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STUDY TO COMPARE THE EFFECTIVENESS OF MODIFIED CONSTRAINT INDUCED MOVEMENT THERAPY AND MIRROR THERAPY ON HAND FUNCTION IN SUB ACUTE STROKE SUBJECTS: A RANDOMIZED CLINICAL TRIAL.

Physiotherapy

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ABSTRACT

Background and Objectives: Modified constraint induced movement therapy (mCIMT) and Mirror therapy (MT) are two techniques which has proved its effectiveness in treatment of stroke subjects. The majority of evidence focuses on chronic stroke. So, the aim of this study is to compare the effect of mCIMT and MT on upper extremity motor recovery and functional status in sub acute stroke subjects.

Materials and methods: Total of 42 stroke subjects were randomized into two group i.e. MT (Group A) and mCIMT (Group B). Pre and post intervention outcome measures were taken using Action research arm test, Box and Block test, Nine-hole Peg test and overall functional status by Functional independence measure.

Result: Subjects of both group showed statistically significant improvements in all the variables measured ($p<0{\cdot}05$) which was more in mCIMT group when compared to the MT group.

Conclusion: The present study confirms that mCIMT is an effective treatment technique to improve upper extremity motor recovery, hand and finger dexterity and functional status in stroke subjects compare to MT.

KEYWORDS

Modified constraint induced therapy, Stroke, Upper extremity, Mirror therapy

INTRODUCTION

The WHO clinically defines stroke as 'the rapid development of clinical signs and symptoms of a focal neurological disturbance lasting more than 24 hours or leading to death with no apparent cause other than vascular origin' WHO 2005. The effects of a stroke depend on the site and severity of brain injury[1] The paretic upper limb is a common and undesirable consequence of stroke that increases activity limitation. It has been reported that up to 85% of stroke survivors experience hemiparesis and that 55% to 75% of stroke survivors have continued to have limitations in upper-extremity functioning.[2] The distal limb impairment is especially problematic because proper hand function is crucial to manual exploration and manipulation of the environment. In fact, finger extension is the motor function most likely to be impaired.[3] Various studies have used proprioceptive neuromuscular facilitation techniques, stretching, biofeedback, compensatory techniques,[4] robot arm training, virtual reality, mental practice and mirror therapy which are based on motor relearning theory[5] to improve hand function in stroke.[6]

Constraint induced movement therapy (CIMT) was developed by Edward Taub and his colleagues in response a concept known as learned non-use.[7] Learned non-use is the idea that if a person tries to use their affected limb and does not get the results they want they will stop using it; this non-use will result in further limitation in functional use of the limb.[8] In 1993 Taub and his colleagues published a standard protocol for CIMT for use with subjects who have sustained a stroke. This standard protocol is what is now referred to as high intensity CIMT.[9] The traditional form of CIMT follows a mass practice schedule; over the 2-week treatment period, restraint of the less affected limb for 90% of waking hours is combined with 6 hours of functionally oriented repetitive task practice using the paretic upper extremity each week day.[10] Behavioral training techniques are also used to help subjects transfer functional gains into real-world activities.[11]

The theoretical basis for CIMT was developed through early research in non-human primates from which the concept of learned nonuse following limb somatosensory differentiation emerged.[12] Taub and colleague described the learned nonuse phenomenon as a behavioral adaptation that occurs in response to the loss of sensory feedback due to decrease in coordinated movement , negative reinforcement from unsuccessful attempt with the impaired limb and positive reinforcement resulting from success in compensatory movement pattern with the unimpaired limb.[13] The result of this sequelae is a decrease in functional use of the impaired upper extremity.[14] According to Taub and Colleagues learned nonuse occurring after somatosensory differentiations in nonhuman primates such as after stroke was asked to perform functional tasks with the more impaired upper extremity with restrain of less affected upper extremity.[15] Restraint in addition to encouraging without formally training mass practice of the impaired upper extremity, result in forced use.[16]

