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Constraint-Induced Movement Therapy: A New Family of Techniques with Broad Application to Physical Rehabilitation--A Clinical Review

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Abstract--A new family of rehabilitation techniques, termed Constraint-Induced Movement Therapy or CI Therapy, has been developed that controlled experiments have shown is effective in producing large improvements in limb use in the real-world environment after cerebrovascular accident (CVA). The signature therapy involves constraining movements of the less-affected arm with a sling for 90% of waking hours for 2 weeks, while intensively training use of the more-affected arm. The common therapeutic factor in all CI Therapy techniques would appear to be inducing concentrated, repetitive practice of use of the more-affected limb. A number of neuroimaging and transcranial magnetic stimulation studies have shown that the massed practice of CI Therapy produces a massive use-dependent cortical reorganization that increases the area of cortex involved in the innervation of movement of the more-affected limb. The CI Therapy approach has been used successfully to date for the upper limb of patients with chronic and subacute CVA and patients with chronic traumatic brain injury and for the lower limb of patients with CVA, incomplete spinal cord injury, and fractured hip. The approach has recently been extended to focal hand dystonia of musicians and possibly phantom limb pain.

Key words: *cerebrovascular accident, CVA, focal hand dystonia, fractured hip, phantom limb pain, physical therapy, rehabilitation, spinal cord injury, traumatic brain injury.*

INTRODUCTION

Cerebrovascular accident (CVA) is the leading cause of disability in the United States. A recent study indicates that the number of CVAs may be dramatically higher than was previously thought to be the case (1). The total number is now estimated to be approximately 730,000 every year and the data suggest that this may be an underestimate. Moreover, more than half of these individuals are left with motor disability (2). There seems little doubt that the number of CVA survivors will increase greatly as the population progressively ages over the next 50 years; a recent projection is that the prevalence of CVA will more than double during this period (3). A 1993 estimate placed the annual costs of CVAs at $30 billion, of which $17 billion were direct medical costs and $13 billion were indirect costs due to lost productivity (4). The American Heart Association estimates that the current direct and indirect costs of CVA are $43.3 billion per year (3). CVAs are a particular problem for the VA because of the large population of World War II and Korean War veterans who are now in the age ranges where CVAs are most frequent; in fiscal year 1997 the national VA system had 22,000 admissions for an acute CVA (5). The consequent motor deficits that veterans sustain result in very large costs to the VA and the Federal Government. The reduction of CVA-related disability thus represents a high VA and national health care priority.

At present, there is little experimental evidence available indicating that physical and occupational therapy is effective for patients with chronic CVA. The literature is even equivocal on the value of physical rehabilitation for sub-acute patients--see literature reviews from the past 10 years (4,6-9). In the Winter 1998 issue of the journal *Topics in Stroke Rehabilitation* devoted to "Functional Implications of Upper Extremity Management," there was minimal discussion of specific therapeutic approaches to improving upper limb function, even though the title suggests that this would be a major, if not the main, topic covered. The small amount of material on upper limb treatment in that special issue may be a meaningful index of the fact that there are few empirically validated treatments to discuss at this time. The special issue did not review Constraint-Induced (CI) Movement Therapy, the treatment approach discussed in this article. The only literature review recent enough to evaluate published studies on CI Therapy cites it as being only one of three treatments for which there is empirical evidence of clinical efficacy and the only one to: 1) be supported with evidence from controlled randomized studies, and 2) have been shown to be effective for the upper limb (6). Moreover, CI Therapy does not involve medications or side effects, and there are no significant risks.

CI Therapy consists of a new set of rehabilitation techniques that data from controlled, randomized studies have indicated can substantially reduce the motor deficit of the more-affected limbs of many patients with chronic CVAs. The therapeutic effect has been demonstrated to transfer from the clinic to the real world; patients show increases in the daily use of their more-impaired limbs that are maintained, in the most powerful intervention, for at least 2 years after treatment (6,10-23). For the upper limb, the therapy involves inducing use of the more-affected limb for a target of 90 percent of waking hours by employing one of several methods for constraining or reducing use of the less-affected limb for 2 or 3 weeks. Concentrated, repetitive training of the more-affected limb is given daily for 6 hours, interspersed with 1 hour of rest, for each of the weekdays over the 2- or 3-week period (i.e., massed practice). The upper limb intervention has been tested to date with all but what we estimate to be the lowest functioning 25 percent of the chronic CVA population with significant residual motor deficit. For the lower limb,

a somewhat different approach is used that does not involve less-affected limb restraint, but does include massed practice of functional lower limb activities (see below). This article reviews the development of CI Therapy from basic research with monkeys to its application to persons with CVA with upper limb deficits and its extension to the treatment of upper limb deficits in traumatic brain injury and lower limb deficits in persons with CVA, spinal cord injury, and hip fracture. The article also describes research suggesting that cortical reorganization is a possible mechanism that accounts for the persistent therapeutic effect of our intervention and discusses further rehabilitation applications that have emerged from this finding.

