Similar effects of two modified constraint-induced therapy protocols on motor impairment, motor function and quality of life in patients with chronic stroke

Wilma Costa Souza,[1]
Adriana B. Conforto,[2]
Marco Orsini,[3] Annette Stern,[4]
Charles André[5]

[1]Federal University of Rio de Janeiro, Rehabilitation Center of Rio de Janeiro, Brazil; [2]Neurostimulation Laboratory, Hospital das Clínicas/São Paulo University, Brazil; [3]Neurology Department, Centro Universitário Augusto Mottta, UNISUAM, Bonsucesso, Brazil; [4]School of Psychology, University of Surrey, Guildford, UK; [5]Department of Neurology, School of Medicine, Federal University of Rio de Janeiro, Brazil

Abstract

Modified constraint-induced movement therapy (CIMT) protocols show motor function and real-world arm use improvement. Meanwhile it usually requires constant supervision by physiotherapists and is therefore more expensive than customary care. This study compared the preliminary efficacy of two modified CIMT protocols. A two-group randomized controlled trial with pre and post treatment measures and six months follow-up was conducted. Nineteen patients with chronic stroke received 10 treatment sessions distributed three to four times a week over 22 days. CIMT3h_direct group received 3 hours of CIMT supervised by a therapist (n=10) while CIMT1.5h_direct group had 1.5 hours of supervised CIMT+1.5 hours home exercises supervised by a caregiver (n=9). Outcome measures were the Fugl-Meyer Assessment, the Motor Activity Log, and the Stroke Specific Quality of Life Scale. The modified CIMT protocols were feasible and well tolerated. Improvements in motor function, real-world arm use and quality of life did not differ significantly between treated groups receiving either 3 or 1.5 hours mCIMT supervised by a therapist.

Introduction

Global ageing is associated with an ever-increasing number of elderly individuals at increased risk for stroke.[1,2] Stroke is a condition with high incidence and mortality, and the most common cause of disability worldwide.[3] Most strokes occur in developing countries,[4,5] presenting a major burden to health care.

In stroke patients, recovery of the upper limb is often limited when compared with that of the lower limb.[6] Loss of upper limb function significantly contributes to overall disability.[7,8] Constraint-induced movement therapy (CIMT) is an evidence-based therapy for upper limb rehabilitation that evolved from basic research.[9,10] The original protocol involved training of the upper limb by shaping and task practice for 6 hours per day and constraint of the unaffected hand for approximately 90% of waking hours during two weeks.[10] The effectiveness of CIMT in post-stroke patients has been shown by randomized clinical trials.[11-13] CIMT improves real-world arm function significantly more than customary care, or no treatment, in the chronic phase after stroke.

A limitation to widespread use of CIMT in stroke rehabilitation is that the original CIMT protocol requires constant supervision by physiotherapists during several hours per day, and is therefore more expensive than customary care.[14] CIMT protocol is very difficult to implement under conditions of developing countries where most strokes occur. Modified CIMT protocols that include less time of direct supervision by a therapist would be more appropriate in developing countries that rely mostly on outpatient rehabilitation.

In recent years, several studies adapted the original protocol,[6,15-19] and showed that modified protocols can also enhance motor function and real-world arm use.[19] However results of modified protocols are conflicting. Supervised CIMT from 30 minutes to 3 hours over 10 sessions,[14-18] led to enhancement of upper limb function in some,[15,18] but not all studies.[14,17]

The present study compares, in a public health facility in Brazil, the preliminary efficacy of two modified CIMT protocols, applied over ten sessions, with direct supervision provided by a therapist for either 3 or 1.5 hours. CIMT durations were based on feasibility of supervised treatment in middle- and low-income countries. The 3-hour supervised protocol was shown to be beneficial to upper limb function in previous studies,[14,17] while the 1.5 hour approach had not been previously tested. We hypothesized that both programs would lead to comparable changes in motor outcomes and quality of life.

Materials and Methods

Study design

In this pilot, randomized, single-blinded clinical trial we compared the feasibility, safety, and efficacy of 10 sessions of either 3 hours of CI-therapy supervised by a therapist (CIMT3h_direct), or 1.5 hours of supervised CI-therapy + 1.5 hours of home exercises supervised by a caregiver (CIMT1.5h_direct), in patients >24 months after stroke. In both groups, patients were instructed to restrain the affected limb during waking hours, for 10 days.