Even though the traditional CIMT approach has been demonstrated to be effective at improving UE function and use post stroke,[7] evidence suggests that it can be difficult to implement clinically due to its high resource demand (eg: time, availability of therapists, and resources).[17-18] To overcome these limitations, the modified methods (mCIMT) have been developed by Page et al which combines structured, 30 min, functional practice sessions using more affected arm with restriction of the less affected arm 5 days/week for 5 h/day. [19] mCIMT has been shown to increase affected arm use and function in case studies[20] and randomized controlled pilot studies enrolling subjects with acute stroke[21] subacute stroke[22] and chronic stroke.[23] In mCIMT, sessions are performed for 30 minutes, 3 times per week over a 10 week period, and incorporate the same 3 key components as CIMT: restraint, RTP, and the application of behavioural techniques including shaping.[24] Despite the use of a distributed practice schedule and thus a reduction in the overall clinical treatment time, mCIMT provide subject with more opportunities to engage.[25]

mCIMT is based on neuroplasticity and cortical reorganization. Nudo and Milliken describe the cortical representation shrinking after lesion or sensory or motor deprivation. Changes in representational areas were prevented or reversed by focused motor training in primates with concurrent improvements in motor function.[26] In addition, functional imaging studies in humans with stroke have found recovery to be associated with shifts of activation during motor tasks involving the affected hand to ipsilateral secondary and tertiary motor areas and to contra lateral homologous motor areas.[27] Most of the previous literature that investigated the effects of CIMT have demonstrated significant gains in upper limb function, as well as increases in the paretic upper limb use during daily activities.[15] Conventional CIMT is proven to improve the gross motor function, but its effectiveness for the fine motor functions remains obscure.[14] The mCIMT shows improvement in all phases of recovery. Furthermore the reduction in clinical treatment time and thus a decreased use of resources in mCIMT may make the treatment easier to manage clinically.[28]

Mirror therapy (MT) aims to create an illusion of normality in the affected limb. It was introduced by Ramachandran in 1992, for use with phantom limb pain and has since been adapted to aid in the management of numerous conditions, including stroke and pain after wrist fracture and hand surgery.[29] The mechanisms for MT are still not fully understood. There are a number of theories described in the literature including increased attention to the limb, improved ownership of the limb, activation of the mirror neurone system and a reduction of sensorimotor incongruence.[30] Many mechanism have been proposed for the effect of MT in motor recovery in stroke subjects. Mirror neuron seem to involved in the mechanism underlying MT.[31] They are nervous cell with visual motor properties discovered in F5 in the brain area of the macaque.[32] This particular types of neuron also present in human brain which are active when an action is in progress and when the action is observed being performed by others.[33]

Lewis Altschuler et al at the end of 1990s introduced MT for stroke rehabilitation. They found that the mirror provides proper visual input and substitutes for the decreased or absent proprioceptive input.[34] The concept of MT has been further substantiated neuro physiologically. An imaging experiment demonstrated that inversion of the visual image of a hand can elicit lateralised cortical activations.[35] In other words, when a right hand is used, but perceived as a left hand this lead to an additional activation of the right hemisphere (and vice versa). As recovery mechanism are known to be most prominent with in the first 3 months after stroke.[36] The improvement of motor function has been demonstrated that observation of mirrored distal movements enhances corticospinal excitability, similar to actual movement execution. Apparently this modulation of excitability contributes to motor recovery, even in an initially plegic limb.[37] This is in accord with previous data, demonstrating a different contribution of both hemiparesis for proximal and distal motor functions.[38] There is evidence that the distal component is organised strictly unilaterally, whereas proximal movements rely more on bihemispheric representations.[39]

Previous literature suggested that MT is beneficial for motor function in the paretic hand in the stroke subjects but lack of evidences comparing mCIMT with MT to our knowledge. Several studies has suggested there is a need for high quality RCT to prove effectiveness of MT and compare with other conventionally applied or newly developed and effective therapies. So, the primary aim of this study was to compare the effect of mCIMT and MT on upper extremity and hand motor recovery and dexterity in sub-acute stroke subjects. The secondary aim was to find functional status of subjects after mCIMT and MT and also to know which is better treatment technique for rehabilitation.

