The learned nonuse phenomenon: implications for rehabilitation

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Research on monkeys with a single forelimb from which sensation is surgically abolished demonstrates that such animals do not use their deafferented limb even though they possess sufficient motor innervation to do so, a phenomenon labeled learned nonuse. This dissociation also occurs after neurological injury in humans. Instruments that measure these two aspects of motor function are discussed. The effects of a neurological injury may differ widely in regard to motor ability assessed on a laboratory performance test in which movements are requested and actual spontaneous use of an extremity in real-world settings, indicating that these parameters need to be evaluated separately. The methods used in Constraint-Induced Movement therapy (CI therapy) research to independently assess these two domains are reliable and valid. We suggest that these tests have applicability beyond studies involving CI therapy for stroke and may be of value for determining motor status in other types of motor disorders and with other types of treatment. The learned nonuse formulation also predicts that a rehabilitation treatment may have differential effects on motor performance made on request and actual spontaneous amount of use of a more affected upper extremity in the life situation. CI therapy produces improvements in the former, but focuses attention on the latter and, in fact, spontaneous use of the limb is where this intervention has by far its greatest effect. The evidence suggests that this result is driven by use of a "transfer package" of techniques, which can be used with other therapies to increase the transfer of improvements made in the clinic to the life situation. The use of CI therapy in humans began with the upper extremity after stroke and was then extended for the upper extremity to cerebral palsy in young children (8 months to 8 years old) and traumatic brain injury. A form of CI therapy was developed for the lower extremities and was used effectively after stroke, spinal cord injury, and fractured hip. Adaptations of CI therapy have also been developed for aphasia (CI aphasia therapy), focal hand dystonia in musicians and phantom limb pain. The range of these applications suggests that CI therapy is not only a treatment for stroke, for which it is most commonly used, but for learned nonuse in general, which manifests as excess motor disability in a number of conditions which until now have been refractory to treatment.

Key words: **Learned nonuse - Rehabilitation - Constraint-Induced Movement therapy.**

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The concept of learned nonuse (LNU) was derived from basic research with monkeys.[1, 2] The formulation was later generalized to include humans after

stroke and other types of damage to the central nervous system (CNS).[2-4] The general principle is that a certain portion of the motor deficit resulting from damage to the nervous system is the result not of the damage per se but of a learning phenomenon stemming from the damage, but whose core is the learned suppression of movement.[2-4] The evidence for this formulation will be reviewed here and, as far as we know, there is no evidence that is inconsistent with it. The concept has become reasonably well known in the rehabilitation community. However, acceptance has not yet risen to the level where its stated implications have influenced clinical practice in any substantial way. The learned nonuse formulation has important applicability: 1) to the theory and practice of measuring motor deficit or other types of deficit after CNS damage, and 2) to the way in which neurorehabilitation is carried out. In this paper, we will review the concept of learned nonuse, how it originated, the evidence for it and its applicability to any damage to the CNS where spontaneous recovery is slow and gradual. We will point out that if the general principle is accepted, significant changes should be carried out in the field of measurement of motor (and possibly cognitive) deficits and in the way therapy is carried out, not just in the case of Constraint-Induced Movement therapy (CI therapy) but other therapies as well.

Learned nonuse and limb deafferentation in monkeys

When sensation is surgically abolished from a single forelimb in monkeys, that extremity is never used again in the free situation. This is a classic observation in neuroscience,[5] that has been replicated many times.[6-11] However, there are two techniques capable of overcoming this nonuse: restraint of the intact forelimb for a period of days or weeks [7, 9, 11-15] and training [12-23] especially the type of training termed shaping.[1, 2]

The question remained, however, of why monkeys would use a deafferented limb in a training situation or after restraint of the intact limb, but not in the free situation, even when it would be to the monkey's advantage to do so. This was one of the central enigmas of the deafferentation literature.

The motivation hypothesis

One possible answer is related to motivation. When unrestricted, a monkey does not use a single deaf-

ferented limb because it can get along in the laboratory environment reasonably well on its 3 intact limbs. Moreover, use of the deafferented limb in concert with the intact limbs might result in incoordination, falling, and loss of food-objects. The monkey, thus, learns not to use the deafferented limb. However, the conditioning and restraint situations force a monkey either to use the affected extremity, or be subjected to electric shock, or to go hungry. The motivation to use the limb is increased and, consequently, the monkey uses it. This explanation, though simple and straightforward, had two important pieces of evidence that seemed to weigh against it. First, situations arise in the colony environment in which independent use of a single deafferented limb would be advantageous. For example, when a monkey is offered food while hanging from the wire mesh of its cage by its intact hand and 2 feet, it does not use the deafferented hand to secure the food even after food deprivation. Under similar circumstances, the animals will not use the deafferented limb to ward off an object that is thrust at it. Second, 2 monkeys were studied following complete hemideafferentation of the spinal cord.[11] In contrast to the consequences of a more limited unilateral procedure involving only the upper extremity, both of these animals were severely incapacitated. Though rendered almost completely unable to ambulate or climb, neither animal made significant use of its deafferented arm and leg.

