Long term effects of Constraint Induced Movement Therapy on the functional recovery of upper limb paresis in stroke patients. - A systematic literature review

Physiotherapy Bachelor Thesis

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Preface

The bachelor thesis is the final part of the four year English Stream Physiotherapy program, allowing the student to enter the career domain. There were several domains which the students could choose and do their thesis on.
The topic neurology and specifically Constraint Induced Movement Therapy was chosen due to my interest in this domain. Stroke is a common cause of illness in the world which requires frequent physiotherapy and rehabilitation in order to recover as much as possible to the previously functioning state. Constraint Induced Movement Therapy has been a therapy which, I've often heard about but never truly seen at the internships I've worked in. Therefore, It was my curiousity in wanting to research whether this therapy has a long term effect on the upper limb motor recovery which could lead to it being used more regularly by therapists.

I would like to thank my supervisor Roderick Wondergem for the guidance and feedback he has given me through out the writing of this thesis. I would like to also say a special thank you to the general thesis coordinator, Chris Burtin and those students who peer-reviewed. Lastly, thanking the English Stream coordinator Paul de Meurichy.

Abstract

Background:
Stroke is one of the leading causes of illnesses, affecting approximately 15 million people worldwide every year. A large amount of stroke patients are left with upper extremity paresis in the long term. Several studies have been made on the effect of Constraint Induced Movement Therapy (CIMT) in the post-intervention; however, none have looked at the effect it has in the long term.

Aim:
Systematically review the benefits of CIMT in the long-term recovery of upper limb functioning in the post-acute and chronic stage of stroke.

Question:
What is the long-term effect of CIMT on the functional recovery of upper limb paresis in stroke patients compared to conventional therapy?

Method:
A systematic search was done to identify relevant randomised clinical trials (RCTs) and controlled clinical trials (CCTs) using PubMed, CINAHL, Cochrane Library and PEDro as databases. The articles, which had a potential relevance, were checked using the in- and exclusion criteria. The study validity was done using the checklist from PEDro. Finally the data was extracted and a best evidence synthesis was done to analyse the results using the Wolf Motor Function Test (WMFT) as the outcome measure.

Results:
Five of the 1,232 articles met the inclusion criteria, four RCT's and one placebo RCT. Log performance time on the WMFT showed conflicting evidence that CIMT was more effective than conventional therapy in the long term. The functional ability from the WMFT outcome showed strong evidence that there were no significant differences between both therapies in the long run.

Conclusion:
Constraint Induced Movement Therapy shows to be effective in the long term in retaining functional abilities of the affected upper limb, however, it has not shown to be more effective than other conventional therapies used in rehabilitation. Further research would need to be done.

Keywords: Constraint Induced Movement Therapy, Stroke, Upper limb motor recovery

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1. Introduction

Background information

Stroke is one of the leading causes of illnesses in the world, affecting around 10% of the world population, which is approximately 15 million people in the world every year. Therefore, it is the second cause of death after heart disease.[1,2] When taking a closer look at these previously mentioned 10%, a publication from the stroke federation states that around 5 million are left with severe disabilities.[1] Individuals suffering from disabilities are often bound to outside help either at home or in professional care homes. As the western world population is constantly growing, the number of individuals with disabilities also increases leading up to a lack in health care professionals for these individuals.[3] When looking at the areas most affected in stroke survivors, research and articles show that the upper limb is the part, which shows the greatest weakness in motor recovery. Feys et al.[4] explains that grasping, holding and manipulating objects results from the complex relation of working muscles from the shoulder to the fingers, which causes stroke patients to still have 55% to 75% of upper limb problems six months post stroke. This therefore results in increased compensation mechanisms of the upper limb in comparison to the lower limb. In addition, the lower limb requires minimal recovery in order to participate in functional mobility.[4]

Using a therapy that results in long-term effects, can help decrease the care needed due to an increased independence in activities of daily life (ADL) of the patient. The importance of a therapy which also looks at the training variables such as the intensity, specificity, salience and repetition greatly influences the results seen in the patient.[5] There are a number of therapies available to help in the rehabilitation of stroke patients to retrain functional motor activity in the affected upper limb, which is a primary goal of the therapist. The therapies which are recommended by the Dutch physiotherapy guideline (KNGF) are: Constraint Induced Movement Therapy (CIMT), Exercise therapy, Neuro-developmental treatment (NDT), Bilateral training, and Functional Electrical Stimulation.[6]

Previous history

CIMT is based on research, which was done on monkeys whereby, Taub et al.[7,8] surgically removed the somatic sensation from a single limb by dorsal rhizotomy. The monkeys immediately stopped using their affected limb, explained by the non-use phenomenon. This phenomenon is a behavioural adaptation, which occurs due to a lack of sensory feedback, negative reinforcement from unsuccessful attempts, and positive reinforcement from successful compensatory movements.[8,9] These results increased the curiosity of Taub[8] and his colleagues to look deeper into the effects of restraining the healthy limb. The immobilization of the healthy limb in monkey's showed to have permanent reuse of the limb due to neuroplasticity.[8] Neuroplasticity is defined as anatomical and functional re-organisation taking place in the brain, which moulds and adapts to the present environment.[10] This explains why CIMT plays a vital role in forcing the brain to produce new pathways in order to recover motor

functioning and could have similar effects in patients with Cerebro-Vascular-Accidents (CVA).[11] CIMT also incorporates the principles of Experience-Dependent plasticity described by Kleim and Jones[5] working with the intensity, repetition and specificity of the therapy.

