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Research Article

Constraint-Induced Movement Therapy (CIMT): Current Perspectives and Future Directions

Aimee P. Reiss, Steven L. Wolf, Elizabeth A. Hammel, Erin L. McLeod, and Erin A. Williams

Division of Physical Therapy, Department of Rehabilitation Medicine, Emory University School of Medicine, Atlanta, GA, USA

Correspondence should be addressed to Aimee P. Reiss, aimee.reiss@emory.edu

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Constraint-induced movement therapy (CIMT) has gained considerable popularity as a treatment technique for upper extremity rehabilitation among patients with mild-to-moderate stroke. While substantial evidence has emerged to support its applicability, issues remain unanswered regarding the best and most practical approach. Following the establishment of what can be called the "signature" CIMT approach characterized by intense clinic/laboratory-based practice, several distributed forms of training, collectively known as modified constraint therapy (mCIMT), have emerged. There is a need to examine the strengths and limitations of such approaches, and based upon such information, develop the components of a study that would compare the signature approach to the best elements of mCIMT, referred to here as "alternative" CIMT. Based upon a PEDro review of literature, limitations in mCIMT studies for meeting criteria were identified and discussed. A suggestion for a "first effort" at a comparative study that would both address such limitations while taking practical considerations into account is provided.

1. Introduction

Recent advances in stroke rehabilitation research, including constraint-induced movement therapy (CIMT), have the potential to change traditional therapeutic approaches in clinical practice. However, communicating best practices and implementing change remain significant challenges for both researchers and practicing clinicians to overcome. In a recent Canadian study, Menon et al. [1] found that, despite the evidence of best practice in stroke rehabilitation, the implementation of best practice in the clinic was inconsistent and underutilized, as clinicians continued to apply traditional neurodevelopmental techniques in the treatment of individuals after stroke. Barriers to incorporating evidence-based practice (EBP) into clinical settings are well documented and fall under two general categories: individual clinician barriers and organization barriers [1–3]. Lack of time and resources is often cited by clinicians as primary limitations to reading or searching the literature [1–3] as well as self-efficacy. In this context, self-efficacy means the degree to which an individual clinician feels capable of searching, reading, analyzing, and implementing evidence-based practice into her daily clinical practice and thought processing. Low self-efficacy may be more prevalent in clinicians who have been working for 15 or more years because of lack of formal education in EBP skills [1, 2]. Organizational barriers can include lack of computers or access to research databases, the absence of active research in clinical settings and limited encouragement of professional development, with a growing emphasis on productivity [1, 2]. The combination of time constraints, productivity pressures, volume of research available, and a dearth in EBP skills may, over time, create an even greater gap between best evidence and current practice [1]. National and international guidelines for evidence-based practice following stroke can assist clinicians in determining best practice by compiling recent advances in stroke research. These guidelines are easily accessible and decrease the burden on clinicians to search and assess the literature themselves. However, they may not always provide sufficient evidence or information regarding a particular intervention, and there may not be a shared consensus among guidelines.

In the case of constraint-induced movement therapy, drawing a solid conclusion after reviewing prominent stroke guidelines is difficult. For instance, in a scientific statement from the American Heart Association [4], CIMT is recommended for chronic stroke patients with greater than 10 degrees finger extension, but no parameters of treatment are provided. Australian stroke guidelines paint a less conclusive picture of CIMT, concluding that CIMT is effective with more than 20 hours of training, but possibly detrimental when provided very early in the rehabilitation process [5]. Here again no treatment parameters were offered for the delivery of CIMT and the lack of methodological consistency in the literature was noted. New Zealand guidelines briefly mention CIMT as a possible rehabilitation approach, but make no recommendations regarding patient criteria or the parameters to deliver CIMT [6]. Canadian guidelines, updated in 2010, offer the most specific details for patient criteria and protocol parameters for signature or modified CIMT (mCIMT) in early stroke rehabilitation [7]. These differences yield a lack of clarity regarding recommendations for CIMT and may in part be precipitated by the lack of methodological quality in the modified CIMT literature. The purpose of this paper is therefore multi-fold: (1) present current perspectives of signature CIMT and the evolution of mCIMT; (2) discuss limitations in current CIMT literature by using PEDro criteria as a basis to; (3) suggest an "alternative" form of modified CIMT, which can subsequently be compared to the signature form in a "head-to-head" comparison, first in preliminary studies and then as a formal clinical trial. This consideration is important since such an effort has not been formally undertaken.

