for just 2 hours/d.[27,28]

The State of the Evidence for Intensive Upper Limb Therapy Approaches

Since the first published randomized controlled trial of constraint-induced movement therapy with children with unilateral cerebral palsy in 2004,[29] there has been a substantial increase in the evidence for this intensive treatment approach. Efficacy of bimanual training (targeting coordinated use of 2 hands together) and models combining constraint-induced movement therapy and bimanual therapy (hybrid therapy) has been investigated to a lesser extent. Twenty-four randomized controlled trials have been published for constraint-induced movement therapy (19 studies; n = 662); hand arm bimanual intensive training (1 study; n = 20); and hybrid therapy (3 studies; n = 116) (Table 1). Eight studies of constraint-induced movement therapy,[28,29,32,34,36,38,40,47,52,54] 1 hand arm bimanual intensive training,[33] and 2 of hybrid therapy[35,42] have compared intervention to a control or usual care group receiving substantially less therapy. Six studies of constraint-induced movement therapy[24,25,40,45,47] and 2 of hybrid therapy[26,53] have compared intervention to an equivalent dose of bimanual therapy or usual care.

Constraint-Induced Movement Therapy

Population. Studies of constraint-induced movement therapy have predominantly targeted children with spastic unilateral cerebral palsy, with the exception of 1 study that included children with quadriplegia.[37] For inclusion in constraint-induced movement therapy, children generally required a degree of active wrist extension and grasping ability on the impaired upper limb.[25,32,34,38,45,47-49,52-54] A smaller number of trials have included children with all degrees of severity of hand function.[27-29,42,43,55] The rationale for limiting inclusion of children based on severity of hand function (ie, no ability to grasp) was to minimize potential frustration, but also related to a possible restricted choice of age-appropriate activities. Despite these concerns, there has been some suggestion that children with minimal hand function can achieve large improvements in upper limb skills following constraint-induced movement therapy.[27]

Constraint-induced movement therapy has been used mainly with children aged between 2 and 16 years. Only 1 randomized controlled trial has included infants less than 1 year of age[29] and a number have involved adolescents.[25,27,33,45,47,51,53,54] Results from animal and infant studies suggest that optimum outcomes of upper limb therapies could occur with earlier onset of intervention in infancy.[56] The use of constraint on the unimpaired limb may assist in balancing hemispheric activity. Inactivation of the unimpaired contralesional corticospinal tract (via use of constraint) while training on the impaired limb competitively advantages the ipsilesional corticospinal tract. This may limit the competitive displacement of intact contralateral corticospinal tract projections in the injured hemisphere by more active corticospinal tract projections in the uninjured hemisphere.[57] It is unknown, however, whether

Table 1. Summary of Studies of Forced Use, Constraint Induced Movement Therapy, HABIT and Hybrid Models of Intensive Upper Limb Activity-Based Therapy.

Author, year	Design	Participants	Age	Intervention	N	Comparison control	N	Outcomes
Willis et al, 2002[30]	RCT	Hemi (stroke, cerebral malformation, trauma)	1 to 8 y	Forced use, 24 h/d, 7 d/wk, 4 wk Restraint: short arm cast Training: maintained regular therapy	12	Maintained regular therapy	13	PDMS, WeeFIM self-care
Taub et al, 2004[29]	RCT	Hemi CP	7 mo to 8 y	CIMT Direct therapy: 6 h/d, 7 d/wk, 3 wk Indirect therapy: NR Restraint: long arm bivalve cast Context: individual, clinic based Training: repetitive task practice, shaping reach, grasp, weight bearing, manipulation, ADLs	9	Regular therapy Direct therapy: 1 session/wk (minimum) to 4 sessions/wk (maximum) Indirect therapy: NR	9	PMAL, EBS, TAUT
Sung et al, 2005[31]	RCT	Hemi CP	≤8 y	Forced use + regular therapy Restraint: short arm cast Direct therapy: 0.5 h/d, 2 d/wk, 6 wk stretch, reach, grasp, manipulate, functional training	18	Regular therapy: 0.5 h/d, 2/wk, 6 wk	13	EDPT, Box and Block
Charles et al, 2006[32]	SB RCT	Hemi CP	4 to 8 y	mCIMT Direct therapy: 6 h/d, 5 d/wk, 2 wk Indirect therapy: 1 h/d during CIMT, 2 h/d, for 6 months post Restraint: sling Context: clinic groups 2-4 Training: movement training, play, functional therapy using shaping, repetitive task practice	11	Control: previous therapy levels	11	Jebsen, BOTMP-8 CFUS
Gordon et al, 2007[33]	SB RCT cross over	Hemi CP	3 to 15 y	HABIT Direct therapy: 6 h/d, 5 d/wk, 2 wk Indirect therapy: 1 h/d during HABIT, 2 h/d for 6 months post Context: clinic groups of 4 Training: bilateral fine motor, manipulative gross motor activities using whole and part task practice and shaping	10	Control: previous therapy levels	10	Jebsen, AHA, BOTMP (6 bim items), CFUS
Smania et al, 2009[34]	RCT cross over	Hemi CP	1 to 9 y	mCIMT Direct therapy: 1 h/d, 2 d/wk, 5 wk Indirect therapy: mitt worn 8 h/d, 7 d/wk, 5 wk Restraint: mitt Context: individual, clinic based Training: repetitive practice, play	5	PT Direct therapy: 1 h/d, 2 d/wk, 5 wk Context: individual, clinic based Training: repetitive practice, play	5	Use Test, Function Test