CIMT is a therapy aiming to force the patient to repeat functional tasks with their affected side by restraining the healthy side. The duration of the therapy lasts two weeks for six hours a day, five times a week. The therapy is mainly used during the post-acute or chronic stage, as the patient's condition is more stable. The post-acute stage is one to six months after the initial stroke and the chronic stage is from six months onwards.[6] Also an important criteria which subjects need, is to have a minimum amount of movement in the fingers and wrist.[8] Seeing that the therapy is very intense and quite costly, people tend to avoid using this therapy despite the effectiveness that the therapy has proven to have.[8] However, no systematic review has been done to show whether the effects can be seen in the long-term. When speaking of the long term, this review will be looking at follow-up outcomes three months or longer after the intervention.

The main outcome assessment tool that was specified for CIMT, is the Wolf Motor Function Test (WMFT) described by Wolf et al. in 1989.[12,13] WMFT is a reliable quantitative assessment tool used to measure the upper extremity motor ability through timed and functional ability.[14,15] It originally had 21 items, which were performed by the subject. The test is split into three sections: performance time (120 seconds), functional ability, and strength. However, the assessment was modified in later years to just 17 items.

If CIMT proves to be an effective alternative to post-stroke rehabilitation, long-term dependency on health care could be reduced by a great amount. The question this review therefore, poses is "*What is the long term effect of CIMT on the functional recovery of upper limb paresis in stroke patients compared to conventional therapy?*"

2. Method

2.1 General description of the search strategy

In order to find the required literature, search terms were placed into four databases. The search procedure was done in such a manner that first titles and abstracts were scanned. Those articles, which could have a potential relevance, were then checked using the in- and exclusion criteria. This method pinpointed articles, which were then assessed for their quality. Lastly the articles were placed into a table to extract information, which is relevant for the research.

2.2 Search procedure

Medical databases were used to find relevant articles for the research paper. The following databases were used: PubMed (1996 - April 2013), Cochrane Library (1995 - April 2013), PEDro (1999 - April 2013) and CINAHL (1984 - April 2013). The initial search took place between November 2012 and April 2013. If full texts were not found in the databases; the articles were searched on biep.nu via the Fonty's Mediatheek webpage or free access to the Technical University of Eindhoven. The remaining articles were accessed either by mailing the authors or through the research supervisor.
Several search terms were placed into the databases in order to create a search string, to find an acceptable amount of articles relevant to the study (Appendix I). All search terms were combined with Boolean operators AND/OR. A filter such as English, RCTs/CCTs and studies on humans were applied to adjust the required searches.

2.3 In- and exclusion criteria for studies

To enable the articles to be used in this review, a set of inclusion and exclusion criteria was applied before the start of the literature search. For this to proceed, the following items were considered: subjects, study design, outcome measure, intervention and language of study. Table 1 gives an outline of the criteria:

Table 1: In-and exclusion criteria

Inclusion	• *Study design:* RCTs, CCTs, Clinical trials and references • *Subjects:* Female/male group > 18 years of age • *Language*: Articles published in English • *Participants:* Post-acute stroke (1 - 6 months) and chronic stroke (> 6 months) • *Intervention:* Constraint induced movement therapy as intervention and conventional therapies as control intervention • *Assessment:* Follow-up three months or more post intervention • *Outcome:* Wolf Motor Function Test (WMFT)
Exclusion	• Studies with just the abstract available • Studies which have not been done on humans

2.4 Selection procedure

To narrow down the number of articles, a procedure following the snowball method was applied. Firstly, keeping in mind the in- and exclusion criteria, the titles of the articles were scanned. If the title was acceptable, the abstract was then screened. Relevant and similar keywords were kept in mind to keep a constant and reliable search. When abstracts were thought to fit the topic, the full article was read to decide whether it was in accordance with the inclusion criteria. The reference list from the read articles was also checked for further studies, which could be included.

2.5 Assessment of literature

Once the articles passed the inclusion and exclusion criteria, the studies were scored on the PEDro scale. The PEDro scale was developed to assess methodological quality of RCTs and CCTs in the field of physiotherapy. It has 11 criteria rating internal validity (ten items) and external validity (one item) to assess the risk of bias in articles. A point was given for each criterion which then gives an overall score out of ten (eligibility criterion is not added to the final score). The achieved scores were listed in the results, so that the reader can see the credibility of the articles. Depending on the grade of the criteria, it gives a score of the quality. Following the KNGF guideline[6], studies are rated by 0-3 (poor), 4-5 (reasonably good), 6-8 (good) and 9-10 (very good) quality. Studies were considered of sufficient quality to use in the research with a level of 4-5 (reasonably good). If there was doubts upon the results, two reviewers "Bogaards J and Kainz J" assessed the results to confirm the quality.

2.6 Data extraction

For the studies, which were identified as possible to be used in the research, they went through the next step of data extraction. A table was composed which provided the necessary information required of each article in order to evaluate the results. The form included the following details: author of study, study design, intervention, mean time after stroke, follow-up time, PEDro score and outcome measure. (Table 3 can be found in the result section)

2.7 Best evidence synthesis

A best evidence synthesis was done using the results found from the inclusion of the articles in the research paper. This gives the overall finding for the literature review. The statistical significance was with a p value of (< 0.05). The data analysis was done using a best evidence synthesis method as proposed by van Tulder et al.[16] The analysis has five levels of evidence, which can be found in Table 2. This was done, by taking into account the methodological quality done with PEDro and consistency of the evidence. The outcomes were then presented in Table 4 and 5, in order to allow the reader to understand the results. The criteria good and very good from the PEDro rating will be regarded as high qualities for the outcomes used in van Tulder's[16] criteria.

