The Behavior-Analytic Origins of Constraint-Induced Movement Therapy: An Example of Behavioral Neurorehabilitation

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Constraint-induced (CI) therapy is a term given to a family of efficacious neurorehabilitation treatments including to date: upper extremity CI movement therapy, lower extremity CI movement therapy, pediatric CI therapy, and CI aphasia therapy. The purpose of this article is to outline the behavior analysis origins of CI therapy and the ways in which its procedures incorporate behavior analysis methods and principles. The intervention is founded on the concept of *learned nonuse*, a mechanism now empirically demonstrated to exist, which occurs after many different types of damage to the central nervous system (CNS). It results from the dramatic alteration of the contingencies of reinforcement that results from substantial CNS damage and leads to a greater deficit than is warranted by the actual damage sustained. CI therapy produces a countervailing alteration in the contingencies of reinforcement. The intervention has been used successfully to substantially improve motor deficits after stroke, traumatic brain injury, spinal cord injury, multiple sclerosis, with cerebral palsy in a pediatric population, and for language impairment in poststroke aphasia. The protocol of CI therapy consists primarily of standard behavior-analytic methods. It produces a marked plastic brain change that is correlated with its therapeutic effect, and therefore provides an example of the way in which behavior change can contribute to a profound remodeling of the brain. CI therapy may be viewed as an example of behavioral neurorehabilitation.

Key words: CI therapy, CI movement therapy, CI aphasia therapy, stroke, central nervous system injury, neurorehabilitation, behavior analysis

Constraint-induced movement therapy (CIMT) is a family of neurorehabilitation treatments developed at

the University of Alabama at Birmingham (UAB). It involves the application of behavior-analytic techniques to the improvement of deficits that result from different types of substantial damage to the central nervous system (CNS), such as stroke, traumatic brain injury, spinal cord injury, multiple sclerosis, cerebral palsy, and other pediatric motor disorders (summarized in Taub & Uswatte, 2009; Taub, Uswatte, & Pidikiti, 1999). The deficits treated are mainly motor in nature but also include verbal behavior in aphasia and phantom limb pain after limb amputation. The first application of CI therapy was to motor deficit after stroke (Taub et al., 1993), and this continues to be the most frequent application. Its efficacy has been demonstrated by a multisite randomized controlled trial (RCT; Wolf et al., 2006), which is rare for the rehabilitation field, and multiple single-site RCTs. There are now well over 300

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CI therapy studies that have reported positive results for improving motor deficit after stroke. Its use is therefore beginning to spread.

CI therapy basically involves the use of operant training techniques in a rehabilitation context. The origin of the therapy is described in publications from this laboratory, but it is not well recognized or understood and is therefore often overlooked, the main reason probably being that there is little familiarity with behavior analysis in the fields associated with neurorehabilitation.

The theoretical roots of CI therapy emerged from principles developed during graduate work at Columbia University with Fred Keller and W. Schoenfeld. The initial laboratory work that led to CI therapy began in the Department of Experimental Neurology in a research institute at the Jewish Chronic Disease Center in Brooklyn, New York. Monkeys received a surgical abolition of somatic sensation from one or both forelimbs, and then were given training based, in part, on operant learning principles. Work continued at the Institute for Behavioral Research (IBR) in Silver Spring, Maryland. The Chairman of the Board of IBR was Joseph V. Brady, who played a leading role in founding behavioral pharmacology. The translation of CI therapy from monkeys to humans was stimulated by Brady's example. CI therapy can be viewed as a type of behavioral neurorehabilitation.

DEAFFERENTATION IN MONKEYS

When somatic sensation is abolished from a single forelimb in monkeys by the serial section of all sensory roots of spinal nerves innervating that extremity, the monkey never again uses the deafferented limb. This is the case even though the motor outflow over the ventral roots of spinal nerves is left intact. This was a classic observation, made

first by Mott and Sherrington (1895) and subsequently replicated (Lassek, 1953; Twitchell, 1954). It formed one of the major pillars underlying Sherrington's formulation of the reflexological position (Sherrington, 1910), which became one of the dominant positions in neurology for the first 70 years of the 20th century. However, we showed that there were two behavioral techniques that could induce a monkey to make use of a single deafferented forelimb.