BASIC RESEARCH

Experiments with Non-Human Primates

CI Therapy is derived from basic behavioral neuroscience research with non-human primates conducted by E.T. and coworkers. When a single forelimb is deafferented in a monkey, the animal does not make use of it in the free situation (24-26). However, Taub and coworkers (27,28) found that monkeys can be induced to use the deafferented limb by restricting movement of the intact limb for several days. A useless limb is thereby converted into a limb capable of extensive movement (10). Conditioned response and shaping techniques are another means of overcoming the inability to use a single deafferented limb in primates (10,26-34).

During this century, several investigators, including Carl Lashley, Sarah Tower, S.I. Franz, William Chambers, and John Liu, have found that a behavioral technique could be employed in animals to substantially improve a motor deficit resulting from neurological damage (35-38). However, none of these observations were embedded in a formal theoretical context that permitted prediction nor was the generality of the mechanism clearly recognized. Consequently, these findings remained a set of disconnected observations that received little attention. Moreover, no attempt was made to apply this approach to humans in a systematic fashion.

Learned Nonuse

Several converging lines of evidence suggest that nonuse of a single deafferented limb is a learning phenomenon involving a conditioned suppression of movement. (For a description of the experimental analysis leading to this conclusion, see references 10 and 34). As a background for this explanation, one should note that substantial neurological injury usually leads to a depression in motor and/or perceptual function that is considerably greater than will eventually be the case after spontaneous recovery of function has taken place. The processes responsible for the initial depression of function and the later gradual recovery of function, which occurs at the level of both the spinal cord and the brain, is, at present, incompletely understood. However, regardless of the mechanism, recovery processes come into operation following deafferentation so that after a period of time movements can, *at least potentially,* be expressed. In monkeys, the initial period of depressed function lasts from 2-6 months following forelimb deafferentation; they progressively regain the *ability* to make coordinated movements of their affected limb during that time (28,34).

Thus, monkeys cannot use their deafferented limb soon after sensation from the forelimb has

been surgically abolished at level of the spinal cord; recovery from the initial depression of function requires considerable time. An animal with one deafferented limb tries to use that limb in the immediate postoperative situation, but it cannot. It gets along quite well in the laboratory environment on three limbs and is therefore positively reinforced for this pattern of behavior, which, as a result, is strengthened. Moreover, continued attempts to use the deafferented limb often lead to painful and otherwise aversive consequences, such as incoordination and falling, as well as to loss of food objects, and, in general, failure of any activity attempted with the deafferented limb. These aversive consequences constitute punishment. Many learning experiments have demonstrated that punishment results in the suppression of behavior (39-41). This response tendency persists, and consequently the monkeys never learn that several months after operation the limb has become potentially useful.

When a movement restriction device is placed on the intact limb several months after unilateral deafferentation so that movements of this limb are constrained, the situation is changed dramatically. The animal either uses the deafferented limb or it cannot, with any degree of efficiency, feed itself, walk, or carry out a large portion of its normal activities of daily life. This change in motivation overcomes the learned nonuse of the deafferented limb, and consequently the animal uses it. However, if the movement-restricting device is removed a short while after the early display of purposive movement, the newly learned use of the deafferented limb acquires little strength and is, therefore, quickly overwhelmed by the well-learned tendency not to use the limb. If the movement restriction device is left on for several days or longer, however, use of the deafferented limb acquires strength and is then able to compete successfully with the learned nonuse of that limb in the free situation. The conditioned response and shaping conditions noted above, just like the restriction of the intact limb, also involve major alterations in motivation. For a fuller account of this mechanism see reference 10.

Experimental Test of Learned Nonuse Formulation

An experiment was carried out to test the learned nonuse formulation directly (34). Movement of a unilaterally deafferented forelimb was prevented with a restraining device in several animals so that they could not attempt to use that limb for a period of 3 months following surgery. Restraint was begun while the animal was still under anesthesia. The reasoning was that by preventing an animal from trying to use the deafferented limb during the period before spontaneous recovery of function had taken place, one should prevent the animal from learning that the limb could not be used during that interval. Learned nonuse of the affected limb should therefore not develop. In conformity with this prediction, the animals were able to use their deafferented limb in the free situation after the restraint was removed 3 months after operation. Suggestive evidence in support of the learned nonuse was also obtained during the course of deafferentation experiments carried out prenatally (42-44). Two animals were studied who were exteriorized by intra-uterine surgery (but not delivered), given prenatal unilateral forelimb deafferentation, and then replaced in utero for the remainder of gestation; one when two-thirds the way through gestation and one when two-fifths the way through gestation. Life in the physically restricted uterine environment imposes major constraints on the ability to use the forelimbs (while not preventing use of the limbs entirely), thereby functioning like the movement restriction device in the mature animals. These animals exhibited purposive use of the deafferented limb from the first day of extrauterine life, at which time they both employed the limb for postural support during "sprawling" and in pushing to a sitting position. Subsequently, though the intact limb was never restrained, the ability to use

the deafferented limb continued to develop in ontogeny until it was similar in all respects to that of animals given unilateral deafferentation and intact limb restraint when mature. This, then, constitutes a second direct line of evidence in favor of the learned nonuse formulation.