Table 2: Quality criteria for methodological quality proposed by van Tulder[16]

Levels	Criteria
Strong	Consistent findings among multiple high quality RCT's*
Moderate	Consistent findings among multiple low quality RCTs and/or CCTs and/or one high quality RCT
Limited	One low quality RCT and/or CCT
Conflicting	Inconsistent findings among multiple trials (RCTs and/or CCTs)
No Evidence	No RCTs or CCTs
*If the proportion of studies that show evidence is < 50% of the total number of studies with the same category of methodological quality and study design, we state no evidence.	

3. Results

3.1 Selection of studies

A total of 1,232 studies were found using the electronic databases CINAHL, Cochrane Library, PEDro and lastly PubMed. Once the titles were screened, 146 articles remained to have their abstract screened. Of these, 21 articles were left to have their full text screened. However, 16 were excluded[9,11,17–30], mainly due to: the type of outcome measure,[17,20] studies not having follow-ups,[23,25,27] not having a control group,[9,11,18,19,21,22,24,26,28,30] or not being able to get the full article[29]. A summary of the search process can be found in Figure 1. In the end, five articles met the inclusion criteria to be used in this systematic review.

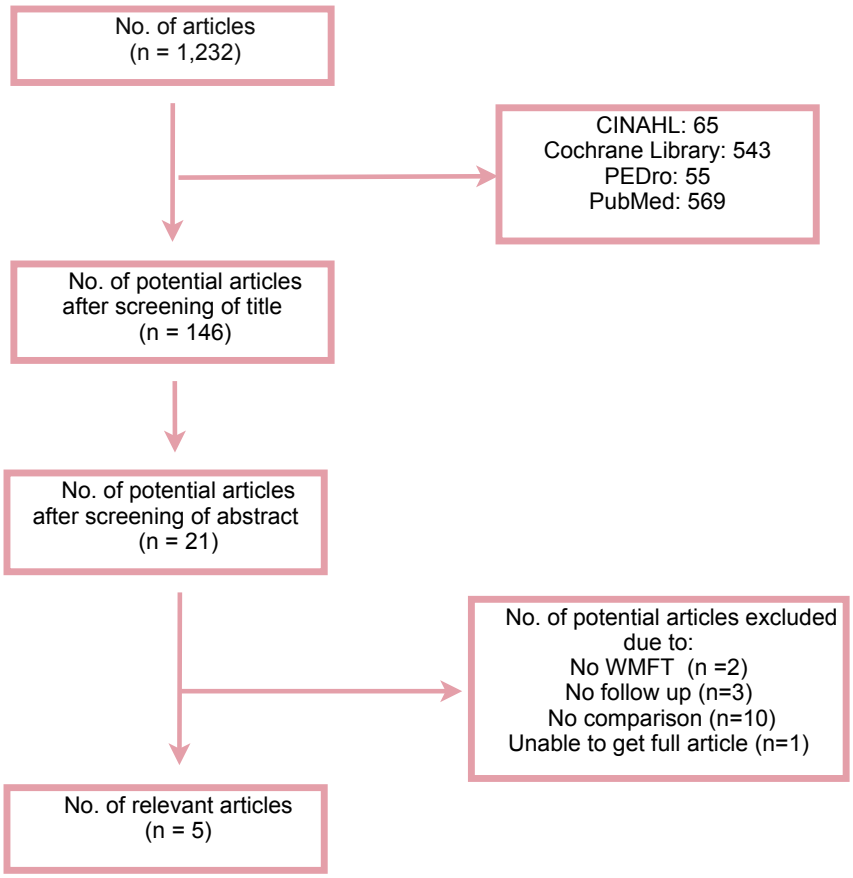

Figure 1: Flowchart of search strategy.

3.2 Methodological quality of included articles

Two of the five trials were defined as reasonably good in quality scoring 5/10 and 4/10 for the study done by Taub et al.[31] and Hayner et al.[32] respectively. The three other trials were assessed as good in quality scoring 7/10[33], 6/10[34], and 8/10[35]. Apart from one trial[31] all studies reported random allocations. In regards to concealed allocation, only one study presented this data.[35] All studies showed that their subjects were similar at baseline in regards to the important prognostic factors. None of the studies met the criteria for neither blinding of subjects nor blinding of the therapists. However, four studies showed blinding of the assessors.[31,33–35] Only one study[32] did not show that more than 85% of the subject who were initially allocated to the groups had the key outcome measured. All trials showed between-group statistical comparisons and lastly, all studies showed point measures and variability. Table 7-9 can be found in Appendix II.

3.3 Data extraction

The interventions and study characteristics were placed into Table 3. The information was given in the following order: author, method of study design, intervention of study, mean time of subject since stroke, follow-up time from intervention, score from the PEDro scale and lastly, results from the primary outcome which was looked at in this study (WMFT).

