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Review Article

Constraint-Induced Movement Therapy for the Paretic Lower Limb in Acute and Sub-Acute Stroke

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Abstract

Stroke is currently one of the major causes of physical incapacity worldwide. Patients with stroke often exhibit impaired movements, frequently aggravated by conditioned suppression of the use of the affected segments (learned disuse). Constraint-Induced Movement Therapy (CIMT), developed from animal experiments in the 1950s and 60s, has proven to be quite efficient in rehabilitating the paretic upper limb after unilateral pathologies, such as stroke. This therapy seeks to stimulate the use of the affected segment, reducing the effects of learned disuse and helping to promote positive changes in brain structure and function. CIMT was also adapted to treat the paretic lower limb, but there are still fewer studies when compared to the upper limb. After stroke, applying this technique to lower limbs has demonstrated good results, with important effects on motor function and functional activities performed with these limbs. In the early phases after stroke, CIMT contributes to acquiring adequate movement patterns in the lower limbs, acting in the phase with the greatest cerebral plasticity to promote better recovery. However, CIMT to lower limbs is more commonly applied in the chronic phase of the disease, similar to the upper limbs. This review discusses the use of CIMT in the lower limbs after stroke, with emphasis on the acute and subacute phases of the disease.

Keywords: Stroke; Rehabilitation; Paresis; Lower extremity; Restraint; Review

Abbreviations

CIMT: Constraint-Induced Movement Therapy; PLL: Paretic Lower Limb; NPLL: Non-Paretic Lower Limb; UPL: Upper Paretic Limb; OCSP: Oxfordshire Community Stroke Project

Introduction

Stroke is one of the main causes of death and physical and mental incapacity worldwide [1], with a growing increase in both its ischemic and hemorrhagic forms in low and middle-income countries [2]. Ischemic stroke, more than twice as common as the hemorrhagic form [2], is characterized by a wide range of clinical outcomes, as well as functional impairments that depend primarily on the location and extent of the lesion [3].

In terms of functional recovery, movement deficits have the greatest impact, when compared to other experimental alterations [4]. In addition to impaired movement itself, conditioned suppression of the use of the affected body segments was also observed, a condition known as learned disuse. This term was created from experiments with deafferented monkeys which, even with preserved motor efference, stopped using the deafferented paw, indicating a post-lesion adaptive behavioral mechanism [5,6]. Similarly, later studies showed that, after a cerebral lesion such as stroke, the motor recovery of some patients is less than that of other patients with similar lesion (in terms of location and extent), suggesting that learned disuse may also account for this difference [7].

Constraint-Induced Movement Therapy (CIMT) was developed based on behavioral neuroscience studies in an attempt at reversing additional impairment caused by learned disuse. It was initially used to treat the upper limb, and later adapted for the lower limb. CIMT for the lower limb is an important approach, since it favors the use of the Paretic Lower Limb (PLL), even without completely restricting the use of the Non-Paretic Lower Limb (NPLL), as occurs in therapy for the upper limb. This allows more equal weight transfer between the lower limbs, resulting in improved motor function and functional activities involved in these limbs. Despite the good results that have been found, there are relatively few studies on this issue, when compared with the upper limb. Most existing studies are conducted in the chronic phase of the disease, where some voluntary movement of the PLL can already be observed. In the early phases after stroke (acute and subacute phases), studies appear even more promising, but are also less common. Thus, the focus of this review will be on the application of CIMT to the lower limb in the early phases after stroke, especially the ischemic type.

Constraint-Induced Movement Therapy

Brief history

The paradigm of constraint-induced movement was initially used in non-human primates by Edward Taub et al., the same team that conducted experiments with deafferented monkeys. They observed that monkeys could be induced to use the deafferented limb, after having movement of the healthy limb restricted for a number of days [8,9]. If use of the healthy limb was restricted for only one or two days, the monkeys used the deafferented limb during this period; after removing the restriction mechanism, they once again used only the healthy limb. However, if the restriction was applied for several

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consecutive days (for example, one week), gains in mobility in the deafferented limb were preserved, and the monkeys continued to use this limb even after the constraint was removed from the healthy limb.

In patients with stroke, this practice was used primarily by Ince [10] and subsequently by Halberstam et al. [11], who observed a successful motor capacity response in these patients. Thereafter, a number of studies were conducted, until Taub et al. [12] described the technique, also investigating its effects on individuals with stroke. In the 1990s the authors published the first randomized clinical trial, in which they modified the previous study design and included aspects of the training in the technique – which became known as constraint-induced movement therapy [13].