MATERIALS AND METHOD

Study population

Stroke subjects were recruited from Central Referral Hospital in Sikkim, India by simple random sampling method. SMIMS Institutional ethics committee approved the study on 23rd April 2015with IEC registration number IEC/321/15-044. This study was not register for clinical trial registry in INDIA. Stroke was defined as an acute event of cerebrovascular origin causing focal or global neurologic dysfunction lasting more than 24 hours, as diagnosed by a neurologist and confirmed by computed tomography or magnetic resonance imaging. Subjects were included in the study if they (1) had a first episode of unilateral stroke with hemiparesis from 14 to 90 days (2) Brunnstrom recovery score between stages II and III for the upper extremity, (3) Both gender of 30-70 years of age, (4) Mini-Mental State Examination score (MMSE) ≥ to 24 (21 for illiterate). (5) Having at least 10° of active extension of each metacarpo-phalangeal joint, Inter-phalangeal joints of all the digits and 10° wrist extension of the affected limb. We also applied the following exclusion criteria: Subjects with severe aphasia, Unable to sit without support for less than 30 minutes, severe shoulder pain affecting therapy or any comorbid condition that could limit upper extremity function, visual or hearing impairment.

Recruitment and randomization

We used a randomized controlled design in which the assessor was blinded to the group allocation of each subject. All assessments were performed by the same investigator who was blinded to the treatment assignment. The baseline data regarding name, age, sex, hospital number, post stroke duration, the side of involvement, MMSE and brunnstorm recovery stage was taken after informed consent for all subjects. Subjects were individually randomized into MT (Group A) and mCIMT (Group B) groups by using computer generated random numbers (fig 1). Blocks were numbered, after which we used a random-number generator program to select numbers that established the sequence in which blocks were allocated to one or the other group. A physical therapist who was blinded to the research protocol and was not otherwise involved in the trial conducted the random-number program. There was total number of 42 subjects out of which 21 were in each group. Both the group received the same usual care rehabilitation programs for thirty minutes and additionally, had each of their own therapies for 45 minutes per session, five days a week for 3 weeks. The usual care was subject-specific and consists of Rood's facilitation techniques, Bobath techniques and Motor relearning program. There were no drop outs in the study.

Interventions

In Group A, stroke subjects received MT as an intervention that uses a mirror to create a reflection of non –paretic upper limb, thus giving the subjects visual feedback of normal movement of the paretic limb. Subjects were seated on a chair, with the Mirror board (65 X 45 cm) positioned the upper limb perpendicular to the subject's midline and with the unaffected upper limb facing the reflective surface. The subjects were asked to perform following exercises under the supervision of the therapist with unaffected upper limb and with affected limb: Wrist: Flexion & Extension, Grasp activities (holding cup, holding pen, crumple a sheet of paper in a ball. Try to spread it back out into a flat piece), Grip activities (flipping card, holding keys, holding spoon, pick up small objects like buttons, coins, and string beads) for 45 min/session, 5 days/week for 3 weeks. The speed of the movements was self- selected & no additional verbal feedback was offered. While doing above exercises, the subjects were asked to observe the reflection of unaffected extremity in mirror (which looks like the affected extremity) and to imagine that his/her affected extremity was moving normally.

In group B, a mitt was used to restrain the unaffected arm which prevented the use of unaffected limb. It was made of cotton material which was extending till the forearm. The subjects were encouraged to wear a mitt during treatment and post treatment as 10 h/day for 3 weeks except for activities like toileting, washing etc. The mitt allowed the unaffected upper extremity to assist in transfers and ambulation, but it was preventing use of the unaffected fingers to manipulate objects and necessitate use of the affected hand to perform daily activities. The total duration for mitt was recorded by subject in the log book, which was provided by the therapist.