Table 3: Extraction table, of inclusion characteristics of studies. (In order of surname of first author)

Author	Method	Intervention	Mean Time after stroke	Follow-up time	PEDro Score	Between group outcome (P value)
Dahl et al.[35] (2007)	RCT feasibility	I: CIMT 6h/day for 10 days wearing a mitt 90% of waking hours. C: 1.7h/week, Upper & lower extremity exercises and 0.8h/week of occupational therapy.	1.9 years	6 months	8/10	WMFT LP: P<0.585 FA: P <0.823
Hayner et al.[32] (2010)	RCT	I: CIMT 6h/day for 10 days plus home exercises using a mitt on unaffected arm. C: Bilateral training 6h/day for 10 days plus home exercises.	3 years	6 months	4/10	WMFT No individual results
Taub et al.[31] (2006)	Placebo-controlled trial	I: CIMT 6h/day with an hour rest on each day for 14 day and wearing the mitt for 90% waking hours. C: General fitness and relaxation program 6 h/day for 10 weekdays.	4.5 years	4 weeks, 3 months and 2 years	5/10	WMFT No P value given
Wittenberg et al.[34] (2003)	RCT	I: CIMT 6h/day for 10 consecutive days (4hrs on weekend) and wearing a mitt during waking hours. C: 3h/day of less intense therapy (1hr involved passive therapy) and also aiming to improve performance task of unaffected arm. No treatment on weekends	2.75 years	6 months	6/10	WMFT No P value given
Wolf et al.[33] (2006)	RCT	I: CIMT 6h/day for 14 days wearing the mitt 90% of waking hours. C: Customary care (no treatment, use of orthotics or Occupational/ physiotherapy.	3 - 9 months	4, 8 and 12 months	7/10	WMFT LP: P<.001 FA: P<.001

RCT: Randomised Controlled Trial, I: Intervention, C: Control, LP: Log Performance, FA: Functional Ability, CIMT: Constraint induced movement therapy.

3.4 Findings

Below one can find the description of the results. The outcome differences can be seen in Appendix III

Participants

In all the studies the time, which the patients had their stroke before the intervention, was between three months to four and a half years. This shows that most of the subjects were in the chronic phase. In all the studies the range age were between thirty and eighty. The percentage of female to male was under 50% for all studies except by Hayner et al.[32] who had 58% of their subjects being female. When looking at the dominant side having the paresis, only three studies stated the percentage of subjects.[31,33,35] Dahl et al.[35] showed that 70% of the subjects had the paresis on their dominant side with Taub et al.[31] and Wolf et al.[33] having 46% and 49% respectively.

Intervention

The duration of CIMT intervention was between ten to fourteen days. The frequency of the training was six hours a day, five times a week except for Wittenberg et al.[34] who also involved four hours of training a day on the weekend. Three studies[31,33,35] had the participants wear a mitt for 90% of waking hours. The remaining two studies mention that their participants wore a mitt during the therapies but do not say for how long during the waking hours. The tasks of all the studies in the experimental group during the training, were functional orientated such as in Hayner et al.[32] and Dahl et al.[35] where participants did activities in personal care, kitchen, household and handicrafts. All studies began with easy tasks and increased the difficulty when the patient was progressing. Apart from Hayner et al.[32], whereby, the CIMT and bilateral group increased the challenge of the tasks; the remaining studies did not mention whether the control groups increased the difficulty of their training.[31,33–35] When looking at the control groups, three of the studies[32,34,35], had general fitness exercises. Dahl et al.[35] had the subjects do 1.7 hours a week of upper and lower extremity exercises and 0.8h/week of occupational therapy. Taub et al[31], had the control group do fitness and relaxation exercises 6h/day for ten days. The study by Wittenberg et al.[34] had the control group do less intense therapy, 3h/day intending to improve task performance of the unaffected arm. In those three hours, one hour was used for passive therapy such as stretching and heat. Wolf et al[33], is the only study which did not give an intervention to the control group. The group just followed their customary care and were regularly in contact to track the care they were receiving.

Follow-up and outcome measure

Dahl et al.[35] did not have drop outs between baseline and the follow-up measurements. At six-month follow-up, the log performance and functional ability of the WMFT showed no significant improvement ($P< 0.585$) and ($P< 0.823$) respectively. When looking at the results more closely both groups improved significantly.

The study by Hayner et al.[32] does not mention if they had a decrease in the number of the participants, nor does the study give the results of the treatment separately but as a group. It is mentioned in the study that there was no significant difference found between the CIMT and bilateral group when looking at the scoring from WMFT.

Taub et al.[31] did not do WMFT measurements at follow-up due to 33% of participants who did not appear at the two year follow-up.

Wittenberg et al.[34] did not have any drop outs from baseline to follow-up measurements. The study however, fails to mention what the WMFT scores are at follow-up and only mention the pre and post intervention results whereby they show no significant difference.

Wolf et al.[33] had 76.1% of the test subjects return at the twelve month follow-up. The study involved, follow-up testing at four, eight and twelve months post intervention. However, the between group difference was only done at 12 months which showed a P value of (< .001) for log performance time and functional ability in the WMFT.

3.5 Best evidence synthesis

The quality of the criteria for the methodological studies was analysed using the description from van Tulder[16] mentioned in Table 2 in the method section. Only the studies by Wolf et al.[33] and Dahl et al.[35] could be used in order to do the best evidence synthesis (BES). The other three articles did not show the results of the outcome and therefore, could not be included in the BES. The best evidence synthesis can be found below in Table 4 and 5.

Table 4. Best evidence synthesis for log performance

Study	Methodological quality	significance for log performance	Level of evidence
Dahl et al.[35] (2007)	High	No significant difference	Conflicting
Wolf et al.[33] (2006)	High	Significant difference	

Table 5. Best evidence synthesis for functional ability

Study	Methodological quality	significance for functional ability	Level of evidence
Dahl et al.[35] (2007)	High	No significant difference	Strong
Wolf et al.[33](2006)	High	No significant difference	

Effects of the intervention

In Table 4, both studies have a high methodological quality, but the study by Dahl et al.[35] showed that there was no significant difference compared to Wolf et al.[33] who showed that there was a significant differences. This leads to the level of evidence being conflicting.

