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Constraint-Induced Movement Therapy for Children with Brain Tumors

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Abstract

Purpose—The purpose of this pilot study was to investigate the feasibility of a 3-week constraint-induced movement therapy program in children with brain tumors and upper extremity hemiplegia and to describe change in extremity use.

Methods—Affected arm use, health-related quality of life, and parent-reported feasibility of program participation were measured before and after the intervention and at a 3-month follow-up visit.

Results—All 9 participants completed the entire study. The quality and amount of affected arm use improved significantly; gains were maintained at the 3-month follow-up evaluation. Some parents (44%) reported that program participation was difficult; however, all reported satisfaction with the program. Participants did not experience negative changes in health-related quality of life during the intervention, indicating that the program was well tolerated.

Conclusions—Findings suggest that a child with hemiplegia as a result of a brain tumor can adhere to and benefit from a CIMT program.

INTRODUCTION AND PURPOSE

The National Cancer Institute estimates that 15,780 children and adolescents in the United States aged 0 to 19 years will be diagnosed with cancer each year.¹ With advances in treatment over the past 5 decades, the 5-year relative survival rates for children with cancers of the central nervous system has reached 73.1%, resulting in an increased focus on the child's post treatment status and quality of life.² Pediatric cancer and its treatment (e.g.

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chemotherapy, radiation therapy and surgery) may result in a wide range of negative sequelae, including psychosocial dysfunction, peripheral neuropathy, cognitive limitations, and decreases in strength, coordination, and balance. One potential neurological impairment in children treated for a brain tumor is hemiparesis,³ prevalent in up to 21% of survivors.⁴

Constraint-induced movement therapy (CIMT) is a rehabilitation intervention that improves function in extremities affected by neurological injury. CIMT is based on research demonstrating that cortical signaling from the damaged cortex is absent or minimal immediately following a neurological insult (stroke, brain injury, etc.), resulting in limb movements that are difficult and inefficient.⁵ Attempts to move the affected extremity perpetuate the initial insult because of learned non-use, or in very young children, because of developmental disregard. Learned 'non-use' describes a pattern of disuse of the hemiplegic arm after a neurological injury, in which repeated failures when the child attempts to use the affected limb result in the child relying on the non-affected limb for function. Non-use causes contraction of the cortical representation of the hand, further limiting use of the affected extremity.^{6,7} Developmental disregard occurs in very young children with hemiplegia when neurological injury interferes with development of neural pathways necessary for controlled volitional movement and proprioceptive feedback. Motor skills are delayed or fail to develop because the child is unaware of the existence of the affected extremity.^{8,9}

Fortunately, research demonstrates that with repetitive practice, cortical reorganization and improved limb function are possible among individuals with neurological injury.⁵ CIMT in pediatric populations constrains the unaffected arm in a splint or cast to encourage use of the affected extremity. Additionally, the high dose therapy engages the affected extremity in repetitive practice of developmentally appropriate movement strategies and employs the behavioral technique of shaping to achieve motor goals during play.^{8,9} Neuroimaging from CIMT studies in adults and children with hemiplegia indicate that facilitated cortical reorganization overcomes learned non-use or developmental disregard, leading to improved function of the limb.^{10,11} CIMT yields results in short-term and long-term improvements in upper extremity function that are superior to those of standard therapies in children with cerebral palsy^{8,12,13,14,15} and can improve upper extremity function in children with brachial plexus injury¹⁶, hemispherectomy¹⁷, and acquired brain injury^{18,19}. Although a few children with brain tumors have participated in CIMT trials²⁰, the effectiveness of CIMT among children with neurological injury related to their history of cancer or its treatment has not been systematically evaluated.

The purpose of this pilot study was to investigate the feasibility impact on quality of life of a 3-week CIMT program in children with brain tumors and upper extremity hemiplegia and to describe the change in amount and quality of extremity use that resulted from participation in the CIMT program.