The technique

The original protocol described by Taub [12] involves the induced use of the Upper Paretic Limb (UPL) for 90% of the waking hours, with some type of restriction mechanism on the UPL (generally a splint or sling), for a period of two weeks. Concentrated and repetitive training of the UPL must occur during this period for six hours a day. The original therapy has undergone changes over past decades, but preserving a large part of the original characteristics. From the outset, CIMT has contained three main elements: massive practice, a focus on functional activities and restricted use of the non-paretic limb. Currently, we can also include multiple components and subcomponents of these elements, as follows: repetitive task-oriented training of the paretic limb for several hours a day, for 10 to 15 days (depending on the severity of initial impairment); application of a "transfer package" or behavioral methods in order to guarantee adherence to the training protocol and transfer these gains to the patient's real environment; and urging patients to use their paretic limb during their waking hours in the training period, primarily by constraining the non-paretic limb [14].

In addition to the issue of learned disuse, a different, albeit interlinked, mechanism (use-dependent cortical reorganization) has been proposed as being largely responsible for the results obtained by CIMT. A recently-published article by Taub et al. [15] describes a number of experiments showing that CIMT is accompanied by significant changes in brain structure and function, and that these changes are related to the degree of improvement in motor function caused by therapy. Brain imaging and mapping techniques demonstrated that after CIMT there is an increase in the area of cortical representation in relation to the paretic limb [16,17], with an increase in gray matter in the bilateral sensorimotor cortex [18,19] and reduced post-lesion brain tissue loss [20]. Reorganization of brain function also takes place in a number of ways: 1 - adjacent areas previously inactive for the function that was compromised become active, playing the role of the injured area [21]; 2 – increased excitability and neuron recruitment related to paretic limb movements; these additional neurons are adjacent to those recruited before treatment [16,17]; and 3 – recruitment of the motor cortex ipsilateral to the affected limb, an area that normally controls contralateral limb movements [22].

CIMT for the lower limb

Given that CIMT was created to treat upper limbs, it is currently much more evolved than therapy for the lower limb. For the upper limb, there are several randomized clinical trials, producing satisfactory results not only in patients with stroke, but also those with traumatic brain injury [23], multiple sclerosis [24], cerebral palsy [25] and neurological disorders in children and adolescents [26,27], exhibiting consistent and reproducible protocols.

Theoretically, the idea of constraint to induce movement could also be easily applied to the lower limb, since after stroke and other brain lesions a hemiparetic pattern often develops, also heightening interest in the treatment of this body segment. However, it is difficult to apply CIMT to the lower limb because the predominantly bilateral characteristic of lower limb activities makes it impractical to contain. Nevertheless, it was found that for the upper limb, non-paretic limb restriction seems to be the least important point of this therapy, with intensive practice and functional activities being most relevant [28]. Thus, this initial restriction difficulty does not preclude the use of the technique for the lower limb. It can be observed that, to date, there are no widely used applicable CIMT protocols for the lower limb. Most authors use CIMT principles and apply the therapy in different ways – sometimes without involving CIMT restraint of the NPLL.

In 1997 Duncan [29], representing E. Taub´s team, published the first manuscript that described the treatment of patients with chronic stroke, using CIMT for the lower limb. Therapy consisted of intensive lower limb activities (for example, treadmill and over ground walking, sitting and rising, climbing stairs and various balance exercises) using partial body weight support, when necessary, for 7 hours per day with rest breaks, over three consecutive weeks. All treated patients exhibited significant improvements in the parameters measured compared to the control group, which performed general physical conditioning exercises. Taub et al. [7] report that most patients with stroke walk again, albeit with degraded walking patterns learned in the early post-lesion phases. For this reason, they prefer to use "learned misuse" instead of "learned disuse", when referring to activities performed with the lower limbs of these patients. Thus, they suggest that repetitive practice of functional activities can correct inadequate movement patterns acquired after the lesion, even without use NPLL restraint.

Since then, a number of studies involving CIMT for the lower limb have been conducted. In addition to investigations involving patients with stroke (most of the studies), these include research with patients suffering from incomplete spinal cord injury [30], hip fracture [31], cerebral palsy [32] and multiple sclerosis [33], indicating the scope of the applicability of this therapy.