The shaping technique for m-CIMT was given for 45 minutes/day for 3 weeks at the frequency of 5 days a week. The "Shaping" is a commonly used operant conditioning method in which a behavioral objective (in this case, movement) is approached in small steps of progressively increasing difficulty. The participant was rewarded with enthusiastic approval for improvement, but never blamed or punished for failure. All tasks were individually selected according to motor ability, to ensure successful experience, and prevent frustration leading to learned non-use. The subjects was asked to perform following exercises under the supervision of the therapist with affected limb; Wrist: Flexion & Extension, Grasp activities (holding cup, holding pen, crumple a sheet of paper in a ball. Try to spread it back out into a flat piece), Grip activities (flipping card, holding keys, holding spoon, pick up small objects like buttons, coins, and string beads).Task difficulty was progressively increased using behavioral techniques of shaping and successive approximation.

Outcome measures

The upper extremity motor recovery was measure by the Action research arm test (ARAT), gross manual dexterity was measure by Box and Block test (BBT), finger dexterity was measure by Nine-hole Peg test (9HPT) and overall functional status of subjects were measure by Functional independence measure (FIM). The ARAT, BBT, and 9HPT was administered as primary outcome whereas FIM as secondary outcome measure. Outcome measures were performed at 0 months (pretreatment) and at 3 weeks (posttreatment).

The ARAT is a standardized ordinal scale that measures upper-extremity (arm and hand) function. The ARAT includes19 items divided into four subscales: grasp, grip, pinch, and gross movements. The items within each subtest are ordered based on a 4-point ordinal scales ranging from 0 to 3 where 3 represents normal performance on each items. A score of 57 indicates normal performance. It is reliable and valid measure to assess upper extremity functions in stroke subjects.[40] The BBT was devised to assess unilateral gross manual dexterity in stroke subjects. It requests subjects to seat at a table, facing a rectangular box that is divided into two square compartments of equal dimension by means of a partition: one of the two compartments contains one hundred and fifty, 2.5 cm, coloured, wooden cubes. The individual is instructed to move as many blocks as possible, one at a time, from one compartment to the other for a period of 60 seconds. The final score is computed by counting the number of blocks moved during the one-minute trial period. The interrater reliability and validity of BBT are excellent.[41]

The 9HPT is design to measure finger dexterity in subjects with various neurological disorders. Only the hand being evaluated should perform the test. Hand not being evaluated is permitted to hold the edge of the board in order to provide stability Scores are based on the time taken to complete the test activity, recorded in seconds. It is a reliable and vailed test that measures manual dexterity. It measure the speed with which the subjects grasp and insert (and removes) 9 pegs into a grid of vertical holes. The test will be discontinued after 50 s if the subject is still unable to insert any pegs.[42]

The FIM is the functional status component of the Uniform Data System for Medical Rehabilitation. It contains 18 items that measure independent performance in self-care, sphincter control, transfers, locomotion, communication, and social cognition. The FIM scores range from 1 to 7: a score of 7 represents "complete independence," and a score of 1 is "complete dependence" (performs less than 25% of task).The FIM self-care subscale23 was used in the present study; the total score ranges from 6 (lowest) to 42 (highest). The reliability and validity of the of the FIM has been documented in stroke.[43]

Statistical analysis

The data was statistically analyzed using SPSS 22.0 version. All statistical analysis was performed on the final 42 subjects. All data was normally distributed. Normal distribution was achieved. Then data was analysed by ANOVA .mean with SD was computed. Post hoc analysis with bonn-feronnitest was used to see changes in the group and between the group .F value i.e., main effect and interaction effect was computed while level of significance was fixed at p value <0.05.