Learned Nonuse after CVA

Learned nonuse could also be relevant to humans after brain injury or CVA (10). The period of temporary, organically based inability to use an affected upper limb would be due to cortical mechanisms rather than processes associated with deafferentation at the level of the spinal cord. The learned nonuse model in no way obviates the general correlation between amount of neural damage following CVA and the amount of motor function that is recovered on the affected side. Such a correlation could be a sufficient explanation for the observed differences in amount of recovery among many patients. However, the fact that some patients with a given extent and locus of lesion recover more movement than others with CVA having similar lesions suggests that additional factors may be involved; one of these might be the operation of a learned nonuse mechanism.

A Linked, But Independent, Mechanism: Use-Dependent Cortical Reorganization

Five recent focal transcranial magnetic stimulation (TMS), neuroelectric source imaging (EEG), and magnetic source imaging (MEG) studies with humans, carried out by four groups of investigators and an intracortical microstimulation (ICMS) study with monkeys suggest that cortical reorganization may be associated with the therapeutic effect of CI Therapy. Following the seminal work of Recanzone, Merzenich, and co-workers on use-dependent cortical reorganization in monkeys (45-48), a number of neuroimaging studies showed that the same phenomenon occurs in humans. For example, Elbert, Taub, and co-workers (49) found that the cortical somatosensory representation of the digits of the left hand was larger in string players, who use their left hand for the dexterous task of fingering the strings, than in nonmusician controls. Moreover, the representation of the fingers of blind Braille readers who use several fingers simultaneously to read was both enlarged and disordered; the latter neurophysiological aberration was associated with a perceptual disturbance in which the subjects could not discriminate which of their fingers was being touched (50). In previous collaborative research, we found that "massive" cortical reorganization takes place after somatosensory deafferentation of an entire forelimb in monkeys (51). In several recent studies, we discovered that the amount of cortical reorganization is strongly correlated with the amount of symptomatology in a number of pathological conditions: phantom limb pain (52), tinnitus (53), and focal hand dystonia in keyboard musicians and guitarists (54). Prior to our findings, these conditions were enigmatic entities in that they had no agreed-upon etiology. Central nervous system (CNS) correlates of these conditions had been long sought; however, it was not possible to identify them until our group (55) and a group in San Diego (56) showed in 1994 that massive cortical reorganization takes place in humans after CNS injury. These results, especially those relating to use-dependent cortical reorganization, suggest that the size of the cortical representation of a body part in adult humans depends on the amount of use of that part. Moreover, Nudo and co-workers carried out a significant ICMS study that demonstrated in adult squirrel monkeys that were surgically given an ischemic infarct in the cortical area controlling the movements of a hand, that training of the affected limb resulted in cortical reorganization. Specifically, the area surrounding the infarct, which would not normally be involved in control of the hand, came to participate in that function (57).

The hypothesis that CI Therapy produces a large use-dependent cortical reorganization in humans with stroke-related paresis of an upper limb was recently confirmed in several collaborative studies. In one study, Liepert and co-workers (58) used focal TMS to map the areas of the brain that control arm movement in 6 patients with a chronic upper limb hemiparesis (mean chronicity = 6 years) before and after CI Therapy. We first replicated the clinical result that CI Therapy produces a very large increase in the patients' amount of arm use in the home over the 2-week treatment period. Over the same interval, the cortical region from which EMG responses of a hand muscle could be elicited by TMS was greatly increased. In a follow-up study with 9 additional subjects (total N=15), we found that both the motor rehabilitation effect and the alteration in brain function persisted for the 6 months tested to date[1]. CI Therapy had led to a recruitment of a large number of neurons in the innervation of movements of the CVA-affected limb adjacent to those originally involved in control of the limb. The effect was sufficiently large that it represented a return of the balance of area of excitability in the innervation of muscular activity between the two hemispheres toward what is, in effect, a normal condition. In a third study, Kopp et al. (59) carried out dipole modeling of steady-state movement-related cortical potentials (EEG) of patients having CI Therapy. We found that 3 months after treatment the motor cortex ipsilateral to the affected arm, which normally controls movements of the contralateral arm, had been recruited to generate movements of the affected arm. This effect was not in evidence immediately after treatment and was presumably due to a sustained increase in affected arm use produced by CI Therapy over the 3-month follow-up period. This experimental evidence that CI Therapy is associated with a use-dependent increase in cortical reorganization has been confirmed by convergent, as yet unpublished data from two other collaborative neuroimaging studies with E.T. using a variety of neuroimaging techniques in association with the administration of CI Therapy[2].

These findings suggest that CI Therapy produces a permanent increase in arm use by two linked but independent mechanisms (23,58,59). First, as noted above, CI Therapy changes the contingencies of reinforcement (provides opportunities for reinforcement of use of the more-affected arm and aversive consequences for its nonuse by constraining the less-affected arm) so that the nonuse of the more-affected arm learned in the acute and early sub-acute periods is counter-conditioned or lifted. Second, the consequent increase in more affected arm use, involving sustained and repeated practice of functional arm movements, induces expansion of the contralateral cortical area controlling movement of the more-affected arm and recruitment of new ipsilateral areas. This use-dependent cortical reorganization may serve as the neural basis for the permanent increase in use of the affected arm. Moreover, to the best of our knowledge, these recent studies are the first to demonstrate an alteration in brain structure or function associated with a therapy-induced improvement in movement after CNS damage. Furthermore, by providing a physiological basis for the observed treatment effect, these results are likely to increase confidence in the clinical findings.