CIMT for the lower limb after stroke

To perform CIMT on the upper limb after stroke, a minimum amount of paretic limb movement is recommended, often defined as 10° finger extension and 20° wrist extension [34]. Therefore, most patients with stroke who undergo CIMT for the upper limb do so in the chronic phase of stroke (at least six months post-lesion), where, in most cases, they display some degree of voluntary movement.

For the lower limb, there is no precise definition of the minimum amount of movement required to perform CIMT. However, it is advisable that some movement be present and, similar to therapy for the upper limb, most studies on CIMT for the lower limb after stroke involve the chronic phase of the disease.

Authors whose studies involve patients with stroke use various

Table 1: Characteristics of studies enrolling CIMT for the lower limbs in chronic stroke.

Study (year)	Number of participants; diagnosis	Age and sequelae time	Focus of intervention	Main results
Aruin et al. [35]	8 participants; nil reported	59.1 ± 6.1 years and 1.46 ± 0.7 years	RESTRICTION (addition of a lift to the shoe on the nonparetic lower limb) + INTENSIVE PRACTICE (exercises to produce dynamic weight transfer, during six weeks)	Increase in symmetrical weightbearing, walking speed and stride length
Vearrier et al. [36]	10 participants; ischemic and hemorrhagic stroke	59 ± 18 years and 4.7 ± 7.3 years	INTENSIVE PRACTICE (6 h/day of one-on-one training for 10 consecutive weekdays, focused predominantly on functional mobility)	Improvements in ability to recover from a balance threat, and in anticipatory and steady-state balance control. In addition, weight-bearing symmetry improved and the number of falls sustained declined
Marklund & Klässbo [37]	5 participants; nil reported	62.4 ± 13.7 years and 35.6 ± 27.3 months	RESTRICTION (Immobilization of knee of unaffected leg with a whole-leg orthosis + INTENSIVE PRACTICE (functional activities on all weekdays, 6 h a day for two weeks)	Improvements in motor function, mobility, dynamic balance, weight-bearing symmetry and walking ability, with maintenance at long-term follow-up
Hase et al. [38]	22 participants; ischemic and hemorrhagic stroke	Experimental group: 60.1 ± 13.0 years and 36.4 ± 25.1 months Control group: 62.3 ± 9.2 years and 44.1 ± 29.4 months	RESTRICTION (gait training using either a below-knee prosthesis on unaffected leg - experimental group - or gait training on a treadmill - control group) + INTENSIVE PRACTICE (3-week program consisted of a 5-minute gait training session 2 to 3 times a day)	Significant increase of the fore-aft ground reaction forces during the paretic propulsion phase and in the relative durations of the paretic and nonparetic single stance, only in the experimental group
Ding et al. [39]	3 participants; nil reported	68 ± 11.8 years and 37 ±36.5 months	RESTRICTION (approach that encourages the use of paretic leg for weight-shifting tasks during balance control training in a virtual reality setting) + INTENSIVE PRACTICE (Interventions also included conventional rehabilitation program. All lasted 3h, each working day for 3 weeks)	Improvement of patients' ability to maneuver their center of pressure during a tracking task, and more symmetrical patient's weight distributions
Bonnyaud et al. [40]	60 participants; nil reported	50.3 ± 13.1 years and 5.7 ± 6.3 years	RESTRICTION (Each patient participated in one of four conditions: overground or on a treadmill while wearing or not wearing an ankle mass fixed on non-paretic lower limb). Interventions occurred in a single gait training session, which lasted 20 minutes	Had no specific effect on gait parameters of the paretic limb, whereas it increased braking force of the non-paretic limb in groups that have restrained the non-paretic lower limb
Kalilo et al. [41]	3 participants; nil reported	71 to 79 years and 14.7 ± 8.5 months	RESTRICTION (a whole-leg orthosis was used to immobilize the unaffected leg) + INTENSIVE PRACTICE (rehabilitation functional exercises of the affected leg for 2 hours each weekday over 4 weeks)	Significant increase in motor function, dynamic balance and functional mobility, which remained after a follow-up period

forms of CIMT for the lower limb. None of them used the protocol described by Taub and his team in 1997 [29]. Whereas some focus on intensive practice, others concentrate on some type of constraint for NPLL movement; however, all report CIMT in their study. Table 1 describes studies conducted with CIMT for the lower limb, in individuals with chronic stroke.

