

COMPARISON OF DIFFERENT PHYSICAL THERAPY INTERVENTIONS FOR UPPER EXTREMITY IN CHILDREN WITH HEMIPARETIC CEREBRAL PALSY

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Abstract:

Background and Objective: Dysfunction in the upper limbs is one of the most common symptoms in children with cerebral palsy (CP), particularly children with hemiparetic CP which intern has the potential to limit the involvement of these children in life activities and cause distress and suffering for both children and their parents. The main purpose of the research was to compare the therapeutic impact among hand-arm bimanual intensive therapy (HABIT), modified constrained induced movement therapy (mCIMT) and task-oriented training (TOT) on upper extremity functions in children with hemiparetic CP.

Subjects and Methods: Sixty hemiparetic CP children of both genders with an age range from five to eight years were randomly divided into three equal-number groups. Group (A) received HABIT, group (B) received mCIMT and group (C) received TOT. Treatment was conducted for 30 minutes, three days per week for three successive months. Peabody Developmental Motor Scale (PDMS-2) and Quality of the Upper Extremity Skills Test (QUEST) were used to assess the function of the upper extremity for all groups. The Assessment was performed before as well as after the period of intervention.

Results: Significant improvement of the visual-motor integration and grasping subsets of PDMS-2 as well as a significant increase in dissociated movements and grasp subsets of QUEST in the three groups after intervention with a higher significant effect for the mCIMT.

Conclusion: It could be concluded that all of the three physical therapy interventions (HABIT, mCIMT and TOT) could improve upper extremity functions for children with hemiparetic CP with a more significant effect on the mCIMT.

Keywords: Cerebral palsy, Modified constrained induced movement therapy, Bimanual intensive, hand-arm bimanual intensive therapy, Hemiparesis, Task-oriented training.

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INTRODUCTION

Cerebral palsy (CP) refers to a group of permanent non-progressive neurodevelopmental disorders affecting the development of movement and posture and occurring in the developing fetal or infant brain, thus limiting activity^{1,2}. It represents the most common and devastating cause of childhood chronic physical disability³. In spite of improvements in antenatal and perinatal care, the incidence rate of CP has been around two to three for every 1000 live births in both developed and developing countries for the past 40 years⁴. In Egypt, a prevalence rate of 2.04/1000 live births was documented⁵.

The most common manifestation of CP is hemiparesis which affects 30% to 40 % of the overall population of children with CP. Children with hemiparetic CP may suffer from predominant upper limb motor impairments, which adversely affect their quality of life because of the negative impacts on reaching, bimanual tasks and functionality during activities conducted at home, school and community setting^{6,7}. It is worth mentioning that popular arm and hand disorders in hemiparetic CP include muscle weakness, muscle imbalance, sensory impairment, spasticity, decreased length of muscle, dystonia and/or disuse. Hemiparetic CP children might experience difficulties performing several functional abilities such as reaching, pointing, grasping, releasing and manipulating objects as a result of combinations of the above mentioned impairments.

Repeated failure to perform the activities with the impacted arm and hand results in spontaneous use diminishing. As a result, children with hemiparesis often, use their affected upper limb less frequently than expected in bimanual activities on the basis of their functional capacity. This disparity between ability

and performance (referred to as disregard for development) is going to lead to a vicious circle of decreasing upper limb use⁹. Therefore, Boyd et al.,¹⁰ explained in his study the urgent need for early interventions that mitigate brain injury which improve early-hand function, and later vocational and life outcomes.

Different rehabilitation intervention procedures addressing upper extremity dysfunction are essential to promote better use of disabled arms and hands in bi-manual daily activities and achieving functional independence at home, in school and in the community¹¹.

Several strategies have been developed to improve the functioning of hands in children with hemiparetic CP with varying evidence of benefits¹². Shierk et al.,¹ listed the categories of intervention based on the number of articles that are most common to the least frequent as follows: (1) constraint-induced movement therapy (CIMT), (2) hand-arm bimanual intensive therapy (HABIT), (3) virtual reality (web and computer-based) interventions, (4) treatment intervention in conjunction with botulinum toxin A (BoNT), (5) Task-oriented therapy (TOT), (6) splints and Kinesio tape, (7) home programmes, (8) surgical intervention, (9) exercise and reinforcement, and (10) Other procedures including handwritten, therapy by mirror, somatosensory training, motivation, electrical stimulation and metronomic training.