The motor learning literature suggests that massed practice has only a neutral or negative effect on the learning of continuous tasks and a variable effect on the learning of discrete tasks (60). However, CI Therapy employs massed practice to increase the tendency of patients to use their more-impaired limb, and thereby induces a use-dependent functional reorganization of brain structures. This is certainly a type of central nervous system plasticity, as is learning; but they probably represent somewhat different processes and their establishment may be, at least in part,

governed by different principles.

CLINICAL APPLICATIONS

Previous Research in Other Laboratories on Overcoming Learned Nonuse with Humans

First Ince (61) and then Halberstam, Zaretsky, Brucker, and Buttman (62) used one of the conditioned response paradigms developed in the primate deafferentation research noted above in successful attempts to improve motor capacity following CVA. For some time there was no follow-up on this work. However, several years ago Wolf, elaborating on the primate deafferentation research and following an initial case study (63), carried out an experiment to test the hypothesis that the movement restriction component of the CI Therapy approach is applicable to humans. The study (64) included 25 CVA and traumatic brain injury patients who were more than one-year post-injury and who possessed a minimum of 10° extension at the metacarpophalangeal and interphalangeal joints and 20° extension at the wrist of the affected arm. The patients were asked to wear a sling on the unaffected arm all day for 2 weeks, except during a 30-minute exercise period and sleeping hours. It is important to note that no attempt was made to combine shaping, any other type of training technique or supervised practice, with the movement restriction procedure. It will be seen below that training techniques, particularly shaping, are especially effective means of promoting transfer of motor improvement to activities of daily living.

The patients demonstrated significant improvements in speed or force of movement, depending on the task, on 19 out of 21 tasks on the Wolf Motor Function Test (WMFT)--a laboratory motor function test. No information was obtained on whether there was transfer to the real-world environment. Though the effect on the laboratory motor function was small, it was significant and promising. The results suggested the value of pursuing work with CI Therapy using one of the training techniques tested with monkeys (shaping) and a reliable means of assuring compliance with the direction to wear a sling on the less-affected limb (such as might be achieved by having a patient stay in the treatment area all day where compliance could be observed and fostered).

Other Successful Physical Rehabilitation Treatments for Patients with Chronic CVA

Successful clinical use has been made of the CI Therapy approach by other investigators on a case history basis for patients with CVA, spinal cord injury[3], and traumatic brain injury (64-66). Bach-y-Rita (67, 68) and Franz, Scheetz, and Wilson (69), not operating within a CI Therapy context, have used training techniques based on physical therapy methods to obtain improvements in limb use in patients with chronic CVA whose greatly impaired motor function was presumably not amenable to further recovery. Wolf (70,71), Basmajian (72,73), and Balliet (74), among others, have used training techniques based on EMG biofeedback to improve motor ability in patients with chronic CVA. Investigators from the laboratory of Mauritz have obtained large therapeutic effects for lower limb function (75-77). Their treatment involves repetitive, concentrated practice, much like the CI Therapy approach, and supports the importance of massed practice for effective rehabilitation.

This Laboratory: Upper Quartile Patients

In a paper published in 1980 (10), learned nonuse was hypothesized to develop in some humans after CVA by similar mechanisms to those that operate after deafferentation in monkeys, with the difference that the initial period of motor incapacitation was primarily due to cortical rather than spinal mechanisms. It was therefore felt that the techniques that overcome learned nonuse in monkeys following unilateral deafferentation also constituted a potential treatment to increase the amount of limb use in patients with an upper limb hemiparesis associated with CVA.

Experimental work began here with a pilot experiment (11) that involved application of both components of the published protocol (i.e., paretic arm training and contralateral arm restraint) to the rehabilitation of patients with chronic CVA with residual hemiparesis. The experiment employed an attention-placebo control group (N=5) and emphasized the transfer of therapeutic gains in the laboratory to the life situation. The treatment group (N=4) wore a sling on their less-affected arm for 14 consecutive days. On 10 of those days, the treatment subjects received 6 hours of supervised task practice using their more-affected arm (e.g., eating lunch; throwing a ball; playing dominoes, Chinese checkers, or card games; writing; pushing a broom; and using the Purdue Dexterity Board and Minnesota Rate of Manipulation Test) interspersed with 1 hour of rest. The control subjects were told that they had the capacity for much greater movement of their affected limb than they were exhibiting, were led through a series of passive movement exercises in the treatment center, and were given passive movement exercises to perform at home. All experimental and control patients were at least 1-year post-CVA (mean=4.4 years) and had passed a minimum motor criterion (64) defining the approximate upper quartile of chronic CVA motor functioning (at least 20° extension at wrist and 10° at each of the fingers). Treatment efficacy was evaluated using two laboratory tests of motor ability, the WMFT (11,64), the Arm Motor Ability Test (AMAT; 78,79), and the Motor Activity Log (MAL; 11,19) which tracks arm use in a number of ADLs through a semi-structured interview (22). The treatment group demonstrated a significant increase in motor ability as measured by both laboratory motor tests (WMFT, AMAT) over the treatment period, whereas the control patients showed no change or a decline in arm motor ability. On the MAL, the treatment group showed a very large increase in real-world arm use over the 2-week period and demonstrated a further small increase in use when tested 2 years after treatment; the controls exhibited no change or a decline in arm use over the same period.

