Constraint-induced movement therapy protocols using the number of repetitions of task practice : a systematic review of feasibility and effects

Title: Constraint induced movement therapy protocols using number of repetitions of tasks practice: a systematic review of feasibility and effects

Auwal Abdullahi[1], Sevim Acaroz Candan[2], Melda soysal Tomruk[3], Abdulsalam Mohammed Yakasia[4], Steven Truijen[5], Wim Saeys[5]

1) Neurological Rehabilitation Unit, Department of Physiotherapy, Bayero University Kano, PMB 3011, Gwarzo road, Kano, Nigeria
2) Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Ordu University, Ordu, 52100, Turkey
3) Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Mehmet Akif University, Burdur, Turkey
4) Medical Rehabilitation Therapists (Reg.) Board of Nigeria, Kano Zonal Office Kano, Nigeria
5) Department of Physiotherapy and Rehabilitation Sciences, Faculty of Health and Medical Sciences, University of Antwerp, Antwerp, D.R.312, 2610, Wilrijk, Belgium.

Corresponding Author: Mr. Auwal Abdullahi, Department of Physiotherapy, Zaria road, Kano, 700001, Nigeria. Email: aabdullahi.pth@buk.edu.ng

Abstract

Background: High repetition of tasks practice is required for recovery of motor function during constraint induced movement therapy (CIMT). This can be achieved into ways: when the task practice is measured in hours of practice or when the number of repetitions is counted. However, it has been argued that using hours of tasks practice as a measure of practice does not provide a clear instruction on the dose of practice. **Aim**: The aim of this study is to determine the feasibility and effects of the CIMT protocol that uses number of repetitions of tasks practice. **Materials/ Method**: The study was a systematic review registered in PROSPERO (CRD42020142140). Five databases: PubMED, CENTRAL, PEDro, OTSeeker and Web of Science were searched. Studies of any designs in adults with stroke were included if they used number of repetitions of tasks practice as a measure of dose. The methodological quality of the included studies was assessed using Modified McMaster Critical Review Form. The results were analyzed using qualitative synthesis. **Results**: Nine studies (n=505) were included in the study. The number of tasks repetitions in the studies ranges between 45 and 1280 per day. The results showed that CIMT protocol using number of repetitions of tasks practice was feasible and improved outcomes such as motor function, quality of life, functional mobility and spasticity. **Conclusion**: Number of repetitions of tasks practice as a measure of CIMT dose can be used in place of the existing protocol that uses number of hours of tasks practice.

Key words: quality of life, disability, activities of daily living, motor function, constraint induced movement therapy, mobility

Declaration

Funding

There was no finding for this study

Conflicts of interest/Competing interests

The authors declare no conflict of interest

Ethics approval

Not applicable

Consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and material

Not applicable

Code availability

Not applicable

Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [Auwal Abdullahi], [Melda Soysal Tomruk], [Steven Truijen], [Wim Saeys]. The first draft of the manuscript was written by [Auwal Abdullahi] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript

Acknowledgment

The authors would like to thank the authors of the studies included in the review for giving us further information where necessary.

Introduction

Stroke results when there is interruption in blood supply to the brain [1]. The interruption is caused by ischaemia or haemorrahge [2-3]. When this happens, the brain gets injured [4]; and its functions such as the control movement, sensation and cognition get impaired [5]. One of the interventions used for the rehabilitation of movement after a stroke is constraint induced movement therapy (CIMT). The CIMT is a widely studied technique based on the goal of counteracting learned non-use [6]. It consists of mainly repetitive practice of functional tasks with the affected limb, restriction of movement of the unaffected limb and encouraging the use of the affected in real life situations [7-9]. It was reported to improve the ability to use the affected limb and the quality and quantity of use of the limb [9]. The mechanisms through which these improvements occur include decreased transcallosal inhibition, structural changes in the brain and changes in the expression of molecular biomarkers such as Growth-Associated Protein 43 (GAP-43), Brain-Derived Neurotrophic Factor (BDNF) and Vascular Endothelial Growth Factor (VEGF) [10].

In the original (standard) protocol of CIMT, patients receive tasks practice with the affected limb for 6 hours and constraint for 90% of the waking hours per day for few to several weeks [7]. Over the years, the standard protocol of CIMT has been modified to comprise of short periods of tasks practice and constraint. This is called the modified CIMT [11]. Consequently, in some studies, patients receive tasks practice for 1 to 4 hours and constraint for 2 to 6 hours per day [12-13]. The reason behind reducing the time for tasks practice and constraint may not be unconnected to some later findings. For instance, Kaplon and colleagues evaluated a standard CIMT protocol, and found out only about 3.65 hours out of the claimed 6 hours were actually used for tasks practice [14]. Similarly, it was observed that, participants did not completely use the time allocated for tasks practice during CIMT [15].