METHODS

Participants were a convenience sample of English speaking children aged 2–12 years who had been diagnosed with a brain tumor and hemiplegia after completion of therapy. Study

exclusion criteria were as follows: uncontrolled seizures, significant pain (at least 5/10 on FACES of Numeric Pain Scale), and 30 degrees of active shoulder flexion or abduction, inability to initiate elbow flexion, extension, or movement of the wrist, or digits in the affected extremity. Institutional review board approval was obtained for the study. Written, informed consent was obtained by parents or guardians, and assent was obtained per institutional policy.

Intervention

The intervention included 15 three-hour therapy sessions in the rehabilitation services clinic (5 days per week for 3 weeks), during which participants were engaged in activities to improve strength, motor skills, range-of-motion, and functional use of the affected upper extremity. The 3-week program was scheduled at the convenience of the participant. The intervention was provided by one clinician who was trained through the University of Alabama at Birmingham (UAB) Constraint Induced (CI) Therapy Pediatric Training Program. Play and age-appropriate functional activities such as self-feeding and dressing were used to employ the core CIMT principles of “shaping” and repetitive task practice in order to motivate the participants. Shaping is a behavioral technique in which small, successive approximations or progressive increases in the difficulty level of tasks are used to achieve a motor or behavioral goal.

During the program, the unaffected upper extremity was restrained in a long arm removable cast to overcome the tendency to use the more functional arm. Every other day, the cast was removed and the skin assessed for redness, irritation, and breakdown. The cast remained in place daily, restraining the unaffected extremity until 2 days prior to program completion, at which time bimanual upper extremity training occurred.

After completing the 3-week program, children and their parents/caregivers were instructed in an individualized home program that included activities and exercises to facilitate maintenance of gained skills. The month following program completion, weekly phone conversations were conducted with the parents/caregivers. The phone assessment asked specific questions regarding the child’s progress and provided recommendations for transferring skills learned from the program into their real-world environment.

Outcomes

Feasibility was defined as successful completion of 12 of 15 sessions during the 3-week intensive intervention program, as well as completion of pre-intervention, post-intervention, and 3-month follow-up assessments. (See Schedule of Assessments, Supplemental Digital Content Table 1)

The Pediatric Grading System for Severity of Motor Deficit (Pediatric Model)²¹ was used to assess each child’s range of motion and severity of motor deficit of the more impaired upper extremity. Range of motion is graded on a 4-point scale, with Grade 2 indicating mild to moderate limitation; Grade 3, moderate limitation; Grade 4, moderately severe limitation; and Grade 5, severe or very severe limitation (see Appendix). The overall grade used to characterize a child’s deficit is dictated by the joint (shoulder, elbow, wrist, fingers, thumb) at which the deficit is greatest.

The Pediatric Motor Activity Log (PMAL) was used to assess the frequency and quality of use of the affected extremity in the real world environment. The parent/caregiver used a 5-point Likert scale to rate “how often” and “how well” their child used the affected extremity during 22 arm/hand functional activities.²² The Motor Activity Log, from which the PMAL was adapted, is a valid and reliable tool with high internal consistency and high inter-rater and test/retest reliability. The minimal detectable change for the PMAL is 0.42.

The Inventory of New Motor Activities and Programs²³ (INMAP), a modified version of the Emerging Behaviors Scale,²⁴ was used to record 32 motor patterns and functional activities that emerged during the intervention. Examples of patterns or activities include reaching, release of objects, pincer grasp, crawling, and using feeding or writing utensils. New motor patterns were recorded during the program if verified by at least 2 sources, including a therapist, parent/caregiver, or video recording.