Table 5 assessed the functional ability. Hereby, both studies showed that there was no significant difference. Therefore, it gave a final result of strong evidence that CIMT did not have a greater effect compared to conventional therapy.

With these results in mind, the next section will interpret these outcomes.

4. Discussion

4.1 Purpose of the study

This review aimed at reviewing evidence that CIMT has a greater effect on motor recovery of the upper limb in the long term compared to conventional therapy in stroke patients. Most literature reviews looked at the effect of CIMT after the intervention and often did not do comparisons with other modalities of treatments. In this study, a systematic search was done which resulted in four randomized clinical trials and one placebo controlled trial meeting the inclusion criteria to answer this research question. The WMFT was used due to its specificity for measuring the effects of CIMT, and on top of that has a high reliability and validity.

4.2 Main findings

The results of this study do not show that CIMT is effective in the long term compared to conventional therapies. Out of the five studies, only Dahl et al.[35] and Wolf et al.[33] conveyed results of a statistically significant difference between both treatments. The studies separated the outcome measures from WMFT into log performance time and functional ability. When looking at the log performance time, Dahl et al.[35] showed no statistically significant difference between CIMT and the control group ($P< 0.585$) whereas Wolf et al.[33] stated a significant difference between the groups ($P< .001$), showing CIMT to be more effective. Therefore, the best evidence synthesis reported that there is conflicting evidence whether CIMT has a greater effect in the long run on motor recovery of the upper limb compared to conventional therapy. When looking at the outcome of the functional ability both studies reported no significant difference. This suggests that there is strong evidence that CIMT is not more effective than conventional therapy in regards to functional ability.
Another measure, which Wolf et al.[33] looked at, was the strength outcome from the WMFT. There was no sign of a significant difference between the groups at post treatment. However, at twelve months follow-up the CIMT group showed a vast improvement. This conveyed a statistical significance ($P< .001$) in comparison to the control group. A possible reason for this, could be that because the subjects in the CIMT group are more accustomed to using their affected limb in daily tasks due to the forced use of the therapy, they increased in muscular strength. Although the control group may use their more affected arm in ADLs, they have more opportunities to compensate with the unaffected arm.

The remaining studies were not included in the synthesis as the outcomes were only mentioned in the method and discussion section and not the results section. The study by Hayner et al.[32] used a split plot and grouped all four treatment sub groups (upper extremity more impaired, upper extremity less

impaired, CIMT and Bilateral group) together to represent the results. However, Hayner et al.[32] mentions that no significant difference between the CIMT and bilateral group was found. The study performed by Taub et al.[31] could not perform the WMFT at follow-up as only half of the participants responded to the request to return for follow-up testing. In the post-intervention, the CIMT intervention reported a significant improvement compared to the control group. Hence, one could argue that the -up results could have shown a significant difference towards CIMT if there had not been a large dropout rate. The last study by Wittenberg et al.[34] did not mention the follow-up results. Therefore, a recommendation would be to have a greater number of participants in studies to not have problems such as this one.

In the study by Wolf et al.[33] apart from the follow-up testing at twelve months, the authors also did testing at four and eight months, but did not do a between group analysis. Studying these outcomes, the CIMT group showed significant improvement compared to the control intervention. At four and eight months the CIMT group for the log performance showed a significant difference ($P < .01$) compared to baseline measure, whereby the control had no significant change. The study shows that at twelve months the difference between both groups in the WMFT outcome measure diminished and there was no significant difference between CIMT and the control intervention.[33] In general, the CIMT group shows a more significant effect on functional recovery of the upper limb post intervention. However, at follow-up the control group showed the same recovery of motor function. As stated by Wolf et al.[33] the participants were in the phase of post stroke between three and nine months, and therefore can indicate that spontaneous recovery could also explain the improvement.

With this in mind, in the study by Hayner et al.[32] the bilateral control group was doing the same intensity, frequency and duration. The only difference between both groups was that the bilateral group could use the unaffected arm to help out with some tasks. This brings out a new point that intensive therapy could be of benefit to the patients in contrast to the general conventional therapy. Even though participants do not appear to show a great inter-group difference at follow-up measures, the CIMT groups do retain their functional ability at the six and twelve month testing.[33,35] In addition, CIMT has shown the use of the affected arm is three times greater than patients undergoing conventional therapy.[33]

In conjunction with this, for the first time a study was done in 2009 looking at a four year follow-up of patients who have had CIMT. The authors found that the patients had retained the functional abilities and were using their affected limb on a regular basis.[36] Unfortunately the study did not include a control group and therefore was unable to indicate whether the effect would be the same for subjects receiving conventional therapy.

This research looked at studies with patients whom had endured a stroke at least one month prior to the intervention. Studies with subjects in the acute stage were not used, as it is not recommended to use CIMT at a stage where the patients are not stable in physical and mental being.[6] Apart from one

study by Wolf et al.[33] most of the subjects were more then one year post-stroke whereby, all subjects, including the control group showed improvement.[31–35] These results bring up doubt, on the traditional belief that rehabilitation after six months post-stroke is no longer efficient.[9,37] Intensive therapy could support patients in regaining their upper limb motor function and reduce their dependency on others. The intense therapy could help many patients whom have been dependent on others, have another try at regaining some of their upper limb motor functioning. There have been a number of reviews done looking at the influence of therapies on the upper limb. These studies state, that the recovery also depends on the severity of the upper limb. It has been shown that the patients with moderate motor impairment have greater gains compared to severely impaired motor functioning.[38] Just as mentioned in the Cochrane review,[39] it is unclear which part of the CIMT intervention has the effect on the recovery; whether it is the intensity, repetition of tasks or restraint of the unaffected arm. In a review by Taub[8] and his colleagues' they mention that it is not the mitt itself which influences the amount of recovery CIMT patients have, but that it is the repetition of the exercises which causes the increase of the paretic arm in ADL's in the long term. Hence, once again more studies such as Hayner et al.[32] should be done where the control group has similar treatments, but has one part of the treatment differ. This would allow the authors to maybe pin point more specifically what gives the effect of the recovery.