The interlimb inhibition hypothesis

An alternate explanation for nonuse of a single deafferented limb in the free situation suggests that movements of one limb have an inhibitory effect on movements of the contralateral limb. This interlimb inhibitory mechanism is normally held in check by the ipsilateral segmental afferent inflow. When this ipsilateral input is abolished, as by deafferentation, the interlimb inhibitory mechanism is released, thereby preventing coordinated movements of the deafferented limb. This hypothesis had the virtue of being able to explain all the data available at the time of its formulation. When the intact limb in a unilaterally deafferented animal is immobilized, as in the straitjacket situation, and is relaxed, crossed inhibition is prevented from operating. Consequently, the animal is able to make use of the deafferented limb. The intact limb had also been restrained in the conditioning experiments conducted up to that time (1965)

in order to prevent it from interfering with conditioned responses of the deafferented member, the possible experimental relevance of this procedure not being appreciated at the time. Neither had any training by shaping been carried out then. To test this hypothesis, it was reasoned that if the postulated mechanism exists, and is relevant, then the ability to make simultaneous use of a normal and a deafferented forelimb should be subject to certain restrictions. In the extreme case, no concurrent use of the limbs should be possible. The initial movements of the intact limb would inhibit movement of the deafferented limb; consequently, the attempt at simultaneous use would end in movement of the intact limb only. This prediction was disconfirmed by the finding that monkeys with one intact and one deafferented forelimb were capable of flexing both forelimbs within a very brief temporal interval, sometimes as short as 10 ms, in order to avoid electric shock.[17] These results invalidate the extreme form of the interlimb inhibition hypothesis. It still remained possible, however, that operation of the interlimb inhibitory mechanism could preclude the possibility of only certain patterns of concurrent movement. While this might not completely abolish the ability to use the deafferented limb in all circumstances, it could be quite disabling. For example, if flexion of the intact limb were to prevent extension of the deafferented extremity, then climbing and the usual mode of ambulation would not be possible. Other combinations of partial inhibition could be equally devastating.

The partial interlimb inhibition hypothesis would be difficult to evaluate experimentally because several combinations of movement would have to be tested separately. Instead, it was decided to re-examine the original motivation or "learned nonuse" explanation.

The learned nonuse hypothesis

In the initial intact-limb immobilization studies, the straitjacket was removed shortly after purposive use of the deafferented extremity was displayed, the main point presumably having been made. In the next experiment, 2 unilaterally deafferented monkeys were placed in a restraining device 9 weeks after operation, but in this case they were kept with their intact forelimb so restrained for 3 days. These animals displayed extensive use of the deafferented limb. However, in contrast to the briefly straitjacketed monkeys, these animals continued to use the deafferented limb in the free situation after removal of the straitjacket. (It may be noted that these results invalidated the partial interlimb inhibition hypothesis).

The data can be accounted for in the following manner: immediately after operation, monkeys cannot use a deafferented limb; recovery of function requires considerable time, as data from animals with bilateral forelimb deafferentation have shown. An animal with one deafferented limb tries to use that extremity in the immediate postoperative situation, but it cannot. It gets along quite well in the laboratory environment on 3 limbs. Moreover, continued attempts to use the deafferented limb often lead to aversive consequences, such as loss of balance and falling, loss of food objects, etc. The monkeys, therefore, learn not to try to use the deafferented limb. This habit persists and, consequently, they never learn that, several months after operation, the limb has become potentially useful.

When the intact limb is immobilized several months after unilateral deafferentation, motivation to use the deafferented limb increases sharply, thereby overcoming the learned nonuse of that limb. The animal then uses the deafferented limb. However, if the straitjacket is removed a short while after the initial display of purposive movement, as was the case in our earlier experiment, the newly learned use of the deafferented limb acquires little strength and is, therefore, quickly overwhelmed by the well learned habit of nonuse. If the straitjacket is left on for several days, 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.

Following pyramidotomy, monkeys exhibit an extensive initial loss of motor capacity. Investigators differed greatly at that time on the amount of recovery of function that can take place afterward.[24] Tower [25] presented evidence that part of the long enduring deficit may be due to a mechanism similar to the learned nonuse phenomenon just described. Previously, Lashley [26] had invoked a motivational mechanism essentially similar to that described by Tower [25] (and to learned nonuse) to explain some of the same long-term motor impairments following pyramidotomy and, subsequently, Goldberger [24] has concurred in this opinion. In this regard it is of interest that section of the bulbar pyramids has been generally thought to permanently abolish thumb-forefinger prehension. However, Chambers (cited in Goldberger [24]) has found that when appropriate training

techniques are employed monkeys can recover these movements. The effects of unilateral forelimb deafferentation in monkeys results in a permanent abolition of purposive movement unless special training or restraint techniques are used; they are, thus, considerably more severe than the effects of pyramidotomy in monkeys. However, the data suggest there may well be some interesting parallels in terms of the participation of a learned nonuse mechanism in the masking of the behavioral capacity actually present after both types of lesions.

Direct test of the learned nonuse hypothesis

All of the evidence cited until now constitutes indirect evidence for the learned nonuse hypothesis. Therefore, we attempted to test the hypothesis in direct fashion. This involved restraining a deafferented limb in several animals so that they could not attempt to use it for a period of 3 months following surgery. By preventing an animal from using the deafferented limb during the period before recovery of function had taken place, one could thereby prevent it from learning that the limb could not be used during that interval. Learned nonuse of the deafferented limb should therefore not develop. That is, the unilateral animal after being released from forelimb restraint should be able to use the deafferented extremity in the free situation, though never again subjected to restraint of the intact limb.

In carrying out the experiment, we decided also to restrain the intact limb as well as the deafferented limb so that the animal could not learn to carry out its daily activities through the use of the intact limb exclusively. This would tend to bias the data against the hypothesis. The animals forelimbs were placed in 3 different positions, which immobilized the limbs in different ways: arms crossed on the chest, arms extended along the sides of the torso, arms tied behind the back. Limb position was changed every other day.

On removal from the restraining situations, 3 months after surgery, we found that the animals had difficulty in using both limbs, the intact limb as well as the deafferented limb. There was increased resistance to passive movement, and it was clear that an insufficient amount of passive exercise had been given. However, notwithstanding this difficulty, the animals did use the deafferented limb immediately after removal from restraint. Over the course of the next several weeks, use of both arms continued to improve. Ability to use

the deafferented arm spontaneously reached the level normally exhibited by animals given deafferentation of both forelimbs. No further interventions were needed to accomplish this.