The Pediatric Arm Function Test²⁵ (PAFT) was administered to assess the frequency and quality of affected upper extremity function. The assessment consists of 26 unilateral and bilateral upper extremity tasks completed by the child and videotaped for later scoring. The quality of affected upper limb function is scored and a quality of use score is obtained. The percentage of items completed spontaneously with the affected upper extremity is also recorded. PAFT has high internal consistency (Cronbach’s alpha = 0.96), and test/retest reliability was adequate (ICC = 0.74).²¹

The Pediatric Grading System for Severity of Motor Deficit (Pediatric Model), the PMAL, the INMAP, and the PAFT were chosen because they are a part of the UAB Pediatric CI Therapy Program.

Health-related quality-of-life (HRQOL) was assessed by using the Pediatric Quality of Life Inventory SF-15 and the Pediatric Quality of Life Inventory (PedsQL) Acute Version.^{26,27} Parents completed the PedsQL SF-15 before the intervention and at the 3-month follow-up visit and the PedsQL acute version at the end of weeks 1, 2, and 3. Items were rated from 0–4, with a score of 0 indicating “never a problem” and 4 indicating “always a problem”. Scale scores were computed as the sum of the item scores divided by the number of items completed, reflecting a summary measure of HRQOL. Those with scores 1 standard deviation (SD) below established population means were classified as having poor HRQOL.

The CIMT Feasibility Scale was completed by the child’s parent at the end of the 3 week intervention period to assess the feasibility of participating in and completing the program. It asked parents to rate levels of difficulty related to adhering to the cast-wearing schedule and participating in routine daily and home activities and to rate the child’s frustration level during the program. (See Feasibility Questionnaire, Supplemental Digital Content Table 2)

Statistical Analysis

Descriptive statistics were used to characterize the study participants and results of the SJCIT Feasibility Questionnaire. Mean values (with SD) were calculated pre-intervention, post-intervention and at the 3-month follow up for the PMAL, PAFT, INMAP, and the PedsQL and compared between time periods by using generalized estimating equations to

account for within-person correlation²⁸. The data analysis was performed using SAS version 9.3 (SAS Institute).

RESULTS

Ten children were recruited and nine (3 boys, 6 girls) consented to participate in the study. All participants completed each phase of the study, including pretesting, 15 intervention sessions, and all follow-up assessments. None of the participants had previously participated in a CIMT or other intensive therapy program. Participant characteristics are shown in Table 1. The mean (SD) age of participants was 7.3 (3.6) years, with a mean (SD) time since diagnosis of 4.2 (3) years. Juvenile pilocytic astrocytoma was the most common brain tumor diagnosis (n = 4), with other participants having a variety of brain tumor types. All participants experienced additional neurological impairments; the most common were visual deficits (n = 9), seizure activity that did not interfere with daily activities (n = 3), and dysarthria (n=1). All participants were ambulatory. All participants underwent resection of the tumor as a component of treatment. Five also received chemotherapy and two received radiation therapy. None of the participants were receiving active cancer therapy at the time of the intervention. However, 1 participant was hospitalized for a shunt infection during the long-term follow-up phase of the study. This hospitalization was lengthy, and her course of care included a period of significant activity restriction due to externalization of her shunt. She was unable to participate in follow-up home activities/exercises to the extent prescribed by the program for a period of approximately 3 weeks but was able to return for her long-term follow-up assessment. Seven participants had a range-of-motion/motor severity score of 4 or greater (mean = 4.1), indicating moderately severe movement impairment (i.e., limitation of between $\frac{1}{3}$ and $\frac{1}{2}$ of normal range of motion) at the most limited joint.

Table 2 provides the mean pre-treatment, post-treatment, and 3-month follow-up scores of the PMAL, PAFT, and INMAP measures and comparison of score between time periods. After intervention, participants demonstrated significant improvements in the amount and quality of use on clinical measures (PAFT) and parent-reported measures of real world function (PMAL). These results were maintained at the 3-month follow-up visit, with the exception of the measured frequency of use on the PAFT. All participants gained at least 1 new motor pattern in the affected arm during the program and maintained these skills at the 3 month follow-up visit. The mean (SD) number of new motor patterns gained from pretreatment to the 3 month follow up visit was 5.6 (3.4) ($p < .0001$); the maximum was 11. The mean (SD) number of new daily living skills gained and maintained at long-term follow up assessment was 7.3 (3.6) ($p < .0001$); the maximum number gained and maintained was 12.