1.1. Current Perspectives of Signature CIMT and the Evolution of mCIMT. Constraint-induced movement therapy (CIMT) is a widely explored treatment protocol to increase functional use of the more impaired upper extremity (UE) for persons with hemiparetic stroke. The theoretical basis for CIMT was developed through early research in nonhuman primates from which the concept of learned nonuse following limb somatosensory deafferentation emerged [8, 9]. Taub and colleagues described the learned nonuse phenomenon as a behavioural adaptation that occurs in response to the loss of sensory feedback due to a decrease in coordinated movements, negative reinforcement from unsuccessful attempts with the impaired limb, and positive reinforcement resulting from success in compensatory movement patterns with the unimpaired limb. The result of this sequelae is a decrease in functional use of the impaired UE [10]. This undesirable adaptation was overcome in monkeys by restraining the insensate limb, thus forcing them to use the impaired UE [11].

According to Taub and colleagues [12], learned nonuse occurring after somatosensory deafferentation in nonhuman primates is comparable to that seen following central nervous system (CNS) insult in humans, such as after stroke. In the first application of a treatment technique to overcome learned nonuse in humans, a patient with hemiparetic stroke was asked to perform functional tasks with the more impaired UE with restraint of the less affected UE [13]. Restraint, in addition to encouraging without formally training massed practice of the impaired UE, resulted in what Wolf et al. called "forced use" [14].

The protocol has evolved to specifically include repetitive and adaptive task practice under clinical supervision. These additional structured elements collectively define the current concept of CIMT. Repetitive task practice (RTP) is continuous blocked practice of a specific functional task, usually for a period of 15–20 minutes. Adaptive task practice (ATP), or shaping, uses a step-wise approximation method, breaking down tasks into successive manageable components to improve overall proficiency [15, 16]. Based upon the underlying operant conditioning through provision of therapist feedback, shaping fosters patient problem solving, resulting in self-motivation to use the affected limb [16]. This intensive practice fosters motor relearning and has been shown to promote neural plasticity in the CNS [15]. Successful application of CIMT is thought to induce a use-dependent increase in cortical reorganization of the areas of the brain controlling the most affected limb [17, 18].

Several studies, primarily in mild to moderately impaired survivors of stroke, have demonstrated clinically relevant results [12, 19–21]. However, limitations, such as small sample sizes within trials, variations in time since stroke, and alternative CIMT protocols, weakened the ability to draw significant conclusions about pertinent findings [22, 23]. In 2006, results from the first Phase III, multisite, randomized clinical study, the EXtremity Constraint-Induced Therapy Evaluation (EXCITE) trial, were published and showed statistically and clinically relevant confirmation of the efficacy of CIMT in patients three-to-nine months posthemiparetic stroke [24].

Signature CIMT, developed by Taub [12, 25] and later used in the EXCITE [24] trial, included restraint of the less impaired upper extremity by donning a protective safety mitt for 90% of waking hours over a two-week intervention period. Subjects were also required to participate in six hours/day (five days/week) of ATP and RTP [10, 24]. Some researchers have criticized this signature protocol as being impractical in clinical settings [26–31]. Patient tolerance, mitt wearing adherence, feasibility in clinics, and reimbursement issues have been emphasized as key weaknesses of the signature CIMT protocol, thus potentially acting as barriers to more pervasive clinical implementation [32, 33].

In response to these critiques, a number of "modified" versions have arisen to address the issues presented by the signature form of CIMT. Some investigators altered intensity protocols by distributing total treatment time over a longer duration. For example, Wu et al. [29, 34, 35] decreased the intensity to two hours/day (five days/week) but increased duration to three weeks, which required only six hours/day of upper extremity restraint. Page et al. [26, 33, 36] increased treatment duration to 10 weeks, with 30 minutes of intervention per day, three days/week and reduced mitt restraint to five hours/day. Other investigators expanded the inclusion criterion for relative chronicity. Ro et al. [37] included subjects 14 days after stroke, and Miltner et al. [38] included subjects up to 17 years after stroke. While all of these modifications claim to have shown effectiveness in

improving motor function, these studies, like early signature CIMT research, are also limited by small sample sizes. Of all trials included in previous reviews of CIMT, only two studies had greater than 30 participants [22, 23].