Consequently, it has been argued that, use of hours of tasks practice as a measure of dose of CIMT seems to be inappropriate since it is now clear on how much tasks is practiced [16]. This is because when patients are asked to practice tasks for a certain period of time, how much tasks they practiced cannot be specified. In order to therefore give a clear instruction on the dose of tasks to practice during CIMT, it was suggested that it is better to use number of repetitions of the tasks practice [16]. This is line with the existing literature whereby tasks repetitions between 300 and 1000 per day was reported to induce recovery of motor function [17-18]. The aim of this systematic review was to therefore investigate the evidence on the feasibility and the effects CIMT protocol using number of repetitions of tasks practice as a measure of dose of CIMT on outcomes after stroke.

Material and Methods

The study was a systematic review looking at the feasibility and effects of constraint induced movement therapy protocols using number of repetitions of tasks practice on outcomes after stroke. The review was registered in PROSPERO, registration number: CRD42020142140. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline was used in carrying out the review [19].

Eligibility criteria and information sources

The following databases: PubMED, Web of Science, PEDro, CENTRAL and OT Seeker were searched from their earliest dates to 16th July, 2020. The reference lists of systematic reviews on CIMT and the included studies were also searched in order to identify eligible studies. Details of the search strategies used according to the requirements of the databases are provided in the appendix. The search was carried out by one of the authors (MTS). The search was confirmed by another author (AA). Following this, one of the authors (MTS) removed duplicate studies using Endnote software.

Studies were selected if they were randomized controlled trials (RCTs) comparing upper or lower limb CIMT with traditional therapy involving stroke patients who were 18 years and above. The studies must have also assessed outcomes such as motor function, gait speed and quality of life post-intervention.

Selection of eligible studies and extraction of data

Selection of the eligible studies based on their titles and abstracts was carried out independently by two of the authors (AA and SAC) using Rayyan software [20]. When studies could not be selected based on their titles and abstracts, AA and SAC read the full texts. However, when there were disputes arising from inclusion or exclusion of studies, consensus discussion was done or a third author (AMY) was consulted. Similarly, two of the authors (AA and SAC) carried out the data extraction independently using a data collection form. Thereafter, they held meeting and agreed based on consensus on the extracted data. The data extracted include the study authors, year of publication, the study design, number of participants, stage of stroke, mean age of the participants, mean scores on the outcomes of interest in the experimental and control groups and the results of the studies..

Assessment of Methodological Quality of the Included Studies

Two of the authors (AA and AMY) independently assessed the methodological quality of the included studies using Modified McMaster Review Form for Quantitative Studies [21].The form has 17 items that assess purpose of the study, design of the study, number of participants, review of the literature, outcomes assessed, interventions used, results and conclusion. Each of the items has four answer options consisting of yes, no, not addressed and not applicable. Answering yes to an item, receives a score of one; but a score of zero is awarded for answering no to a question. When a particular item is not relevant to a study design, no score is awarded, but it is designated as not applicable (NA). When the assessment is done, the total scores are rated as poor (1/4 or less), fair (≤2/4), good (≥2/4 but ≤3/4) and excellent (>3/4 to 4/4). Any disputes arising from the assessment, were resolved through discussion or consulting another author (SAC). Similarly, the National Health and Medical Research Council's (NHMRC) evidence hierarchy was used to determine the level of evidence [22].

Synthesis of the Results

Qualitative synthesis was used to summarize the results. The synthesis involved summarizing the characteristics and methodological quality of the included studies. The results were reported in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guideline. However, meta-analysis was not performed due to lack of adequate information and data.

Result

Study selection

The total number of hits provided by the searched databases and the reference lists of related studies and systematic reviews was 2997. Out of this number, 1235 studies remained after removing 1762 duplicates. In addition, 1198 studies were excluded after screening the abstracts of the remaining studies, resulting in the balance of only 37 studies. When the full texts of the remaining 37 studies were read, only eight studies were eligible for inclusion in the study. See figure 1 for the study flowchart.

Characteristics of the Included Studies

Eight studies including four RCTs, two observational studies, one case report and one experimental study (pre-test-post-test design) published between 2010 and 2019 were included in the study. The total number of participants in the studies was 205, comprising of 109 men and 96 women. The sample size in the studies ranges between one and 58 participants. However, only two studies gave the details of how the sample sizes were calculated [23-24]. Inadequate sample size can undermine the generalizability of findings of a study.