The pre-test mean (SD) PedsQL summary score was 65.1 (14.5), with scale scores of 59.4 (17.9) for physical and 66.9 (17.4) for psychosocial function. The percentage of children with an overall PedsQL score at least 1 SD below the expected population mean was 66%. Nearly all (7/9) of the parent-reported child quality-of-life scores improved or remained stable over the study period. There were no significant changes in quality of life from pre to post assessment or from the post to 3-month follow up time point. Of the 2 participants whose parent reported a decline in quality of life, 1 was clinically significant, with a change

score of -40. This participant's parent provided additional information, indicating that other factors, unrelated to the program influenced their child's score: 1) the need for a new lower extremity orthotic to improve independent mobility and 2) difficulties adjusting to living in a new city and school. No significant associations were found between the child's age at diagnosis, severity score, sex and changes on the PedsQL, INMAP, PAFT or PMAL.

One parent reported that participation in the program was easy. Of the other participants, 44% felt that their child's participation in the program was difficult and 44% reported a neutral feeling about program difficulty. Seven of nine parents reported that their child wore the cast at least 90% of the prescribed time during the intensive phase of the program; 8 of 9 parents reported that enforcing that the child wore the cast as instructed was easy or very easy. One-third of parents rated participating in the P-CIMT program as frustrating, and one-third rated it as not frustrating, with the remaining third reporting a neutral level of frustration. All parents reported satisfaction with the program. Bathing, dressing, and eating were the activities of daily living most frequently reported by parents as being difficult or very difficult for their children (7/9). Detailed results of the Feasibility Questionnaire are provided in Feasibility Questionnaire Results, Supplemental Digital Content Table 3.

DISCUSSION

Applications of evidence-based rehabilitation interventions among children with brain tumors and hemiplegia are limited. This study indicates that children who survive brain tumor with hemiplegia can successfully complete a 3-week CIMT program and that such a program has potential to significantly improve the amount and quality of affected upper extremity use in this population.

Although the pediatric literature describing the efficacy of CIMT is primarily focused on children with hemiplegia due to cerebral palsy, one small pilot study that employed CIMT for children with acquired brain injury had findings similar to ours. Karman et al¹⁸ evaluated outcomes following CIMT among 7 children aged 7 to 17 years: 3 with traumatic head injury, 2 with cerebrovascular events from arteriovenous malformations, and 2 with stroke. Five demonstrated significant improvements in at least 1 measure of upper extremity function. Although this was a 2-week, 6-hour-per-day program and these children tended to be older at the time of participation, participants were similar to those in the present study in terms of time since initial injury and baseline function in the affected limb. However, another CIMT trial in which children with acquired brain injury due to ischemic stroke (N=8, ages 6–15 years) participated in 2 hours per day of direct treatment over the course of 4 weeks did not find improved sensorimotor function or quality of upper limb movement function.¹⁹ On average, the children in that study were older than those in our study, closer to their initial insult, and had more severe impairment in the affected limb at baseline than did the children in our study. More work is needed to determine the effects of age, timing, treatment dosing/duration, and severity of impairment on CIMT efficacy among children with acquired brain injury.