Hand-armed bimanual intensive training is a bimanual approach of rehabilitation that addresses impairments specific to the upper extremity of children with hemiparetic CP that have shown positive results. HABIT is not only based on ordinary bilateral coupling or mirror movements, but also on asymmetric movements of both hands using the motor learning

concepts and neuroplasticity, which can be defined as practice mediated brain changes resulting from repetition, increasing the complexity of movement, motivation, and reward. Moreover, one of the principles of HABIT involves increasing the complexity of functional activities that require both hands use and repetitions to achieve functional goals¹³. It is a successful therapeutic approach used to improve motor action, improve hand/arm function and bimanual coordination of children with hemiparetic CP. The cortical changes associated with these therapy enhancements are correlated with the reconfiguration of the topology of the sensorimotor cortex, the increase in the volume of white matter and preserving the integrity of the corticospinal fiber tract¹⁴.

The modified CIMT (mCIMT) protocol had been developed as an alternative to the CIMT's intensive nature and includes fewer time consuming restrictions over a longer duration of intervention¹⁵. It is a form of rehabilitative treatment involving restricting the less-affected limb while the more affected limb is in training simultaneously. This is an analytical-behavioral approach intended to enhance deficits that arise from different forms of damage to the central nervous system, such as stroke, traumatic brain injury, spinal cord injury, multiple sclerosis, cerebral palsy and other conditions. Similarly, the protocol involves restraint of the unaffected limb with variants in the type of constraint applied (e.g. gloves, slings) and is accompanied by repetitive unimanual practice¹⁶.

Task-oriented training complies with the modern concepts of motor learning that support the precision of the training and requires the execution of tasks that are relevant for the expected outcome and meaningful to the individual. Use of TOT as a strategy for rehabilitation to improve motor function has been gaining momentum in the last decade¹⁷. TOT is a therapeutic approach that offers children with CP interesting activities in objective functional aspects and intensive environmental training that can promote movement and involvement that can eventually enhance motor performance^{18,19}.

Improvement of function and independence was the primary target in hemiparetic CP rehabilitation. Many of the conventional neurorehabilitation approaches have focused on the management of impairment. However, there is little evidence that impairment-related intervention is effective on disabled children, and improvement in impairment cannot be generalized to function²⁰. Therefore, this study was designed to compare the effects of HABIT, mCIMT and TOT to improve functions of the upper extremity in children with hemiparetic CP. To the best of our knowledge, this is the first study investigating the relationship between upper extremity impairments and the efficacy of HABI, mCIMT and TOT interventions for children with hemiparetic CP.

MATERIALS AND METHODS

Study design and sampling method:

This study is a randomized control trial that was conducted during the period from September 2018 till March 2020. The study was conducted in the out clinic of the physical therapy department of Children's Hospital-Cairo University (Abu El-Resh) and different pediatric rehabilitation centers in Cairo, Egypt. The children were randomly assigned into three groups by a blinded, independent research assistant who was not involved in the patient selection and who open envelopes that contained a computer-generated randomization card.

Sample size calculation:

Before the study, the sample size was calculated using the statistical software G*POWER (version 3.1.9.2; Franz Faul, University Kiel, Germany) [F tests- MANOVA: repeated

interaction measurements, $\alpha=0.05$, $\beta=0.2$, and large effect size] and revealed that the appropriate sample size for this study is 60 participants (N=60).

Participants:

Sixty children of both genders participated in this study. They have participated if they met the following inclusion criteria: (1) diagnosed as hemiparetic CP, (2) age ranged from six to eight years, (3) degree of spasticity measured for wrist and elbow flexors of the affected upper limb ranged from 1 to 1+ depending on the modified Ashworth scale (MAS), (4) capacity to handle objects without continuous assistance (level I or II in accordance with the Manual Ability Classification System [MACS]) and (5) the capability to manipulate and grasp objects with or without limitations (level I or II according to Bimanual Fine Motor Function [BFMF]).