In all the studies, participants were included if they were ≥18 years of age. In addition, in most of the studies, participants were included if they had mild to moderate disability. In three studies the participants had scores of one to three on National Institute of Health Stroke scale (NIHSS) [18, 23, 25]. In one study, the participant had 20° of active wrist extension and 10° of metacarpophalangeal and interphalangeal joints extension [26]. In one study, the participants had scores of 20 to 33/34 on motor arm sub-scale of lower limb Fugl-Meyer [27]. In three studies, the participants had ability to walk at least 10 meters independently [24, 27-28]. However, in one study, the level of disability was not specified [29].

Similarly, most of the studies included participants who had no significant cognitive impairment. Two studies used a score ≥ 24 points on Mini Mental state Examination (MMSE) [24, 29]. Three studies used a score of ≤1 on the consciousness and communication items of NIHSS [18, 23, 25]. One study used the ability to perform two steps command and a score of <8 on the Short Blessed memory, Orientation and Concentration scale [23]. In the case report, the patient had no obvious cognitive impairment according to the authors [26]. However, two studies did not specify whether they included only participants with no significant cognitive impairment [27-28]. Significant cognitive impairment can affect patients' ability to obey command and perform tasks or exercise.

Four studies included participants who had no balance problem [24, 27-29]. Five studies included participants with no neglect [18, 23-26]. This includes a score of < 2 on NIHSS extinction and inattention item in two studies [18, 25]; and normal performance on line bisection test in one study [26]. Similarly, there were ≤ 3 errors on star cancellation test in one study [28]; and a cut-off point > 44 on the star cancellation test in another study [24]. Hemineglect interferes significantly with rehabilitation and its outcomes [30]. In addition, only six studies (n=175) provided information on the types of stroke used [23-24, 26-29]. Participants with ischaemic stroke were 143; while those with haemorrhagic stroke were 32 in number. Type of stroke is an important predictor of recovery following stroke. Consequently, the ischaemic type has been presumed to have a more favourable outcome in most cases [31-32].

Only seven studies with n=167 provided details on the side of the lesion, 68 right and 99 left side lesions [18, 23-27, 29]. According to the literature, there is difference in pattern of symptoms presentation between left and right sided lesions. Patients with right side lesion usually present with neglect [33-34]; whereas those with left sided lesion present with language difficulties such as comprehension and expression problems [35-36]. Similarly, only two studies with n= 30 provided information on the number of cases involving the dominant limb which was 16 [18, 25]. Pre-stroke limb dominance does not affect impairment and disability after stroke, and there is no difference between dominant and non-dominant limbs [37-38].

In addition, only one study reported adverse events [24]. In the study, two participants in the experimental group (CIMT protocol using number of repetition of tasks practice) reported mild low back pain and calf muscle pain respectively. Adverse events can limit the use of a particular intervention.

Only one of the studies reported adequate follow-up [25]. Three studies reported that high repetition of tasks practice was feasible during CIMT [18, 24-25]. In all studies, the outcomes of interest improved better in the CIMT group compared to the control. However, in one of the RCTs, there was no significant difference between groups in quality of life and temporal symmetry index post-intervention [24]. The number of tasks repetition in the studies ranges between 45 and 1280 per day. In addition, one of the studies was only published yet as a protocol, and we had to request for the unpublished results from the authors [24]. See table 1 for the details of the characteristics of the included studies.

Methodological Quality and Level of Evidence of the Included Studies

Seven studies have excellent methodological quality [18, 24-26 28-29]; while one study has good methodological quality [27]. Four studies are Level II evidence studies [23-24, 28-29]. Three studies are Level III-3 evidence studies [18, 25, 27]. One study is a Level IV evidence study [26]. See table 2 for the details of methodological quality and Level of evidence and table 3 for the interpretation of the evidence.

Table 1: Characteristics of the Included Studies

Study	N	Stroke phase	Mean age (years)	Intervention	Outcomes	Findings
Birkinmeier et al. (2010)	15	Chronic ≥6 months	53.73±15.30	222 mean repetition of tasks practice/day, 3 times a week for six weeks.	Motor function (ARAT), grip strength(Jamar hydroaulic hand held dynamometer) quality of life (SIS) and ADL (COPM)	High tasks repetition was feasible within one hour. Attendance was 97%. After intervention, subjects rated and fatigue as low. All outcomes improved.
Billinger et al. (2010)	12	Chronic	60.60±14.5	Isokinetic flexion, extension protocol using Biodex system (single leg exercise), 40 repetitions per set with 30 seconds rest breaks in between each set. Participants were instructed to self-progress with the goal of reaching 40 sets. Exercises were carried out 3 times a week for 4 weeks.	Cardiopulmonary fitness (maximal exercise test), gait velocity (10 meter fast walk test), motor function (Fugl-Meyer), lean tissue mass (DEXA) and knee extensor strength (Biodex system).	Oxygen uptake (VO_2) and gait velocity improve post-intervention.
Abdullahi et al. (2014)	1	Acute	55 years	320 repetitions of tasks practice divided in 2 sessions/ day, 5 times a week for 8 weeks. Constraint of the unaffected limb for 90% of the waking hours.	Motor function (WMFT)	Improved motor function post-intervention that reached MCID at 4, 6 and 8 weeks.