(continued)

Table 1. (continued)

Author, year	Design	Participants	Age	Intervention	N	Comparison control	N	Outcomes
Brandao et al, 2010[35]	SB RCT	Hemi CP	4 to 8 y	mCIMT and BIM Direct therapy: 3 h/d, 5 d/wk, 2 wk CIMT then BIM 0.75 h/d, 3 d/wk, 1 wk Indirect therapy: Immobilization during waking hours for 10 h/d Restraint: resting splint and sling Context: individual Training: shaping of fine motor, ADLs	8	Regular therapy Direct therapy: 0.75 h/d, 1 d/wk, 3 wk: bimanual activities, sensory stimulation	8	Jebsen, PEDI,
Aarts et al, 2010[26]	SB RCT	Hemi CP	30 mo to 8 y	mCIMT-BiT 3 h/d, 3 d/wk, 6 wk mCIMT then 3 h/d, 3 d/wk, 2 wk BIM: Restraint: sling Context: rehab center, groups of 6 Training: mCIMT shaping and repetitive task practice, bimanual training goal-directed, ADLs, pirate themed	28	Regular therapy 1.5 h/wk, 2 d/wk, 8 wk Context: individual, rehab center Training: stretch, weight bearing, bimanual therapy	24	ABILHAND-Kids, MelbA, AHA, COPM, GAS
Al-Oraibi et al, 2010[36]	SB RCT	Hemi CP	22 to 105 mo	mCIMT Direct therapy: 1 d/wk, 8 wk Indirect therapy: 2 h/d, 6 d/wk, 8 wk Restraint: mitt Context: individual, clinic Training: repetitive practice, play	7	NDT 1 h/wk, 2 d/wk, 5 wk Context: individual, home based Training: weight bearing, facilitation arm movement	7	AHA
Lin et al, 2011[37]	SB RCT	Hemi CP (n = 11) Quad CP (n = 10)	4 to 9 y	mCIMT Direct therapy: 4 h/d, 2 d/wk, 4 wk Indirect therapy: bandage worn 4 h/d, 5 d/wk, 4 wk Restraint: elastic bandage Context: individual, home based Training: shaping and repetitive task practice	10	Therapy Direct therapy: 4 h/d, 2 d/wk, 4 wk Indirect therapy: bandage worn 4 h/d, 5 d/wk, 4 wk Context: individual, home based Training: functional activities, NDT, motor learning	11	BOTMP-8, PDMS-G and V, PMAL, CFUS
Sakzewski et al, 2011[25]	SB RCT	Hemi CP	5 to 16 y	mCIMT Direct therapy: 6 h/d, 5 d/wk, 2 wk Indirect therapy: Nil Restraint: mitt Context: community groups 8-13 Training: repetitive whole task practice, circus themed	32	BIM training Direct therapy: 6 h/d, 5 d/wk, 2 wk Indirect therapy: Nil Context: community groups 8-13 Training: repetitive bimanual activities, circus themed	31	MelbA, AHA, Jebsen, COPM, CAPE, SFA, LIFE-H, CPQOL-Child
Wallen et al, 2011[38]	SB RCT	Hemi CP	19 mo to 7 y	mCIMT Direct therapy: 1 h/d, 1 d/wk, 8 wk Indirect therapy: 2 h/d, 7 d/wk, 8 wk Restraint: mitt Context: home, school, preschool Training: goal-directed, ADL, repetitive movements in play	25	Standard OT Direct therapy: 1 h/d, 1 d/wk, 8 wk Indirect therapy: 0.3 h/d, Context: home, school, preschool Training: goal-directed, stretch, splint, motor training, environmental modification	25	PMAL, AHA, COPM, GAS, PMAL

(continued)

Table 1. (continued)