Thus, the learned nonuse hypothesis was confirmed by direct test. In this regard, it is interesting to recognize that life in the physically restrictive uterine environment imposes major constraints on the ability to use the forelimbs (while not preventing the use of the limbs entirely). Consequently, prenatal deafferentation of a single limb could provide a means of testing the learned nonuse hypothesis, particularly if the results were positive (*i.e.*, if the animal used the deafferented limb without requiring restraint of the intact limb). This is so because the intrauterine environment, which permits some use of the intact forelimb, should bias the outcome in the direction of learned nonuse of the deafferented extremity (*i.e.*, against the hypothesis).

Three animals were studied that had received unilateral forelimb deafferentation during the prenatal period: 2 when 2/3 of the way through gestation and 1 when 2/5 of the way through gestation. Early illness and a muscular deformity prevent a clear interpretation of the results from 1 of the 2/3 through gestation animals. However, the other two animals exhibited purposive use of the deafferented extremity from the first day of extrauterine life, at which time they both employed the limb for postural support during age-appropriate "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 spontaneously with the emergence of all age-appropriate motor patterns (though clumsy) at the appropriate times with the exception of prehension (as noted earlier). Thus, the results from the prenatally deafferented animals provide additional evidence in favor of the learned nonuse explanation for the lack of purposive movement following unilateral forelimb deafferentation in adolescent monkeys.

In humans, an index of learned nonuse would be the difference between a measure of what a person can do in the laboratory when requested to do the best he can and a measure of what a person actually does do spontaneously in the real world situation. In this laboratory, our measure of the former is the score on a laboratory motor function test (Wolf motor function test, WMFT) and our primary measure of the latter is score on the motor activity log (MAL). It was found that the
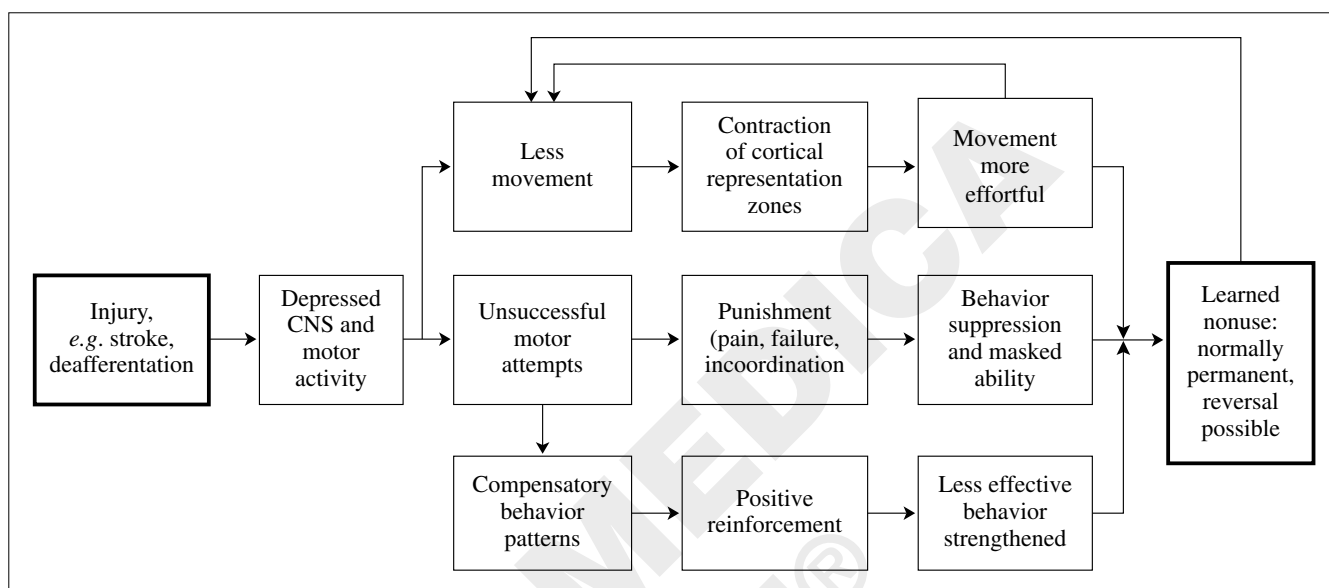
Figure 1.—Development of learned nonuse. CNS: central nervous system.

magnitude of this difference in score predicted CI therapy outcome (r=0.49, P<0.0001; Mark, Taub and Uswatte, unpublished data), whereas the individual components of this composite variable did not predict treatment outcome. That is, the greater the pretreatment learned nonuse the greater the increase in real world more affected arm use as a result of CI therapy. The fact that this measure does not account for all of the variance in treatment outcome suggests that CI therapy has other actions in the rehabilitation of poststroke motor function other than overcoming learned nonuse. For example, the data from each of our experiments with humans after CNS injury shows that CI therapy significantly improves the quality and speed of movement in a laboratory motor function test: an effect that may be attributable to motor learning induced by the shaping or repetitive task practice carried out in the CI therapy protocol.

Brain plasticity: a complementary mechanism

After stroke, there is a marked contraction in the size of the cortical representation of the more affected limb.[27-29] This phenomenon is probably related to the reports of individuals with stroke that movement of the more affected extremity is effortful. This is not surprising since the person is trying to make movements of that extremity on the basis of activation of half the neurons that were operative for that purpose before the stroke. This contraction of the arm's cortical representation interacts with the other two processes noted above (i.e., punishment of use of the more affected limb and reinforcement of use of the intact limb) to produce a vicious spiral downward that results in learned nonuse of the affected extremity that is normally permanent.[30, 31] The process is depicted in Figure 1.

However, learned nonuse of an affected extremity can be overcome by the application of an efficacious treatment, such as CI therapy. As noted above, both intensive training and restraint of the less affected arm induce increased purposive movement of that extremity. That increases the size of the cortical representation zone of that arm,[27, 28] which presumably makes movement less effortful. This establishes the basis for further movement and reward for using the more affected arm, and so on. In this way the learned nonuse, which is normally permanent, is reversed. This process is depicted schematically in Figure 2.