Key: ARAT= action research arm test, SIS=stroke impact scale, DEXA=Dual Energy X-ray Absorptiometry, WMFT=Wolf motor function test, MCID=Minimal clinically important difference.

Table 1: Characteristics of the Included Studies

Study	N	Stroke phase	Mean age (years)	Intervention	Outcomes	Findings
Waddell et al. (2014)	15	Acute and chronic	53.73±15.30	≥ 300 repetition of supervised tasks practice/day, 4 times a week for the duration of inpatient rehabilitation.	Feasibility measures (number of repetition) achieved during single session, fatigue (Standford fatigue visual scale), motor function (ARAT), grip strength (JHHD), pinch strength (pinch gauge)quality of life (SIS) and ADL (FIM)	High tasks repetition was feasible. All outcomes improved post-intervention.
eSilva et al. (2017)	38	Acute	21-70 years	CIMT =Lord discharge exercise in anterior-posterior and latero-lateral directions, 3 sets of 15 repetitions every day. The non-paretic limb was constrained with a mass equivalent of 5% body weight. Control=Treadmill training for 30 minutes per day for 9 days	Balance (BBB), functional mobility (TUG), spatio-temporal and kinematic parameters (Qualysis motion system), gait performance and mobility (PWV, FWV, SSI, TSI, TUG and RMI) and quality of life (SSQOLTV).	FUT improved better in most gait parameter. However, there was no significant difference in quality of life and TSI between groups

Key: PWV=preferred walking velocity, FWV=fast walking velocity, TSI=temporal symmetry index, SSI=spatial symmetry index, RMI=Rivermead mobility index, SSQOL=Stroke specific quality of life.

Table 1: Characteristics of the Included Studies

Study	N	Stroke phase	Mean age (years)	Intervention	Outcomes	Findings
Danlami & Abdullahi (2017)	18	Chronic	sCIMT=48.2±7.89 tCIMT=55.67±99.00 Control=54.14±6.87	sCIMT =480 repetition of tasks practice/day. tCIMT Performed the same tasks, 2 hours per day. Control received usual physiotherapy for 2 hours per day. Interventions were carried out 5 times a week for 4 weeks in each group.	Motor impairment (Fugl-Meyer).	Higher improvement in sCIMT .
Abdullahi (2018)	48	Acute	Control=58.83±10.57 mCIMT=54.62±6.00 300 rep=59.42±13.93 600 rep=57.60±10.27	Control group received 3 hour of traditional therapy. mCIMT received 3 hours of CIMT. 300 rep group received 300 repetitions of tasks practice. . 600 rep group received 600 repetitions of tasks practice. All the groups except the control received constraint for 90% of the waking hours.	Motor function (WMFT & FM), real world arm use (MAL) and self-efficacy (UPSET).	No significant difference between the 3 experimental groups. Improvement in the 3 groups attained MCID in all the outcomes.

Key: FM=Fugl Meyer, WMFT=Wolf motor function test, MAL= Motor activity log, UPSET=Upper limb self-efficacy test, MCID=Minimal clinically important difference

Table 1: Characteristics of the Included Studies

Study	N	Stroke phase	Mean age (years)	Intervention	Outcomes	Findings
Abdullahi et al. (2021)	58	Acute, sub-acute and chronic	CIMT rep=50.20±13.90 mCIMT=47.80±14.70	CIMT rep received 600 repetitions of tasks practice (200 repetitions per session) x 3 per day. mCIMT received 3 hours of tasks practice per day. Each group practiced 5 times a week for 4 weeks.	Motor function (FM), balance (BBS), functional mobility (RMI), walking speed (10MWT), spasticity (MAS), and walking endurance (6MWT).	Significant improvement in all outcomes in both groups. Better improvement in spasticity in the CIMT repetition group. .

