

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.

© The Authors 2020;

This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike. (<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited. The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 02.01.2020. Revised: 25.01.2020. Accepted: 04.02.2020.

Constraint-induced movement therapy in stroke patients

Joanna Ilzecka

Independent Neurological Rehabilitation Unit, Medical University of Lublin

SUMMARY

Stroke is an important cause of disability and death of patients. The consequence of a stroke may be weakness of limbs or hemiplegia. Constraint-induced movement therapy (CIMT) is a technique of rehabilitation, whose mission is to provoke the patient to use the paretic upper limb. In the literature is presented many clinical studies on the effectiveness of CIMT therapy in patients after stroke. The aim of the work was a review of the literature on CIMT in stroke patients.

Keywords: constraint-induced movement therapy, rehabilitation, stroke

INTRODUCTION AND PURPOSE OF WORK

Patients with hemispheric stroke may have limited use of the affected upper limb. In the first days after stroke onset, this concerns about 80% of the patients, while deficits in upper limb capacity persist at 6 months poststroke in 30% to 66% of the hemiplegic stroke patients (1-4).

Constraint-induced movement therapy (CIMT) is a multifaceted neurorehabilitation technique that aims to improve motor function and increase use of the hemiparetic upper limb in real-world activities (5). CIMT is a behavioral technique that is based on reversing learned nonuse to improve functional use of the upper extremity after a stroke (6,7). The original protocol of CIMT consists of three components: immobilization of the nonparetic arm with a padded mitt for 90% of the waking hours, task-oriented training with a high number of repetitions for about 6 h a day, and behavioral strategies to improve from the clinical setting to the patient's home environment (8,9). Modified forms of constraint-induced movement therapy (mCIMT) have been developed including reducing training during the period of

restraint or concentrating only on the use of restraint without additional treatment of the affected arm in a forced-use intervention (9,10).

Wittenberg et al. (11) described current understanding of the changes in brain function and structure that occur in response to CIMT. Studies using transcranial magnetic stimulation have demonstrated an increase in the size of the representation of paretic hand muscles in the ipsilesional motor cortex after CIMT. This motor map expansion occurs in response to CIMT delivered at all time periods after stroke, from within days to after several years. Functional neuroimaging studies have shown varying patterns of change in activation within the sensorimotor network after CIMT. This variability may depend on the extent of stroke-induced damage to the corticospinal tract, the major descending motor pathway in the brain. This variability may also stem from interacting plastic changes in brain structure occurring in response to CIMT. The authors concluded that CIMT is the first well defined poststroke motor rehabilitation to have identified changes in brain function and structure that accompany gains in motor function of the paretic upper limb.

The aim of the work was a review of the literature on CIMT in stroke patients.

CONSTRAINT-INDUCED MOVEMENT THERAPY IN STROKE PATIENTS – *REVIEW OF THE LITERATURE*

The review conducted by Etoom et al. (9) aimed to investigate evidence of the effect of CIMT on upper extremity in stroke patients and to identify optimal methods to apply CIMT. Randomized clinical trials that studied the effect of CIMT on upper extremity outcomes in stroke patients compared with other rehabilitative techniques. The authors revealed a heterogeneous significant effect of CIMT on upper extremity. There was no significant effect of CIMT at different durations of follow-up. The effect of CIMT changed in terms of sample size and quality features of the articles included. A findings indicate that evidence for the superiority of CIMT in comparison with other rehabilitative interventions is weak.

Corbetta et al. (10) assessed the efficacy of CIMT, mCIMT, or forced use (FU) for arm management in people with hemiparesis after stroke. Eleven trials assessed disability immediately after the intervention, indicating a non-significant standard mean difference favouring CIMT compared with conventional treatment. For the most frequently reported outcome, arm motor function it was showed a significant effect in favour of CIMT. Three studies involving explored disability after a few months of follow-up and found no significant difference. The authors found that CIMT was associated with limited improvements in motor impairment and motor function, but that these benefits did not convincingly reduce disability.