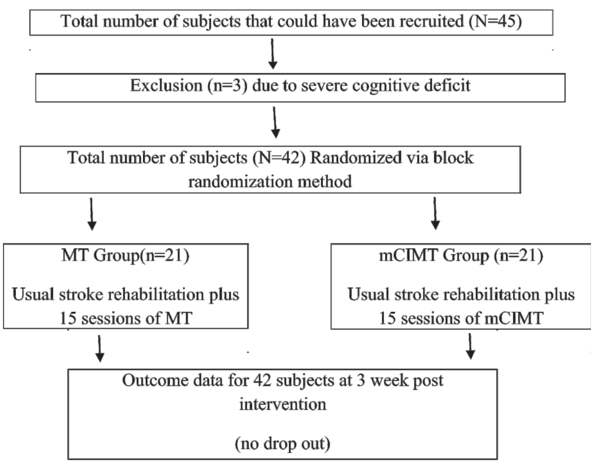

Fig 1: Flow diagram for randomized subject assignment in this study

RESULTS

Mean age in MT group was58.1± 9.05 and in mCIMT group, it was 57.9± 7.1. Out of 21 subjects in MT group, 14 were males and 7 were females. In mCIMT group, 15 were males and 6 were females. Demographic and clinical characteristics of the 42 subjects, as well as baseline comparisons of the groups, are presented in table 1. Baseline comparisons revealed that age, sex, duration, type, side of involvement, MMSE scores did not differ between the groups. At baseline subjects of both groups showed no significant differences regarding ARAT, BBT, 9HPT and FIM scores (Table 2 and 3). Data given in the Table 2 and 3 shows the changes in variables from pre to post intervention in MT and mCIMT group. After 3 weeks of intervention, subjects of both groups showed statistically significant improvements in all the variables measured (Table 2 and 3). No relevant adverse event was noted during the study in both groups. Table 4 presents the between-group comparisons of the change score for ARAT, BBT, 9HPT and FIM scores from baseline to post intervention. ANOVA test was performed to analyse the change within resistance group.

Table 1: Demographic Characteristics of the Mirror and Control Groups and Baseline Measurements

Variable	MT group n =21	mCIMT group n=20
Age (Years)	58.1± 9.05(40- 75)	57.9± 7.1 (40-70)
Female/male	07/14	06/15
Duration of stroke (days)	94.0± 33.5 (50-150)	93.5± 39.8 (50-150)
Paretic side (right/left)	12/09	11/10
Type of stroke (ischemic/hemorrhagic)	13/08	11/10
MMSE score	26.0 ± 2.04 (24-30)	26.4± 1.9 (24-30)
Brunnstrom recovery stage (2/3)	12/09	10/11

Values are number or mean ± standard deviation, ranges provided for continuous variable

MMSE: Mini-mental state examination.

Table 2: Motor Recovery and Motor Functioning Scores of stroke subjects at Pre and Post intervention in MT group

Variables	Pre Intervention		Post intervention		P value
	Mean ± SD	**CI**	**Mean ± SD**	**CI**	**<0.05**
ARAT	24.3±4.3	22.3- 26.4	34.0±4.2	31.9 –36.0	<0.05
9HPT	270.0±13.4	263.7-276.2	198.8±13.7	192.4- 205.2	<0.05
BBT	13.7±3.6	12.0- 15.4	25.0± 5.3	22.5- 27.5	<0.05
FIM	26.2±3.9	24.3- 28.0	33.3±4.2	31.3- 35.3	<0.05

Table 3: Motor Recovery and Motor Functioning Scores of stroke subjects at Pre and Post intervention in mCIMT group

Variables	Pre Intervention		Post intervention		P value
	Mean ± SD	**CI**	**Mean ± SD**	**CI**	**<0.05**
ARAT	22.6±4.0	20.7- 24.5	41.4±2.6	41.1-42.6	<0.05
9HPT	268.8±23.1	257.2- 27.8	161.5±25.3	149.6- 173.3	<0.05
BBT	23.6±8.7	19.5- 27.7	43.3±11.9	41.7- 52.8	<0.05
FIM	23.4±5.0	21.0- 25.8	36.9±4.0	35.0- 38.8	<0.05