Our study was a non-randomized feasibility study with a small sample size. Although we were unable to identify patient- or program-specific factors that predicted improvement, this

study did demonstrate that children who survive brain tumors with chronic hemiplegia and moderately severe movement impairment can benefit from CIMIT intervention. Continued research aimed at identifying potential predictors of CIMIT outcomes will assist clinicians in targeting children who will benefit most from the specific therapy. For example, Wolf et al. reported that, among adult stroke survivors, (N=222), those who were at least 3 months post neurological injury demonstrated improvement with CIMIT therapy that was not seen in those in the acute recovery phase (i.e., first few weeks after stroke).²⁹ Others have reported that outcomes are dependent on the severity of the initial impairment, with individuals who initially demonstrated higher functional levels and range of motion abilities improving more than those with greater deficits.³⁰

Although this program was modeled after current evidence that supports a 3-week, 3-hours-per-day program rather than the previously recommended 6-hours-per-day program,³¹ it remains a time- and resource-demanding intervention for children, families, and therapists. Although it was time consuming, all 9 participants were able to successfully complete the CIMIT program, and although some parents reported participation in the program was difficult, all reported satisfaction with the program at the end of the 3-week intervention. In addition, the children did not report statistically significant declines in HRQOL during the 3-week intervention, indicating that the program was well tolerated. These data are consistent with those of 2 other studies that described perceptions and experiences of parents, therapists, and children who participated in intensive therapy programs, reporting increased stress but perceived benefit including improved motor function and goal attainment.^{32, 33}

We found that although there were no significant changes in HRQOL during the CIMIT intervention, there was also no significant lasting positive effect on HRQOL. Information describing the effect of CIMIT on HRQOL of children is limited. A previous study assessed HRQOL following CIMIT in a group of children with cerebral palsy (N=40; ages, 5–16 years) by using a condition-specific quality-of-life outcome measure (The Cerebral Palsy Quality of Life Assessment for Children) and found significant improvements in reported participation, physical health, psychosocial health, and social well-being, which were maintained at long-term follow-up assessments.³⁴ A randomized controlled trial evaluating the effects of a home-based CIMIT program found that although the CIMIT group and the control group had significant differences in HRQOL at a 3-month follow-up visit, there were no such differences post treatment, indicating gains in quality of life are greater over the long term than the short term.³⁵

This intervention was completed in a clinical setting. A recent systematic review of randomized controlled trials of CIMIT in children with cerebral palsy concluded that intervention setting was significantly associated with a study's effect size, reporting that effect size was larger in a home-based constraint-induced movement therapy program than in a clinic-based one and smallest in a camp-based program.³⁶ Further research is needed to compare the effect of intervention setting on CIMIT effectiveness in children who survive brain tumors.

CONCLUSION

Our findings suggest that a child with hemiplegia as a result of a brain tumor can adhere to and benefit from participation in a CIMT program, including up to 10 years from diagnosis and with other tumor or treatment related co-morbidities. Ongoing investigation into the efficacy of CIMT within the pediatric oncology population, the efficacy of CIMT as compared to other equally intensive interventions, and identification of potential predictors for successful CIMT outcomes are warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Appendix

Appendix 1

Grading System for Severity of Pediatric Motor Deficit

Amount of Deficit	Shoulder	Elbow	Wrist	Fingers	Thumb
Grade 2 Mild/Moderate	WNL/ mild limitation in flexion or abduction	WNL/ mild limitation in extension	WNL/mild limitation in extension	WNL/mild limitation in extension	WNL/mild limitation in lateral abduction
Grade 3 Moderate	Moderate limitation flexion or abduction	Moderate limitation in extension	Moderate limitation in extension	Moderate limitation in extension	Moderate limitation in lateral abduction
Grade 4 Moderately Severe	Severe limitation in flexion or abduction, but >30°	Severe limitation in extension	Severe limitation in extension	Severe limitation in extension	Severe limitation in lateral abduction
Grade 5A Severe	30° flexion or abduction	Initiation of flexion or extension	Initiation of movement	Initiation of movement	Initiation of movement
Grade 5B Very Severe	30° flexion or abduction	Initiation of flexion or extension	No initiation of movement	No initiation of movement	No initiation of movement

The overall grade used to characterize a child's deficit is dictated by the joint (shoulder, elbow, wrist, fingers, thumb) at which the deficit is greatest.