The study conducted by Stock et al. (12) aimed to compare the long-term effects of CIMT applied 6 months after stroke with the results of CIMT applied within 28 days post-stroke. Both groups received standard rehabilitation and were tested at 5 time points. The results revealed that both groups showed significant improvements after 12 months. No significant differences between the 2 treatment groups were found before and after the delayed intervention group received CIMT at 6 months and during the 12-month follow-up. Both groups showed only minor impairment after 6 months. The first group showed an initially faster recovery curve of Wolf Motor Function Test (WMFT), Nine-Hole Peg Test (NHPT), and Modified Rankin Scale (MRS) scores. The authors concluded that commencing CIMT early is as good as delayed intervention in the long term, specifically in this group of patients who might have reached a ceiling effect during the first 6 months after stroke.

Uswatte et al. (13) evaluated the efficacy of an expanded form of constraint-induced movement therapy (eCIMT). At post-treatment, the immediate eCIMT group showed

significant gains relative to the combination of the control groups on the Grade-4/5 Motor Activity Log and a convergent measure, the Canadian Occupational Performance Measure. The short and long-term outcomes of the crossover eCIMT group were similar to those of the immediate eCIMT group. The authors concluded that eCIMT produces a large, meaningful, and persistent improvement in everyday use of the more-affected arm in adults with severe upper-extremity hemiparesis long after stroke.

Banq et al. (14) measured the effects of mCIMT, additionally modified by adding trunk restraint (TR), on upper-limb function and activities of daily living (ADLs) in early post-stroke patients and concluded that mCIMT combined with TR may be more effective than mCIMT alone in improving upper-limb function and ADLs in patients with early stroke.

Takebayashi et al. (15) investigated the effects of dual-hemisphere transcranial direct current stimulation (dual-tDCS) of both the affected (anodal tDCS) and non-affected (cathodal tDCS) primary motor cortex, combined with peripheral neuromuscular electrical stimulation (PNMES), on the effectiveness of CIMT as a neurorehabilitation intervention in chronic stroke. Twenty chronic stroke patients were randomly allocated to the control group, receiving conventional CIMT, or the intervention group receiving dual-tDCS combined with PNMES before CIMT. The findings suggest a novel pretreatment stimulation strategy based on dual-tDCS and PNMES may enhance the therapeutic benefit of CIMT.

Takebayashi et al. (16) aimed to clarify the relationship between several non-corticospinal neural pathway integrities and the short- and long-term benefits of CIMT. The patients showed significant improvements in all functional assessments at both short- and long-term follow-ups. Immediate the Fugl-Meyer Assessment (FMA) score improvements were significantly correlated with fractional anisotropy (FA) of the affected anterior limb of the internal capsule (ALIC), body of the corpus callosum, column and body of the fornix (CBF), cingulate cortex (CgC), cerebral peduncle (CP), and posterior limb of the internal capsule. Six-month FMA score improvements were significantly correlated with FA of the affected ALIC, CgC, CBF, CP, and superior frontooccipital fasciculus. The authors concluded that the integrity of the affected corticospinal and non-corticospinal motor pathways was associated with CIMT-induced motor learning at least 6 months after CIMT.

Doussoulin et al. (7) determined the effectiveness of a group therapy, compared with individual modified CIMT, in increasing the use and functionality of movement of a paretic upper limb. Thirty-six patients who had had a stroke more than 6 months previously were divided randomly into two intervention groups. Both types of intervention generated increases in the function and use of the upper extremity, with these increases being higher in the group therapy. The effects of the group therapy modality were maintained 6 months after the intervention ended.

E Silva et al. (17) examined the effects of CIMT for lower limbs on functional mobility and postural balance in stroke patients. A 40-day follow-up, single-blind randomized controlled trial was performed with 38 subacute stroke patients (mean of 4.5 months post-stroke). Participants were randomized into: treadmill training with load to restraint the non-paretic ankle (experimental group) or treadmill training without load (control group). Both groups performing daily training for two consecutive weeks (nine sessions) and performed home-based exercises during this period. It was observed improvements after training in postural balance and functional mobility, showed by Timed Up and Go test (TUG) and by kinematic turning parameters. All these improvements were observed in both groups and maintained in follow-up. The authors concluded that two weeks of treadmill gait training associated to home-based exercises can be effective to improve postural balance and functional mobility in subacute stroke patients.