Motor neglect and other formulations

The terms "motor neglect" or "motor amnesia" have been used to describe the selective deficit of sponta-
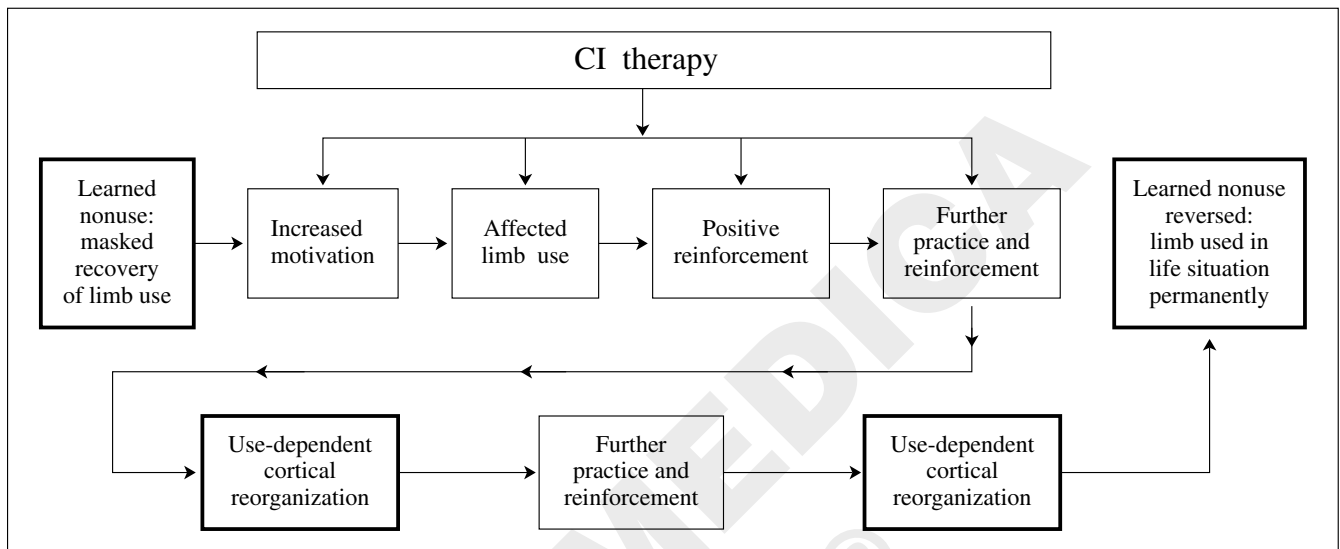
Figure 2.—Overcoming learned nonuse. CI: Constraint-Induced Movement therapy.

neous limb use. The earliest clinical description of a conditional failure of purposive limb movement was by Meige in 1905,[32] who inferred that some stroke patients fail to "remember" how to move the limb effectively, leading to an inhibition of attempted limb movement that has a general resemblance to the formulation of LNU presented here. Moreover, Meige anecdotally indicated that such movement failure could be counteracted by massed practice training. However, he did not present data. Meige did not elaborate on why the movement failure could be regarded as a memory disorder. Nevertheless, as discussed below, many patients exhibiting learned nonuse have explicitly not forgotten how to make movements not performed spontaneously. Meige's observations, though astute, have unfortunately been overlooked.

Critchley in 1953 [33] first used the term motor neglect, which he thought resulted from a severe general unilateral attentional deficit that nonetheless could be overcome by "deliberate willed actions". The term was subsequently resurrected in the extensive clinical studies by Castaigne, Laplane, and Heilman and other authors [34-44] In these reports, patients during acute focal brain injury were described as lacking spontaneous movement of the more affected limb while retaining movement when requested to use the extremity. The finding was not regarded as a conditioned learned response but rather as a spontaneous unilateral deficit of attention, akin to other forms of

unilateral spatial neglect that reflect impaired awareness of contralesional phenomena but which can nonetheless be overcome by cuing.

However, absence of a correlation between motor neglect and other forms of hemi-inattention [45] indicates that the unilateral deficiency of spontaneous limb use cannot strictly result from a multimodal unilateral attentional deficit. This suggests that it is a separate phenomenon. There are a number of other reasons to believe that what is called "motor neglect" or "motor amnesia" is not an attentional or memory disorder involving the more affected side of the body.

Motor neglect usually remits spontaneously in the first year after stroke (as is the case for lateral visual neglect). Some cases of motor neglect can persist into the chronic phase but most resolve spontaneously early in recovery. In contrast, this does not occur with learned nonuse. It is assumed to begin developing in the first few days after CNS damage and then gets progressively stronger. We have never seen learned nonuse resolve spontaneously and we routinely observe its presence decades after injury.

An argument against learned nonuse involving simple inattention to the more affected upper extremity or a lapse in memory is that virtually all of our subjects have been aware of the lack of use of their more affected arm. They sometimes believe that the reason they do not use it is that they cannot, and are surprised in laboratory motor testing to find that they

can do a particular task when they are encouraged to try it. Most subjects, though, are aware that they could use the limb if they wanted to, they just lack the motivation to. Both cases are consistent with the operation of a learned nonuse mechanism.

Many cases of hemi-inattention occur more frequently on the left side of the body than on the right. This is not the case for learned nonuse, which is equally common for right and left hemiparesis.

An important consideration is the speed at which learned nonuse resolves with the application of CI therapy. Most of the therapeutic progress is made in the first few days after the initiation of treatment. In fact, it is common for the greatest progress to be made during the first day of treatment, even when the lack of use of the limb has been present for years or decades. The usual period of treatment is 2 weeks and improvement almost always describes a negatively accelerated curve. This speed of improvement is consistent with the lifting of a conditioned inhibition, which can frequently be rapid.