Author, year	Design	Participants	Age	Intervention	N	Comparison control	N	Outcomes
Gordon et al, 2011,[24] and Brandao et al, 2012[39]	SB RCT	Hemi CP	3 to 10 y	mCIMT Direct therapy: 6 h/d, 5 d/wk, 3 wk Indirect therapy: 1 h/d during and 2 h/d for 6 mo postintervention Restraint: sling Context: day camp groups 2-5 Training: whole and part task practice of unimanual functional activities and play	21	HABIT Direct therapy: 6 h/d, 5 d/wk, 3 wk Indirect therapy: 1 h/d during and 2 h/d for 6 mo postintervention Context: day camp groups 2-5 Training: goal-directed, symmetrical and asymmetrical fine and gross motor bimanual activities	21	Jebsen, QUEST- G and DM, AHA, GAS, COPM, PEDI, accelerometry
Facchin et al, 2011,[40] and Fedrizzi et al, 2012[41]	Cluster RCT	Hemi CP	2 to 8 y	mCIMT Direct therapy: 3 h/d, 3 d/wk, 10 wk Indirect therapy: 3 h/d, 4 d/wk, 10 wk Restraint: glove Context: individual, rehab center Training: perceptual motor, reach, grasp, hold and manipulation, postural and balance, ADLs	39	(*a*) BIM training: Direct therapy: 3 h/d, 3 d/wk, 10 wk Indirect therapy: 3 h/d, 4 d/wk, 10 wk Context: individual, rehab center Training: bimanual play and ADLs (*b*) Standard Care Direct therapy: 1 h/d, 1-2 d/wk, 10 wk	33 33	QUEST-T and G, Besta, CBC
Eliasson et al, 2011[28]	SB RCT cross over	Hemi CP	1.5 to 5 y	Eco mCIMT 2 h/d, 7 d/wk, 8 wk with 1/wk supervision by therapist Restraint: glove Context: individual, home, or community based Training: based on AHA assessment, repetitive whole task practice.	12	Usual care: PT 2/m and OT 1/m Training: consultative, functional activity-based training	13	AHA
Taub et al, 2011[42]	RCT cross over	Hemi CP	2 to 6 y	CIMT Direct therapy: 6 h/d, 7 d/wk, 18 d (13 d CIMT, 2 d BIM) Indirect therapy: NR Restraint: long arm cast Context: individual, home based Training: repetitive task practice, shaping in play and ADLs	10	Usual care Direct therapy: 1-2 h/d, 1 d/wk Indirect therapy: NR	10	PMAL-R, INMAP, PAFT
Case-Smith et al, 2013,[43] and Deluca et al, 2012[44]	SB RCT	Hemi CP	3 to 6 y	CIMT Direct therapy: 3 h/d, 5d/wk, 3 wk Indirect therapy: NR Restraint: full arm cast Context: individual, home or clinic based Training: 18 d CIMT, 3 d BIM, shaping new skills, block and random practice	9	CIMT Direct therapy: 6 h/d, 5 d/wk, 3 wk Indirect therapy: NR Restraint: full arm cast Context: individual, home, or clinic based Training: 18 d CIMT, 3 d BIM, shaping new skills or movements	9	QUEST-G and DM, PMAL, SHUEE, AHA

(continued)

Table 1. (continued)

Author, year	Design	Participants	Age	Intervention	N	Comparison control	N	Outcomes
Xu et al, 2012[45]	SB RCT	Hemi CP	2 to 14 y	mCIMT and FES Direct therapy: 3 h/d, 5 d/wk, 2 wk Indirect therapy: 1 h/d during and 2 h/d for 6 mo posttherapy Restraint: splint Context: hospital groups 2-4 Training: structured play and functional activities; FES: 50 hz pulse rate, 30 pulse/s, 300 us amplitude, 12 s on time, 12 s off time	22	(*a*) mCIMT Direct therapy: 3 h/d, 5 d/wk, 2 wk Indirect therapy: 1 h/d during and 2 h/d for 6 mo post therapy Restraint: splint Context: hospital groups 2-4 Training: structured play and functional activities (*b*) OT Direct therapy: 3 h/d, 5 d/wk, 2 wk Indirect therapy: 1 h/d during and 2 h/d for 6 mo post therapy Training: NDT, task specific training, strength, stretch, goal directed	23 23	9-hole peg
Hsin et al, 2012[46] and Chen et al, 2013[47]	SB RCT	Hemi CP	6 to 12 y	mCIMT (home) 3.5-4 h/d, 2 d/wk, 4 wk Restraint: elastic bandage and glove Context: individual, home based Training: shaping, repetitive task practice	24	Standard care 3.5-4 h/d, 2 d/wk, 4 wk Context: individual, home based Training: positioning, strengthening, task training based on NDT, task oriented approaches	23	PDMS-G and V, BOTMP-8, PMAL-R,
Rostami et al, 2012a[48]	SB RCT	Hemi CP	74 mo (mean)	mCIMT (home) Direct therapy: 1.5 h/d, 3 d/wk, 3 wk Indirect therapy: 1 h/d, 7 d/wk, 3 wk Restraint: splint Context: individual, home based Training: reach, grasp, manipulate, fine motor, ADL	7	mCIMT (clinic) Direct therapy: 1.5 h/d, 2 d/wk, 3 wk Indirect therapy: 1 h/d, 7 d/wk, 3 wk Restraint: splint Context: individual, clinic based Training: as per intervention group	7	PMAL, BOTMP-5 and 8
Rostami et al, 2012b[49]	SB RCT	Hemi CP	6 to 11 y	mCIMT Direct therapy: 1.5 h/d, 3 d/wk, 4 wk and 0.5 h/d, 2 d/wk, 4 wk regular therapy Indirect therapy: splint worn 5 h/d, 7 d/wk, 4 wk Context: individual, research center Training: a/a	8	(*a*) mCIMT and VR Direct therapy: 1.5 h/d, 3 d/wk, 4 wk and 0.5 h/d, 2 d/wk, 4 wk regular therapy Indirect therapy: splint worn 5 h/d, 7 d/wk, 4 wk Context: individual, research center Training: E-Link Evaluation and Exercise System: active, active resistive grip and pinch, ROM exercises (*b*) VR: 1.5 h/d, 3/wk, 4 wk and 0.5 h/d, 2 d/wk, 4 wk regular therapy (*c*) Control: 0.5 h/d, 2 d/wk, 4 wk Training: NDT, stretching, ROM	8 8 8	PMAL, BOTMP-8