One technique was training of the deafferented extremity. At first a discrete-trial avoidance conditioning procedure was used. The monkey had to make a simple flexion of the deafferented limb at the sound of a buzzer (Knapp, Taub, & Berman, 1959, 1963) or click (Taub & Berman, 1963, 1968) to avoid an electric shock. When the research shifted to the IBR, shaping was used. It proved to be a particularly effective means of improving the motor deficit of the deafferented extremity. When discrete-trial procedures were used, transfer of limb use from the conditioning chamber to the colony environment was never observed (Taub & Berman, 1963, 1968; Taub, Ellman, & Berman, 1966; Taub, Goldberg, & Taub, 1975; Taub, Williams, Barro, & Steiner, 1978). However, when manual shaping with food reward was employed in subsequent experiments, there was a substantial improvement of movement in the life situation as well (Taub, 1977). The actions shaped included pointing at visual targets (Taub, Goldberg, & Taub, 1975) and prehension in juveniles deafferented on day of birth (Taub, Perrella, & Barro, 1973) and prenatally (Taub, Perrella, Miller, & Barro, 1975) that had never exhibited prehension previously. In both cases, the manual shaping-with-food-reward procedure produced an almost complete reversal of the motor disability, which progressed from total absence of the target behavior to very good (although not normal) behav-

ior. In the case of thumb–forefinger prehension, this took approximately 30 half-hour sessions. The steps involved in the shaping progression are described in Appendix A.

Another technique resulting in use of the deafferented limb was restraint of the intact limb while the deafferented limb was left free (Knapp et al., 1959, 1963; Taub & Berman, 1968). This rendered the animal virtually helpless. However, within several hours of the imposition of restraint, the animal began to use the deafferented extremity extensively. If the restraint was left in place for 1 week, then on removal of the restraint the animal continued to use the limb when the intact limb was not restrained, and that use was permanent. The movements were not normal; they were clumsy because somatic sensation had been abolished, but they were extensive and effective (Taub, 1977, 1980).

Thus, both the training and shaping conditions and the situation in which the intact limb was restrained induced the monkeys to make purposive use of the deafferented extremity. In trying to understand whether these two experimental manipulations involved a common mechanism, it was noted that in the unrestricted colony environment the monkeys were free to use the intact limb to accomplish objectives including those normally carried out by both forelimbs in concert, rather than attempting to coordinate use of the intact forelimb with an impaired extremity. However, both the restraint and the training situation reversed the contingencies of reinforcement. Either the monkeys used the deafferented limb or they were punished: In the training situations, they were either subjected to a noxious electric shock or could not obtain food or water reinforcement when 22 hr hungry or thirsty; in the restraint situation, they were rendered virtually helpless. Consequently, the monkey used the deafferented limb.

This set of results seemed to resolve the enigma posed by the absence of purposive movement by a deafferented limb posed originally by the Mott and Sherrington experiment (1895): Why didn't the monkeys use a single deafferented limb? Sherrington's reasonable answer had been that extremity deafferentation interrupted the afferent limb of spinal reflexes, and it was this that abolished use of the extremity even though motor innervation remained intact. Hence the idea emerged that spinal reflexes were the basic building blocks from which behavior was elaborated, which was the fundamental tenet of Sherringtonian reflexology. This was a pervasive view for decades, whose influence, as the exemplar of the "peripheralist position," extended into a number of behaviorist systems. For example, the second half of the first chapter of Skinner's (1938) *The Behavior of Organisms* is devoted to Sherrington's laws of the reflex. However, the two simple behavioral techniques noted above (and later control experiments) showed that this formulation could not be correct. What then could account for the absence of purposive movement after unilateral forelimb deafferentation? The need to address that salient question led to the formulation of the concept of learned nonuse.

LEARNED NONUSE

Several converging lines of evidence suggested that the nonuse of a single deafferented forelimb in monkeys is a learning phenomenon that involves a conditioned suppression of movement that was termed *learned nonuse* (LNU). The restraint and training techniques appeared to be effective because they overcame LNU (Taub, 1977, 1980; Taub, Uswatte, Mark, & Morris, 2006).

Substantial neurological injury usually leads to a depression of CNS excitability and a consequent reduction

Figure 1. Schematic model for the development of learned nonuse.

or even elimination of the motor or sensory function with which the affected CNS area is associated. Subsequently, a spontaneous recovery of CNS excitability takes place, but this process can require considerable time in both nonhuman and human primates (Taub, 1980, Taub, Heitman, & Barro, 1977). Thus, immediately after surgical deafferentation of a single forelimb, monkeys cannot use that extremity. Efforts to use it often lead to painful and otherwise aversive consequences, such as incoordination and falling, loss of food objects, and in general, failure of any activity attempted with the deafferented limb. Many learning experiments have demonstrated that punishment has the effect of suppressing the behavior that precedes it (Azrin & Holz, 1966; Catania, 1998; Estes, 1944). The monkeys, meanwhile, get along reasonably well in the laboratory environment on three limbs and are therefore reinforced for this pattern of less effective compensatory behavior that, as a result, is strengthened. Thus, the response tendency to not use the affected limb persists and, consequently, monkeys never learn that the limb had become potentially useful several months after surgery. The mechanism

by which LNU develops is depicted schematically in Figure 1.