Children excluded if they have the following exclusion criteria: (1) fixed contracture or deformities in the upper extremities, (2) inability to tolerate touching of the affected upper extremity, (3) phenolisation or botulinumtoxin injection in the last six months prior to participating in the study, (4) previous surgery to the upper extremities and/or (5) visual, auditory behavioral or mental impairments.

Participants were split randomly into three equal-number groups: group (A) received HABIT, group (B) received m CIMT while group (C) received TOT.

Materials and Procedures:

Ethical considerations

The research was accepted by the ethical committee of the Department of Physical Therapy for Pediatrics, Faculty of Physical Therapy, Cairo University. Approval from Children's Hospital-Cairo University (Abu El-Resh) and different pediatric rehabilitation centers in Cairo, Egypt, were obtained. The consent forms were distributed to the parents or guardians after an explanation of the procedures in detail. A signed consent form was obtained before starting the study.

Participants' selection

The MAS was used to measure the degree of spasticity of wrist and elbow flexors of affected upper extremity (grade 1 or 1+)²¹. The MACS was used to measure object handling capability without continuous assistance (level I or II)²². The BFMF was used to measure the ability to grasp and manipulate objects with or without limitations (level I or II)²³.

Evaluation measures:

1. Evaluation of fine motor hand skills: Peabody Developmental Motor Scale (PDMS-2) has been used to assess fine-handed skills including grasping (24-item) and visual-motor integration (VMI) (72-item) subtests to measure the ability of a child to use his/her visual perception skills to perform complex tasks of eye-hand coordination activities, such as reaching and grasping certain objects, building specific shapes with blocks and copying different designs²⁴. Each child sat on chair-with feet rested on the ground in front of a table wide enough and of appropriate height opposite to the therapist side. All materials were within the reach of the examiner and outside the child's view. Scoring of PDMS-2 ranged from 0-2 for each item according to criteria in the manual. The raw scores for each sub-test were accumulated then transformed to a standard score for each subtest and were recorded.

2. Evaluation of upper extremity quality of movement:

Quality of Upper Extremity Skills Test (QUEST) was used to assess the functional ability of upper extremity. It includes 25 items in two domains which are essential components of normal patterns of development; dissociated movements (19 items with one level of response for each item) and grasp (6

items with 3-5 level of response for each item). Each child sat in a quiet room on a chair with hips and knees at right angles and feet flat on the floor, with the front table just above the waist level. The therapist sat on the other side of the table with equipment reachable to his hands, facilitating the movements through verbal encouragement, toys or demonstrations. The score of each item entered in every scoring box even if not tested. A percentage score had been calculated for each domain. According to the instruction manual, domain scores are based on a summation of the affected and unaffected side, ranging from negative to 100.

Treatment measures:

Group (A):

This group received HABIT for 30 minutes, three days per week for three successive months. Children were given age-appropriate fine motor and manipulative gross motor activities which needed both hands to be used. Task requirements have been graded to enable success and with specific rules linked to success, difficulties were progressed. Task performance has been recorded, and both positive comprehension of knowledge of performance were used to motivate performance and reinforce target movements. Structured HABIT is characterized by three key components: 1) progress of the difficulty of the task (the difficulty of the task was graded either by increasing the spatial and temporal complexity of the movements or by increasing the complexity of how the affected hand was used), 2) repeated practice of isolated movements (part-task practice [shaping] emphasized the practice of a single movement component). Task performance, time on task and number of repetitions have been logged and 3) functional goals were practiced (play goals and activity of daily living (ADL) goals were identified by the participant and his/her family prior to training. During training, goals were practiced.

Group (B):

This group received mCIMT. Children wore a splint or arm sling on unaffected arm for seven hours a day and took part in activities promoting the use of the affected arm under parents' observation for two hours per day. This was performed in addition to 30 minutes of a therapy sessions, three days per week for three successive months. Every child has received personal instructions, motivation and encouragement from the therapist, which involves the specific practice of targeted movements. Children engaged in therapeutic functional activities using the involved hand which provided organized and intensive practice. The difficulty of the selected activities was gradually increased by changing the task's time or spatial/accuracy constraints after successful execution of the target move. Gross handling tasks as well as accuracy tasks have been highlighted in everyday activities such as finger painting, crafts and team-building activities.