(continued)

Table 1. (continued)

Author, year	Design	Participants	Age	Intervention	N	Comparison control	N	Outcomes
Choudhary et al, 2013[50]	SB RCT	Hemi CP	3 to 8 y	mCIMT Direct therapy: 2 h/d, 2-3 d/wk, 4 wk Indirect therapy: 1 h/d 2-3 d/wk and 2 h/d 4-5 d/wk Restraint: arm sling Context: groups of 4, outpatient department Training: repetitive task practice, shaping	16	Regular therapy Indirect therapy: 0.3 h/d, 5 d/wk, 4 wk Context: individual, home based Training: stretching, strengthening, bilateral hand activities, ADLs	15	QUEST-T, G, DM, WB, PE, 9 hole peg
Eugster-Buesch et al, 2012[51]	SB RCT	Hemi CP	6 to 16 y	Forced use, 6 h/d, 5 d/wk, 2 wk Restraint: removable cast Direct therapy: 1 session/wk Indirect therapy: 2 h/d	12	Control: regular therapy 1 session/wk, 2 wk	11	Melb A
Hoare et al, 2013[52]	SB RCT	Hemi CP	18 mo to 6 y	BoNT-A and CIMT Direct therapy: 1 h/d, 2 d/wk, 8 wk Indirect therapy: 3 h/d, 7 d/wk, 8 wk Restraint: glove Context: individual, clinic based Training: Repetitive task practice of movement and skills	17	BoNT-A and Bim OT Direct therapy: 1 h/d, 2 d/wk, 8 wk Indirect therapy: time not specified Context: individual, clinic based Training: motor learning and cognitive based on AHA hierarchy	17	QUEST-G and DM, AHA, COPM, PEDI
Deppe et al, 2013[53]	SB RCT	Hemi CP and ABI	3 to 12 y	mCIMT 4 h/d, 5 d/wk, 3 wk and then BIM 4 h/d, 5 d/wk, 1 wk Restraint: elastic bandage Context: individual, inpatient rehabilitation Training: sensory, mobilization, reach, grasp, release, stabilization, manipulation using shaping.	26	Bimanual training 4 h/d, 5 d/wk, 4 wk Context: individual, inpatient rehabilitation Training: sensory, mobilization and activity and functional ADL and play	21	Melb A AHA PEDI SC
Klingels et al, 2013[54]	SB RCT	Hemi CP	4 to 12 y	mCIMT Direct therapy: usual care Indirect therapy: 1 h/d, 5 d/wk, 10 wk Restraint: rigid hand splint Context: individual home Training: structured skills practice	26	mCIMT+ intensive strength training Direct therapy: usual care + 0.75 h/d, 3 d/wk, 10 wk Indirect therapy: 1 h/d, 5 d/wk, 10 wk Context: individual, home and clinic Training: structured skills practice, unimanual and bimanual, strength training 3 sets of 10 reps wrist extensors and supinators	25	AHA, Melb A, Jebsen, ABILHAND kids