Table 4: Between-Group differences in change Scores for outcome measures

Variables	Group A (MT)	Group B (mCIMT)	P value	F value
ARAT	9.6	18.7	<0.05	13.54
9HPT	-71.1	- 106.5	<0.05	326.45
BBT	11.3	23.6	<0.05	136.2
FIM	7.1	13.5	<0.05	9.36

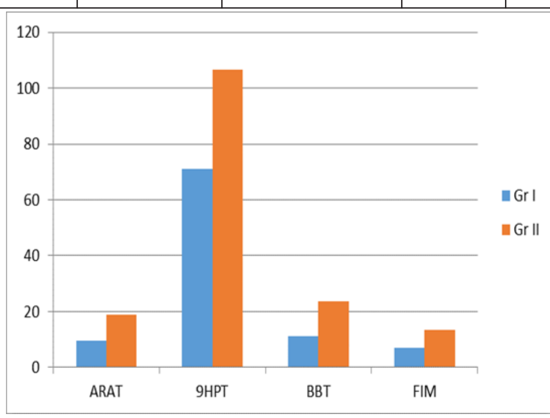

Fig 2: Shows comparison between the two groups where group II (mCIMT) shows significant improvement compares to group I (MT).

DISCUSSION

The present study demonstrated that 3 weeks of MT and mCIMT can safely improve the motor recovery, hand and finger dextrity and functional status in sub- acute stroke subjects. The result has shown more significant improvement in ARAT, BBT and 9HPT in mCIMT group compared to MT group, which is similar to a study by Jin A Yoon et al where they showed greater improvement in the BBT and 9HPT i.e. the fine motor functions as well as the grip strength were improved.

The improvement in mCIMT group for our study can be explained by following mechanism: that motor or functional recovery of CIMT is because of enhanced neural plasticity and cortical reorganisation of the learned function in the undamaged surrounding cortex and even in opposite hemisphere.[1] A study reports that human brain respond to training through its special ability called neural plasticity which is the ability of the neural circuit to undergo change in functions or organisation due to previous activity and change in response to environmental cues, experience, injury or disease.[44] Stephen Page, Peter Levine et al also pointed that mCIMT given for 30 min per day showed significant improvement in the functional outcome of the upper limb and further they suggested that even a therapy session as less as 15 mins of task specific training is sufficient for Cortical Reorganization and Motor learning to occur. Hummelsheim H et al emphasised that importance of frequent movement repetition for 15 min can also show the changes in the motor rehabilitation.[45] Classen J also believed that rapid plasticity of human cortical movement representation can be induced by as less time as 15 min per day.[46]

There was significant improvement in all components of ARAT in this study which was more in mCIMT compare to MT group. This findings are in accordance with a study by Dromerick and colleagues who found improvement in ARAT scores in the CIMT group.[47] These improvements in response to mCIMT could be explained by the guiding theory that impairment in hand function is exacerbated by" learned non-use" process and this in result lead to loss of cortical representation of the upper limb. It is claimed that these process can be reversed by 2 weeks of constraint of unaffected limb combined with practice and use of the paretic hand.[48] Yue X et al also reported that mCIMT has some specific advantages such as reducing the level of disability, increasing the use of the more affected upper limb in daily living, and enhancing the motor automaticity of the more affected arm during movement which was similar to the present finding. It is possible that repeated affected limb use can bring about cortical reorganization and then improve motor function and overcome the learned nonuse.

In the present study there is improvement in hand function in all the variables measured (Fig.2). There was significant improvement for BBT in mCIMT group and 9HPT in MT group compare with other variants. There was also improvement in hand related functioning (self-care item) on FIM instrument. Previous studies on stroke suggested that MT may be beneficial for motor function in the paretic hand which is similar to the finding of the present study. The beneficial effect of MT had also functional consequences for regaining useful reach and grasp movements, which was assessed with the ARAT which is also similar to the result of the present study.[40] The task-oriented and proprioceptive integrated exercises which was performed by the subject in the present study might activate the extended motor cortex strongly (including the parietal cortex, premotor cortex, and primary motor cortex), which can result in cerebral motor cortical facilitation which is in accord with previous study done by Kang et al .