Although most rehabilitation professionals are now aware of the learned nonuse phenomenon, relatively little attention has been paid in the literature to discrepancies between motor ability and actual use of an extremity in real-world situations. A notable exception is an article published by Andrews and Stewart in 1979, titled "Stroke recovery: he can but does he?" This article reported that among 29 consecutive admissions of stroke patients to a day hospital program, activities of daily living (ADL) were performed less well in the home situation than in the hospital in 25-45% of cases.[46] This isolated finding is amply supported by data from our laboratory. Among chronic stroke patients, who were enrolled in a clinical trial of CI therapy (n=21) [47] with mild to moderate motor impairment of their more affected arm, there was no association before treatment between motor ability, as measured by a laboratory motor performance test [3, 47-50] and real-world arm function, as indexed by an objective measure of arm movement outside the laboratory.[51]

Finally, one should note that there is nothing inconsistent between a neural basis for nonuse and the operation of a learning mechanism. Indeed, the learned nonuse mechanism is consistent with a CNS lesion or an injury of some type that gives rise to a period of real inability to use an extremity during which a learning not to try to use the extremity takes place. Moreover, the learned nonuse formulation

asserts that only part of a motor deficit following CNS damage is due to learning. A very large part of the deficit is the direct effect of the lesion. The quantitative contribution of the two factors is a question for empirical determination in individual cases.

Constraint-induced movement therapy

The same primate research that gave rise to the learned nonuse formulation described above also gave rise to the development of a technique for substantially reducing the incapacitating motor deficit of the upper extremity in many stroke patients and greatly increasing use of the more-impaired extremity in the life setting.[3, 4, 30, 31, 47] The technique is termed CI therapy and it has been demonstrated to be effective in multiple studies using between-and within-subject controls, placebo controls, and convergent measures from multiple domains. A recently concluded multisite randomized clinical trial (EXCITE) with subacute patients 3-9 months poststroke reports positive results. In addition, CI therapy has been shown to produce a large transfer of increased limb use to the ADL in the home situation. The procedures involved in its administration have been described in detail in another article in this journal.[52] In brief, CI therapy involves 3 main elements: 1) intensive training of the more affected arm; 2) a "transfer package" of techniques to promote transfer of therapeutic gains from the laboratory to the real world environment; and 3) motor restriction of the less affected arm during the entire period of treatment.

One of the most striking aspects of the results from CI therapy is the difference between the effect the intervention has on the quality and speed of movement patients make when requested to do so in the laboratory on a motor function test and the amount of spontaneous use of the more affected extremity in the real world situation, as measured by the MAL. To compare the magnitude of a change on different tests as result of a therapy where the scores are not directly comparable, one can use effect size (ES) statistics as is commonly done in the meta-analysis literature. For present purposes, the within subject statistic d' will be used.[53] According to the conventions of the field a large ES is d'=0.5. Over a number of different experiments from this laboratory the ES for movements made on the WMFT, a laboratory motor function test, is approximately 0.9. Thus, CI therapy pro-

duces a large improvement in quality and speed of movement when a subject is asked to do the best they can. However, the ES on the actual amount of spontaneous movement in the life situation is much larger: 4.5 times as large as a large ES. This disparity in scores on the two types of tests has important implications for the measurement of motor status after neurological injury, and for the type of procedures that are important to use during any type of rehabilitation therapy to achieve transfer to the life situation.

Implications of learned nonuse for measurement of motor function

The current consensus in physical rehabilitation, including the perspectives of patients, researchers, clinicians, and health care payers, is that functional activity in the life situation is the most important outcome to pursue and measure.[54-56] The standard assessment tools, however, do not provide direct measures of affected extremity motor function in the real world.[56] Traditional instruments [57-59] in physical rehabilitation focus on measuring strength, flexibility, and coordination in the clinic or laboratory setting.[56] More recent instruments [60-62] measure functional ability in the home indirectly; that is, clinicians observe ADL performed in the laboratory or clinic. However, the relationship between performance on these instruments and activity in the life situation has not been rigorously tested.[54, 56, 63] When investigators have measured behavior in the home, they have focused on functional independence rather than extremity function.[63-65]

As noted, experimental work by Taub *et al.* and Uswatte *et al.*[3, 56] and the observations of others [46] suggest that laboratory motor tests indicate a rehabilitation patient's maximum motor ability, but that patients frequently do not make full use of that ability in the life setting. There is frequently a very large gap between the two, and CI therapy has the effect of reducing that gap.[56] Thus, to measure the major result of CI therapy, new instruments were developed to measure real world upper extremity (UE) outcome, including the MAL, and accelerometry.[56] Five different laboratories have found that CI therapy for the UE produces a larger effect on real world outcome, as measured by the MAL, than on laboratory motor function, as measured by either of two tests of motor ability carried out in the laboratory: the WMFT or the arm motor ability test (AMAT).[3, 47, 66-69] This difference

in gains in real-world motor function *vs* motor capacity has been confirmed using accelerometry, which is an objective measure.

Real-world use and motor capacity measures correlate significantly but the strength of the correlation is only modest (*e.g.* r=0.34, P<0.05). Furthermore, as noted above, the difference in ES (*i.e.* d') after CI therapy recorded by these two types of measures is very large (*e.g.* MAL d'=3.3; WMFT performance time d'=0.9). Consequently, to determine the full range of the effect of CI therapy, one must measure both parameters separately.[56] Moreover, as noted, changes in real-world function are of greater interest than changes in motor capacity from multiple perspectives.