Group (C):

This group received TOT in which sessions were divided into three parts. Each session began with three minutes of preparatory activity (slow-sustained stretching, mobilization and passive range of motion of the hemiparetic upper extremity, focusing on normalization of elbow and wrist flexors and shoulder abductors. In a structured setting, children then conducted 20 minutes of TOT uni- and bimanual activities on vertical and horizontal planes. The sessions brought to an end with 10 minutes of functional training that included the practice

of a challenging activity chosen by the child or his family. Activities were progressed with increasing levels of difficulty according to child/therapist preference and clinical goals reinforced by verbal instructions and feedback.

All groups received the intended program for 30 minutes, three days per week for three successive months.

Data analysis:

Descriptive statistics and ANOVA tests were carried out to compare age between groups. Chi-squared test has been used to compare sex, affected side and spasticity grade distribution among the three groups. Kruskal-Wallis test was conducted for comparison of the median values of MACS and BFMF among groups. The normal data distribution was checked for all variables using the Shapiro-Wilk Test. To test for homogeneity between groups, Levine's test for homogeneity of variances was carried out. Mixed MANOVA was performed to compare effects within and between the groups on PDMS-2 and QUEST. For subsequent multiple comparisons, post-hoc tests were conducted using the Bonferroni correction. For all statistical tests, the significance level was set at $p \leq 0.05$. All statistical analysis was carried out by the Statistical Package of Social Studies (SPSS) version 22 for Windows (IBM SPSS, Chicago, IL, USA).

RESULTS

Subject characteristics:

Table (1) shows the characteristics of the participants in the three groups prior to the intervention. There were no significant differences across groups regarding age, MACS, BFMF, sex distribution, spasticity grade as well as the affected side distribution ($p > 0.05$).

Effect of exercise on PDMS and QUEST:

Mixed MANOVA revealed a significant interaction ($F=32.2$, $p=0.001$) between treatment and time. Time's principal effect was significant ($F=69.45$, $p=0.001$). Treatment mainly had a significant effect ($F=10.71$, $p=0.001$).

Table (2) shows PDMS-2 and QUEST descriptive statistics and the high level of group comparison, as well as the high level of pre- and post-treatment comparison in each group. The Within-group comparison revealed a significant increase in standard score of VMI and grasping subsets of PDMS-2, substantial increase in the standard score of dissociated movement and grasp subsets of QUEST in the three groups post-treatment compared with that of pre-treatment ($p < 0.001$).

Among groups, comparison pre-treatment revealed a non-significant difference in all measured parameters ($p > 0.05$). Comparison among groups post-treatment revealed a significant increase in standard score of VMI and grasping subsets of PDMS-2, a standard score of dissociated movement and grasp subsets of QUEST of a group (B) compared to that of a group (A) and (C) ($p < 0.01$). There was a significant increase in standard score of VMI and a standard score of dissociated movement and grasp subsets of QUEST of a group (C) compared to that of a group (A) post-treatment ($p < 0.01$) while no significant difference was found in the standard score of grasping subset of PDMS-2 between-group (A) and (C) ($p > 0.05$) (Table 2).

Table (1): Participants' characteristics among groups.

Variables	Group (A)	Group (B)	Group (C)	p-value
Age in months: Mean±SD	75.7±9.06	75.65±9.08	75.5±9.0	0.99
MACS: Median	1.5	1.5	1.5	1

BFMF: Median		2	2	2	0.79
Sex: N(%)	Girls	9(45%)	9(45%)	10(50%)	0.93
	Boys	11(55%)	11(55%)	10(50%)	
Spasticity grade: N(%)	Grade I	9(45%)	8(40%)	10(50%)	0.81
	Grade I+	11(55%)	12(60%)	10(50%)	
Affected side: N(%)	Right	11(55%)	10(50%)	8(40%)	0.62
	Left	9(45%)	10(50%)	12(60%)	

SD: Standard deviation. MACS: Manual Ability Classification System. BFMF: Bimanual Fine Motor Function. N: Number. %: Percentage. p-value: Level of significance.