Another interesting point to mention is in regards to the study done by Fritz et al.[18] They looked at six characteristics, which could be potential influences on the recovery of the patient when doing CIMT. These were: side of stroke, time since stroke, dominant hand, age, sex and ambulatory status. What the authors concluded was that, only age could be used as a predictor, showing that younger subjects maintained the gained function more easily in the long term compared to elderly individuals. However, all the other characteristics did not influence the outcome. This shows that these criteria should not be used to exclude patients from having CIMT.

4.3 Clinical relevance

When looking at the clinical relevance, the Minimal Clinical Important Difference (MCID) is used in this study. MCID is said to be the smallest difference in score in the domain of interest.[40] In this study, only the MCID of the log performance could be looked at. What was found is that there is a clinical relevance in one study for the performance time.[33] For the other study, there was no clinical important difference.[35] However, it needs to be noted, that the MCID for the WMFT was done for stroke patients who were in the acute phase. Also it looks at the results with subjects using their dominant hand.[14] In both studies, the results do not state the dominant hand and therefore, the overall score was looked at. Minimal Detectable Change (MDC) could not be used due to the single item scores of the WMFT not being shown in the studies.

4.4 Quality of studies

The methodological quality of these studies had been rated with the PEDro scale before using them for the best evidence synthesis. There were mixed results in the studies ranging between four and eight out of ten on the PEDro scale. Having a limited number of high quality studies can affect the end results of this research by giving a possibility of bias. However, in this research the two studies which did have a high quality were used for the best evidence synthesis.[33,35] The search strategy had very specific in- and exclusion criteria, which therefore could have also caused some high quality studies, having been missed out. Another aspect, which could influence the results, was the sample size. All the studies except Wolf et al.[33] (n = 222) had a small sample size ranging from 12 - 41, which affects the outcome. In all the studies, the authors tried to stay as close as possible to the traditional CIMT. They all wore a mitt for 90% of waking hours, except for the study by Hayner et al.[32], who does not mention how long their subjects had the mitt on for. All the studies had the same intensity of therapy for the CIMT group of six hours a day with the exception of the study by Taub et al.[31] who gave their subjects an hour break each day. This allowed congruence between all the studies when looking at the CIMT group. On the other hand, each study had different treatment intensity for the control group. Therefore, a future recommendation would be to have more parallel interventions with the control group.

4.5 Strengths and limitations

The strength of this systematic review was that it has a clearly explained method, which allows future replica of the results.

As in all reviews, there were limitations. Firstly, there was a limited amount of articles that were suitable for the best evidence synthesis. Initially, the expectations of comparative studies using WMFT as an outcome measure was expected to be higher than the number it actually resulted in. Out of the five articles, which were used for the results, three of them could not be used in the best evidence synthesis. This was either due to the small sample size (n=12) which led to drop outs and unable to do follow-up tests and see an inter-group difference or by the authors not mentioning the individual results of the WMFT at the follow-up.

4.6 Future research

It is recommended to do further research in this domain in order to come to a definite conclusion. More studies with a greater number of participants at baseline would be required, so that in the case of dropouts, it does not have such a great effect on the outcomes. A recommendation for future research would also be to limit the follow-up period between six months to twelve months and not longer. Limiting the follow-up period may help avoid dropouts due to deaths, recurrent stroke, and reduce

problems with adherence due to loss of interest in the experiment. The future research should also put emphasis on the treatment intensity that is ideal for stroke patients, which has been seen in the study by Hayner et al.[32] The bilateral and CIMT group had no significant difference after the same amount of intensity and frequency. Therefore, further research would be required. Lastly research with a higher methodological quality would be recommended in order to have more reliable results.
When looking at the implication of CIMT in practice, it can be seen that it is effective in the long term, revealing that there is retention of the upper extremity function and a greater use of the affected arm. But there were no significant differences, observed in the long term. However, more RCTs need to be done in order to confirm these results.

4.7 Clinical recommendations

There are a few recommendations, which need to be looked at, if one wishes to apply CIMT in practice. First of all, not all stroke patients are suited for this therapy. The patient's cognition and physical state needs to be at a certain level in order to not cause dangerous situations. Seeing that it is an intense therapy of six hours a day, it would be recommended that the therapy takes place in a clinical setting such as a hospital or rehabilitation center. Lastly, in order to have the patient motivated to participate in CIMT, it would be wise to do functional tasks which are relevant and of importance towards the individual patient. Ideally as it has been shown in previous studies, this should be done in the form of 'shaping', whereby, the challenges of the tasks increases when the patient succeeds.

5. Conclusion

In summary, results show that CIMT is beneficial in the long term. The subjects retained the functional use of their affected limb from post-intervention to follow-up measure. However, it does not show an advantage over conventional therapies. There was no significant difference found between the CIMT and control groups with the WMFT. The best evidence synthesis also showed that there was conflicting evidence that CIMT was not more effective than conventional therapy in the log performance. The synthesis for the functional ability showed strong evidence that CIMT was not more effective than conventional therapy From this study, it appears that high intensity and repetitive training are beneficial for stroke patients, and that recovery can still be expected at twelve months post stroke. Therefore, further studies are recommended to compare CIMT, intensive therapy, and conventional therapy.