Yu et al. (18) evaluated the therapeutic effects of mCIMT in patients with acute subcortical infarction. The role of mCIMT was investigated in patients experiencing

subcortical infarction in the preceding 14 days. mCIMT group was treated daily for 3 h over 10 consecutive working days, using a mitt on the unaffected arm for up to 30% of waking hours. Results showed that treatment significantly improved the movement in the mCIMT group compared with the control group. The mean Wolf Motor Function (WMF) score was significantly higher in the mCIMT group. It was also showed that the appearance of motor-evoked potentials (MEPs) were significantly higher in the mCIMT group compared with the baseline data. Moreover, a significant change in ipsilesional silent period occurred in the mCIMT group compared with the control group. The authors concluded that mCIMT resulted in significant functional changes in timed movement immediately following treatment in patients with acute subcortical infarction. Further, early mCIMT improved ipsilesional cortical excitability. However, no long-term effects were seen.

Choi et al. (19) determined whether game-based CIMT is effective at improving balance ability in patients with stroke. Thirty-six patients with chronic stroke were randomly assigned to game-based CIMT, general game-based training, and conventional groups. All interventions were conducted 3 times a week for 4 weeks. All 3 groups showed significant improvement in anterior-posterior axis (AP-axis) distance, sway area, weight-bearing symmetry, Functional Reach Test (FRT), modified Functional Reach Test (mFRT), and Timed Up and Go (TUG) test after therapy. The statistical analysis showed significant differences in AP-axis, and sway area, weight-bearing symmetry of the game-based CIMT group compared with the other group. The authors concluded that although the general game-based training and the game-based CIMT both improved on static and dynamic balance ability, game-based CIMT had a larger effect on static balance control, weight-bearing symmetry, and side-to-side weight shift.

Barzel et al. (20) assessed the efficacy of home CIMT, a modified form of CIMT that trains arm use in daily activities within the home environment. 96% patients in the home CIMT group and 100% patients in the standard therapy group completed treatment and were assessed at 4 weeks. Patients in both groups improved in quality of movement. Patients in the home CIMT group improved more than patients in the standard therapy group. Both groups also improved in motor function performance time, but the extent of improvement did not differ between groups. According to authors home-based CIMT can enhance the perceived use of the stroke-affected arm in daily activities more effectively than conventional therapy, but was not superior with respect to motor function.

Thrane et al. (21) evaluated the effect of a mCIMT within 4 weeks poststroke. This trial investigated the effects of CIMT in 47 individuals who had experienced a stroke in the preceding 26 days. The CIMT program was 3 h/d over 10 consecutive working days, with mitt use on the unaffected arm for up to 90% of waking hours. The follow-up time was 6 months. The study showed that after therapy, the mean timed Wolf Motor Function test (WMFT) score was significantly better in the CIMT group compared with the control group. Moreover, posttreatment dexterity, as tested with the Nine-Hole Peg test (NHPT), was significantly better in the CIMT group, whereas the other test results were similar in both the groups. At the 6-month follow-up, the 2 groups showed no significant difference in arm impairment, function, or use in daily activities. The authors concluded that despite a favorable effect of CIMT on timed movement measures immediately after treatment, significant effects were not found after 6 months.

Sawaki et al. (22) compared the differential degree of cortical reorganization according to chronicity in stroke subjects receiving CIMT. Seventeen early and 9 late individuals were included to the study. Each patient received CIMT for 2 weeks. The authors observed that the early group showed greater improvement in Wolf Motor Function Test (WMFT) compared with the late group. Transcranial magnetic stimulation motor maps showed persistent enlargement in both groups but the late group trended toward more

enlargement. The map shifted posteriorly in the late stroke group. The authors concluded that CIMT appears to lead to greater improvement in motor function in the early phase after stroke. Greater cortical reorganization in map size and position occurred in the late group in comparison.