Despite significant variability in protocols, each form of treatment delivery claims the name "modified" CIMT [35, 39]. The issue therein is the lack of standardization by which to establish a consistent reference point for monitoring treatment dosage, creating confusion among the researcher, therapist and reimbursement communities. Therefore, an analysis of existing modified CIMT protocols, to devise a reasonable synthesis of approaches called "alternative" CIMT, should be performed and becomes a necessary precursor before a best model alternative intervention that incorporates key elements, such as intensity, duration, and subject chronicity [40, 41], can be constructed. This best model alternative protocol can then be formally compared to signature CIMT to determine if an alternative, more feasible approach is equally effective.

An important first step, intended to increase the veracity of these future studies, is the analysis of the methodological quality of current CIMT literature using a valid and reliable tool to determine worthy inclusion in development of the alternative treatment protocol. To build a strong study at any level, including only the highest quality literature as a foundation for study design and in support of findings, becomes a critical consideration. Not only do these factors increase the integrity of any immediate study, but also that of future studies. Unlike previous reviews which explored only CIMT efficacy [22, 23], we sought to critically analyze existing CIMT methodologies in order to systematically determine specific deficiencies within articles. Worthy articles can then be selected for use in determining an alternative form CIMT, which can then compared to the signature form in a "head-to-head" comparison.

The evaluation tool chosen for analyzing methodological quality of CIMT research was the Physiotherapy Evidence Database (PEDro). PEDro applies 11 criteria, 10 of which are scored (see Appendix A) to assign a quantitative measure of study strength [42]. This particular set of criteria was chosen for its specificity to physical therapy literature; use by novice and expert researchers alike; reliability [43]; strength in assessing methodological quality specifically in stroke literature [44].

Although the authors did not intend to perform a systematic review of the CIMT literature, several articles were selected from 1998–2008 as a comprehensive sampling to use as the basis for this discussion. The list of CIMT literature was compiled using the following electronic databases: PubMed, Cochrane Library, MEDLINE, and Ovid. Key terms included constraint-induced movement therapy, modified CIMT, hemiparetic stroke, and constraint-induced therapy.

Approximately 75 studies were deemed relevant for further review, based upon title and abstract containing CIMT or "modified" CIMT. Studies were excluded if all three components of CIMT (ATP, RTP, and restraint) were not administered in at least one group; they contained paediatric participants (<18 years of age), used subjects other than patients with stroke, were systematic reviews/meta-analyses, or were nonexperimental literature (case studies, letters to the editor, or perspectives). Experimental literature accepted for use in this review included Sackett's levels of evidence: 1b, 2b, and 3b (see Appendix B) [45]. After employing this procedure, 27 articles, published between 1999 and 2008, were chosen for inclusion in this discussion [24, 26–31, 33, 34, 37, 38, 46–61].

Therapist raters with comparable experience in research design, independently rated each of 27 CIMT articles using PEDro criteria. A series of detailed discussions regarding the nature and interpretation of these criteria preceded the actual rating exercise. All raters were blinded to each other's assessments. A "yes" was given for each criterion the rater believed was satisfied by the article. Total scores reflected the total number of "yes" answers given on eligible criteria (2–11 are considered "eligible" for scoring). One reviewer compiled the results of the three raters. Scores were not discussed among raters prior to compilation or statistical analysis. A post-hoc analysis showed that raters could not agree upon whether some studies met three particular PEDro criteria: baseline similarity between groups, outcome measures obtained for at least 85% of participants, and clarity regarding successfully meeting the "intention to treat" directive (see Appendix A).

There may be several explanations for interrater discrepancies. Lack of clarity in some PEDro operational definitions may have contributed to varying interpretations among reviewers. Hence there may have been some uncertainty about whether studies clearly articulated and implemented an intention to treat strategy. A discussion amongst raters suggested that disagreement between raters may have been precipitated by alternative interpretations or poorly defined aspects of methodologies or outcomes. Such misinterpretations could be overcome through clearer precision in the delineation of methods. For criterion four (baseline similarity), some articles calculated significant differences between groups for only a few characteristics, but claimed overall "baseline similarity." This discrepancy in approach left the reader unsure if the criterion was completely fulfilled. Raters were commonly uncertain if outcomes measures were collected in at least 85% of subjects (criteria eight). Finally, report of attrition (criteria nine) was another source of reader confusion due to unclear documentation. Subject dropout had to be inferred in some cases from tables, rather than explicitly stated in the text.