The studies mentioned in table 1 do not define one specific type of stroke (ischemic or hemorrhagic) as inclusion criterion. This is because most stroke cases are ischemic, almost always leading to hemiparesis. Attributing stroke unilaterality as criterion and stipulating that this causes hemiparesis as a sequel means cases of hemorrhagic stroke can also be included, since they will exhibit similar behavior to that of ischemic stroke.

Even though most studies on chronic stroke have reported good results for CIMT on the lower limb, it is expected that even better results can emerge if the therapy is applied in the early phases after stroke. This is justified because most cases of stroke – particularly ischemic – occur in the middle cerebral artery, compromising the upper more than the lower limb [42], which generally restores function more quickly. Considering all types of stroke (according to classification proposed by the Oxfordshire Community Stroke Project - OCSP), it is estimated that the median time to assume the upright position for 10 seconds is 3 days post-stroke, 6 days to walk 10 steps and to 10 meter-walk, 9 days after the event [43].

The relatively early recovery of lower limb function is accompanied by the emergence of inadequate movement patterns in this initial post-stroke phase. Even after assuming the upright position, there is still significant imbalance and asymmetry in body weight unloading, with much more weight being sustained by the NPLL. This pattern is reflected during gait and in other lower limb activities, making individuals more dependent on the NPLL and causing biomechanical changes in this limb. In an attempt at moving around satisfactorily, a process of acquiring compensatory strategies was initiated, involving both the PLL and NPLL [44,45].

Thus, it can be observed for example, that individuals with stroke take relatively short steps, in order to minimize single stance time with the PLL and return to the more stable phases of double stance [44,46]. Another example occurs in the swing phase of gait, in which the PLL takes much longer to displace forward, resulting from inadequate propulsion of the hip and ankle flexors of this limb. As compensation, many used hip circumduction, which also compensates reduced ankle dorsiflexion for total foot lifting during the swing phase [47]. In general, particular excursion of the PLL is limited, and to counterbalance, patients tend to increase cadence rather than step length, in order to raise gait speed and move comfortably [48,49]. All of this promotes inter-limb asymmetry, resulting in greater displacement of the center of body mass when compared to normal subjects, thereby increasing energy expenditure [50].

By acting in the initial phases after stroke, especially when the upright position is achieved and the first activities involving the lower limbs are performed (especially gait), it is believed that CIMT can intervene more effectively, avoiding the development and consolidation of inadequate movement patterns. Learned “misuse”, more than learned “disuse”, is characteristic of the lower limbs and needs to be combatted. To that end, it seems to be more effective to promote the adequate acquisition of a motor skill (that is, in the acute and subacute phases of the disease) than correcting the execution of a previously consolidated skill, in a more chronic phase.

Finally, it is known that spontaneous recovery tends to occur in the first weeks after stroke [51], representing an active process of brain plasticity, which tends to reach a plateau between 3 and 6 months after the event [52]. Early application of CIMT can therefore exploit the window of the best response to motor training, and therefore obtain better results than if applied late. It is important to underscore, however, that stimulation must occur preferentially after one week of lesion, since studies in rats showed that in the first week the forced use of the affected limb promotes an increase in the lesion area [53] and worse functional recovery [54], which does not occur after the first week [55].

Even with all these premises, studies with CIMT for the lower limb in the acute and subacute of stroke are still less common, although promising. Table 2 presents the characteristics of the studies using CIMT in the early phases after stroke.

Comparison between studies conducted by Regnaux et al. [58] (Table 2) and Bonnyaud et al. [40] (Table 1) corroborate the predictions of a better response to CIMT for the lower limb in the initial post-stroke phases. Regnaux’s study was performed with 10 patients in the subacute phase after stroke. He obtained significant gains in gait speed, cadence and kinematics of the PLL, after restricting the NPLL using load fixed to the ankle, in a single treadmill gait training session. These gains were maintained 20 minutes after removal of the load. Bonnyaud’s study was composed of 15 chronic patients in the group that underwent the same protocol as in Regnaux’s investigation; however, the patients did not exhibit the same results, showing no gain in PLL. He observed only an increase in arm strength in the NPLL, which contributed to greater asymmetry between limbs.

Table 2 shows that all the studies in the acute and subacute phases used the non-paretic limb constraint approach, which seems to be effective, even without intensive practice with the PLL. The study by Numata et al. [57] had the longest intensive practice time (19.5 hours over two consecutive days). Studies conducted in the chronic phase after stroke (Table 1) tended to use massive practice, but also sought to create restrictions for the NPLL, which is not an easy task. Developing effective constraints poses a challenge, since this can inhibit mobility, making it more difficult to maintain postural stability [39]. On the other hand, according to the studies cited here (especially in Table 2), restriction seems to have been the preferred principle of CIMT for the lower limb after stroke, given that it favors weight transfer to the PLL, increasing its use and making the lower limb less asymmetrical.