Key: FM=Fugl Meyer, BBS=Berg balance scale, RMI=Rivermead mobility index, 10MWT=Ten meter walk test, MAS=modified Ashworth scale, 6MWT=Six minute walk test

Table 2: Levels of Evidence and Methodological Quality of the Included Studies

Study	**Design**	**Level of Evidence**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**Total score**
Birkinmeier et al. (2010)	Cohort (repeated measures)	III-3	Yes	No	Yes	No	NA	NA	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	No	Yes	Yes	11/14
Billinger et al. (2010)	Within subjects design	III-3	Yes	Yes	Yes	No	NA	NA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	11/15
Abdullahi et al. (2014)	Case report	IV	Yes	Yes	Yes	NA	NA	NA	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes	NA	Yes	11/12
Waddell et al. (2014)	Cohort (repeated measures)	III-3	Yes	Yes	Yes	No	NA	NA	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	No	Yes	Yes	12/14
Danlami & Abdullahi (2017)	RCT	II	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	15/17
eSilva et al. (2017)	RCT	II	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	14/17
Abdullahi. (2018)	RCT	II	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	15/17
Abdullahi et al. (2021)	RCT	II	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	16/15

Key: Yes=1, No=0, NA=Not applicable

Table 3: NHMRC Form Framework

Component	Grade	Comments
1) Evidence	A-Excellent Several Level II studies	Quantity: a total of 8 studies Participants: 205 stroke patients Level II: 4 studies Level III-2: 0 study Level III-3: 3 studies Level IV: 1 study
2) Consistency	C-Satisfactory Some inconsistency reflecting genuine uncertainty around clinical question	Consistent reporting of statistical significance (this was only absent in one case report, Abdullahi et al., 2014). Studies used different designs
3) Clinical Impact	B-Moderate	Statistical significance was reported by seven studies. However, only three studies (Billinger et al., 2010; Abdulahi, 2018; Abdullahi et al., 2014) reported clinical significance. One study (Abdullahi et al., 2021) reported adverse events.
4) Generalizability	B-Good	The population of the studies was similar to the target population (stroke patients).
5) Applicability	A-Excellent Applicable internationally	Studies were carried out in 3 countries in 3 different continents
Recommendation	C-Good (evidence), but more studies are needed to confirm it.	There is significant heterogeneity between studies

Discussion

The results showed that using number of repetition of tasks practice as a measure of dose during CIMT is feasible. The number of tasks repetition in the studies ranges between 45 and 1280 per day. In addition, the protocol is effective at improving many outcomes after stroke such as motor function, quality of life, oxygen uptake, gait velocity, activities of daily living, functional mobility and spasticity. These findings are important as it has been argued that, the existing protocol of CIMT which uses hours of tasks practice as a measure of dose is not clear on the amount of tasks practiced [16]. Similarly, when CIMT studies using number of hours of practice were evaluated, it was found out that not all the hours claimed were used for tasks practice [14-15]. Furthermore, it was reported that, the modified form of CIMT using < 3 hours of practice is more effective than the ones using > 3 hours of practice [39]. Consequently, hours of tasks practice cannot be used as a measure of dose of practice. In lieu of this, it has been argued that, it is better to use number of repetitions of tasks practice as a measure of dose of practice [16].

The reason for the above is that, already the number of tasks repetition required for recovery has been reported [17-18, 40-42]. This number ranges between 300 and 1000 per day; and is as high as possible to help induce recovery of motor function [43]. Improvement in motor function translates into the ability to carry out activities of daily living in which in turn translates better quality of life [44-45]. Another advantage of using number of repetitions of tasks practice as a measure of dose is that, it gives clear instructions the amount of tasks to practice. This is important since patients can keep track of the number of times they practiced tasks [46]. Consequently, patients may be encouraged to achieve the number of repetitions required for recovery if they are aware of the number of times to practice. A further advantage of this protocol is that, the amount of practice is said to be possible within one hour [18].

Although, the length of time taken to perform the tasks is not the most important, rather the ability to carry out the required number of repetitions, the finding is still is significant. This is because it seems to suggest that, practicing for many hours such as six hours could be wastage of patients' and therapists' time. However, it seems unknown whether the ability to perform such a high amount of tasks practice may be influenced by the patients' personal and clinical characteristics such as age, time since stroke, side affected and dominant limb stroke. Therefore, the effects of these factors on the patients' ability to carry out high repetitions of tasks practice needs to be investigated. In addition, development or the use of technological aids such as virtual reality gaming system and automated devices may help patients achieve the number of repetitions of tasks practice required for motor recovery during CIMT. Such aids have been used with success in previously during CIMT that used number of hours of tasks practice [47-49].

Furthermore, one of the ways to know whether a particular protocol can be used is in the way it affects outcomes positively. As previously noted, the protocol improved outcomes including motor function, quality of life, oxygen uptake, gait velocity, activities of daily living, functional mobility and spasticity. These outcomes are the ones that get impaired after stroke [47]. In addition, they may have relationship with each other. For instance, when motor function improves, activities of daily living also improves, which also in turn affects the patients' quality of life [44-45]. The strength of the study is that different study designs such as RCTs, observational studies, case reports and pre-test-post-test experimental studies were included. However, one of the limitations of the study was that there was no information to carry out meta-analysis.