Additionally, raters agreed that blinding of evaluators to subject allocation and intervention received were not adequately addressed in the current review. Collectively, these methodological weaknesses present a challenge for clinicians to confidently interpret and apply the principles of these alternative forms of CIMT. These discrepancies became the basis for the selection of elements that needed greater clarification and inclusion in an alternative form of CIMT against which one can then undertake a comparison with the signature CIMT.

1.2. Efforts to Create a Standardized Alternative Form of CIMT. A recent article attempted to compare a version

of modified CIMT to signature CIMT. Barzel and colleagues [62] compared signature CIMT to a 4-week home-based modified CIMT program (CIMThome). CIMThome patients and a family member received an initial day of training from a physiotherapist regarding the two primary components of signature CIMT: shaping and constraint of the nonaffected upper extremity. CIMThome patients and their caregivers then performed a self-managed program at home for four weeks, with weekly visits by the physiotherapist to supervise and advance therapeutic exercises as appropriate. Despite the home-based program, patients still received nearly 15 hours of supervision from a physiotherapist. Results showed CIMThome to be as effective as signature CIMT; however, the sample size was small with just seven chronic stroke patients in the CIMThome group.

Hosomi and colleagues also developed a self-training protocol using elements of signature CIMT [63]. Forty patients were recruited based on signature CIMT criteria. Patients were then instructed in a self-training protocol that included instruction in shaping tasks to address individual limitations. The protocol consisted of 20 minutes of self-training per shaping task, culminating in 10–15 different training tasks per day (five hours a day for 10 consecutive weekdays). Direct supervision by a physiotherapist occurred every 20 minutes to evaluate patient performance and advance therapeutic exercise as appropriate. Results showed significant improvements on the Fugl-Meyer Assessment, the Wolf Motor Function Test, and The Motricity Index. However, a major limitation of this study was having no comparison to a control group or other modified CIMT protocol. Therefore, the weaknesses of methodology discussed in this paper have still not been addressed in recent studies either, and a need exists to generate a best-model alternative CIMT option that incorporates weaknesses extracted from the literature.

1.3. Implications. In designing future studies, methodologies must be clearly defined and controlled to improve clarity for readers and replication for clinical researchers. Specifically, discrepancies were noted for attrition and diffusion of intervention, and report of baseline statistics.

To provide evidence-based practice, increased numbers of therapists are accessing and reading clinical trials in order to choose appropriate interventions. When attempting to qualify an article's strength, clinicians and researchers may use a system like PEDro. Therapists may be assumed to use high- rather than low-scoring articles when choosing interventions. However, if criterion satisfaction is unclear, interpretation is left to the reader, leading to discrepancies in perception of the value of a clinical trial that can ultimately impact clinician interest in utilization of treatment protocols. A more appropriate course of action would be to place responsibility upon researchers to give greater attention to clarity when describing methodological considerations.

Recently, within the field of neurorehabilitation, there has been a call to improve the value of studies [64, 65]. Dobkin [65] proposed performing a thorough qualitative assessment of current literature as a key to accomplishing a more systematic approach to method design, to increase the integrity of multisite randomized clinical trials for motor interventions. In the case of CIMT, we have performed a comprehensive literature search and assessed the methodological quality of several articles to determine specific deficiencies within the articles.