Boe et al. (23) investigated whether cognitive and emotional status affects motor improvement during two weeks of CIMT and retention of the gain at three months follow-up. Twenty stroke patients (3-12 months post stroke) completed two weeks of CIMT. Motor performance was measured using the Wolf Motor Function Test (WMFT). Cognitive and emotional status was measured with a comprehensive neuropsychological test battery and a questionnaire on emotional status. All measures were performed at baseline, after two weeks of training, and at three months follow-up. The authors found no significant correlation between cognitive or emotional measures at baseline and improvement in motor performance post training. Also, cognitive and emotional status did not correlate with motor retention at three months follow-up. The authors found no evidence to support that cognitive performance in stroke patients can predict motor gain from CIMT.

The aim of the study conducted by Kitago et al. (24) was to demonstrate the feasibility of using kinematic measures in conjunction with clinical outcome measures to better understand the mechanism of recovery in chronic stroke patients with mild to moderate motor impairments who undergo CIMT. Ten participants with chronic stroke were included in a modified CIMT protocol over 2 weeks. There was a clinically meaningful improvement in Action Research Arm Test (ARAT) from the second pre-CIMT session to the post-CIMT session compared with the change between the 2 pre-CIMT sessions. However, the Upper-Extremity Fugl-Meyer score (FM-UE) and kinematic measures showed no significant improvements. The authors concluded that functional improvement in the affected arm after CIMT in patients with chronic stroke appears to be mediated through compensatory strategies rather than a decrease in impairment or return to more normal motor control.

Treger et al. (25) evaluated the effect of mCIMT on improving paretic arm function in patients after stroke. Twenty-eight subacute stroke patients with arm paresis were randomized into a mCIMT or control group. The mCIMT group received 1-hour daily physical rehabilitation sessions for 2 weeks. The unaffected arm was restrained during the sessions. Subjects were encouraged to wear a restrictive mitten up to 4 hours a day. The subjects were asked to perform the following tasks, with the affected hand for 30 seconds: (1) transfer pegs from a saucer to a pegboard; (2) grasp, carry, and release a hard rubber ball; and (3) "eating," using a spoon to remove the jelly from the plate, bring it towards the mouth, and then place it on another plate. Results showed that the mCIMT group showed significantly higher changes in all 3 tests compared to the standard rehabilitation group. The authors concluded that the study provides additional support for the use of mCIMT during a subacute rehabilitation period of poststroke patients. According to authors, CIMT may facilitate functional improvement of a plegic hand.

Smania (26) compared the effects of a reduced-intensity mCIMT program that included splinting the unaffected arm for 12 hours daily with the effects of a conventional rehabilitation program for arm paresis in patients with stroke. Sixty-six participants with hemiparesis (3-24 months poststroke) who could extend the wrist and several fingers at least 10° were randomly assigned to mCIMT or conventional rehabilitation. Each group underwent 10 (2 h/d) treatment sessions (5 d/wk for 2 weeks). Results showed that the mCIMT group overall had greater improvement than the control group in terms of the Wolf Motor Function Test (WMFT-FA), the Motor Activity Log (MAL-AOU, and MAL-QOM). Differences between groups were significant both after treatment and at the 3-month follow-up. Furthermore, the mCIMT group showed a greater decrease of Ashworth Scale score than the control group at 3 months. The authors concluded that two hours of CIMT may

be more effective than conventional rehabilitation in improving motor function and use of the paretic arm in patients with chronic stroke.

Fuzaro et al. (27) evaluated the effect of Modified FUT (mFUT) and mCIMT on the gait and balance during four weeks of treatment and 3 months follow-up. The study included thirty-seven hemiparetic patients after stroke. Participants were evaluated at Baseline, 1st, 2nd, 3rd and 4th weeks, and three months after randomization. The Stroke Impact Scale (SIS), Berg Balance Scale (BBS) and Fugl-Meyer Motor Assessment (FM) for the evaluation were used. Gait was analyzed by the 10-meter walk test (T10) and Timed Up & Go test (TUG). Results showed that participants had better health status (SIS), better balance, better use of lower limb (BBS and FM) and greater speed in gait (T10 and TUG), during the weeks of therapy and months of follow-up, compared to the baseline. The results of the study conducted by Fuzaro et al. showed that mFUT and mCIMT are effective in the rehabilitation of balance and gait.