Abbreviations: ABI, acquired brain injury; AHA, Assisting Hand Assessment; ADL, activities of daily living; BIM, bimanual training; BoNT-A, botulinum toxin A; BOTMP, Bruininks Oseretsky Test of Motor Proficiency (subtest 8 or 5 as indicated); CAPE, Children's Assessment of Participation and Enjoyment; CBC, Child Behavior Checklist; CFUS, Caregiver Functional Use Survey; COPM; Canadian Occupational Performance Measure; CP, cerebral palsy; CPQOL, Cerebral Palsy Quality of Life; EBS, Emerging Behavior Scale; EDPT, Erhardt Developmental Prehension Test; GAS, Goal Attainment Scale; HABIT, Hand Arm Bimanual Intensive Training; Hemi, hemiplegia; INMAP, Inventory of New Motor Activities and Programs Instrument; mCIMT, modified-constraint induced movement therapy; Melb A, Melbourne Assessment; NDT, neurodevelopmental treatment; NR, not reported; OT, occupational therapy; PAFT, Pediatric Arm Function Test; PDMS; Peabody Developmental Motor Scales (G, grasp domain; V, visual motor integration domain); PEDI, Pediatric Evaluation of Disability Inventory (SC, Self-Care subtest); PMAL, Pediatric Motor Activity Log (R, revised version); quad, quadriplegia; QUEST; Quality of Upper Extremity Skills Test (T, total score; G, grasp; DM, dissociated movements WB, weight bearing; PE, protective extension); RCT, randomized controlled trial; ROM, range of motion; SB, single blind; SFA; School Function Assessment; SHUEE, Shriner Hospital Upper Extremity Evaluation; TAUT, Toddler Arm Use Test.

long periods of restraint during infancy can impact normal development of the unimpaired limb; therefore, caution is warranted and less intensive models of constraint-induced movement therapy should be considered. Although this research suggests that intervention should commence earlier than what has currently occurred, it is important to note that older children have demonstrated significant and clinically meaningful gains following constraint-induced movement therapy.[24,25] In a direct comparison, older (aged 9-13 years) compared with younger (aged 4-8 years) children achieved similar gains following constraint-induced movement therapy.[58] Nevertheless, the optimum timing throughout child development that would be most amenable to constraint-induced movement therapy to improve upper limb function remains unclear.

Methods of restraint. There has been significant variation across studies according to the model of therapy (length, frequency, and duration), type of restraint used, and differing contexts in which therapy was delivered. Signature constraint-induced movement therapy proposed by Taub used continuous wear of a cast,[29,42,44] whereas modifications to ensure a more "child friendly" approach have included use of individually constructed gloves or mitts,[25,27,28,34,36,38,52,55] slings,[24,32,50] splints,[35,54,45,48,49] or elastic bandages.[37,47] Use of a continuously worn cast completely restricts use of the impaired upper limb. Alternative forms of restraint, such as mitts or splints worn for specified hours throughout the waking day, changes the role of the unimpaired limb so that it becomes an assisting hand, allowing the impaired upper limb to act as the dominant hand. There is no clear evidence that one method of restraint is superior to another; therefore, choice needs to consider safety, comfort, family preferences, and the context in which therapy is delivered.

Intensity, dose, and context of intervention. Models of therapy delivery can broadly be categorized as short-length, high-duration or long-length, low-duration (distributed model). There has been considerable variation in both the total dose of therapy provided as well as the proportion of direct "hands on" intervention provided by therapists and indirect therapy via use of home/preschool programs. Short-length, high-duration therapy models have been carried out over a 2- to 4-week period, with frequency ranging from 2 to 7 sessions per week.[24,25,29,32,37,42,43,45,47,49,50] Session times (duration) ranged from 1.5 to 6 hours, with the total dose of direct "hands on" therapy varying between 18 and 126 hours. Accompanying home practice was required in most studies with the expected dose between 21 and 240 hours. Distributed models of intervention ranged from 5 to 10 weeks in length with between 1 and 3 sessions per week.[28,34,36,38,52,55] The dose of direct therapy ranged from 8 to 90 hours, with proportionally greater expectations for home practice (28-168 hours). To date, there has been no direct comparison of intensive versus distributed models of constraint-induced movement therapy.

Constraint-induced movement therapy has been provided on an individual basis or in groups (2-13 children). Groups have been used primarily with school-aged children. There is no indication that group-based intervention is less effective than individually tailored therapy; however, a number of the group-based programs used a child-to-therapist ratio of 1:1[24,45] or involved caregivers.[50] This can allow individualization of the program within the group context while drawing upon the benefits of a group such as peer modeling and support, relating to others with similar difficulties and social interaction. The context of therapy delivery has predominantly been in hospital or clinic settings.[24,29,32,34,36,40,45,49,50,52] Several studies have provided constraint-induced movement therapy using a more ecological approach embedding intervention in naturalistic home,[28,37,38,47,54,42] school,[38] or community leisure environments.[25] Findings of home and community delivered constraint-induced movement therapy have consistently demonstrated gains in upper limb function.[28,37,38,42,47,54] A direct comparison of home- versus center-based constraint-induced movement therapy ($n = 14$) demonstrated no immediate differences between the 2 therapy contexts.[48] There was some suggestion, however, of greater gains by the home base group at 3 months postintervention,[48] supporting the notion of generalization of skills. Despite the large variation in models of therapy delivery, findings suggest that constraint-induced movement therapy is superior to usual care to improve spontaneous use,[29,42,49] efficiency and quality of movement of the impaired upper limb,[32,49,55] and bimanual hand use.[27,28,36]

