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CONSTRAINT-INDUCED MOVEMENT THERAPY: SOME THOUGHTS ABOUT THEORIES AND EVIDENCE

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Constraint-Induced Movement Therapy (CIMT) is a type of treatment for hemiparetic stroke patients in which the patient is strongly encouraged to use the affected arm. One way of doing this is to immobilise the unaffected arm. This treatment is meant to help patients overcome 'learned non-use'. The learned non-use theory is based on deafferentiation experiments in monkeys. In this review four randomised clinical trials are presented systematically. Although the authors of all four studies reported positive results, the effect sizes calculated without covariates yielded no statistically significant differences. In one of the studies a differential effect was found for patients with sensory disorders and hemineglect, leading to the hypothesis that learned non-use may be primarily related to afferent impairments. It is concluded that the learned non-use theory requires further exploration and that the evidence regarding the effectiveness of CIMT is not yet conclusive.

Key words: constraint-induced movement therapy, stroke, cerebrovascular accident, review literature, upper extremity, arm, somatosensory disorders

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INTRODUCTION

Promising results have been presented in a number of clinical studies investigating the effectiveness of Constraint-Induced Movement Therapy (CIMT) (1). This treatment is intended to help stroke patients overcome 'learned non-use' of the paretic arm by discouraging the use of the unaffected or less affected arm in combination with intensive training of the paretic arm. In spite of the positive conclusions of several authors, critical appraisal of the theory and the available evidence may lead to a less optimistic view. This paper covers the following topics: 1) the theories underlying CIMT, 2) the evidence provided by the literature and possible causes of differences between the results of clinical studies, and 3) a critical interpretation, based on the author's experience and opinion.

THEORIES

The learned non-use theory is based on experiments with monkeys, in which one forelimb was deafferented by dorsal rhizotomy (2). Due to the loss of sensory feedback, the monkeys never used this forelimb again after the operation, unless they were forced to do so due to restricted movement of the intact limb (3). If restriction of the intact forelimb was maintained for 1 to 2 weeks, this led to a permanent change in the ability to use the deafferented forelimb. According to Taub (2), learned non-use develops during the initial post-lesional phase of central nervous system shock (either spinal shock, in the case of dorsal rhizotomy, or diaschisis or cortical shock in the case of stroke). The lesioned animal (or the stroke patient) learns to avoid using the affected limb, due to a learning process in which attempts to use the affected limb are punished by the negative consequences of these attempts, e.g. falling or failure to accomplish the intended goal. If the ability to use the affected limb gradually appears after a period of weeks or months, the learned non-use behaviour remains, and the actual use of the affected limb will be much less than its potential use (3). The hypothesis of learned non-use in human stroke patients is based on the impression of clinicians that some patients use their affected arm less than could be expected on the basis of the severity of their arm impairment (4). However, there is no validated instrument to diagnose the presence or severity of learned non-use. The notion that shock to the central nervous system leads to learned non-use lacks empirical support. Transferring findings from monkeys that have undergone dorsal rhizotomy to human stroke patients cannot be done by a simple one-to-one comparison. Considering the pathological differences between the circumscribed dorsal root lesions in the monkeys studied by Taub and the variety of hemisphere lesions in the stroke patients included in clinical studies, the external validity of extrapolating the findings in deafferented monkeys to human stroke patients must be called into question. The existence of a learned non-use phenomenon in human stroke patients is only based on clinical impressions, and may be associated with sensory disorders or hemineglect (5). Our knowledge about the existence of a learned non-use phenomenon in human stroke victims and its possible pathological mechanisms is still poorly developed.

EVIDENCE

Despite the lack of knowledge, many attempts have been made to help patients overcome their learned non-use by means of CIMT

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(1, 3, 5–17). Does the literature on CIMT provide evidence of the method's success? From the history of medical science there are several examples showing that uncontrolled studies can lead to treatments which are eventually found to be ineffective or even detrimental instead of beneficial (18). Controlled, but non-randomised, studies that may generate hypotheses are often found to overestimate the effects of interventions. Therefore, the current review is limited to randomised clinical trials. In a recent systematic review on the effectiveness of exercise therapy for arm function in stroke patients (19), two randomised clinical trials were identified that evaluated the forced use treatment in chronic stroke patients (5, 8). Since August 2000, two additional randomised controlled trials have been published (14, 17), which evaluated CIMT in patients who had more recently suffered a stroke. Several characteristics of these four studies are summarised in Table I, showing that there are many differences between the four studies regarding: 1) patient inclusion criteria, 2) the contrast between the experimental and the control interventions, and 3) outcome measures (20).