Mild – Limitation of < $\frac{1}{3}$ to just below normal range

Moderate – Limitation of between $\frac{1}{3}$ and $\frac{1}{2}$ of normal range

Severe A – Limitation of > $\frac{1}{2}$ of normal range but can initiate movement

Severe B – No initiation of movement

Abbreviation: WNL, within normal limits

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Table 1

Participant Characteristics

Participant	Age at CIMT (y)	Years since diagnosis	Diagnosis	Treatment Completed and Functional Deficits	Months since last treatment	Severity Score
(1)	11	10	Juvenile pilocytic astrocytoma, suprasellar hypothalamus	Tumor resection, chemotherapy. Seizure activity, L hemiplegia, optic atrophy, and related visual acuity and field deficits.	23	4
(2)	5	5	Choroid plexus carcinoma, right hemisphere	Tumor resection, chemotherapy. Left hemiplegia, left homonymous hemianopia	52	3
(3)	10	8	Multiple recurrent juvenile pilocytic astrocytoma, temporal lobe.	Tumor Resection Right hemiplegia, right visual field deficit.	44	2
(4)	10	4	High-grade glioma, left frontoparietal	Tumor resection, chemotherapy, radiation therapy. Right hemiplegia, right incomplete homonymous hemianopia. Dysarthria	41	5
(5)	3	3	High-grade infantile glioneuronal tumor, frontoparietal	Tumor resection resulting in intracranial hemorrhage, shunt placement, seizure activity. Right hemiplegia, right visual field cut.	27	5
(6)	2	2	Anaplastic astrocytoma, thalamus	Tumor resection, shunt placement, chemotherapy, seizure activity. Right hemiplegia, visual deficits	16	4
(7)	6	2	Atypical teratoid rhabdoid tumor, midbrain and thalamus	Tumor resection, radiation therapy, chemotherapy. Left hemiplegia, visual deficits (Left Cranial Nerve VI impairment)	23	5
(8)	7	1	Juvenile pilocytic astrocytoma, medullary	Tumor resection. Right hemiplegia, visual deficits (mild - nystagmus, strabismus, Horner's syndrome).	38	4
(9)	12	3	Juvenile pilocytic astrocytoma, thalamus.	Tumor resection. Left hemiplegia. Optic atrophy and Left Hemianopia.	18	5
TOTAL	Mean (SD) = 7.3 (3.6)	Mean (SD) = 4.2 (3)			Mean (SD) = 31.3 (12.7)	Mean (SD) = 4.1 (1.1)

Abbreviations: CIMT, constraint-induced movement therapy

Table 2

Scores on Motor Activity Measures at Each Time Point

Measure	Pre-intervention, Mean (SD)	Post-intervention, Mean (SD)	3-month follow-up, Mean (SD)	P, pre to post	P, pre to 3-month follow up	P, post to 3-month follow up
Pediatric Motor Activity Log (parent-reported)						
Frequency of use	1.3 (0.7)	2.3 (1.0)	2.4 (1.1)	<0.001	<0.001	0.60
Quality of use	1.4 (0.7)	2.7 (0.8)	2.5 (1.0)	<0.001	<0.001	0.20
Pediatric Arm Function Test (measured)						
Frequency of use	59.0 (29.5)	77.1 (27.9)	69.6 (27.3)	<0.001	0.002	0.01
Quality of use	30.9 (10.4)	38.9 (10.6)	38.5 (9.1)	<0.001	<0.001	0.63
Inventory of New Motor Activities and Programs						
Motor skills	10.9 (5.8)	17.3 (4.5)	16.4 (5.4)	<0.001	<0.001	0.20
Activities of daily living	10.9 (4.7)	20.6 (3.3)	18.2 (4.5)	<0.001	<0.001	0.09
Pediatric Quality of Life Inventory						
Total Score	65.1 (14.5)	72.3 (10.6)	66.5 (15.1)	0.08	0.83	0.31