Könönen et al. (28) used multimodal functional imaging to assess the relationship of clinical gain and imaging changes in patients with chronic stroke whose voluntary motor control improved after CIMT. Eleven patients were included to the study. Results showed that increase in functional MRI (fMRI) activation in the sensorimotor areas was greater amongst those subjects who had poor hand motor behavior before therapy and/or whose motor behavior improved notably because of therapy than amongst subjects with relatively good motor behavior already before therapy. The magnitude of CIMT-induced changes in task-related fMRI activation differed between lesioned and non-lesioned hemispheres, and the fMRI laterality index was different for paretic and non-paretic hand tasks. The corticospinal conduction time in transcranial magnetic stimulation (TMS) was significantly decreased after CIMT therapy. The authors concluded that alterations in sensorimotor cortical activations (fMRI) and corticospinal conductivity (TMS) were observed after intensive rehabilitation in patients with chronic stroke. Activation and functional changes in fMRI and TMS correlated significantly with the degree of clinical improvement in hand motor behavior.

McCall et al. (29) investigated the efficacy of a mCIMT protocol on participation, activity, and impairment in a population of older individuals after subacute stroke. Four older adults were assessed before and after therapy. Although none of the participants adhered to the 6-hr per day self-practice aspect of the CIMT protocol, considerable improvements were noted in participation, as measured using the Canadian Occupational Performance Measure. Some improvements were also noted at the level of impairment and activity.

Brunner et al. (30) examined eligibility for modalities such as CIMT and mCIMT in the subacute phase after stroke. Patients with arm paresis 1 to 2 weeks post stroke were investigated. Participants who were cognitively intact, medically stable, and able to extend the wrist and 3 fingers 10° as a lower limit were included to CIMT therapy. Motor function was assessed by the Action Research Arm Test (ARAT) and the Nine Hole Peg Test at 1 to 2 weeks, 4 weeks, and 3 months post stroke. Results showed that 46% patients were eligible according to motor function of the hand at 1 to 2 weeks post stroke, whereas in the other patients motor function was either too good or too poor. The share of patients eligible declined to 31% after 4 weeks and 15% after 3 months. Results indicate that eligibility for CIMT or mCIMT should not be considered before 4 weeks post stroke because much improvement in arm function was shown to occur during the first month post stroke with standard rehabilitation.

The objective of study conducted by Barzel et al. (31) was to evaluate the effects of a 4-week homebased CIMT program among chronic stroke patients and to compare them with a 2-week CIMT program. Seven adults with chronic stroke completed a newly developed variant of CIMT, performed at patients' homes (group1, CIMThome), supervised by an instructed family member, constraint of unaffected hand for a target of 60% of waking hours.

Effects on improvement in upper extremity function were compared with patients treated according to the original protocol (group2, CIMTclassic), supervised by a physiotherapist, constraint of unaffected hand for a target of 90% of waking hours. Patients from both groups showed almost identical improvement of their motor function according to scores on the Wolf Motor Function Test (WMFT) and the Motor Activity Log (MAL) immediately after the treatment period as well as at follow-up after 6 months. The authors concluded that CIMThome is not only feasible but also as effective as CIMTclassic.

Azab et al. (32) investigated the effectiveness of CIMT on the Barthel Index (BI) scores in patients after stroke. Twenty-seven patients participated in the study as an experimental group. The experimental/treatment group received traditional therapy with the CIMT where the intact contralateral upper limb was placed in a removable cast for 6 hours a day during waking hours for 4 weeks. The control group received traditional therapy only. Results showed significant improvement in the BI for the experimental group compared to the control group. The authors concluded that following stroke, patients who received CIMT every day for 4 weeks in conjunction with traditional rehabilitation therapy showed significant changes in the BI upon discharge and this positive outcome was preserved after 6 months follow-up.