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* In accordance to Vancouver referencing

7.Appendices

Appendix I - Search Strategy

Table 6: Search Strategy

Category	Intervention	Patient	Outcome
Keyword/Synonyms	Constraint Induced movement therapy (CIMT)	Stroke (MeSH)	Upper limb motor recovery
	CI therapy	Sub-acute Stroke	Follow up
	Physiotherapy	Chronic Stroke	Functional recovery
	Forced use therapy	Cerebrovascular Accident (CVA)	Wolf motor function test
	Rehabilitation		
	Conventional therapy		

Search String:

The following search string was placed into PubMed, which was then also reused or rephrased in the previously mentioned databases:
Stroke OR sub-acute stroke OR chronic stroke OR cerebrovascular Accident AND Constraint induced movement therapy OR CIMT OR CI therapy OR Physiotherapy OR forced use therapy OR rehabilitation AND Upper limb motor recovery OR follow up OR functional recovery OR Wolf motor function test.

This resulted in the following search detail:

("stroke"[MeSH Terms] OR "stroke"[All Fields]) AND (sub-acute[All Fields] AND ("stroke"[MeSH Terms] OR "stroke"[All Fields])) AND (chronic[All Fields] AND ("stroke"[MeSH Terms] OR "stroke"[All Fields])) OR ("stroke"[MeSH Terms] OR "stroke"[All Fields] OR ("cerebrovascular"[All Fields] AND "accident"[All Fields]) OR "cerebrovascular accident"[All Fields])) AND (constraint[All Fields] AND induced[All Fields] AND ("movement"[MeSH Terms] OR "movement"[All Fields]) AND ("therapy"[Subheading] OR "therapy"[All Fields] OR "therapeutics"[MeSH Terms] OR "therapeutics"[All Fields])) OR CIMT[All Fields]) OR (("chemically induced"[Subheading] OR ("chemically"[All Fields] AND "induced"[All Fields]) OR "chemically induced"[All Fields] OR "ci"[All Fields]) AND ("therapy"[Subheading] OR "therapy"[All Fields] OR "therapeutics"[MeSH Terms] OR "therapeutics"[All Fields])) OR ("physical therapy modalities"[MeSH Terms] OR ("physical"[All Fields] AND "therapy"[All Fields] AND "modalities"[All Fields]) OR "physical therapy modalities"[All Fields] OR "physiotherapy"[All Fields])) OR (forced[All Fields] AND ("therapy"[Subheading] OR "therapy"[All Fields] OR "therapeutics"[MeSH Terms] OR "therapeutics"[All Fields])) OR ("rehabilitation"[Subheading] OR "rehabilitation"[All Fields] OR "rehabilitation"[MeSH Terms])) AND (("upper extremity"[MeSH Terms] OR ("upper"[All Fields] AND "extremity"[All Fields]) OR "upper extremity"[All Fields] OR ("upper"[All Fields] AND "limb"[All Fields]) OR "upper limb"[All Fields]) AND motor[All Fields] AND recovery[All Fields])) OR ("recovery of function"[MeSH Terms] OR ("recovery"[All Fields] AND "function"[All Fields]) OR "recovery of function"[All Fields] OR ("functional"[All Fields] AND "recovery"[All Fields]) OR "functional recovery"[All Fields])) OR (("wolves"[MeSH Terms] OR "wolves"[All Fields] OR "wolf"[All Fields]) AND motor[All Fields] AND ("physiology"[Subheading] OR "physiology"[All Fields] OR "function"[All Fields] OR "physiology"[MeSH Terms] OR "function"[All Fields]) AND ("research design"[MeSH Terms] OR ("research"[All Fields] AND "design"[All Fields]) OR "research design"[All Fields] OR "test"[All Fields]))

Appendix II - PEDro Score

Rating of the studies done by the author can be found in table 4. In table 5 the rating was done by the PEDro website.

Table 7: Methodological quality assessment by author

Study	Intervention	1	2	3	4	5	6	7	8	9	10	Total
Dahl et al.[35] (2007)	CIMT compared with traditional rehabilitation	1	1	1	0	0	1	1	1	1	1	8/10
Hayner et al.[32] (2010)	CIMT vs Bilateral treatment	1	0	1	0	0	0	0	0	1	1	4/10
Taub et al.[31] (2006)	CIMT vs placebo controlled group	0	0	1	0	0	1	1	0	1	1	5/10
Wittenberg et al.[34] (2003)	CI therapy vs less intensive intervention control group	1	0	1	0	0	1	1	0	1	1	6/10
Wolf et al.[33] (2006)	CIMT vs usual & customary care	1	0	1	0	0	1	1	1	1	1	7/10

CIMT: Constraint Induced Movement Therapy

Table 8: Methodological quality assessment from PEDro website

Study	Intervention	1	2	3	4	5	6	7	8	9	10	Total
Dahl et al.[35] (2007)	CIMT compared with traditional rehabilitation	1	1	1	0	0	1	1	1	1	1	8/10
Hayner et al.[32] (2010)	CIMT vs Bilateral treatment	1	0	1	0	0	0	1	0	1	0	4/10
Taub et al.[31] (2006)	CIMT vs placebo controlled group	0	0	1	0	0	0	1	0	1	1	4/10
Wittenberg et al.[34] (2003)	CIMT therapy vs less intensive intervention control group	1	0	1	0	0	1	1	0	1	1	6/10
Wolf et al.[33] (2006)	CIMT vs usual & customary care	1	0	1	0	0	1	0	1	1	1	6/10

CIMT: Constraint Induced Movement Therapy

Table 9: Reason for scoring in PEDro.