Participants

Inclusion and exclusion criteria were based on previous CIMT research.[12]

Inclusion criteria: age >18 years; history of ischemic or hemorrhagic stroke leading to upper limb paresis in the previous 24 months; minimal active range of motion of 10 degrees for wrist extension, 10 degrees for abduction/extension of the thumb and at least 2 additional digits, 90 degrees for shoulder flexion and abduction, 45 degrees for shoulder external rotation, 30 degrees for elbow extension, 45 degrees for forearm supination and pronation (from neutral position), wrist extension (from neutral), and finger extension of all digits; amount-of-use score on the Motor Activity Log >2.5;[9] balance and stability to move using a glove in the unaffected hand; safe and independent transfer to toilet; ability to stand for two minutes with and without the glove (with support of upper limbs, if necessary); availability of a family member to supervise home exercises.

Exclusion criteria: medical problems or cognitive deficit (mini mental status examination score <24)[20] that could interfere with study completion; aphasia or hemineglect; intended or actual participation in any other study; significant pain (≥4 in the visual analog scale) in

any joint; upper limb treatment with anti-spasticity drugs in the previous 6 months; and severe upper limb spasticity (≥3 in the Modified Ashworth Scale).[21]

The protocol was approved by the institutional review board for human studies of Federal University of Rio de Janeiro. Stroke patients were recruited in a public outpatient rehabilitation center and gave informed written consent to participate.

Baseline measures

The following characteristics were evaluated at baseline: gender, age, time from stroke, type of stroke, handedness and side of hemiparesis.

Experimental design

Patients were randomized to one of the two groups by a staff member not involved in the study. Randomization information was stored in sealed envelopes that were kept in a cabinet accessible solely to the principal investigator. Each patient received 10 treatment sessions distributed three to four times a week over 22 days. In the $CIMT_{1.5h\_direct}$ group, patients performed exercises with the paretic upper limb for 1.5 hours at an outpatient facility and home exercises, supervised by a caregiver or family member, for additional 1.5 hours. Two days before treatment started, the caregiver was trained for one hour by the researcher providing CIMT on how to supervise the prescribed exercises performed by the patient at home. Each caregiver was instructed to make notes in a log book about the exercises performed, the number of repetitions and difficulties experience by the patient. At the beginning of each session the homework was discussed and when necessary, the level of difficulty was increased or new tasks were prescribed.

Patients in the $CIMT_{3h\_direct}$ group performed exercises under direct supervision of the same therapist that treated patients in the $CIMT_{1.5h\_direct}$ group for 3 hours per session, at the outpatient facility.

In both groups, training was provided in an individual basis and consisted of shaping principles, as outlined by Taub *et al.*,[10,22] and task specific practice. Shaping exercises comprised a battery of tasks including grasping and releasing objects of different shapes, playing cards and board games, clay activities, drawing and painting. Tasks were tailored to needs of each patient. Task-specific practice for both groups involved preparing a snack (sandwiches and juice), including arranging dishes and cutlery on a table, washing and drying them, and putting them in a cupboard. Treatment regimens were designed to ensure that both groups received the same amount of task practice and shaping.

In both groups, patients were required to use a padded mitt in the unaffected hand at home, as much as possible during waking hours. The mitt prevented use of the unaffected hand to perform fine motor activities and should be used during activities of daily living (ADL) and household activities. The $CIMT_{1.5h\_direct}$ group received written assignment of practice at home. All patients were instructed to record the use time of the mitt and any difficulties perceived at home, in log books. At the beginning of each outpatient session the notes were discussed and, if necessary, problem-solving strategies were applied.

Outcome measures

Primary outcome

The primary outcome measure was the Motor Activity Log (MAL).[9] The MAL was developed to measure the use of the affected arm in real world,[23,24] and consists of a semi-structured interview that can be applied to both patients and caregivers. It is capable of detecting phenomena not evaluated in other instruments, such as the *learned nonuse*.[24] The present study applied the original version (14 activities) of the MAL quality of movement scale (QOM). Although the original instrument presents two subscales, *i.e.*, quality of movement (QOM) and amount of use (AOU), it has been shown that the QOM scale is able to capture components of both quality and quantity of use of the affected extremity in stroke patients.[25] The MAL-14 presents a 5-point ordinal scale and individuals are asked to rate how well they have used the affected arm in the past week. Higher scores reflect great quality of movements of the more affected arm in real world.[25]

Secondary outcomes

Secondary outcomes included the Fugl-Meyer Assessment of Sensorimotor Recovery after Stroke (FMA)[26-28] and the Stroke Specific Quality of life Scale (SSQOL).[29-31]

The FMA measures the level of motor impairment in stroke patients (best possible score for the upper limb, 66) and has excellent test-retest reliability and construct validity.