Acceptability and feasibility. Despite evidence suggesting that constraint-induced movement therapy is an effective treatment, there is limited knowledge about the feasibility of providing constraint-induced movement therapy in different environmental contexts or to what extent the restraint may or may not negatively impact the child's emotional and psychological well-being. Acceptability of constraint-induced movement therapy from a child's perspective could depend on both the type and length of time the restraint is used as well as how the training is organized. Young children in particular will not cooperate if the training is not fun and engaging. Therapy must provide the "just right" challenge. If it is too difficult, the child may not persist and if it is too easy, they are likely to find it boring and lose interest. The cooperation of children and the acceptance of the restraint are therefore highly dependent on the therapist's skills to engage and appropriately target therapy to the child's abilities. The type of restraint could additionally impact acceptability. Most commonly, higher-quality studies have used *removable devices* such as a sling, mitt, splint, or glove, whereas there are several studies using *nonremovable devices* such as casting.[24,38,52,59,60] A nonremovable cast is typically worn at all times during the day, resulting not only in much greater intensity of unstructured training but also a heavier burden on the child.[29,42,44] Removable restraints have predominantly been applied during the structured skills training period. There is currently no evidence to suggest use of *nonremovable devices* compared with *removable devices* achieves superior results, and issues around compliance when using different types of constraints requires further investigation.

Few adverse events have been reported for nonremovable restraints.[42,43] The average participant drop-out rate for constraint-induced movement therapy and comparison groups across 21 published randomized controlled trials of constraint-induced movement therapy in children is 9%.[60] Tolerance of wearing the restraint has rarely been investigated from a child perspective. In a number of studies, parents have reported that a fabric mitt, custom made for comfort and fit, was well tolerated and emphasized that a long splint was less acceptable.[61,62] School-aged children attending a day camp circus themed constraint-induced movement therapy group highlighted the frustration and discomfort of wearing a restraint. However, these barriers were moderated with supports that enabled, engaged, and motivated participation (eg, fun experiences of camp, circus, positive connections with others).[63] Therefore, the rate of drop-outs can depend on the type of restraint used but also other child and environmental factors.

Constraint-induced movement therapy has been provided in various environments using different models of therapy provision. The development of different models appears to reflect practical issues and the social and economic systems in different countries. For example, day camps for school-aged children are often run during school holidays. For families that are at a distance to the therapy setting or where both parents work, the training can occur at home or in school. Findings suggest that intervention can be carried out effectively by family members, teachers, or students as long as they receive training and supervision from therapists.[24,28,38] When the training is provided by others in a nonstandardized environment, the expected dosage of training has not been fulfilled, and it is unclear whether children complete the intervention as intended. However, it appears that reported results are similar to more controlled intervention programs.

A major consideration for implementing constraint-induced movement therapy in clinical practice relates to the cost benefit of this potentially resource-intensive intervention. Home-based or daily environmental programs are possibly more cost effective than hospital-based programs as they provide less therapy-guided sessions although still requiring planning and education. Education of the constraint-induced movement therapy-provider is important and supervision from therapists needs to occur to ensure the provider remains motivated and the training occurs as intended. Resources such as handbooks and manuals for the implementation of constraint-induced movement therapy programs are required.

Bimanual Therapy and Hybrid Models

Despite showing strong levels of efficacy,[5,64] constraint-induced movement therapy has some limitations even with the modifications described earlier. Most important, constraint-induced movement therapy focuses only on training unimanual dexterity, which does not greatly influence functional independence and quality of life because they have a well-functioning (dominant) hand.[1] Children with unilateral cerebral palsy have impairments in spatial and temporal coordination of the 2 hands,[65-68] as well as global impairments in motor planning.[69] Constraint therapies cannot address these problems without a transfer protocol,[70] and thus generalization of training cannot apply. These limitations drove the modification of bimanual training, already used as one tool by occupational/physical therapists, such that it was delivered with the same intensity as constraint-induced movement therapy. One highly structured form of bimanual training, HABIT (Hand Arm Bimanual Intensive Training),[24,33,71] aimed to improve the amount and quality of impaired upper limb use during bimanual tasks. Hand Arm Bimanual Intensive Training retained the intensive structured practice of constraint-induced movement therapy but engaged the child in bimanual activities rather than relying on use of a restraint to encourage use of the more affected upper limb. Children's goals and parental involvement were integral and consistent with family-centered practice.[72] Functional activities requiring the use of 2 hands were used, with particular consideration of the role of the impaired upper limb (to stabilize by grip, manipulate, etc). Children were required to actively problem-solve in order to complete tasks. Initial findings from a small randomized controlled trial ($n = 20$) of Hand Arm Bimanual Intensive Training (60 hours of intervention) compared to usual care for children with unilateral cerebral palsy demonstrated improved bimanual performance, but limited gains in movement efficiency of the impaired upper limb.[33] Direct comparisons of bimanual therapy to an equal dose of constraint-induced movement therapy have demonstrated minimal differences between the 2 approaches to improve upper limb outcomes[24,25,55] that was confirmed in a recent systematic review and meta-analysis highlighting both interventions led to similar improvements in upper limb outcomes.[59] Two important caveats are that bimanual training resulted in greater improvements in goals identified by caregivers[24,39] and in the spatial-temporal coordination of the 2 hands during a functional bimanual activity.[73]