Real-world measures

MOTOR ACTIVITY LOG

This is a structured interview during which respondents are asked to rate how they use their more-impaired arm for 28 ADL in the home over a specified period.[3, 70, 71] The MAL is administered independently to the patient and an informant. Activities include brushing teeth, buttoning a shirt or blouse, and eating with a fork or spoon. For each item the participant must report whether, how well (6-point, quality of movement or QOM scale), and how often (6-point, amount of use or AOU scale) each activity was performed during a specified period. The data suggest the QOM scale captures both how well and how much stroke survivors use their more-impaired arm (*e.g.*, the correlation between the QOM and AOU scales is 0.92).[71] Currently, we use only the QOM scale for literature reports, which will be referred to as the Arm Use scale.[47, 70-72]

The MAL has an established reliability and validity.[56, 70, 71, 73] Data from our laboratory, for example, indicate that the Arm Use scale has high internal consistency (α>0.81) and test-retest reliability (r>0.91), and has high convergent validity for measuring treatment changes with an objective accelerometer-based measure of more-impaired arm movement outside the laboratory (r=0.91, P<0.01).[70] These findings have been confirmed by data from a multisite randomized clinical trial of CI therapy (EXCITE).[71, 74, 75]

Information is obtained about motor activity from all participants in the year prior and week prior to the subject's participation in the project, the day before and the day after the intervention, daily during treatment, weekly for the first 4 weeks after treatment and

at 6- and 12-month follow-up time points. Caregivers or other informants complete the MAL just prior to the beginning of treatment, on one of the testing days just after the completion of treatment, and at the same time points as the patient thereafter. The method of conducting the interview and eliciting information is standardized according to a specified protocol. Our laboratory has made a video depicting stroke patients carrying out 8 of the MAL tasks at each rating step of the Arm Use scale. This video is shown as often as is appropriate to participants to help establish a common frame of reference for scoring the MAL across subjects.[70]

ACCELEROMETRY

The accelerometers [76] used in our laboratory are plastic units about the size and weight of a large wristwatch that are worn proximal to the wrist on modified wristbands. They are based on piezoelectric crystal technology. When the piezoelectric crystal in an accelerometer is subjected to acceleration, it deforms and produces a charge. This charge is digitized at a 10 Hz sampling rate, integrated over a user-specified time epoch, and reported as an activity count for each epoch.[76, 77] Approximately 20 activity counts, for example, are recorded in response to a human arm movement such as lifting a book from a stool 78 cm off the floor to a shelf 80 cm away in 1 s. The acceleration recordings are stored in the unit's RAM and can be downloaded to a personal computer using an interface reader unit. When a 2-s recording epoch is specified, the units can record continuously for approximately 72 h. These devices are durable with only two incidents of breakage (repaired within 1 week) among 14 accelerometers worn over 6 years.

A series of studies conducted by one of us (G. U.) show that accelerometry provides an accurate, reliable and stable measure of the duration of arm movement, and that this parameter is a valid measure of real-world use of the limb. In one study a short recording epoch (2 s) was used and simple data transformation of the raw accelerometer recordings was carried out to obtain an accurate measure of the duration of extremity movement. The transformation involved setting raw values above a low threshold to 1 and values below the threshold to 0. The number of 2-s epochs with a transformed value of 1, multiplied by 2, represents the duration of movement in seconds. With this "threshold-filter" approach, the accelerometer recordings gave a virtually perfect reflection of the duration

of movement for subjects tested in a series of two studies.[51] For example, in the second study healthy subjects and stroke patients were videotaped at home and in an occupational therapy clinic while carrying out their usual activities wearing a set of 4 accelerometers (one on each arm, the chest and a leg). Correlations between threshold-transformed accelerometer values and observer coding of the duration of impaired-arm, torso, and ambulatory movements were 0.93, 0.93, and 0.99, respectively.[51] In a more recent paper accelerometer recordings were obtained for 3 consecutive days from upper-extremity CI therapy patients before and after 2 weeks of treatment and stroke survivors in the community before and after a 2-week no-treatment period. Because one would expect that changes in overall levels of physical activity would affect recordings from the more-impaired and less-impaired arms roughly equally, the ratio of more- to less-impaired arm accelerometer recordings was examined as a measure of treatment outcome. The CI therapy patients showed a significant increase in this ratio (P<0.05, d'=0.9), while the no-treatment controls did not show a significant change (NS, d'=0.3), suggesting that the ratio measure provides a responsive and stable measure of upper-extremity rehabilitation outcome. In data from the EXCITE trial,[78] the ratio measure was strongly correlated with other measures of arm activity (r>0.52), but only weakly correlated with a measure of mobility (r=0.16). More-impaired arm recordings alone, however, were influenced by differences in overall levels of physical activity; they were correlated moderately with both measures of arm activity (r>0.38) and mobility (r=0.32). Test-retest reliability of the ratio measure in the previous experiment [79] and the EXCITE trial [78] was 0.88 and 0.9, respectively.

The accelerometers are removed when subjects are sleeping or in contact with water. The use of only two accelerometers is supported by the findings summarized above showing that the ratio of affected to unaffected arm accelerometer recordings controls for changes in the overall level of activity and is a reliable, stable, responsive, and valid index of upper-extremity rehabilitation outcome.

Laboratory measures

WOLF MOTOR FUNCTION TEST

This impairment-based test was developed by Wolf *et al.*[50] and modified by Taub *et al.* and Morris *et al.*[3,

[48] to quantify motor function in stroke and traumatic brain injury patients. The WMFT has 17 items, 2 of which involve strength measures and 15 of which involve timed performance on various tasks. Performance time (up to 120 s), quality of motor function (6-point scale of functional ability) and force are assessed. The first half of the test involves simple limb movements, primarily of the proximal musculature. The second half of the test involves tasks performed in the life situation using the distal musculature.