Criteria	Dahl et al.[35] (2007)	Hayner et al.[32] (2010)	Taub et al.[31] (2006)	Wittenberg et al.[34] (2003)	Wolf et al.[33] (2006)
Random Allocation	Methods: Study Design	Methods: Study design	/	Methods: Subject Paragraph 2	Methods: Recruitment
Concealed Allocation	Methods: Study Design	/	/	/	/
Baseline Similarity	Results: Study Sample	Methods: Study design	Method: Participants	Methodology: Paragraph 2	Methods: Key Outcomes
Blinding of Participants	/	/	/	/	/
Blinding of Therapists	/	/	/	/	/
Blinding of Assessors	Methods: Study Design	/	Method: Measures	Methodology: Paragraph 2	Methods: Outcome measure paragraph 2
Measure of key outcomes from more than 85% of participants	Results: Figure 1 & Discussion paragraph 8		Results: Changes from pre to post treatment and Persistance of improvement	Results: Patient characteristics	Results: Figure 1
Intention to treat analysis	Methods: Statistical Analysis Paragraph 1	/	/	/	Methods: Data analysis paragraph 1
Between group statistical comparisons	Methods: Statistical Analysis Paragraph 2	Method: Statistical Analysis: paragraph 2	Results: Initial difference.	Results: Baseline and outcome measure	Methods: Data analysis paragraph 2
Point measures of variability.	Results: Study Sample paragraph 2 & table 2	Method: Statistical Analysis: paragraph 1	Results: Table 2.	Results	Results: paragraph 1
Eligibility criteria	Yes	Yes	Yes	Yes	Yes

Appendix III - Data Extraction

Table 10 Results of Intervention

Study	Intervention	Outcome Measure	Treatment			Control			Difference between group (P Value)
			n	Baseline	FU	n	Baseline	FU	
Dahl et al.[35] (2007)	CIMT compared to traditional therapy	WMFT a)LP b) FA	18	a)2.17 ± 0.78 b)3.51 ± 0.53	a)1.82 ± 0.80 b)3.95 ± 0.61	12	a)2.27 ± 0.85 b)3.31 ± 0.58	a)1.77 ± 0.92 b)3.73 ± 0.58	a)P< 0.585 b)P< 0.823
Hayner et al.[32] (2010)	CIMT compared to bilateral training	WMFT a)LP b) FA	6	No individual results.	No individual results.	6	No individual results.	No individual results.	No individual results.
Taub et al.[31] (2006)	CIMT compared to placebo fitness group	WMFT a)LP b) FA	21	a)5.3 ± 3.1 b)3 ± 0.4	Could not obtain results	20	a)4.1 ± 2.5 b)2.9 ± 0.4	Could not obtain results	No P value given.
Wittenberg et al.[34] (2003)	CIMT compared to customary care	WMFT a)LP b) FA	9	6.7	No results were given	7	5.5	No results were given	No P value given.
Wolf et al.[33] (2006)	CIMT compared to customary care	WMFT a)LP b) FA	106	a)2.96 b)2.39	a)2.23 b)2.75	116	a)3.179 b)2.21	a)2.873 b)2.47	a)P < .001 b)P < .001

FU: Follow-up, LP: Log-performance, FA: Functional ability

Appendix IV - Project approval

B4 Assessment form project plan

Name: Hortensia Luxen Student no: 2141275

Date: ~~26-6-2013~~ 26-6-2013

Title: Long term effects of CIMT on the functional recovery of upper limb paresis in post-stroke patients.

General

- The project plan is according to format yes / no
- Spelling and language are correct yes / no

Problem description and problem definition (introduction)

- The problem description is sufficiently clearly formulated yes / no
- The problem description reflects social and paramedical relevance yes / no
- A concrete and relevant research question (or questions) can be formulated based on the problem definition, including possible sub questions yes / no

Objective

The objective is:

- Sufficiently clearly and concretely formulated yes / no
- Relevant for a selected target group within the (paramedical) professional practice yes / no
- Practically feasible yes / no
- Achievable within the set time yes / no

Project product

The project product:

- Is in line with the problem definition, research question and objective yes / no
- Is usable for the selected target group yes / no
- Is in line with the client's wishes yes / no
- The product requirements are accurately described yes / no

Activities/method

Sufficient insight is given into the type of activities and types of sources for the performance of the research and the realization of the product yes / no

Time schedule

- The time schedule gives a global phasing and time investment for the project as a whole and for the coming weeks an increasingly detailed schedule yes / no
- Important moments are recorded in the table (typographically noticeable) (e.g. contact moments, handing-in moments) yes / no
- The time schedule gives a global task division of the planned activities yes / no

Estimated costs

Clear insight is given in:

- The costs to be expected concerning money and hours — yes / no
- The division of these costs (project leader, student, programme) — yes / no

Literature

- Used and planned literature is specific and mentioned to a sufficient extent — yes / no
- Relevant and recent literature is referred to — yes / no
- Literature references, in the text and in the literature list, are made according to the Writer's Guide (Wouters 2012) — yes / no

Comments:
Some definitions has to be ~~clear~~ clarify in the introduction.
The funnel ~~has~~ in the introduction is not sharp enough for the final product.
Method section is clear enough for project plan

All points under B3.1 up to and including B3.8 must be answered with a 'yes' in order to receive a GO for the project. The supervisor discusses with the student which points need adjustment.

GENERAL:	GO

Name assessor: Date + Signature

R. Wondergem — 26-4-2013

Jaap Jansen — 26-4-2013