Table (2):PDMS-2 and QUEST results before and after treatment among groups.

Variables		Mean±SD			p-value		
		Group A	Group B	Group C	A vs B	A vs C	B vs C
VMI	Pre-treatment	4.20±1.10	4.25±1.06	4.30±0.86	0.980	0.940	0.980
	Post-treatment	5.95±1.31	10.5±1.7	7.70±1.50	0.001	0.002	0.001
	p-value	0.001	0.001	0.001			
Grasping (PDMS-2)	Pre-treatment	1.25±0.44	1.2±0.41	1.25±0.44	0.920	1	0.920
	Post-treatment	3.10±0.96	4.25±1.06	3.40±1.04	0.002	0.620	0.03
	p-value	0.001	0.001	0.001			
Dissociated Movement (%)	Pre-treatment	39.98±2.71	39.55±2.86	39.68±2.88	0.880	0.930	0.980
	Post-treatment	48.51±2.13	68.94±4.08	56.30±2.40	0.001	0.001	0.001
	p-value	0.001	0.001	0.01			
Grasping (%) (QUEST)	Pre-treatment	34.4±4.50	32.76±4.53	33.07±4.51	0.480	0.620	0.970
	Post-treatment	62.95±3.43	82.27±2.65	71.80±2.12	0.001	0.001	0.001
	p-value	0.001	0.001	0.001			

PDMS-2: Peabody Developmental Motor Scale. QUEST: Quality of Upper Extremity Skills Test. SD: Standard deviation. p-value: Level of significance. vs: Versus.

DISCUSSION

The findings of the study revealed a substantial improvement in all measuring variables in the three groups after three successive months of treatment. There was a substantial difference among the three groups regarding the standard score of the VMI subtest of PDMS-2, and regarding the standard score of dissociated movement and grasp subtests of QUEST. Although upper extremity functions and grasp hand skills were improved in three study groups but this improvement did not show a significant difference in standard score of grasping subtest of PDMS-2 between groups (A) and (C) after intervention.

Results revealed that the higher statistical significant difference in the upper extremity functions and activity performance and quality of movements was observed in group (B) (mCIMT) regarding standard score of VMI and grasp subtest of PDMS-2 as well as the standard score of QUEST in dissociated movement and grasp subtests rather than groups (A) and (C). This might be explained by the intension to move the upper extremity of the affected side is a notable difference in this group of treatment. It was observed that the children were willing to move the paralyzed upper limbs in functional activities, even though the paralyzed upper extremity does not perform the tasks in an efficient way. In addition, the attempt to execute movement leads to the reorganization of the brain's motor area, leading to improved motor skills and higher performance on ADL25.

This finding comes in agreement with Ju and Yoon¹¹ who compared the effects of mCIMT and therapy by mirror for upper extremity function and its influence on ADL. In their study, they explained the significant improvement in the mCIMT group to the execution of motor processes, from merely attempting to move the affected arm to actually move the affected arm, is effective in performing daily living activities. The above

mentioned findings suggest that the performance of entire motor actions had clinical importance compared to increased mechanical muscle function. It was found that mCIMT have substantial rehabilitative effects on motor function. It is essential to consider the impact of motor function improvement on daily living activities performance with respect to the child's ability to live independently.

Another analytical point of view was described by Kong et al.,²⁶ whose study showed that mCIMT appears to alter local cerebral perfusion in the area known to involve in the planning and execution of movements. Regional cerebral perfusion increased in frontal areas, occipital areas of the hemisphere affected, cerebellum and occipital, temporal areas of the hemisphere not affected but decreased in frontotemporal and white matter of the hemisphere affected. These alterations in young children with hemiplegic CP may be a sign of active cortical reorganization processes following CIMT. Improved hand function after receiving CIMT with corresponding changes occurring in cerebral perfusion on the single-photon emission computerized tomography were recorded.