Lin et al. (33) evaluated the benefits of CIMT relative to traditional intervention equal in treatment intensity and use of restraint mitt outside rehabilitation on motor performance and daily functions in stroke patients. The subjects were randomized to receive CIMT (restraint of the less affected limb combined with intensive training of the affected limb) or traditional intervention (control treatment) during the study. The treatment intensity was matched between the two groups (2h/d, 5d/wk for 3 wk). Both groups of patients received restraint of the less affected limb outside rehabilitation (ca. 3h/d). The CIMT group showed significantly greater improvements in motor performance, level of functional independence, and the mobility domain of extended activities of daily living.

Dahl et al. (34) determined the effect and feasibility of CIMT compared with traditional rehabilitation in short and long term. The patients were assessed at baseline, post-treatment and at six-month follow-up. The CIMT group showed a statistically significant shorter performance time and greater functional ability than the control group on the Wolf Motor Function Test at post-treatment assessment. There was a non-significant trend toward greater amount of use and better quality of movement in the CIMT group according to the Motor Activity Log. No such differences were seen on Functional Independence Measure at the same time. At six-month follow-up the CIMT group maintained their improvement, but as the control group improved even more, there were no significant differences between the groups on any measurements. The authors concluded that CIMT seems to be an effective and feasible method to improve motor function in the short term, but no long-term effect was found.

The aim of the study conducted by Wolf et al. (35) was to compare the effects of a 2-week program of CIMT vs usual and customary care on improvement in upper extremity function among patients who had a first stroke within the previous 3 to 9 months. Two hundred twenty-two individuals with predominantly ischemic stroke were included to the study. From baseline to 12 months, the CIMT group showed greater improvements than the control group in both the Wolf Motor Function Test (WMFT) Performance Time and in the Motor Activity Log (MAL) Amount of Use. The authors concluded that among patients who had a stroke within the previous 3 to 9 months, CIMT produced statistically significant and clinically relevant improvements in arm motor function that persisted for at least 1 year.

Dettmers et al. (36) evaluated the effectiveness of a distributed version of CIMT. Eleven persons with chronic stroke took part in the study. All had active extension of at least 20 degrees at the wrist and at least 10 degrees for each finger of the more-affected hand. Real-

world (Motor Activity Log) and laboratory motor activity (Wolf Motor Function Test, Frenchay Arm Test, Nine Hole Peg Test), strength (grip force) and spasticity (Ashworth Scale), and quality of life (QOL; Stroke Impact Scale) were assessed. Participants showed significant improvements in more-affected arm real-world motor activity, laboratory motor activity, strength and spasticity, as well as in some aspects of QOL, up to 6 months after treatment. The authors concluded that distributed CIMT is a promising intervention for improving motor function and QOL in patients with chronic stroke.

CONCLUSION

CIMT is a rehabilitation technique for improving the function of the paretic upper limb after stroke. Review of the literature points to the beneficial effect of the use of this technique in stroke patients.