Conclusion

The protocol of CIMT using number of repetitions of tasks practice is feasible and effective. Therefore, it can be used in place of the existing protocol that uses number of hours of tasks practice. However, it is not known when the ability to carry out this type of protocol may be influenced by the personal and clinical characteristics of the patients. Consequently, use of technological aids such as virtual reality gaming system and robotic devices may help patients achieve the number of repetitions of tasks practice required for motor recovery during CIMT.

Reference

[1] Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A et al (2013) An updated definition of stroke for the 21st century: A statement for healthcare professionals from the American Heart Association/ American Stroke Association. Stroke **44**(7):2064-2089. DOI: 10.1161/ STR.0b013e318296aeca

[2] Del Zoppo JD, Hallenbeck JM (2000) Advances in the vascular pathophysiology of ischemic stroke. Thrombosis Res 98(3):73-81

[3] Frizzell JP (2005) Acute stroke: Pathophysiology, diagnosis, and treatment. AACN Clinical Issues: Advanced Practice in Acute and Critical Care 16(4):421-598

[4] Deba P, Sharma S, Hassan KM (2010). Pathophysiologic mechanisms of acute ischemic stroke: An overview with emphasis on therapeutic significance beyond thrombolysis. Pathophysiol 17:197-218. DOI: 10.1016/j.pathophys.2009.12.001

[5] Hachinski V, Iadecola C, Petersen C, Breteler MM, Nyenhuis DL, Black SE et al (2006) National institute of neurological disorders and stroke—Canadian stroke network vascular cognitive impairment harmonization standards. Stroke 37:2220-2241. DOI: 10.1161/01.STR.0000237236.88823.47

[6] Taub E, Berman AJ (1963) Avoidance conditioning in the absence of relevant proprioceptive and exteroceptive feedback. J Comp Physiol Psychol 56: 1012–6

[7] Wolf SL, Lecraw DE, Barton LA, Jann BB (1989) Forced use of hemiplegic upper extremities to reverse the effect of learned nonuse among chronic stroke and head-injured patients. Exp Neurol 104(2): 125–32

[8] Taub E, Miller NE, Novack TA, Cook IEW, Fleming WC, Nepomuceno CS (1993) Technique to improve chronic motor deficit after stroke. Arch Phys Med Rehabil 74(4): 347–54

[9] Etoom M, Hawamdeh M, Hawamdeh Z (2016) Constraint-induced movement therapy as a rehabilitation intervention for upper extremity in stroke patients: systematic review and meta-analysis. Int J Rehabil Res 39:197–210.

[10] Abdullahi A, Truijen S, Saeys W (2020) Neurobiology of Recovery of Motor Function after Stroke: The Central Nervous System Biomarker Effects of Constraint-Induced Movement Therapy. Neural Plasticity. https://doi.org/10.1155/2020/9484298

[11] Yadav RK, Sharma R, Borah D, Kothari SY (2016) Efficacy of Modified Constraint Induced Movement Therapy in the Treatment of Hemiparetic Upper Limb in Stroke Patients: A Randomized Controlled Trial. J Clin Diagn Res 10(11): YC01–YC05.

[12] Shi YX, Tian JH, Yang KH, Zhao Y (2011) Modified constraint-induced movement therapy versus traditional rehabilitation in patients with upper-extremity dysfunction after stroke: a systematic review and meta-analysis. Arch Phys Med Rehabil 92:972-82.

[13] Yu C, Zhang Y, Wang Y, Hou W, Liu S, Gao C, Wang C, Mo L, Wu J (2017) The Effects of Modified Constraint-Induced Movement Therapy in Acute Subcortical Cerebral Infarction. Front. Hum. Neurosci. https://doi.org/10.3389/fnhum.2017.00265

[14] Kaplon RT, Prettyman MG, Kushi CL, Winstein CJ (2007) Six hours in the laboratory: Quantification of practice time during Constraint Induced Therapy. Clin Rehabil 21(10):950–8

[15] Stock G, Thrane G, Askim T (2015) "Norwegian constraintinduced therapy multisite trial: Adherence to treatment protocol applied early after stroke," J Rehabil Med 47(9): 816–823.

[16] Abdullahi A (2014) Is time spent using constraint induced movement therapy an appropriate measure of dose? A critical literature review. Inter J Therap Rehabil 21(3): 140-146

[17] Schröder J, Truijen S, Van Criekinge T, Saeys W (2019) Feasibility and effectiveness of repetitive gait training early after stroke: a systematic review and meta-analysis. J Rehabil Med 51: 78–88

[18] Birkenmeier RL, Prager EM, Lang CE (2010) "Translating animal doses of task-specific training to people with chronic stroke in 1-hour therapy sessions: a proof-of-concept study," Neurorehabil Neural Repair 4(7)7:620– 635.