The results of this study also concur with Johansen-Berg et al.,²⁷ who revealed that improved hand function after rehabilitation therapy is correlated with increased fMRI activity in the premotor cortex and secondary somatosensory cortex contralateral to the affected hand and in the superior bilateral superior posterior cerebellar hemispheres. This indicates that modified recruitment of sensorimotor cortex and cerebellum after restricted movement therapy may contribute to recovery.

Modified CIMT has faced major challenges to be accepted in clinic and research bases, including controversial opinions on the strict limitation of the unaffected arm and the forced use of the affected arm. However, findings of this study indicate that the attempt to move the affected arm voluntarily, conduce

improved enthusiasm and eventually cause functional improvement of the performance of activities by the affected upper extremity 11.

The results in this study revealed that group (B) (mCIMT) showed better improvement than group (A) (HABIT) in dissociated movements and grasp which come in agreement with the results of Zafer et al.,²⁸ who reported that mCIMT has superior outcomes as compared to HABIT in improving functional status of children with CP. Significant improvement in dissociated movements and grasp of QUEST is noted in mCIMT treated group as compared to the HABIT treated group. The mCIMT group received personalized ADL task training of affected limb two hours a day, six days a week, for two weeks. Restraint of that limb was provided during the waking period for six hours a day. The HABIT group received personalized training on ADL tasks for both limbs, with the same therapy sessions.

Our study results also come in agreement with Atteya et al.,²⁹ whose study revealed that mCIMT and HABIT improved upper extremity function with the superiority of mCIMT than HABIT in improving gross manual dexterity.

Robert et al.,³⁰ characterized the relationship between the integrity of the corpus callosum and hand functions, and assessed the relationship between changes in the hand functions and the integrity of the baseline of the corpus callosum on 44 unilateral spastic CP children. One group received 90 hours of HABIT and the other group received CIMT. Both groups have shown improvement in hand function. Furthermore, children with poorer corpus callosum integrity have been associated with better bimanual changes for group of CIMT but not for HABIT group.

Corpus callosum could be a predictor of bimanual changes after receiving CIMT training, but not HABIT training, that could be explained by two possible mechanisms. First; CIMT can help to improve the motor function by decreasing transcallosal inhibition pathway activation³¹. For this situation, due to poor integrity of the corpus callosum, interhemispheric inhibition is most likely marginal relative to those with a near-intact corpus callosum that promotes better recovery. The results of this study strengthened the hypothesis that reduced inhibitory connection activation leads to a better recovery³². Secondly; unlike those activities practiced in CIMT, the essence of the activities performed in HABIT represents bimanual coordination skills. Thus, regardless of corpus callosum integrity, the fact that more bimanual practice has been performed in the HABIT group enabled all children to improve in bimanual functions. Together, these two interpretations suggest that corpus callosum integrity can only be used as a biomarker following CIMT, not HABIT³⁰.

Our findings after intervention revealed that the TOT group showed substantially more progress of the paretic upper extremity in all outcomes than the HABIT group regarding VMI and grasp as well as dissociated movement. This might be explained by Shumway-cook and Woollacott³³ who stated that TOT causes cortical reorganization and focuses on the study of motor control, motor learning and rehabilitation science; active participation and skill acquisition are essential components of patient recovery.

The results of this study also agree with Thant et al.,³⁴ who reported that task oriented training can induce greater neural plastic changes and transfer to real-life due to the practiced tasks that are meaningful as well as familiar everyday tasks. Task-specific training can restore function through the use of spared brain parts adjacent to injured areas, and/or by recruiting additional brain areas.

CONCLUSION

The results of this study have provided the evidence that the HABIT, mCIMT and TOT could enhance upper extremity functions in children with hemiparetic CP in which the modified constrained induced movement therapy provides higher significant improvement followed by task-oriented training while the least improvement showed with HABIT treatment.