Patient inclusion criteria

Dromerick et al. (14) included acute patients, and Page et al. (17) included sub-acute patients, while the other two studies included chronic patients (5, 8). Although forced use immediately after the lesion was found to result in a dramatic exaggeration of the neuronal injury in rats, accompanied by severe and chronic behavioural deficits (21), no adverse effects were reported when intervening earlier in the human studies. The statistical power of intervention studies depends on the probability of a type 1 error (usually 0.05), the number of subjects and the variability of the study population, and the expected effect size (22). The study by

Table I. *Main study characteristics of four RCTs evaluating the effect of constraint-induced therapy in stroke patients*

Author, year	Patients	Experimental intervention	Control intervention	Outcome measures	SMD (95% CI)	Follow-up period	Authors' conclusions
Taub et al., 1993 (8)	4 exp/5 control (10 at the start) Chronic (median 4 years)	Restraint of unaffected arm for over 90% of waking hours + 6 hours of supervised task practice 5 days/week 2 weeks	Procedures to focus attention on the involved extremity	Emory Motor Function Test Arm Motor Activity Test MAL	Insufficient data	2 years post-interv-ention	Restraint and practice was effective in restoring substantial motor function; effect was maintained during follow-up
Van der Lee et al., 1999 (5)	31 exp/31 control (66 at the start) Chronic (median 3 years)	Immobilisation of unaffected arm + intensive arm function training 6 hours a day 5 days/week 2 weeks	Intensive bimanual arm function training 6 hours a day 5 days/week 2 weeks	ARA RAP-PC RAP-Occ FMA MAL Problem Score	ARA 0.34 (-0.16; 0.84) RAP-PC – 0.18 (-0.68; 0.31)	1 year post-intervention	Small but lasting effect on dexterity (ARA); No effect on ADL (RAP)
Dromerick et al., 2000 (14)	11 exp/9 control (23 at the start) Acute (range 4 – 14 days)	Discouragement to use unaffected hand (padded mitten) 6 hours/day + occupational therapy and CIM circuit training 2 hours a day 5 days/week 2 weeks	Standard occupational treatment + circuit training (bilateral) 2 hours a day 5 days/week 2 weeks	ARA Barthel Index FIM	ARA 0.45 (-0.44; 1.34)	None	CIM was associated with less arm impairment at the end of treatment
Page et al., 2002 (17)	4 exp 5 control therapy 5 no therapy Sub-acute (range 4– 6 months)	0.5 hour PT and 0.5 hour OT including Shaping 3 times a week 10 weeks + restraint during 5 hours of frequent arm use, 5 days a week 10 weeks	Control: 0.5 hour PT and 0.5 hour OT including PNF 3 times a week 10 weeks	ARA FMA MAL Wolf (= Emory) Motor Function Test	Insufficient data	None	Evidence suggesting that a modified CIT protocol is effective

SMD: Standardised Mean Difference between improvement in both groups immediately post-intervention. SMD: Mean difference eperimental group minus mean difference control group devided by Pooled Standard Deviation; 95% CI: 95% Confidence Interval; MAL: Motor Activity Log; ARA: Action Research Arm test; RAP-PC: Rehabilitation Activities Profile; domain Personal Care; RAP-Occ: Rehabilitation Activities Profile; domain Occupation; FMA: upper extremity motor section of the Fugl-Meyer Assessment scale; CIM: Constraint-induced movement; FIM: Functional Independence Measure: PNF: Proprioceptive Neuromuscular Facilitation.

Van der Lee et al. (5) included the largest number of patients and therefore, supposing all other factors being equal, this study can be considered to be the most powerful statistically.

Contrast between interventions

The most intensive treatment was given by Taub et al. (8), with patients in the control group receiving much less active treatment and much less in the area of non-specific aspects, such as the attention from therapists and being in the outpatient department for many hours a day. In several systematic reviews and meta-analyses of exercise therapy, a positive relationship has been found between effect sizes and the contrast in intensity (23–26). In two studies (5, 14) this contrast in intensity, a potential confounder, was taken into account by giving the control patients equally intensive training during which time both hands could be used. Dromerick et al. (14) and Page et al. (17) applied much less intensive training schedules. In Page's study there were two contrasts, i.e. the experimental group had the unaffected arm restrained for 5 h/day, 5 days a week in addition to the treatment (1 h/day, 3 times weekly) which was also given to the patients in the regular therapy group, and a second control group received no treatment at all.