These results have since been confirmed in further work from this laboratory (19,23) using less-affected arm sling-constraint and training (by shaping) of the affected arm instead of task practice with a larger sample (N=40). The shaping procedure (80-83) involved: 1) selecting tasks that were tailored to address the motor deficits of the individual patient 2) helping the patient to carry out parts of a movement sequence if they were incapable of completing the movement on their own at first, and 3) providing explicit verbal feedback and verbal reward for small improvements in task performance (13). Modeling and prompting of task performance were also used. The placebo control group (N=20) was designed to better control for the duration and intensity of therapist-patient interaction and the duration and intensity of therapeutic activities than in the previous study. The controls received a general fitness program in which they performed strength, balance, and stamina training exercises, played games that stimulated cognitive activity, and practiced relaxation skills for 10 days. As in the first experiment, the treatment group (N=20) demonstrated a significant increase in motor ability, as measured by the WMFT, and a very large increase in real-world arm use, as measured by the MAL, over the intervention period, whereas the controls

did not. The placebo control subjects' answers to an expectancy and self-efficacy questionnaire about their expectations for rehabilitation prior to the control intervention and their reported increase in quality of life after the intervention, as measured by the SF-36 (84), suggested that they found the control intervention to be credible.

Other experiments have indicated that there is a family of techniques that can overcome learned nonuse (19,23). The other interventions that have been tested are: 1) placement of a half-glove on the less-affected arm as a reminder not to use it and shaping of the paretic arm, 2) shaping of the paretic arm only, and 3) intensive physical therapy (e.g., aquatic therapy, neurophysiological facilitation, and task practice) of the paretic arm for 5 hours a day for 10 consecutive weekdays. The half-glove intervention was designed so that CI Therapy could be employed with patients who have balance problems and might be at risk for falls when wearing a sling; this intervention expanded the population of patients with CVA amenable to CI Therapy threefold. More recently, a padded "protective safety mitt" has been used; it leaves the unaffected arm free so as not to compromise safety, but prevents use of the hand and fingers in ADLs. The intensive physical therapy intervention did not involve physical constraint of the less-affected arm; however, the subjects were requested to not make use of their less-affected arm and this regimen was monitored. To our knowledge, such a concentrated application of physical therapy had not been evaluated before this trial. All three groups showed very large increases in arm use in the life situation over the treatment period. These changes were equivalent to those observed for the sling constraint and task-practice and sling constraint and shaping groups. Two years after treatment, however, the three groups showed some decrement in arm use, while the sling constraint and task practice/shaping groups showed either no decrease (sling plus task practice) or a smaller decrease (sling plus shaping).

The mean effect size (ES) for the WMFT, a laboratory motor function test, in all of these studies was 0.9; however, the mean ES for the MAL, which records ADL in the life situation, was 3.3. The much larger ES for the MAL than for the WMFT indicates that CI Therapy has its greatest effect on increasing the actual amount of use of a more affected upper limb in the real world setting, though the improvement in quality of movement as indexed by the WMFT is still substantial. In the meta-analysis literature, ESs of 0.2 are considered small, 0.4-0.6 ESs are deemed moderate, while ESs of 0.8 and above are judged to be large (85). Thus, by the standards of the meta-analysis literature, the ES of CI Therapy for real-world outcome in patients with chronic CVA from the upper quartile of motor functioning is extremely large.

Other Laboratories: Replications with Upper Quartile Patients

The sling plus shaping results have been replicated with patients with chronic CVA in published studies from the laboratories of W. Miltner (20) and H. Flor (21) and in work read at meetings from laboratories in the United States (3), Germany (2), and Sweden (4). The results have been replicated in a teenager with cerebral palsy in a case study (86). There has also been pilot work with positive results at six sites in this country in the planning of a national clinical trial of CI Therapy for upper limb paresis in patients with subacute CVA including: this laboratory, Emory University (Dr. Steven Wolf), UCLA (Dr. Carolee Winstein), University of North Carolina and Wake Forest School of Medicine (Drs. Carol Giuliani and David Good), University of Florida at Gainesville (Drs. Kathye Light and Carl Kulkulka) and Ohio State University (Dr. Deborah Nichols). To date 89 patients have received CI Therapy for the upper limb in several experiments

in this laboratory, while 102 patients to our knowledge have been treated in other laboratories. Only two quite low functioning patients from this laboratory can be characterized as frank treatment failures. All other subjects showed large treatment effects. The confirmatory results from other laboratories are of value in establishing the generality of CI Therapy.