REFERENCES

1. Jorgensen H, Nakayama H, Raaschou H, Olsen T. Stroke. Neurologic and functional recovery the Copenhagen Stroke Study. *Phys Med Rehabil Clin N Am.* 1999;10:887-906.
2. Nijland R, Van Wegen E, Harmeling-Van der Wel B, Kwakkel G. Presence of finger extension and shoulder abduction within 72 hours after stroke predicts functional recovery: early prediction of functional outcome after stroke: the EPOS cohort study. *Stroke.* 2010;41:745-50.
3. Kwakkel G, Kollen B, Van der Grond J, Prevo A. Probability of regaining dexterity in the flaccid upper limb: impact of severity of paresis and time since onset in acute stroke. *Stroke.* 2003;34:2181-6.
4. Veerbeek JM, Langbroek-Amersfoort AC, van Wegen EE, Meskers CG, Kwakkel G. Effects of robot-assisted therapy for the upper limb after stroke. *Neurorehabil Neural Repair.* 2017;31:107-21.
5. Taub E, Miller NE, Novack TA, Cook EW, Fleming WC, Nepomuceno CS, et al. Technique to improve chronic motor deficit after stroke. *Arch Phys Med Rehabil.* 1993;74:347-54.
6. Doussoulin A. Terapia de restricción inducida y su impacto en revertir el “no uso aprendido en neurorehabilitación. *Rev Kinesiología.* 2011;30:14-9.
7. Doussoulin A, Rivas C, Rivas R, Saiz J. Effects of modified constraint-induced movement therapy in the recovery of upper extremity function affected by a stroke: a single-blind randomized parallel trial-comparing group versus individual intervention. *Int J Rehabil Res.* 2018;41(1):35-40.
8. Morris D, Taub E, Mark V. Constraint-induced movement therapy: characterizing the intervention protocol. *Eura Medicophys.* 2006;42:257-68.
9. Etoom M, Hawamdeh M, Hawamdeh Z, Alwardat M, Giordani L, Bacciu S, et al. Constraint-induced movement therapy as a rehabilitation intervention for upper extremity in stroke patients: systematic review and meta-analysis. *Int J Rehabil Res.* 2016;39(3):197-210.
10. Corbetta D, Sirtori V, Castellini G, Moja L, Gatti R. Constraint-induced movement therapy for upper extremities in people with stroke. *Cochrane Database Syst Rev.* 2015;(10):CD004433.
11. Wittenberg GF, Schaechter JD. The neural basis of constraint-induced movement therapy. *Curr Opin Neurol.* 2009;22(6):582-8.
12. Stock R, Thrane G, Anke A, Gjone R, Askim T. Early versus late-applied constraint-induced movement therapy: A multisite, randomized controlled trial with a 12-month follow-up. *Physiother Res Int.* 2018;23(1).

13. Uswatte G, Taub E, Bowman MH, Delgado A, Bryson C, Morris DM, et al. Rehabilitation of stroke patients with plegic hands: Randomized controlled trial of expanded constraint-induced movement therapy. *Restor Neurol Neurosci.* 2018;36(2):225-44.
14. Bang DH, Shin WS, Choi HS. Effects of modified constraint-induced movement therapy with trunk restraint in early stroke patients: A single-blinded, randomized, controlled, pilot trial. *NeuroRehabilitation.* 2018;42(1):29-35.
15. Takebayashi T, Takahashi K, Moriwaki M, Sakamoto T, Domen K. Improvement of upper extremity deficit after constraint-induced movement therapy combined with and without preconditioning stimulation using dual-hemisphere transcranial direct current stimulation and peripheral neuromuscular stimulation in chronic stroke patients: A pilot randomized controlled trial. *Front Neurol.* 2017;8:568.
16. Takebayashi T, Marumoto K, Takahashi K, Domen K. Differences in neural pathways are related to the short- or long-term benefits of constraint-induced movement therapy in patients with chronic stroke and hemiparesis: a pilot cohort study. *Top Stroke Rehabil.* 2018;25(3):203-8.
17. E Silva EMGS, Ribeiro TS, da Silva TCC, Costa MFP, Cavalcanti FADC, Lindquist ARR. Effects of constraint-induced movement therapy for lower limbs on measurements of functional mobility and postural balance in subjects with stroke: a randomized controlled trial. *Top Stroke Rehabil.* 2017;24(8):555-61.
18. Yu C, Wang W, Zhang Y, Wang Y, Hou W, Liu S, et al. The effects of modified constraint-induced movement therapy in acute subcortical cerebral infarction. *Front Hum Neurosci.* 2017;11:265.
19. Choi HS, Shin WS, Bang DH, Choi SJ. Effects of game-based constraint-induced movement therapy on balance in patients with stroke: A single-blind randomized controlled trial. *Am J Phys Med Rehabil.* 2017;96(3):184-90.
20. Barzel A, Ketels G, Stark A, Tetzlaff B, Daubmann A, Wegscheider K, et al. Home-based constraint-induced movement therapy for patients with upper limb dysfunction after stroke (HOME CIMT): a cluster-randomised, controlled trial. *Lancet Neurol.* 2015;14(9):893-902.
21. Thrane G, Askim T, Stock R, Indredavik B, Gjone R, Erichsen A, et al. Efficacy of constraint-induced movement therapy in early stroke rehabilitation: A randomized controlled multisite trial. *Neurorehabil Neural Repair.* 2015;29(6):517-25.
22. Sawaki L, Butler AJ, Leng X, Wassenaar PA, Mohammad YM, Blanton S, et al. Differential patterns of cortical reorganization following constraint-induced movement therapy during early and late period after stroke: A preliminary study. *NeuroRehabilitation.* 2014;35(3):415-26.
23. Boe EW, Pedersen AD, Pedersen AR, Nielsen JF, Blicher JU. Cognitive status does not predict motor gain from post stroke constraint-induced movement therapy. *NeuroRehabilitation.* 2014;34(1):201-7.
24. Kitago T, Liang J, Huang VS, Hayes S, Simon P, Tenteromano L, et al. Improvement after constraint-induced movement therapy: recovery of normal motor control or task-specific compensation? *Neurorehabil Neural Repair.* 2013;27(2):99-109.
25. Treger I, Aidinof L, Lehrer H, Kalichman L. Modified constraint-induced movement therapy improved upper limb function in subacute poststroke patients: a small-scale clinical trial. *Top Stroke Rehabil.* 2012;19(4):287-93.
26. Smania N, Gandolfi M, Paolucci S, Iosa M, Ianes P, Recchia S, et al. Reduced-intensity modified constraint-induced movement therapy versus conventional therapy for upper extremity rehabilitation after stroke: a multicenter trial. *Neurorehabil Neural Repair.* 2012;26(9):1035-45.