The SSQOL assesses health-related quality of life in stroke patients and encompasses three dimensions of the International Classification of Functioning, Disability and Health: impairment, activity and participation.[31,32] The instrument has proven its validity, reliability and sensitivity. It includes 49 items dealing with energy, family role, language, mobility, mood, personality, self-care, social role, reasoning, upper limb function, vision, and work/productivity. Each item is rated in a 5-point scale and the scale has a maximal score of 245 points with higher scores meaning better health-related quality of life. Outcomes were assessed at baseline, two days after the intervention program (end of treatment) and 6 months after end of treatment by a trained physiotherapist blinded to group assignment.

Analyses

In order to compare treatment effects between the two groups, the Effectiveness Index – EI for MAL,[33] FMA and SSQL was calculated in each group, comparing results before and post-treatment and before and 6 months after treatment using the following formula:

$$EI = \frac{\text{(Total test score at T1)} - \text{(Total test score at T2)}}{\text{(Maximum test score)} - \text{(Total test score at T1)}} \times 100$$

The Effectiveness Index (EI) takes into account the fact that potential improvement for patients with high initial scores is lower than that for those with low initial scores. Thus, the EI reflects the proportion of potential improvement that was actually achieved during treatment.[34,35]

After calculating the IE for each of the variables, Mann-Whitney U tests were applied to detect significant differences in treatment effects between the two groups, immediately after treatment and six months later ($P \leq 0.025$, Bonferroni correction). Statistical analyses were performed using the Statistical Package for the Social Science (SPSS) version 17, software for Windows (SPSS, Chicago, IL, USA).

Results

One hundred seventy four patients were screened and 24 were randomized (Figure 1).

Two patients in each group did not complete the treatment protocol. In the $CIMT_{1.5h\_direct}$ group, one patient moved far from the outpatient rehabilitation center and the other had financial limitations that impeded compliance with treatment three times a weak. One additional subject from this group had a fatal recurrent stroke before the last follow-up session at six months. In the $CIMT_{3h\_direct}$ group, one patient considered that the exercises were too difficult and the other one returned to work. Therefore, we analyzed data from nine patients in the $CIMT_{1.5h\_direct}$ and ten patients in the $CIMT_{3h\_direct}$ group.

Table 1 shows characteristics of the 19 subjects that completed the treatment and follow-up protocol. There were no significant differences in baseline characteristics between patients in the two groups.

In the $CIMT_{1.5h\_direct}$ group, patients wore the mitt for an average of 3.3±1.5 daily hours and in the $CIMT_{3h\_direct}$ group, for 2.8±1.2 daily hours. However two patients in the $CIMT_{1.5h\_direct}$ group and three patients in the $CIMT_{3h\_direct}$ group did not log this information appropriately.

Primary outcome

Figure 2A show results of EI for the MAL immediately after treatment and 6 months later. Immediately after treatment, there were no significant differences in EI results between the two groups (P=0.24). Likewise, no significant differences were observed between the groups, 6 months later (P=0.97), indicating comparable benefits from the two programs on real-life motor improvements.

Secondary outcomes

There were no significant differences in EI results regarding FMA scores between $CIMT_{1.5h\_direct}$ group and the $CIMT_{3h\_direct}$ group immediately after treatment (P=0.60). Similarly, no significant differences between $CIMT_{1.5h\_direct}$ and the $CIMT_{3h\_direct\ group}$ after 6 months (P=0.84) indicating similar effects of therapies on motor impairment (Figure 2B).

Quality of life

Figure 1C shows EI results. There were no significant differences between the two groups immediately after treatment (P=0.90) and at six months post-treatment (P=0.04).