This viewpoint seems to be contradictory to that proposed by Taub and his team for training of the lower limb in patients with chronic stroke, in which restriction of the NPLL was not used, but rather intense activity aimed at correcting the learned misuse of the PLL [29]. Later, they also demonstrated that, at least for the upper limb, restraint seems to be less important than intense functional activities to promote the use of the paretic limb, also in patients with chronic stroke [28]. As previously discussed, in the initial phases after stroke, it appears that constraint of the lower member is important in promoting acquisition of functional movement patterns; in the chronic phase, restriction may be relevant, but intense activity is crucial to adapt the movements already acquired. It is important to underscore the need for larger studies to compare the role of constraint and intense functional practice in lower limbs after stroke, especially considering the different phases of the disease.

Studies conducted with CIMT for the lower limb use the principles of the technique, with each author developing their own protocol. Jonsdottir et al. [59] suggest that to maximize the results of treatment in patients with stroke, the principles of motor learning must be applied in the protocols. The main factors of motor learning include the stages of learning, types of tasks, types of practice and feedback [60]. Analyzing the learning stage in which patients find themselves – whether cognitive, associative or autonomous [61] – will make all the difference in therapy preparation. For example, patients in the early phases after stroke, who will acquire a motor skill such as sitting down, are in the cognitive (initial) stage; at this stage, skills involve inaccurate and slow motor actions, which require a great deal of attention to process information. Certainly, the protocol must not be the same as that used in the chronic phases, given that the chronic patient is often already in the autonomous stage of learning, in which the movement is automatic and does not require as much attention to perform. Following the same reasoning used for stages of learning, the type of task, type of activity and feedback must also be considered.

For the training of patients with stroke, Jonsdottir et al. [59] indicate that the use of feedback is conducive to learning new motor skills. These authors suggest the use of feedback at the onset of therapy, with a gradual reduction at the end of the session, in order to reduce the patient’s dependency on this external information. In relation to

Table 2: Characteristics of studies enrolling CIMT for the lower limbs in acute and subacute stroke.

Study (year)	Number of participants; diagnosis	Age and sequelae time	Intervention	Main results
Rodriguez & Aruin [56]	9 participants; ischemic and hemorrhagic stroke	36 - 78 years and 2 to 8 weeks	RESTRICTION (addition of a lift or wedge to the shoe on the nonparetic lower limb), in 1 day	Improvements in symmetry of weight bearing and stance
Numata et al. [57]	1 participant; ischemic stroke	72 years and 14 days	RESTRICTION (immobilization of knee of unaffected leg with a whole-leg orthosis) + INTENSIVE PRACTICE (immobilization for 19.5 h during 2 consecutive days)	Appearance of voluntary movement of the affected leg and functional improvement of lower limbs
Regnaux et al. [58]	10 participants; ischemic and hemorrhagic stroke	48.4 years and 3 to 7 months	RESTRICTION (treadmill training while wearing an ankle mass fixed on the non-paretic lower limb). Interventions occurred in a single gait training session, which lasted 20 minutes	Improvements in gait speed, step length and cadence; greater weight-bearing on paretic leg and greater hip and knee paretic excursion

the type of activity, the aforementioned authors recommend varied activities, which allow the development and retention of effective motor control strategies. In the meantime, the type of task that will be proposed to the individual, involving the use or not of restricted movement to make the task more or less difficult, must be analyzed in conjunction with the other factors related to motor learning. Once again, it is important to reinforce the need for future studies involving the concepts of motor learning associated to CIMT protocols for the lower limb after stroke, with the aim of providing patients with optimized therapy and a more effective recovery.

Conclusion

CIMT has attracted attention recently since it consists of a widely used and consolidated treatment for upper limb impairments after unilateral pathologies, primarily stroke. With respect to the lower limb, it can be said that this therapy is starting, with studies showing good results but without the use of a defined protocol, in contrast to that observed for the upper limb. For treatment with the PLL after stroke, CIMT has exhibited exciting and promising results in motor recovery, particularly in the acute and subacute phases of the disease. However, the small number of studies in the initial phases after stroke still foments discussion regarding the best time to apply this therapy to the lower limb.

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