Bimanual training embedded in a cognitive-based intervention framework has been compared to constraint-induced movement therapy following upper limb injections of botulinum toxin A.[52] This cognitive problem-solving approach actively guided children to develop strategies to address difficulties faced during task performance. The recent development of the Assisting Hand Assessment has expanded our understanding of how children with a unilateral impairment use their impaired upper limb as an assisting hand in bimanual activities.[74] The Rasch analyzed measure provided a hierarchy of item difficulty that was used to inform treatment goals. Findings demonstrated similar gains in bimanual and unimanual upper limb function following a cognitive-based bimanual therapy program compared to constraint-induced movement therapy, despite the bimanual group receiving on average less intervention than the constraint-induced movement therapy group (47 vs 114 hours).[52]

Researchers have consistently reported greater difficulty in provision of bimanual therapy compared with constraint-induced movement therapy.[25,52,33] The restraint in constraint-induced movement therapy forces the child to use their impaired upper limb, requiring less prompting than typically required in bimanual therapy. Therapists need to be more vigilant in bimanual therapy, as children will often revert to using 1 hand despite it being less efficient than 2. The structured presentation of bimanual activities, with clearly enunciated rules as to how the impaired hand should be used to complete tasks is vital. Use of cognitive strategies and verbal mediators have been useful techniques within this therapy framework.[24,52] Bimanual therapy, however, allows a potentially greater variety of activities compared with constraint-induced movement therapy, most of which tend to be more motivating than unimanual activities.[33]

Despite these nuances, in reality, these approaches are not mutually exclusive, and can be performed concurrently with sufficient intensity or over time.[26,44,75] Sequential application of constraint-induced movement therapy and bimanual therapy (hybrid therapy) has been investigated in a number of studies, which aimed to capitalize on the relative benefits of each approach. The notion is that constraint-induced movement therapy can "turn on" the upper limb by increasing spontaneous use and functional unimanual capacity, and bimanual training then facilitates the translation of these gains to improve goal-directed bimanual performance. Six weeks of constraint-induced movement therapy followed by 2 weeks of bimanual therapy (3 hours/d, 3 days/wk) demonstrated significant gains in unimanual capacity and bimanual performance compared to usual care.[26] An alternate model of constraint-induced movement therapy delivered in a 2-week period (3 hours/d, 5 days/wk), followed by 1 week of bimanual training (3/4 hour/d, 3 d/wk) demonstrated gains in self-care skills, but not efficiency of movement of the impaired upper limb, suggesting that the dose of therapy may not have been sufficient.[35]

Evidence for Critical Dose and Neuroplasticity

Although constraint-induced movement therapy and bimanual training have been provided for varying durations, surprisingly little is known about dosing. Three hours of active constraint-induced movement therapy training seemed to yield similar clinical improvements compared to 6 hours, but this was likely washed out by the passive (forced use) component since children were casted 24 hours/d.[43] Comparisons across studies where conditions were held constant except duration generally suggest more training is better. Results of the Jebsen Taylor Test of Hand Function and Assisting Hand Assessment for children in separate studies who received either 60 hours over 10 days or 90 hours over 15 days of constraint-induced movement therapy[23,24] or Hand Arm Bimanual Intensive Training[24,33] found improvement after constraint-induced movement therapy for both dosages. Gains were greater for those receiving 90 compared to 60 hours. Although Assisting Hand Assessment scores improve for both the 60- and 90-hour Hand Arm Bimanual Intensive Training groups, the improvement deteriorated by 1 month for the 60-hour group, whereas it was retained 6 months later for the 90-hour group. Thus, dose effects cannot be determined simply by the initial pre-post results because retention of improvements is the ultimate goal. In a similar comparison of 2 randomized controlled trials providing 60[25] or 30 hours of constraint-induced movement therapy or bimanual training,[76] findings suggested 30 hours (half dose) of constraint-induced movement therapy or bimanual training was insufficient to yield significant changes in upper limb function. Achievement of individualized goals, however, was similar across both doses of therapy for constraint-induced movement therapy and bimanual training.[76]

Irrespective of the type of intervention, variability in response to therapy has been evident. Forty-six percent to 60% of children receiving constraint-induced movement therapy have achieved clinically important gains in bimanual performance postintervention.[27,28,52,77] The characteristics of children that impact meaningful clinical outcomes remain unclear. Larger gains in bimanual performance postintervention have been attributed to younger children,[28,52] older children,[27,78] and greater impairment at baseline.[26,27,52-54] Poorer baseline unimanual outcomes have been attributed to greater gains on unimanual outcomes following constraint-induced movement therapy.[30,77]