REFERENCES

1. Shierk A, Lake A and Haas T. Therapeutic interventions for the upper limb classified by manual ability in children with cerebral palsy. *Seminars in Plastic Surgery*, 2016;30:14-23.
2. Schnackers M, Beckers L, Janssen-Potten Y, Aarts P, Rameckers E et al. Home-based bimanual training based on motor learning principles in children with unilateral cerebral palsy and their parents (the COAD-study). *BMC Pediatrics*, 2018;18:139-147.
3. Colver A, Fairhurst C and Pharoah PO. Cerebral palsy. *Lancet*, 2014;383:1240-1249.
4. Korzeniewski SJ, Slaughter J, Lenski M, Haak P and Paneth N. The complex aetiology of cerebral palsy. *Nature Reviews Neurology*, 2018;14:528-543.
5. El-Tallawy HN, Farghaly WM, Shehata GA, Rageh TA, Metwally NA, Badry R, et al. Cerebral palsy in Al-Quseir City, Egypt: prevalence, subtypes, and risk factors. *Neuropsychiatric Disease and Treatment*, 2014;10:1267-1272.
6. James S, Ziviani J, Ware RS and Boyd RN. Relationships between activities of daily living, upper limb function and visual perception in children and adolescents with unilateral cerebral palsy. *Developmental Medicine Child Neurology*, 2015; 57: 852-7.
7. Junior PRF, Filoni E, Setter CM, Berbel AM, Fernandes AO and Moura RC. Constraint-induced movement therapy of upper limb of children with cerebral palsy in clinical practice: systematic review of the literature. *Cochrane Systematic Review*, 2017;24:334-346.
8. Fehlings D, Rang M, Glazier J and Steele C. Botulinum toxin type A injections in the spastic upper extremity of children with hemiplegia: child characteristics that predict a positive outcome. *European Journal of Neuroscience*, 2001;8:145-149.
9. Geerdink Y, Aarts P, Holst M, Lindeboom R, Burg JVD and Steenbergen B. Development and psychometric properties of the Hand-Use-at-Home questionnaire to assess amount of affected hand-use in children with unilateral paresis. *Developmental Medicine and Child Neurology*, 2017;59:919-925.
10. Boyd RN, Ziviani J, Sakzewski L, Novak I, Badawi N, Pannek K et al. REACH: Study protocol of a randomized trial of rehabilitation very early in congenital hemiplegia. *British Medical Journal*, 2017;7:e017204. doi:10.1136/bmjopen-2017-017204.
11. Ju Y and Yoon I. The effect of modified constrained induced movement therapy and mirror therapy on the upper extremity function and its influence on activities of daily living. *Journal of Physical Therapy Science*, 2018;30:77-81.
12. Basu AP, Pearse J, Kelly S, Wisher V and Kisler J. Early intervention to improve hand function in hemiplegic cerebral palsy. *Frontiers of Neurology*, 2015;5:281-289.
13. Meng G, Meng X, Tan Y, Yu J, Jin A, Zhao Y, et al. Short-term efficacy of hand-arm bimanual intensive training on upper arm function in acute stroke patients: a randomized controlled trial. *Frontiers of Neurology*. 2017;8:726-734.
14. Surkar SM, Hoffman RM, Willett S, Flegle J, Harbourne R and Kurz MJ. Hand-arm bimanual intensive therapy improves prefrontal cortex activation in children with hemiplegic cerebral palsy. *Pediatric Physical Therapy*, 2018;30:93-100.