Secondarily, the most substantial elements that might serve as the foundation of a "best model" alternative CIMT protocol can also be proposed. Three articles in our mCIMT review scored 8/10 on the PEDro scale [29, 31, 34], the highest scores in our review. The frequency and intensity of the modified CIMT interventions were very similar across these studies: 2 h/d, 5d/wk for 3 wk. This treatment intensity may be more feasible and practical than signature CIMT. In addition, we propose further elements drawn from signature CIMT, including two hours of home task practice for three days per week for three weeks including specification and rationalization for this practice. Participants in this alternative form of CIMT would also undergo 30 minutes of a nonspecific but documented functional activity six days per week and wear the restraining device 90% of waking hours. This dosing approximates 75 hours over a three-week interval using a distributed practice model that would be comparable to almost 80 hours (up to six hours per day, five days per week for two weeks in a clinic/laboratory environment in addition to about two hours per day for 10 days of home-based activities) of signature CIMT. For both interventions, restriction of better limb use would occur for 90% of waking hours throughout the intervention period. Inclusion criteria would match that established for the EXCITE Trial [24]. The alternative CIMT plan would include therapist guided on-sight training for two hours the first day of each of three weeks with home based assignment of mutually agreed tasks throughout the remainder of the week for each of three weeks. Participants in both groups would be evaluated before and after the intervention with subsequent followups at 3 and 6 months after intervention. The evaluator would be blinded to group and the selected outcome measure would be standardized. Dropouts would have last values carried forward (imputation), a typical procedure in intention to treat studies. The study would be powered based upon the selected outcome measure. For example, if the outcome was the WMFT, a reasonable change could be a 30 percent reduction in median time to complete tasks associated with a patient impression of percent improvement in function as suggested by Fritz et al. [53]. Collectively, such a comparison would address several issues. All the limitations observed in the present PEDro review would be overcome, dose equivalency would be established, a reasonable home based, patient driven program could be standardized and compliance measured, and immediate and intermediate end points would optimize difficulties often encountered in tracking participants over a longer period of time. A future pilot study will assess the feasibility and efficacy of this proposed "best model" alternative CIMT protocol to signature CIMT with the intent to develop a signature mCIMT protocol.

2. Possible Limitations

The exclusion of meta-analyses and case-studies presents a possible limitation to the extensiveness of the PEDro review. The PEDro system used in this review pertained only to single clinical trials. Moreover, while there were only 27 articles comprising this review, such a number is relatively high compared to previous systematic CIMT reviews. Three existing systematic reviews in CIMT research, conducted by Hakkennes and keating [22], Bonaiuti et al. [23], and Corbetta et al. [66], included 14, nine, and 18 studies respectively, and each review used only two reviewers. In the Hakkenes and Keating [22] and Bonaiuti et al. [23] reviews disagreements were discussed until scores were agreed upon. Unlike these studies, disagreements between raters in this study were viewed as valuable, and utilized to note limitations in current research methods in hopes that the design of future studies might address these considerations. In addition, the Corbetta review [66] described a majority of the articles chosen as "underpowered and imprecise," making the case for a larger RCT and underscoring the weak methodology of the CIMT literature.

3. Conclusion

The model proposed in this paper is not only useful for analysis of CIMT literature, but may serve as a template for future studies in any genre of scientific inquiry. The quality of CIMT literature, specifically modified and signature methods, was examined closely in an attempt to increase the integrity of a future pilot study comparing a "best model" alternative CIMT protocol with the signature form of CIMT. A direct comparison approach that addressed limitations in the literature extracted from the PEDro review was suggested. Efforts by researchers to improve methodology and standardization of protocols can greatly assist the practicing clinician in analyzing EBP and incorporating best practices into clinical practice. Establishing a standardized best-model alternative CIMT protocol would also allow stroke guidelines to make clearer, more definitive recommendations regarding CIMT.

Appendices

A. PEDro Criteria

(1) Eligibility criteria were specified.

(2) Subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received).

(3) Allocation was concealed.

(4) The groups were similar at baseline regarding the most important prognostic indicators.

(5) There was blinding of all subjects.

(6) There was blinding of all therapists who administered the therapy.

(7) There was blinding of all assessors who measured at least one key outcome.

(8) Measures of at least one key outcome were obtained from more than 85% of the subjects.

(9) All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analyzed by "intention to treat."

(10) The results of between-group statistical comparisons are reported for at least one key outcome.

(11) The study provides both point measures and measures of variability for at least one key outcome [42].

B. Sackett's Levels of Evidence

Levels of evidence for interventions [67]:

(1a) systematic reviews of randomized controlled trials (RCTs),

(1b) individual RCTs with narrow confidence interval,

(2a) systematic reviews of cohort studies,

(2b) individual cohort studies and low-quality RCTs,

(3a) systematic reviews of case-control studies,

(3b) case-controlled studies,

(4) case series and poor-quality cohort and case-control studies,

(5) expert opinion.

Conflict of Interests

The authors report no of interests. The authors alone are responsible for the content and writing of the paper.

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