Main Therapeutic Factor

The question arises as to the common factor or factors underlying the therapeutic effect in the several CI Therapy interventions worked with to date. Although most of the techniques involve constraining movement of the less-affected arm, the shaping-only and intensive physical therapy interventions do not. There is thus nothing talismanic about use of a sling or other constraining device on the less-affected limb. The common factor appears to be repeatedly practicing use of the paretic arm. Any technique that induces a patient to use an affected limb many hours a day for a period of consecutive days should be therapeutically efficacious. This factor is likely to produce the use-dependent cortical reorganization found to result from CI Therapy (23, 58,59) and is presumed to be the basis for the long-term increase in the amount of use of the more-affected limb. As noted previously, Mauritz and co-workers (75-77) have also shown that repetitive practice is an important factor in CVA rehabilitation interventions.

Studies that make use of sling-restraint of the less-affected arm but do not give concentrated, extended practice in use of the more-affected arm cannot be said to have validly administered CI Therapy. There is already evidence that this type of procedure yields a markedly reduced treatment effect (64). For example, investigators in one study[4], who trained in this laboratory, were counseled before they left that the attenuated, group, hobby-type practice they were planning would not work well. Not surprisingly, their attenuated intervention did not produce consistent, positive results. It should also be noted that when an intensive conventional physical therapy intervention, which concentrates the administration of therapy far beyond the schedule with which it is usually delivered, is contrasted with an attenuated form of CI Therapy, this comparison is not meaningful in terms of relevance to the results of CI Therapy when it is administered correctly. We have already shown with our intensive physical therapy group (17,19; see above) that massing practice of conventional therapy gives results as good as those achieved with sling restraint of the less-affected arm and intensive task practice or shaping. Indeed, because of the massed practice element, intensive conventional physical therapy can be considered a member of the CI Therapy family of treatments.

Lower Functioning Patients

Until recently, the patients we worked with all met or exceeded a minimum motor criterion of 20° of extension of the wrist and 10° of extension of each finger. It is estimated that approximately 20-25 percent of the chronic CVA population with residual motor deficit meet this motor criterion--that is, first quartile patients (70). However, more recent work with patients who are lower functioning than these individuals is proving to be very promising, suggesting that CI Therapy may be applicable to up to 75 percent of the CVA population with a chronic unilateral motor deficit. In the first study along these lines [5], the minimum motor criterion for inclusion into therapy was 10° extension of the wrist, 10° abduction of the thumb, and 10° extension of any two other digits. Eleven patients whose initial motor ability fell below the minimum motor criterion for the higher functioning group and above the minimum criterion for this lower functioning group were given CI Therapy. All 11 of these lower functioning patients exhibited very

substantial improvement on the MAL (P<0.0001) and the Functional Ability (FA) Scale of the WMFT Test (P<0.0001). The treatment gain on the MAL was somewhat smaller for these lower functioning patients (mean change=1.7, SD=0.44) than for the higher functioning patients (mean change=2.2, SD=0.68; P<0.02). However, due to the lower variability in the scores for the lower functioning group, the Effect Size for the lower functioning patients (d=4.0) was actually larger than for the higher functioning patients (d=3.3). The treatment gain on the WMFT was larger for the lower functioning patients (mean FA change=0.4, SD=0.29) than for the higher functioning patients (mean FA change=0.3, SD=0.30); this difference was also reflected in the Effect Sizes for the two groups (lower functioning d=1.4, higher functioning d=1.0).

In ongoing work, subjects are being treated who have minimal hand function. The minimum motor criterion for this subgroup is that they are able to lift a wash rag off a table top using any type of prehension they can manage and then release it. If the patients in the study described above can be characterized as being from the second quartile of patients with chronic CVA in terms of motor ability, we estimate that the patients in the current study are from the third quartile. To date, we have worked with seven patients from this population. One of these individuals was a frank treatment failure. (We have had only two other treatment failures; one was from the fourth quartile of motor ability and had almost no ability to move his fingers, the other was a first quartile patient who terminated therapy after 4 days because his marked improvement threatened the substantial secondary gains he received from his functional dependence). However, the other six third-quartile patients exhibited substantial improvement. The treatment gain was 1.4 steps on the MAL, which is not quite as large as it was for the second quartile patients (1.7). Thus, the amount of improvement produced by CI Therapy appears to diminish as the initial motor ability of patients decreases. In addition, we have preliminary data to suggest that the use of shaping to train arm function is more important for treating second and third quartile patients than first quartile patients, for whom concentrated task practice without shaping is sufficient to produce large motor gains. Second and third quartile patients appear to need more assistance and guidance from the treatment team to help them use their impaired arm for functional activities. However, CI Therapy does produce a substantial improvement in the real-world function and motor ability of patients with CVA in the second and third quartiles of motor ability. It, therefore, appears that the motor capacity of chronic patients is modifiable in a larger percentage of the population than our research originally suggested (11); as noted, the proportion may be as high as 75 percent.