The underlying neuroplastic changes associated with training have only recently begun to be explored. In one small functional magnetic resonance imaging (MRI) study,[79] an increase in the magnitude of functional MRI signal in the primary motor area (M1) of the contralateral hemisphere was found in some children, indicating clinical improvement after constraint-induced movement therapy. Another small study used several methods to quantify neuroplasticity following constraint-induced movement therapy.[80] Magnetoencephalography demonstrated a significant increase in activation of the primary somatosensory cortex. Changes in M1 excitability, measured with transcranial magnetic stimulation, differed depending on whether the children maintained the normal contralateral corticospinal tract projections from M1 to the spinal cord and hand muscles (contra group), or whether there was a reorganization[57,81] whereby the ipsilateral corticospinal tract innervated the paretic hand (ipsi group). Transcranial magnetic stimulation showed an increase in M1 excitability in the contra group, but a decrease in M1 excitability in the ipsi group. Similarly, functional MRI showed an increase in activation in the M1-S1 region in the contra group, but a decrease in M1 activation in the ipsi group. In a larger randomized controlled trial directly comparing equal doses (60 hours) of constraint-induced movement therapy and bimanual training (n = 30), increased cortical excitability of the impaired motor cortex (transcranial magnetic stimulation) was evident following constraint-induced movement therapy but not bimanual training.[82]

Future Directions

The substantial increase in number of studies investigating intensive models of upper limb therapies has demonstrated the clear need to consider intensity of treatment in the delivery of therapy to children with unilateral cerebral palsy. Three key questions, however, have been proposed as the most important for further research: (1) optimal dosage, (2) repeated treatment sessions, and (3) age responsiveness.[60] Irrespective of whether the therapy is constraint-induced movement therapy, bimanual therapy or hybrid model, the critical threshold dose to achieve sustained upper limb outcomes needs to be further investigated.

Constraint-induced movement therapy was developed as a ''one off'' intervention, but this premise can be questioned, especially when considering a life span perspective. There is some preliminary evidence to suggest a cumulative effect of repeat doses of constraint-induced movement therapy,[30] but this requires further exploration. It is unclear whether there is a ceiling effect in terms of functional skill acquisition, or if there needs to be repeat bursts of treatment to maintain children's skill level. Although repeat doses of bimanual therapy have not been investigated, it could be hypothesized that given the very similar outcomes achieved after an episode of either bimanual therapy or constraint-induced movement therapy, similar cumulative responses could be expected. Therefore, from a life span perspective, the choice between a unimanual, bimanual, or combined approach of therapy at any particular point in time should reflect the specific goals and preferences of families combined with possibilities of different service delivery models.

The third remaining question relates to the importance of age on therapy outcomes. There is limited evidence for upper limb interventions for children under 1 year of age; however, research findings demonstrate that children of any age, even adolescents, will improve. There can be windows for increased neuroplasticity in infancy suggesting earlier provision of therapy may be optimal; however, further investigation is required. Finally, there has been considerable interindividual variability in response to intensive upper limb training approaches. Exploration of specific child characteristics (eg, age, severity of impairment, side of hemiplegia, motivation, cognition, cortical motor reorganization) that lead to clinically meaningful changes in upper limb function requires further investigation.

The challenge with any new approach or innovation is the uptake of evidence into clinical practice. Notwithstanding the considerable body of evidence available, it appears there is a lag in adoption of these intensive approaches in clinical practice.[83,84] Translating evidence into practice can take a variable and unpredictable amount of time.[85] As such, specific knowledge translation strategies may be required to ensure that evidence is applied in routine clinical practice in a timely manner. Therapists need to consider which models of intervention can be adapted to their local context and embed these within their current clinical framework. Methods to increase dose include use of more group-based interventions, augmenting direct hands on therapy with evidence-based occupational therapy home programs,[86] embedding intervention in naturalistic leisure settings or providing intensive holiday programs. Given the resource-intensive nature of many of these models of intervention, further investigation of the cost benefits of each is warranted.

Key Take Home Messages

- There is strong evidence that constraint-induced movement therapy and intensive bimanual therapy work for children with unilateral cerebral palsy of different age groups to improve upper limb function, achieve individualized goals, and promote plasticity.
- Key components of service provision should be that therapy is goal directed, use contemporary motor learning–based approaches such as constraint-induced movement therapy or bimanual task-oriented therapy and be provided at an adequate dose.
- Most studies use a therapy dose varying from 40 to in excess of 120 hours.
- Therapy can be effectively provided individually or in group sessions, augmented by a home program.
- Services for children with unilateral cerebral palsy need to consider how these therapy approaches can be embedded within current clinical frameworks.
- Neurologists can support children and families in achieving optimal upper limb outcomes by early referral to occupational therapy.

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