Discussion and Conclusions

In the present study, improvements in motor

function, real-world arm use and quality of life did not differ significantly between treated groups receiving either 3 or 1.5 hours mCIMT supervised by a therapist. Results immediately after treatment and six months after that suggest that both protocols are equally efficient. Both groups had the same total training time (30 hours). However, $CIMT_{1.5h\_direct}$ group may
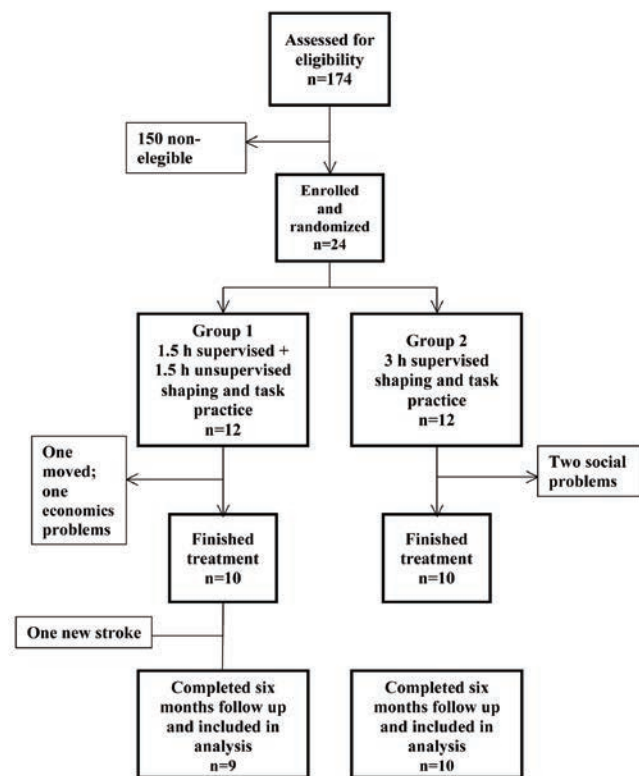
Table 1. Characteristics of study participants.

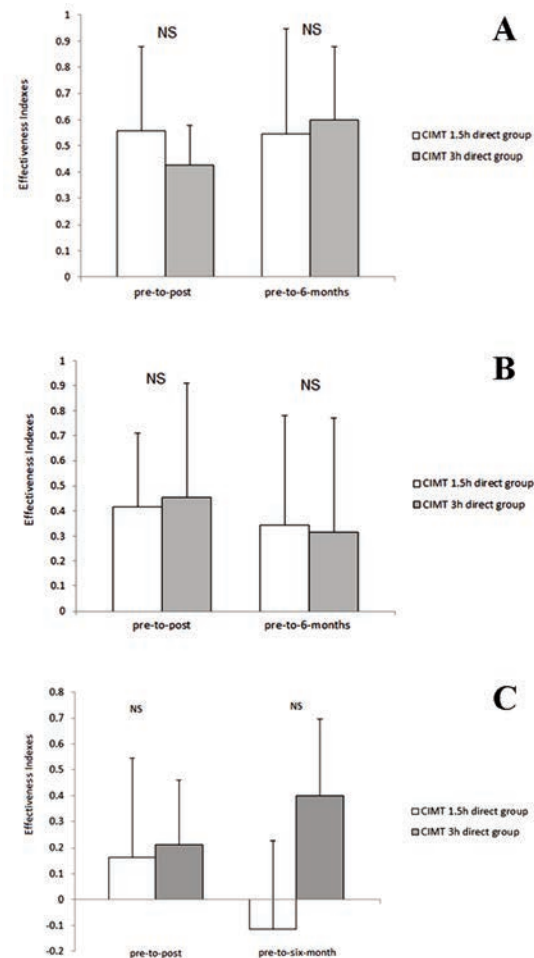|	CIMT 1.5h_direct	CIMT 3h_direct	P
Age, years, means (SD)*	61.7 (12.7)	59.5 (9.1)	0.93
Gender (men/women)**	6/3	9/1	0.55
Months after stroke, mean (SD)*	27.6 (20.9)	35.3 (33.8)	0.71
Type of stroke (ischemic/hemorrhagic)**	7/2	7/3	0.55
Handedness (right/left)**	7/2	9/1	0.45
Years of education*	5.0 (1.7)	6.6 (3.2)	0.44
Affected hemisphere (right/left)**	4/5	4/6	0.60
Motor Activity Log*	1.2 (0.8)	0.7 (0.5)	0.27
Stroke Specific Quality of Life Scale*	163.1 (39.3)	143.3 (25.3)	0.21
Fugl-Meyer assessment*	53.4 (10.8)	51.4 (8.6)	0.44

Data are mean and standard deviation (SD); *Mann-Whitney U test; **Fisher's Exact Test.

Figure 2. Effectiveness indexes results regarding Motor Activity Log (A), Fugl-Meyer Assessment (B) and Stroke Specific Quality of Life (C) scores between CMIT$_{1.5h\_direct}$ group and CIMT$_{3h\_direct}$ group pre-to-post treatment and pre-to-6 months after treatment. Mann Whitney Test (P<0.025). NS, not statistically significant.

Figure 1. Flowchart of participants through the study.

be considered less expensive due to less demand on therapist's time.