15. Page SJ, Sisto SA, Levine P and McGrath RE. Efficacy of modified constraint-induced movement therapy in chronic stroke: a single-blinded randomized controlled trial. *Archives of Physical Medicine and Rehabilitation*, 2004;85:14-18.
16. Ferrari A and Cioni G. The Spastic Forms of Cerebral Palsy. A Guide to the Assessment of Adaptive Functions [Internet]. Italia: Springer, 2010. Available at: <https://doi.org/10.1007/b139073> (Accessed 8 October 2018).
17. Thompson AME, Chow S, Vey C and Lloyd M. Constraint-induced movement therapy in children aged 5 to 9 years with cerebral palsy: a day camp model. *Pediatric Physical Therapy*, 2015;27:72-80.
18. Kwon H and Ahn S. Effect of task-oriented training and high-variability practice on gross motor performance and activities of daily living in children with spastic diplegia. *The Journal of Physical Therapy Science*, 2016;28:2843-2848.
19. Ko EJ, Sung IY, Moon HJ, Yuk JS, Kim H and Lee NH. Effect of group-task-oriented training on gross and fine motor function, and activities of daily living in children with spastic cerebral palsy. *Physical and Occupational Therapy in Pediatrics*, 2020;40:18-30.
20. Salem Y and Godwin EM. Effects of task-oriented training on mobility function in children with cerebral palsy. *Neurorehabilitation*, 2009;24:307-313.
21. Bohannon RW and Smith MB. Inter-reliability of modified Ashworth scale of muscle spasticity. *Physical Therapy*, 1987;67:206-207.
22. Eliasson A, Krumlinde-Sundholm L, Rösblad B, Beckung E, Arner M, Öhrvall A, et al. The Manual Ability Classification System (MACS) for children with cerebral palsy: scale development and evidence of validity and reliability. *Developmental Medicine and Child Neurology*, 2006;48:549-554.
23. Elvrum AKG, Andersen GL, Himmelmann K, Beckung E, Öhrvall AM and Lydersen S. Bimanual Fine Motor Function (BFMF) classification in children with cerebral palsy: aspects of construct and content validity. *Physical and Occupational Therapy in Pediatrics*, 2016;36:1-16.
24. Folio MR and Fewell RR. *Peabody Developmental Motor Scale*. 2nd edition. Austin: Pearson, 2000.
25. Michielsen ME, Selles RW, Geest JN, Eckhardt M, Yavuzer G, Stam HJ, et al. Motor recovery and cortical reorganization after mirror therapy in chronic stroke patients: a phase II randomized controlled trial. *Neurorehabilitation & Neural Repair*, 2011;25:223-233.
26. Kong E, Chun K, Jeong J and Cho I. Brain SPECT analysis after constraint-induced movement therapy in young children with hemiplegic cerebral palsy: case report. *Nuclear Medicine and Molecular Imaging*, 2013;47:119-124.
27. Johansen-Berg H, Dawes H, Guy C, Smith SM, Wade DT and Matthews PM. Correlation between motor improvements and altered fMRI activity after rehabilitative therapy. *Brain*, 2002;125:2731-2742.
28. Zafer H, Amjad I, Malik AN and Shaukat E. Effectiveness of constraint induced movement therapy as compared to bimanual therapy in upper motor function outcome in child with hemiplegic cerebral palsy. *Pakistan Journal of Medical Sciences*, 2016;32:181-184.
29. Atteya A, Mansour WT, Fahmy EM and El Balawy YM. Efficacy of constrained induced movement therapy versus bilateral arm training on upper extremity functional outcomes in stroke patients. *Medical Journal of Cairo University*, 2015;83:79-85.
30. Robert MT, Gutterman J, Ferre CL, Chin K, Brandao MB, Gordon AM and Friel K. Improvements in upper extremity function in children with unilateral spastic cerebral palsy after intensive training correlates with interhemispheric connectivity. *Developmental Medicine and Child Neurology*, 2018; 60. Available at: <https://doi.org/10.1111/dmcn.10314017>
31. Liepert J. Motor cortex excitability in stroke before and after constraint-induced movement therapy. *Cognitive and Behavioral Neurology*, 2006;19:41-47.
32. Manning KY, Fehlings D, Mesterman R, Gorter JG, Switzer L, Campbell C, et al. Resting state and diffusion neuroimaging predictors of clinical improvements following constraint-induced movement therapy in children with hemiplegic cerebral palsy. *Journal of Child Neurology*, 2015;30:1507-1514
33. Shumway-Cook A and Woollacott M. *Motor control: translating research into clinical practice*, 4th ed. Philadelphia: Lippincott Williams and Wilkins, 2012.
34. Thant AA, Wanpen S, Nualnetr N, Puntumetakul R, Chatchawan U, Hla KM, et al. Effects of task oriented training on upper extremity functional performance in patients with sub-acute stroke: a randomized controlled trial. *Journal of Physical Therapy Science*, 2019;31:82-87.