27. Fuzaro AC, Guerreiro CT, Galetti FC, Jucá RB, Araujo JE. Modified constraint-induced movement therapy and modified forced-use therapy for stroke patients are both effective to promote balance and gait improvements. *Rev Bras Fisioter.* 2012;16(2):157-65.
28. Könönen M, Tarkka IM, Niskanen E, Pihlajamäki M, Mervaala E, Pitkänen K, et al. Functional MRI and motor behavioral changes obtained with constraint-induced movement therapy in chronic stroke. *Eur J Neurol.* 2012;19(4):578-86.
29. McCall M, McEwen S, Colantonio A, Streiner D, Dawson DR. Modified constraint-induced movement therapy for elderly clients with subacute stroke. *Am J Occup Ther.* 2011;65(4):409-18.
30. Brunner IC, Skouen JS, Strand LI. Recovery of upper extremity motor function post stroke with regard to eligibility for constraint-induced movement therapy. *Top Stroke Rehabil.* 2011;18(3):248-57.
31. Barzel A, Liepert J, Haevernick K, Eisele M, Ketels G, Rijntjes M, et al. Comparison of two types of constraint-induced movement therapy in chronic stroke patients: A pilot study. *Restor Neurol Neurosci.* 2009;27(6):673-80.
32. Azab M, Al-Jarrah M, Nazzal M, Maayah M, Sammour MA, Jamous M. Effectiveness of constraint-induced movement therapy (CIMT) as home-based therapy on Barthel Index in patients with chronic stroke. *Top Stroke Rehabil.* 2009;16(3):207-11.
33. Lin KC, Wu CY, Liu JS. A randomized controlled trial of constraint-induced movement therapy after stroke. *Acta Neurochir Suppl.* 2008;101:61-4.
34. Dahl AE, Askim T, Stock R, Langørgen E, Lydersen S, Indredavik B. Short- and long-term outcome of constraint-induced movement therapy after stroke: a randomized controlled feasibility trial. *Clin Rehabil.* 2008;22(5):436-47.
35. Wolf SL, Winstein CJ, Miller JP, Taub E, Uswatte G, Morris D, et al.; EXCITE Investigators. Effect of constraint-induced movement therapy on upper extremity function 3 to 9 months after stroke: the EXCITE randomized clinical trial. *JAMA.* 2006;296(17):2095-104.
36. Dettmers C, Teske U, Hamzei F, Uswatte G, Taub E, Weiller C. Distributed form of constraint-induced movement therapy improves functional outcome and quality of life after stroke. *Arch Phys Med Rehabil.* 2005;86(2):204-9.