Application of CI Therapy to the Lower Limb

Work with Patients with CVA

To date, our laboratory has treated the lower limb of 16 patients with chronic CVA with substantial success[6]. These patients have had a wide range of disability extending from being close to nonambulatory to having moderately impaired coordination. The therapy consists of massed or repetitive practice of lower limb tasks (e.g., treadmill walking, over-ground walking, sit-to-stand, lie-to-sit, step climbing, various balance and support exercises) with a partial body weight support harness when necessary for 7 hours/day with interspersed rest intervals over 3 weeks; task performance is "shaped" as in our upper limb work. The control group for this intervention is the General Fitness Control Group before and after both the placebo treatment and crossover to the upper limb intervention; the fitness control subjects had all been given our battery of lower limb tests to provide a basis for comparison with the lower limb subjects. Among the 16

lower limb patients, four minimally ambulatory patients requiring support from one person for progression improved to the status of fully independent (but impaired) ambulation in two cases and ambulation with minimal assistance in two other cases. Each of the 12 subjects with a moderate level of impairment improved substantially on most or all of our measures; on a group basis, the improvement was significant for each of the parameters measured. The treatment gain obtained for the upper limb and the lower limb interventions is difficult to compare because different instruments are used to measure upper and lower limb function. The Effect Sizes (ESs) for the improvement of the upper limb after CI Therapy have been above 2.0 on our measure of real-world limb use throughout this laboratory's work. The ES on the measure of real-world limb use for the lower limb after treatment is somewhat smaller (ES=1.6 to date). However, since 0.8 is generally considered a large ES, the lower limb ES we have observed is still very large.

Approximately 90 percent of patients with chronic CVA ambulate but do so with a degraded pattern of coordination. These disordered patterns of movement may be partly due to the persistence of patterns learned in the early post-injury period before spontaneous recovery of function would have permitted an improved mode of ambulation. This phenomenon may be viewed as learned *mis*use rather than learned *non*use. Initially, we thought that it might be more difficult to overcome learned misuse than learned nonuse, if it was possible at all. In the case of learned misuse, bad habits of coordination need to be overcome before more appropriate patterns of coordination can be substituted. In the case of learned nonuse, as with the upper limb after CVA, there is simply an absence or greatly reduced amount of limb use in the life situation; surmounting improper coordination as an initial step is not a primary problem. We were surprised that this expectation proved to be incorrect. We, however, still do not have sufficient long-term lower limb Motor Activity Log data to draw conclusions about the permanence of the transfer of these gains in motor ability to use in the real world.

Pilot Work with Patients with SCI and Patients with Fractured Hip

Two incomplete SCI patients have been treated. Both patients were ambulatory but with severe initial deficits: they spent most of their time in a wheelchair and reported that they never ambulated over distance of greater than 5 feet. These self-reports were confirmed in laboratory tests. Both subjects improved substantially; the results with them were just as good as with the more-affected lower limb of the patients with chronic CVA described above. They both became less dependent on their wheelchairs and at the end of treatment could ambulate a mean of 103 and 78 feet, respectively, in the 3-Minute Walk Test (87).

The single fractured hip/joint replacement subject we have treated to date was 2-years post-surgery, used a cane much of the time for ambulation, and had trouble ascending and descending stairs. At the end of 3 weeks of treatment, she used her cane infrequently, negotiated stairs without an assistive device, and had increased the velocity of her ambulation without a cane from 66 percent of normal to the middle of the normal range. She made gains in stride length that were commensurate with her improvement in gait velocity.

One-month follow-up has been carried out with the two SCI patients; they showed no decrement in their treatment gains. At the time of this writing, the fractured hip/joint replacement subject has not yet received the 1-month follow-up evaluation. The results from these pilot subjects have been good, but it would be inappropriate to generalize from this very small sample.

Initial Work on Other Applications of CI Therapy

Traumatic Brain Injury (TBI)

We have treated two TBI patients with predominantly unilateral upper limb motor deficits to date. One higher functioning patient with TBI had motor function consistent with the first quartile of patients with chronic CVA; the other patient was within the inclusion criteria for the second quartile. Both patients showed gains in motor function as a result of treatment that were similar to the gains demonstrated by patients with CVA with equivalent initial deficits. One patient with approximately equal deficits bilaterally was given treatment of both upper limbs at the same time using unilateral tasks for each arm in sequence and some bilateral tasks. This subject improved, but not as much as the other two patients. It may be that the diffusion of treatment across the two arms reduced the amount of use of either arm below a threshold that would yield optimal results. This case suggests the possibility that with bilateral upper limb deficits, it might be advisable to treat one arm for a period of time, allow a waiting period of several weeks, and then treat the second arm.

Focal Hand Dystonia of Musicians

Focal hand dystonia is a condition involving manual incoordination that occurs in individuals, including musicians, who engage in extensive and forceful use of the digits. To date, no treatments have been found to be effective. Using a noninvasive neuroimaging technique (magnetic source imaging), we found that musicians with focal hand dystonia exhibit a use-dependent overlap or smearing of the representational zones of the digits of the dystonic hand in the somatosensory cortex (54). Digital overuse had previously been found to produce a similar phenomenon in monkeys in the laboratory of M. Merzenich. Since behavioral mechanisms apparently underlie both the cortical disorder and the involuntary incoordination of movement, we hypothesized that a behavioral intervention could be of value in reducing or eliminating these conditions. The procedures employed in our treatment approach to focal hand dystonia (88) were derived in part from CI Therapy.