The WMFT has an established reliability and validity in stroke patients with mild-to-moderate UE impairment.[48, 49, 80] For example, test-retest reliability, inter-rater reliability, and internal consistency coefficients for the Functional Ability scale were 0.95, 0.88, and 0.92, respectively. Corresponding coefficients for the Performance Time scale were 0.9, 0.97, and 0.92. Validity of the WMFT has been supported, for example, by showing that WMFT Functional Ability and Performance Time scores were significantly worse in stroke patients with UE motor impairment of moderate severity (Grade 3) than in patients with impairment of only mild-to-moderate severity.[80] The grip strength item on the WMFT was borrowed from Mathiowetz *et al.*[58] This item has inter-rater reliability coefficients of >0.8, while inaccuracy in measurement has been shown to be only ±3% for the Jamar dynamometer.[58] For lower functioning patients (moderate to moderately severe impairment), a modified version of the WMFT, named the graded WMFT (gWMFT), is used because it has been shown to be sensitive to changes in motor capacity in this population.[4] An ongoing study in our laboratory (unpublished data) indicates that its clinimetric properties are similar to that of the standard WMFT.

The WMFT is first administered to the less-affected upper extremity and then to the more-affected upper extremity. The former provides a point of comparison indicating how marked the initial and post-treatment motor deficits of the more-affected extremity are, compared to the less-affected arm. The tester measures time to completion of tasks and forces generated on two tasks. In addition, the WMFT performances of all subjects are videotaped and rated independently by two clinicians according to a 6-step scale of functional ability. These clinicians are trained to have a reliable common frame of reference. The mean of the two clinician's scores is taken as the test score. The clinicians are "blind" to group membership and to pre- or post-treatment status of the testing sessions.

Implications of learned nonuse for therapy

As noted, the learned nonuse formulation predicts that for patients with stroke or other types of CNS damage, the ability to make movements on request on a laboratory motor function test and the actual amount of spontaneous use of a more affected extremity in the life situation constitute two different domains of movement. The results of many experiments amply bear this out. Almost all current therapy is directed toward improving movement that is observed in the laboratory and testing concentrates almost exclusively on that domain. However, virtually all stakeholders agree that the ultimate objective of a rehabilitation therapy is or should be producing improved extremity function in the life situation. Unless a rehabilitation therapy does that, it cannot be considered successful.

CI therapy focuses primarily on improving real world function. Through concentrated practice and shaping, the treatment also attempts to improve quality and speed of movement in the laboratory. The data reveal that this objective is accomplished: the ES on the WMFT is d'=0.9. However, the transfer of what is learned in the laboratory to the real world environment is much larger (MAL treatment change scores are approximately d'=3). How does CI therapy accomplish this outcome?

As described previously, CI therapy consists of 3 main elements: 1) concentrated practice of use of the more affected upper extremity on behaviorally relevant tasks; 2) a "transfer package" of behaviorally-based techniques; 3) restraint of the less affected arm. In recent research, we very unexpectedly found that the transfer package (*i.e.* focusing on use of the more affected arm in the life situation) made a much more important contribution to CI therapy treatment outcome than type of training, and that the restraint component was relatively unimportant. Until the recent research (still in progress) was begun, we had viewed the transfer package as a transparent aspect of CI therapy. It was something we had routinely done, but not directed much attention towards, though several rehabilitation professionals on joining our research team had remarked that the procedures were radically different from those generally carried out in rehabilitation treatment centers. The transfer package consists of a number of components, that include: 1) daily administration of the MAL, which collects information about use of the more affected arm in 30 important ADL; 2) a patient-kept daily diary, which

details what a patient did when out of the laboratory overnight and the extent to which there was compliance with an agreed-upon amount of use of the more affected arm (monitoring and accountability component); 3) problem solving to help the patients overcome apparent barriers to real-world use of the more affected arm reported during monitoring; 4) behavioral contracts for patients and caregivers specifying agreed-upon real world activities for which the more affected arm would be used exclusively; 5) home practice of specified exercises; 6) restraint of the less affected arm; and 7) weekly telephone contacts with patients for the first month after the end of treatment in which the MAL is administered and problem solving is carried out (monitoring plus accountability after treatment). In most physical rehabilitation regimens, there is a passive element: the patient is responsible primarily for carrying out the therapist's instructions during the treatment period. A major difference in CI therapy is the involvement of the patient as an active participant in all requirements of the therapy not only during the treatment period but also (and especially) after laboratory therapy has been completed. The description of the transfer package components is included in another paper in this issue of this journal.[52] The strategies used in the CI therapy transfer package are used commonly in behavioral interventions for treating problems, such as disruptive classroom behaviors, drug addiction, and medication adherence, but have not been employed in a systematic way in physical neurorehabilitation.[81]

Self-monitoring is one of the most commonly used strategies and involves asking participants to observe and document their target behaviors.[82-89] For example, Rhode *et al.* showed the importance of self-monitoring in obtaining behavior treatment gains that generalize from a resource room to regular classroom situation.[90] When self-monitoring interventions were utilized in the resource room only, children's behavior improved only in this setting. However, when these same interventions were implemented in the classroom, behavior gains generalized to the classroom setting and were persistent even after termination of the intervention.[90] Just the act of monitoring a target behavior is thought to be effective because it helps patients attend to appropriate stimuli and is self-reinforcing. In CI therapy, for example, recording instances when the more-impaired arm is used in a daily diary may help patients to immediately notice small, gradual improvements in use of their arm that patients

would not notice otherwise until later on in treatment when improvements are more pronounced. Self-monitoring has also been used to improve compliance with home exercise regimens of demonstrated efficacy in back pain patients.

Monitoring of more-impaired arm use also takes place when therapists administer MAL to patients during treatment and in the 4 weekly follow-up telephone contacts made in the first month after treatment. These occasions, along with review of the daily diary at the start of each treatment day, permit therapists to reward patients with verbal praise when they use their more-impaired arm outside of the laboratory setting and adhere to other portions of the treatment protocol, *e.g.*, wearing the restraint device on the less-impaired arm.