[19] Liberati A, Altman DG, Tetzlaff J et al (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies evaluate health care interventions: explanation and elaboration. PLoS Med 6: e1000100.

[20] Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A (2016) Rayyan- a Web and Mobile application for Systematic reviews. Syst Rev 5(1): 2. https://doi.org/10.1186/s13643-016-0384-4

[21] Law HK, Cheung CY, Ng HY et al (2005) Chemokine upregulation in SARS coronavirus infected human monocyte derived dendritic cells. Blood 106:2366–2376

[22] Council-NHaMR. NHMRC levels of evidence and grades for recommendations for guideline developers. Canberra: National Health and Medical Research Council; 2009.

[23] Abdullahi A (2018). Effects of Number of Repetitions and Number of Hours of Shaping Practice during Constraint-Induced Movement Therapy: A Randomized Controlled Trial. Neurol Res Int. https://doi.org/10.1155/2018/5496408

[24] Abdullahi A, Umar NA, Ushotanefe U, Abba MA, Akindele MO, Truijen S, Saeys W (2021) Comparing two different modes of tasks practice during lower limbs constraint-induced movement therapy in people with stroke: a randomized clinical trial. Neural plasticity. https://doi.org/10.1155/2021/6664058

[25] Waddell KJ, Birkenmeier RL, Moore JL, Hornby TG, Lang CE (2014) Feasibility of high-repetition, taskspecific training for individuals with upper-extremity paresis. Am J OccuP Ther 68: 444–453. http://dx.doi.org/10.5014/ajot.2014.011619

[26] Abdullahi A, Shehu S, Dantani BI (2014) Feasibility of High Repetitions of Tasks Practice during Constraint Induced Movement Therapy in an Acute Stroke Patient. Int J Ther Rehabil 21(4): 190-195

[27] Billinger SA, Guo LX, Pohl PS, Kluding PM (2010) Single Limb Exercise: Pilot Study of Physiological and Functional Responses to Forced Use of the Hemiparetic Lower Extremity. Top Stroke Rehabil 17(2): 128–139. doi:10.1310/tsr1702-128.

[28] eSilva EMGS, Ribeiro TS, da Silva TCC, Costa MFP, Cavalcanti FADC, Lindquist ARR (2017) Effects of constraint-inducedmovementtherapy for lower limbs on measurements of functional mobility and postural balance in subjects with stroke: a randomized controlled trial. Top Stroke Rehabil 24(8):555-561. doi: 10.1080/10749357.2017.1366011.

[29] Danlami KA, Abdullahi A (2017) Remodelling the protocol of lower limb constraint-induced movement therapy: a pilot randomized controlled trial. Arch Physiother Glob Res 21 (4): 21-27

[30] Spaccavento S, Cellamare F, Falcone R, Loverre A, Nardulli R (2017) Effect of subtypes of neglect on functional outcome in stroke patients. Annals Phys Rehabil Med 60(6): 376-381. https://doi.org/10.1016/j.rehab.2017.07.245

[31] Vermeer SE, Algra A, Franke CL, Koudstaal PJ, Rinkel GJE (2002) Long-term prognosis after recovery from primary intracerebral hemorrhage. Neurol 59(2):205-209

[32] Andersen KK, Olsen TS, Dehlendorff C, Kammersgaard LP (2009) Hemorrhagic and Ischemic Strokes Compared Stroke Severity, Mortality, and Risk Factors. Stroke 40:2068-2072

[33] Reinhart S, Schmidt L, Kuhn C, Rosenthal A, Schenk T, Keller I, Kerkhoff G (2012) Limb activation ameliorates body-related deficits in spatial neglect. Front Human Neurosci 6:188. doi: 10.3389/fnhum.2012.00188

[34] Stein MS, Kilbride C, Reynolds FA (2016) "What are the functional outcomes of right hemisphere stroke patients with or without hemi-inattention complications? A critical narrative review and suggestions for further research." Disabil Rehabil 8(4):315–328

[35] Mohr B, MacGregor LJ, Difrancesco S, Harrington K, Pulvermüller F, Shtyrov Y (2016) "Hemispheric contributions to language reorganisation: An MEG study of neuroplasticity in chronic post stroke aphasia," Neuropsychol 93:413–424

[36] Maeshima S, Toshiro H, Sekiguchi E, Okita R, Yamaga H, Ozaki F et al (2002) Transcortical mixed aphasia due to cerebral infarction in left inferior frontal lobe and temporo-parietal lobe. Neuroradiol 44:133–137

[37] Menezes K, Faria CD, Scianni AA, Avelino PR, Faria-Fortini I, Teixeira-Salmela LF (2017) Previous lower limb dominance does not affect measures of impairment and activity after stroke. Eur J Phys Rehabil Med 53(1):24-31. doi: 10.23736/S1973-9087.16.04349-5.