Ten professional musicians (seven pianists and three guitarists) with long-standing symptoms were studied; they had previously received several different treatments each without success. Our therapy involved immobilization by splint(s) of one or more of the digits other than the focal dystonic finger. The musicians were required to carry out repetitive exercises with the focal dystonic finger in coordination with one or more of the other digits for 1.5-2.5 hours daily (depending on patient fatigue) over a period of 8 consecutive days (14 days in one case) under therapist supervision. The practice was thus massed; practice of this intensity and duration was very taxing and was at the limit of patient capability. After the end of the primary period of treatment, the patients subsequently continued practicing the exercises with the splint for 1 hour a day at home in combination with progressively longer periods of repertoire practice without the splint. Patient status was quantified with two measurement instruments: 1) a dexterity/ displacement device which continuously recorded digital displacement during metronome-paced movements of two fingers (spectral analysis of the records provided information concerning the smoothness of the movements before, during, and after training); and 2) a dystonia evaluation scale (DES) on which patients, when not wearing the splint, rated how well they were performing movement sequences and passages from their repertoire that had tended to generate dystonic movements in the past.

All patients showed significant and substantial improvements without the splint at the end of treatment on both measures. Half of the subjects have returned to the normal or almost normal range of digit function in music performance. The improvement has persisted for 23 months in the first patient and for varying periods of presently attained follow-up for the remainder. There was one regression 9 months post-treatment following noncompliance with the home practice requirement for 6 months. Four of the patients were orchestral musicians and had never stopped their professional activities. However, four of the patients were soloists who had been forced to stop performing because of focal dystonia; they have now resumed performing in concert.

Phantom Limb Pain

In a recent study (89), the experience of phantom limb pain, non-painful phantom limb sensation, and telescoping was ascertained by questionnaire in a group of persons with upper limb amputation wearing a functionally effective Sauerbruch prosthesis which permits extensive use of the residual limb, and in a group of patients wearing a cosmetic prosthesis which did little to increase the utilization of the amputation stump. The Sauerbruch prosthesis group reported a significant and very large decrease in amount of phantom limb pain, while the cosmetic prosthesis group reported no change. Neither group experienced a decrease in non-painful phantom limb sensation or telescoping.

As noted above, work by E. Taub in collaboration with H. Flor and others had shown that the amount of phantom limb pain is highly correlated with the amount of injury-related, afferent-decrease cortical reorganization (52, 90). It is possible that the increased use of the residual limb induced by wearing a Sauerbruch prosthesis produced a countervailing use-dependent afferent-increase type of cortical reorganization that reduced the amount of injury-related afferent-decrease cortical reorganization and thereby reversed the phantom limb pain.

These preliminary results require replication and direct experimental test. However, phantom limb pain is a condition that has proved to be refractory to any of the many therapeutic approaches that have been applied to it to date. If the preliminary observations reported in this study are confirmed, it would suggest that it might be of value to fit persons with upper limb amputation with functional prostheses in order to reduce the occurrence of phantom limb pain. This treatment would differ from the use of CI Therapy with CVA, TBI, SCI, and hip fracture patients in that it would not involve overcoming learned nonuse. However, it would share the important common feature of employing increased use of a body part, in this case a residual limb, to, presumably, produce a use-dependent cortical reorganization that results in a therapeutic effect.

Consistency of CI Therapy Efficacy with General Clinical Experience

In 1979, Andrews and Stewart (91) published an article entitled "Stroke Recovery: He Can But Does He?" To quote their abstract, "... it was found that there was a difference in what the patients could do in the unit and what they did do at home. Each activity of daily living was less well performed in the home situation in 25-45% cases" (p. 43). Most clinicians recognize the veracity of this statement. Indeed, decrement in performance outside the clinic environment is frequently reported as a source of intense frustration. Clinicians often work with patients intensively for one or more sessions with the result that there is a substantial improvement in some aspect of movement. However, by the time of the next therapy session, there have been varying degrees of

regression. In fact, some clinicians report that they sometimes see degradation in motor patterns as soon as the patient crosses the threshold into the corridor just outside the therapy room.

Very little explicit attention is paid to this dimension of treatment. A reasonably intensive search of the literature failed to reveal a single reference to this phenomenon. Similarly, very little attention has been paid to the Andrews and Stewart paper (91), which has been virtually "lost in the literature." However, for many CVA and other types of patients we have worked with, there is undeniably a gap between performance in the clinic on laboratory motor tests when specific activities are requested and the actual amount of limb use in the home. This gap may be viewed as an index of learned nonuse; CI Therapy operates in this window. It establishes a bridge between the laboratory or clinic and the life setting so that the therapeutic gains made in the clinic transfer maximally and contribute to the functional independence of the patient in the real world. Thus, many patients, though exhibiting a pronounced motor deficit, might have a considerable latent capacity for motor improvement that could be brought to expression by CI Therapy.

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