The present study also showed improvement in functional status of the subjects and these findings are in accord with previous study done by Lin KC et al who found that mCIMT has significant improvement in functional performance on the FIM. Most of the studies that investigated the effects of CIMT have demonstrated significant gains in upper limb function, as well as increases in the paretic upper limb use during daily activities.[7] Kwakkel G et al, reported that clinically meaningful impact on subject's outcomes for arm-hand activities, self reported amount and quality of arm-hand use in daily life, and basic ADL, making mCIMT one of the most effective interventions for the upper paretic limb post stroke.[49]

Mirror therapy may be a suitable alternative because of its low cost and simplicity.[21] Many studies have applied this therapy to hemiplegic subjects, to investigate and validate its clinical effects based on the hypothesis that the visual illusion evoked by the mirror reflection of the unaffected arm, while blocking the visualization of the affected arm, would improve the motor abilities of the subjects.[2]

There were improvements in hand function in MT group also for which several mechanisms have been suggested to explain how MT works for motor recovery. Some have proposed that the visual illusion during MT generates positive feedback to the motor cortex and might remodulate cortical mechanisms of sensation and movement. In addition, the benefits of MT on ADL are not yet conclusive.[4] Stevens and Stoykov hypothesized that congruent visual feedback from the moving nonparetic hand, as provided by a mirror, would restore the function of the affected hand.[34]

The effect of mirror visual illusions on brain activity has been investigated in a number of studies. Garry et al performed transcranial magnetic stimulation during mirror illusions in healthy subjects and showed increased excitability of primary motor cortex (M1) of the hand behind the mirror. Mirror neurons are bimodal visuo motor neurons that are active during action observation, mental stimulation (imagery), and action execution. [37] Mirror neurons are now generally understood to be the system underlying the learning of new skills by visual inspection of the skill. In addition to previously reported "observation with intent to initiate" or "stimulation through simulation" mechanisms based on increased visual or mental imagery feedback, another possible mechanism for the effectiveness of the mirror therapy might be bilateral arm training.[50] Another theory suggests the possibility that the improvement induced by MT can depend on bilateral training which may facilitate rebalancing of the asymmetry of post stroke hemispheric corticomotor excitability. The contralesional cortex increases in excitability and the injured cortex decreases. In many bilateral training studies a decrease in cortical excitability in contralesional motor cortex was associated with an improvement in motor skill of the affected arm.[39] So, overall there was better improvement in mCIMT in all variables compare to MT on hand dexterity and function in subacute stroke subjects.

Study limitations

According to our inclusion criteria, our findings and conclusions are based on the population of subacute stroke inpatients (all within 3 months post stroke) who survived from first stroke without severe cognitive deficits but with severe motor impairment of the hand. A potential limitation of this study is the generalizability of the results that these findings may not be applicable to chronic stroke subjects with severe cognitive deficits. Another limitation could be muscle tone which was not assessed and it is an important component because any activity/intervention that involves attempted repetitive effortful muscle contraction can result in increase motor unit activity and changes in spasticity after stroke. Other possible limitations could be lack of follow up at post intervention.

Future studies may investigate the effectiveness of mCIMT on other impairments like apraxia, neglect etc and also follow up subjects to know its long term effect. Lastly, it should also be compared with other stroke rehabilitation technique.

CONCLUSION

In conclusion, this study found impressive positive effects of mCIMT compared with MT on motor recovery, especially manual dexterity, grasping performance, functional transfer ability as well as gross motor recoveries and motor functioning in stroke subjects. This study is important to help to inform the health professionals about the mCIMT in treatment for sub acute stroke subjects. It also provides benefits on the prognosis of stroke subjects.

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