When the movements of the intact limb are restricted beginning several months or longer after unilateral deafferentation, the situation is changed dramatically. Animals either must use the deafferented limb or cannot with any degree of efficiency feed themselves, locomote, or carry out large portions of their daily activities. This new constraint on behavior increases the tendency to use the deafferented limb, thereby overcoming LNU. Moreover, current ongoing conditions, such as the relative inefficiency of the affected upper extremity compared with the unaffected forelimb, continue to affect the contingencies of reinforcement associated with use of the affected extremity. If the movement-restriction device is removed a short while after the early display of purposive movement, the newly learned use of the deafferented limb will have acquired little strength and is quickly overwhelmed by the well-learned tendency not to use the limb. However, if the movement-restriction device is left on for several days or longer, use of the deafferented limb acquires strength and, then when the device is removed,

Figure 2. Schematic model of mechanism for overcoming learned nonuse.

can compete successfully with the strongly overlearned nonuse of that limb. The counterconditioning of LNU is depicted schematically in Figure 2.

The training situations described in the previous section, just like the restriction of the intact limb, place major constraints on the animals' behavior. In the discrete-trial training situation, if the monkeys do not perform the required response with the deafferented limb, they are either punished by such aversive consequences as falling to the deafferented side, or do not receive food pellets or fluid when hungry or thirsty, respectively. Similarly, during shaping, reward is contingent on making progressively improved movements with the deafferented limb. The monkeys cannot get by using just the intact forelimb as they can in the colony environment. These new sets of conditions, just like the movement-restriction device, constrain the animals to use their deafferented limbs to avoid punishment or obtain reward and thereby induce the use of the deafferented limb. As a result, LNU is overcome.

As noted, use of the deafferented limb does not transfer from the discrete-trial situation to the colony environment. This lack of transfer

may be due to the restriction of training in the conditioning paradigm to a few specific movements within a narrow context, with the result that arm use is not generalized to a variety of movements or situations. The shaping situation, however, is more flexible and free-form; there is freedom for the animal to use many different types of movement and movement strategies to attempt to achieve behavioral objectives that are differentially reinforced. Therefore, what is learned in the shaping situation transfers to the colony environment and even generalizes to movement categories other than those trained. The shaping process appears to provide a bridge from the training to the life situation.

Direct Test of the LNU Hypothesis

An experiment was carried out to test the LNU formulation directly (Taub, 1977, 1980). Movement of a unilaterally deafferented forelimb was prevented immediately after surgery with a restraining device in several animals so that they could not attempt to use that extremity for a period of 3 months. Restraint was begun while the animals were still under anesthesia. The reasoning was that by preventing animals from

using the deafferented limb during the period before spontaneous recovery of function had taken place, they would not learn that the limb could not be used. LNU of the affected extremity should therefore not develop. In addition, the intact limb was restrained for the same period so that the animals could not receive reinforcement for use of that extremity alone. In conformity with the prediction, which without the LNU formulation would have been counterintuitive, the animals were able to use their deafferented extremity in the free situation after the restraint was removed 3 months after surgery, and this was permanent, persisting for the rest of the animals' lives.

Suggestive evidence in support of LNU was also obtained during deafferentation experiments carried out prenatally (Taub et al., 1973; Taub, Perrella, Miller, & Barro, 1975). Life in the physically restrictive uterine environment imposes major constraints on the ability to use the forelimbs for such purposes as altering body orientation to adjust for shifts in maternal position. Although use of the fetal limbs is not prevented entirely, their movement is restricted in utero, thereby functioning like a sling or a padded mitt in a human CI therapy experiment (to be discussed below). Four animals were studied who had received unilateral forelimb deafferentation by an intrauterine approach during the prenatal period; three when two-thirds the way through gestation and one when two-fifths the way through gestation. These animals exhibited functional use of the deafferented extremity from the first day of extrauterine life, in contrast to animals deafferented after maturity that did not use the affected extremity unless given training of the deafferented arm or restraint of the intact arm. At birth, the prenatally deafferented animals all used that limb for postural support during "sprawling" and for pushing into a sitting position. Sub-

sequently, although the intact limb was never restrained, the ability to use the deafferented limb continued to develop as the animals matured until it was similar to the extensive (though impaired) use of a limb when animals were given limb deafferentation as adults. This, then, constitutes a second line of evidence that supports the LNU formulation.