[38] Nam HUK, Huh JS, Yoo JN, Hwang JM, Lee BJ, Min Y-S, Kim C-H, Jung T-D (2014) Effect of Dominant Hand Paralysis on Quality of Life in Patients With Subacute Stroke. Ann Rehabil Med 38(4): 450–457. doi: 10.5535/arm.2014.38.4.450

[39] Nijland R, Kwakkel G, Bakers J, van Wegen E (2011) Constraint-induced movement therapy for the upper paretic limb in acute or sub-acute stroke: a systematic review. Int J Stroke **6**(5): 425–33

[40] Kleim JA, Barbay S, Nudo RJ (1998) "Functional reorganization of the rat motor cortex following motor skill learning," J Neurophysiol 80(6): 3321–3325.

[41] Boyd, Winstein CJ (2006) "Explicit information interferes with implicit motor learning of both continuous and discrete movement tasks after stroke," J Neurologic Phys Therap 30(2): 46–57.

[42] Carey JR, Kimberley TJ, Lewis SM, Auerbach EJ, Dorsey L, Rundquist P, Ugurbil K (2002) Analysis of fMRI and finger tracking training in subjects with chronic stroke. Brain 125(Pt 4): 773–88

[43] Nudo RJ, Milliken GW (1996). Reorganization of movement representations in primary motor cortex following focal ischemic infarcts in adult squirrel monkeys. J Neurophysiol 75(5): 2144–9

[44] Huang YH, Wu CY, Hsieh YW, Lin KC (2010) Predictors of change in quality of life after distributed constraint-induced therapy in patients with chronic stroke. Neurorehabil Neural Repair 24(6):559-66. doi: 10.1177/1545968309358074

[45] Kelly KM, Borstad AL, Kline D, Gauthier LV (2018) Improved quality of life following constraint-induced movement therapy is associated with gains in arm use, but not motor improvement. Topics in Stroke Rehabil 25(7): 467–474. doi:10.1080/10749357.2018.1481605

[46] Bagley P, Hudson M, Green J, Forster A, Young J (2009) Do physiotherapy staff record treatment time accurately? An observational study. Clin Rehabil 23(9): 841–5

[47] Taub E, Lum PS, Hardin P, Mark VW, Uswatte G (2005) AutoCITE: automated delivery of CI therapy with reduced effort by therapists 36(6):1301-4. doi: 10.1161/01.STR.0000166043.27545.e8.

[48] Lum PS, Taub E, Schwandt D, Postman M, Hardin P, Uswatte G. Automated Constraint-Induced Therapy Extension (AutoCITE) for movement deficits after stroke. J Rehabil Res Dev. 2004 May;41(3A):249-58. doi: 10.1682/jrrd.2003.06.0092.

[49] Borstad AL, Crawfis R, Phillips K, Lowes LP, Maung D, McPherson R, Siles A, Worthen-Chaudhari L, Gauthier LV. In-Home Delivery of Constraint-Induced Movement Therapy via Virtual Reality Gaming. J Patient Cent Res Rev. 2018 Jan 30;5(1):6-17. doi: 10.17294/2330-0698.1550. PMID: 31413992; PMCID: PMC6664341.

[50] Lawrence ES, Coshall C, Dundas R, Stewart, J, Rudd AG, Howard R,Wolfe CDA (2001) Estimates of the Prevalence of Acute Stroke Impairments and Disability in a Multiethnic Population. Stroke 32:1279-1284

Figure Legend

Figure 1: Study Flowchart

Appendix

PubMed Search Strategy

(1) Cerebrovascular disorders

(2) Stroke

(3) Cerebrovascular accident

(4) Cerebrovascular disease

(5) Hemiplegia

(6) Hemiparesis

7) 1 OR 2 OR 3 OR 4 OR 5 OR 6

(8) Forced use

(9) Constraint induced movement therapy

(10) Constraint induced movement therapy

(11) Tasks practice

(12) Shaping practice

(13) Motor rehabilitation

(14) 8 OR 9 OR 10 OR 11 OR 12 OR 13

(15) 7 and 14

(16) Motor Function

(17) Motor impairment

(18) Real world arm use

(19) Quality of movement

(20) Quantity of movement

(21) 16 OR 17 OR 18 OR 19 OR 20

(22) 15 AND 21

Figure

Click here to access/download;Figure;Figure 1.tif