All previous studies that addressed the effectiveness of unsupervised practice at home also suggested similar effectiveness of different versions of modified CIMT. Supervision for only 25 to 50% of the time was as effective as standard one-to-one CIMT.[36] Likewise, similar gains in motor skill and real-world arm use were reported after and one hour of supervised outpatient practice coupled with 5 hours of unsupervised practice during two weeks at home.[37] Furthermore, An exclusive home-based mCIMT program supervised by an instructed family member was equally effective as a totally supervised protocol and persisted for the next six months.[38]

The development of flexible schedules may increase the number of treated patients. When questioned about their interest in participating in an original CIMT protocol,[39] 68% of inquired patients said they were not interested because of concerns about the number of hours spent daily in therapy and the length of time required for wearing the restrictive device.

In mCIMT studies, participants are typically requested to wear the constraint from five to six hours daily,[14,16,40] to 90% of the waking hours.[41-43] Nevertheless, few studies reveal the real average number of daily hours with restraint in their results.[40,44]

In the present study, besides the declared mitt time use, some patients informed they consciously avoided the use of the less affected arm in ADLs during the treatment period, so the actual restraint time is somewhat difficult to measure precisely. The contribution of the restraint component of CIMT is in fact not fully established.[45] A mCIMT study with random assignment comparing protocols with and without restraint in 24 patients found similar motor improvements after a one-year follow-up.[46] A recent study,[47] evolving 47 participants, showed no difference between two groups of post stroke patients treated with a combination of CIMT and physiotherapy plus different constraint regimens (sling *versus* voluntary constraint). It seems that using a sling were not an advantage over voluntary constraint.

As to functional outcomes, the present study indicates a substantial improvement in real world arm use after intervention in both groups. In a partially supervised CIMT program based on Taub's protocol,[37] gains in MAL were lost six months after therapy. Training in the present study was less intensive (three hours a day) and distributed over a longer period of time (21 days). This may have contributed to retention of therapeutic gains in both groups of patients. MAL scores at the six-month follow-up exhibited significant improvements in both groups with total score >2.5, indicating a perception of recovery above 50%.[48,49] The MAL

results in our study were consistent with those observed in another protocol with the same intensity and duration.[41]

There is evidence that many post stroke patients do not use their paretic hand spontaneously due to *learned non-use*.[50,51] The detected benefits in the FMA were partially but still meaningfully sustained after six months, although in $CIMT_{1.5h\_direct}$ results did not reached statistical significance. FMA is a laboratory test that assesses motor function, showing what patients can do when requested.

Although CIMT protocols results in improved function it is not clear whether CIMT is necessary to reach the results reported in several studies or whether exposure to task-specific and high-intensity training are the main components for recovery.[52,53] Recently Taub *et al.*[54] discussed the relevance of the *transfer package* that is a set of techniques to help transfer of therapeutic gains from laboratory to real life. The study concluded that the transfer package seems to be an important element of CIMT protocols increasing real-world treatment outcomes. The present study applied some principles of the transfer package like written assignment of practice at home, daily home diary and problem solving strategies to increase arm use in ADL. Health-related quality of life (HRQOL) is a multidimensional concept and can be impacted by several factors besides physical or mental status.[55] A Chinese study with chronic stroke patients found that *having a lower income* was the strongest predicting variable for low HRQOL scores.[56] The effect of exercises on HRQOL in stroke survivors is not fully studied. A recent meta-analysis showed small to medium effects of exercises in HRQOL outcomes after intervention but not 12 to 24 weeks at follow-up.[57] In the present study, the absence of significant differences in EI for the SSQOL may be related to the small sample size, because within-group analysis showed significant improvements only in the $CIMT_{3h\ group}$.

The limitations of the present study are related to its small sample size and to the absence of a control group not receiving CIMT. Strict study criteria akin to those of EXCITE led to the inclusion of only 13.8% of screened subjects. Hence, our results should necessarily be considered preliminary. Future trials should involve a larger number of participants. This should allow investigating the ideal amount of daily training and the influence of each CIMT element in functional recovery. In conclusion, our modified CIMT protocols were feasible and well tolerated. Results in both $CIMT1.5h_{\_direct}$ group and $CIMT_{3h\_direct}$ group were associated with similar improvements in real world arm use after stroke. As protocols involving less therapist supervision can reduce treatment costs, these results, if confirmed, could lead to a wider dissemination of CIMT as a standard

treatment in large numbers of stroke survivors. This would be of special importance in developing countries, which should be prepared to take a greater part of the expected stroke burden in the future.

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