Contracting, *i.e.* negotiating specific behaviors that participants agree to do, has also been shown to be efficacious in promoting behavior change. Contracting indicates the behaviors that will be rewarded and those that are not acceptable in participants. Positive findings for contracting have been observed in treatment of cocaine-dependent outpatients [91] and adherence to behavior modification training for parents of children with behavior problems.[92] The CI therapy transfer package uses contracting by both participants and caregivers to increase compliance with home-based portions of the therapy, *i.e.* attempting to use the more-impaired arm at home, wearing the restraint device on the less-impaired arm, and doing home practice exercises.

Telephone contacts may also be an effective means for increasing treatment compliance. They have been successful at promoting behavior changes in a variety of areas, such as increasing fruit and vegetable consumption,[93] reducing HbA1c levels in diabetics,[94] increasing physical activity,[95] and complying with mammography recommendations.[96] Mixed results have been obtained in studies employing telephone interventions to promote compliance with pharmacological management of hypertension [97, 98] and to reduce coronary disease.[99] However, the interventions used varied widely between studies, possibly accounting for the array of findings. In CI therapy, the 4 weekly follow-up phone calls in the first month after treatment, which include administration of the MAL, may be effective at increasing adherence to CI therapy at home by extending therapist-reinforcement of increased more-impaired arm use into the home setting and the post-treatment period. The fol-

low-up phone calls also provide an opportunity for therapists to continue to model problem-solving for patients.

Problem-solving interventions can also be effective for overcoming barriers to behavior change. Problem-solving interventions teach individuals to identify obstacles that hinder them, generate potential solutions, select a solution to implement, evaluate the outcome, and choose another solution if needed.[83, 88, 98, 100] Problem-solving interventions have been associated with positive health behavior changes such as managing diabetes,[101] compliance with rheumatoid arthritis treatment,[102] and relief of anxiety/depression symptoms.[103] In CI therapy, therapists help patients to find solutions to apparent obstacles to use of their more-impaired arm that patients raise when reviewing the daily diary or completing the MAL. It is thought by modeling appropriate problem-solving behavior during CI therapy and in the follow-up MAL telephone contacts, the therapists will stimulate patients to effectively solve new problems that arise in using their more-impaired arm after contact with therapists has ended.

Other applications of constraint-induced movement therapy

An important adaptation of CI therapy has been used to treat lower limb impairments, first after stroke, then after spinal cord injury and fractured hip.[4] For the leg, the less impaired extremity is not restrained because training under these conditions would simply substitute one degraded pattern of coordination (gait with one leg prevented from having full movement) for another. However, patients are given intensive shaping to promote an improved pattern of walking and other uses of the legs for many hours on each weekday over a period of 3 weeks. The results from 48 patients to date have been virtually as good as for the arm.

The original therapy has been extended to successfully treat deficits in young children with cerebral palsy [104-106] arm use in persons with traumatic brain injury,[107] aphasia,[108, 109] focal hand dystonia,[110] and phantom limb pain.[111] Phantom limb pain is not a motor disorder, but it does seem to be amenable to reduction by increasing the use of the residual stump accomplished by using a functional prosthesis. This embodies one of the main principles of CI therapy,

and the idea for this approach emerged from a CI therapy context.

Constraint-induced movement therapy as a treatment for excess motor disability

CI therapy has been used for the treatment of stroke more frequently than for other motor disorders. It has, therefore, come to be known as a treatment for stroke. As the effective extensions of CI therapy to other disorders indicate, this involves an unnecessarily restrictive view of the nature of CI therapy. CI therapy is a therapy for stroke, but it is not only that. CI therapy is a treatment for "excess motor disability", that is motor disability, that is greater than would seem to be warranted by the organic condition of the individual. This occurs in a large number of conditions that are or had been refractory to treatment. There may, for example, be learned nonuse involved in such conditions as multiple sclerosis, frailty in the elderly, and chronic pain syndromes. There is much that remains to be explored in terms of the applications of CI therapy. Pursuing this approach would be helped greatly if CI therapy was viewed not as a treatment for stroke, but as a treatment for excess motor disability.

Conclusions

CI therapy is beginning to spread at an accelerating pace. There have been more than 150 papers on adult and pediatric CI therapy published to date. To our knowledge all of the studies that have appeared report positive results. Some of the papers report outcomes as large as those obtained in this and related laboratories. However, many studies have results that are significant, but 1/2 to 1/3 as large as those obtained here. The reasons for this disparity are, we believe, two-fold: 1) incomplete or complete lack of use of the "transfer package" of procedures described above, which, though reported in the papers from this laboratory, had been largely unremarked and underemphasized, 2) use of an attenuated protocol. For example, in one study by Van der Lee *et al*.,[73] patients were given hobby-type activities of their choosing in a relaxed accommodating atmosphere. The results were positive but again just 1/3 of what is routinely obtained here.

Our current data suggests that the "transfer package" of techniques that this laboratory had used since the original development work was done [3] is the most important element of CI therapy in producing a treatment effect in the real world environment when used in combination with intensive practice and, paradoxically, it is more important than the intensive practice itself. Thus, the intensive practice may produce improvement in the laboratory/clinic, but if nothing else is done the therapeutic gains will remain largely in the clinic where they can be measured in a laboratory motor test, such as the WMFT. However, they will not transfer importantly to the life situation to improve quality of life or independence, unless appropriate techniques are applied to effect this transfer. We have already shown that use of at least some of the transfer techniques, when used with an ineffective rehabilitation technique, will not produce a treatment effect in a placebo control experiment.[47] The subjects in the placebo group, which was measured by questionnaire to be credible before treatment, kept a daily movement diary, were given the MAL daily, and problem solving was carried out. They did not improve significantly on any test. Thus, intensive training of the more affected arm is a critical aspect of CI therapy, but without the transfer package, there is a reduced effect on real world function.

Our data also imply that the general principles learned about the importance of the transfer components in CI therapy can be applied to other rehabilitation approaches to enhance their real-world effect. There is no reason why the use of the transfer package techniques need be confined to CI therapy.

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