Outcome measures

In all four studies arm function tests were used at the impairment level (Wolf Motor Function Test, or its predecessor the Emory Motor Function Test, Fugl-Meyer assessment scale) and at the (focal) disability level (Arm Motor Activity Test, Action Research Arm (ARA) test). The Motor Activity Log (8) was used in three of the four studies. This instrument has been developed specifically for the evaluation of CIMT, but its psychometric properties have not yet been investigated (27). Two studies seem to put more emphasis on a general disability level (Rehabilitation Activities Profile, Barthel Index and FIM) (5, 14).

Results

The first step in a meta-analysis is to calculate the effect sizes (e.g. standardised mean differences) for the individual studies from the available data, which are subsequently combined to a (weighted) pooled effect size. When reading the last column in Table I, it would appear that the experimental treatment is effective. In the sixth column, however, the standardised mean differences (SMD) are presented for each study, with 95% confidence intervals, calculated from the available data on arm function tests (28). Calculation of effect sizes was hampered by insufficient data presentation (8, 17), or by baseline differences between the experimental and the control groups, which were incorporated as covariates in the analysis (5, 14). Although both these papers presented statistically significant effects, the SMD calculated without these covariates do not reach statistical significance, as is demonstrated by the 95% confidence intervals, which contain 0. Because of this discrepancy between reported effects and calculated SMD and because SMD could only be calculated from two studies, calculation of a pooled effect size does not appear to be useful. All four papers reported positive results at the level of arm and hand function. However, at the disability level, no statistically significant differences were found (5, 14).

Apart from the statistical significance of the results, the clinical relevance should also be taken into account. Even the smallest effect becomes statistically significant if the study population is large enough. Although the decision about what is clinically relevant is always somewhat arbitrary (29), it is an important issue and should not be ignored. There is no consensus about the magnitude of a minimal clinically important difference (MCID) (30) and, moreover, there is not even consensus about the most suitable and valid outcome measures (14, 27). In the only study in which an MCID was estimated on each of the outcome measures before the analysis (5), the statistically significant differences on the Motor Activity Log and the ARA were smaller than the MCID. However, the presence or absence of hemineglect and sensory disorders appeared to be effect modifiers for the results on the Motor Activity Log and ARA test, respectively. The difference between the mean improvement in patients with sensory disorders receiving forced use treatment and the mean improvement in patients with sensory disorders who received the bimanual training exceeded the MCID. These differences in treatment effect on the ARA test in patients with sensory disorders and on the Motor Activity Log in patients with hemineglect had not been postulated in advance. The authors suggested that in this study patients with no sensory disorders had already reached the upper limit of dexterity and that the patients with sensory disorders had developed some degree of learned non-use, despite comprehensive rehabilitation in the past. It was concluded that either forced use was not effective in treating learned non-use symptoms or the included patients had developed little or no learned non-use (5).

In conclusion, the learned non-use theory requires further exploration. The evidence regarding the effectiveness of CIMT is not yet convincing. However, no evidence of effect does not necessarily imply evidence of no effect (31).

INTERPRETATION

The differential effect of CIMT in patients with sensory disorders (5) is intriguing, given the fact that the learned non-use theory was originally developed in research on deafferented monkeys with no permanent motor impairment, but only a severe sensory deficit (32). In the descriptions of earlier studies on CIMT or forced use, the patients included were reported to have no severe sensory disorders (6–8), or no information was provided about the presence or absence of sensory disorders in the included patients (7, 11–15, 17). If the learned non-use phenomenon really

exists, it may be a consequence of the loss of sensory feedback, and a generalisation of the learned non-use theory to apply to all stroke patients should therefore be examined critically. Besides, the type and intensity of the rehabilitation in the early period after stroke may be of crucial importance in determining whether learned non-use is developed. In stroke patients who receive comprehensive rehabilitation during the first months post-stroke, which is customary in the Netherlands, the occurrence and severity of learned non-use may be much less than in patients in the USA, where the amount and duration of rehabilitation depends on the type of health insurance (33, 34). Another factor which may be of importance in the development of learned non-use is the patient's home environment. If patients are encouraged by spouses or other family members to manage by themselves, this may be of crucial influence. In any case, there is still a problem of not being able to assess the presence or severity of learned non-use objectively.

The choice of outcome measures is a difficult one. Generic outcome measures at the disability level are probably not responsive enough to this type of treatment. This notion is not surprising, since most activities of daily living can be performed with one hand. Arm function tests measure what a person can do using the affected arm, but as yet there are no objective instruments which measure the relative use of the affected arm in daily life. The idea of overcoming learned non-use places great emphasis on the affected arm, but in my opinion the individual patient and not the arm should be the central target of treatment and of measurement. For many stroke patients, coming to terms with the full range of their impairments is extremely difficult. The principal question regarding any treatment is whether it is beneficial for the patient in terms of independence and quality of life.

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