Translation of the LNU Model from Deafferentation in Monkeys to CNS Injury in Humans

The results of the experiments described above show that simple behavior-analytic techniques employed in discrete-trial or shaping contexts resulted in the conversion of a useless deafferented upper extremity to a limb that could be used extensively. Later, it became apparent that this could be viewed as a rapid and substantial rehabilitation of movement (although that term was not usually applied to primates at the time). Thus, it appeared possible that the same two techniques might be appropriately used to rehabilitate motor disability in humans. An implication of the concept of LNU as the outcome of the punishments and rewards that result from early post-injury attempted use of an impaired extremity is that it should, in principle, operate after any CNS injury when the initial effect is to temporarily abolish movement, regardless of the injury's location or extent. There was also no a priori reason to suppose that it would not operate in humans as well as monkeys. Specifically, stroke often leaves patients with an apparently permanent loss of function in an upper extremity, although the limb is not paralyzed. In addition, the motor impairment is preponderantly unilateral. These factors are similar to those that pertain after unilateral forelimb deafferentation in monkeys. Therefore, it seemed reasonable to formulate a protocol that simply transferred the behavior-analytic techniques used for overcoming LNU of a deafferented

limb in monkeys to humans who had experienced a cerebrovascular accident (Taub, 1980; Taub, Uswatte, Mark, et al., 2006).

At the time that the LNU mechanism was proposed (Taub, 1977; Taub & Berman, 1968) and its applicability to humans suggested (Taub, 1980), there had been little attempt to translate basic research findings in neuroscience to pathological conditions in humans, and none as far as I know in neurorehabilitation. However, given a belief in the generality of the laws of behavior for all mammals, and the example of Brady's pioneering use of operant conditioning techniques to evaluate the effect of pharmacological agents on behavior in animals and subsequent use of the resultant data as a basis for estimating the possible effects of those agents on humans, the translation of what was to be called CI therapy from monkeys to humans seemed straightforward. The nervous systems might be different, but the principles of behavior were the same.

A series of studies was then carried out starting in 1986 (Taub et al., 1993) in which chronic stroke patients were trained in the laboratory, initially for 6 hr per day with an hour of interpolated rest for 10 consecutive weekdays; later it was found that 3 hr per day of training for 10 consecutive weekdays was equally effective (Taub et al., 1999). In addition, the less affected arm was restrained for a requested 90% of waking hours (i.e., both in the laboratory and at home). A timer was inserted into the restraining device that was activated by contact with the hand so there was an objective record of the amount of time the patient was compliant with the instruction to wear the restraint outside the laboratory.

The primary training technique employed was shaping (Taub et al., 1994), which had been so successful with deafferented monkeys. In addition, a set of behavioral techniques

termed the *transfer package* (TP; described below) was also employed to promote transfer of the improvements in motor ability achieved in the laboratory to the life situation. All subjects in the studies were at least 1 year poststroke ($M = 4.4$ years). The subjects in the early studies had upper extremity motor deficits that could be characterized as mild or moderate, which actually involves a substantial deficit compared to normal motor function. Two of the early studies employed placebo control groups (Taub et al., 1993; Taub, Uswatte, King, et al., 2006). The results showed that the treatment produced very large improvements in the patients' ability to use the more affected arm, just as in the case of the deafferented monkeys.

To date, several hundred subjects with mild or moderate stroke symptoms have been treated with CI therapy in the UAB laboratory. The magnitude of the treatment change can be evaluated with effect size (ES) statistics. By convention, a d' statistic of 0.47 is considered large (Cohen, 1988). The ES for the treatment change on our measure of actual use of the more affected arm in the life situation ranged from a d' of 2.1 to 4.0 ($M = 3.3$), depending on the experiment. In a key experiment (Taub, Uswatte, King, et al., 2006), the amount of real-world spontaneous arm use compared to before stroke increased from 9% prior to treatment to 52% after treatment, a more than five times improvement. Similar results have been obtained in other experiments from this laboratory.

The deafferented monkeys in the experiments in which the CI therapy rehabilitation techniques were developed were all in the chronic phase, more than 1 year after their surgical procedures. It therefore seemed that these techniques should work well with patients in the chronic phase if the translation of the approach was efficacious at all. However, the general, essentially axiomatic belief in

the rehabilitation field at the time was that the impaired movement of a stroke victim could not be modified in the chronic phase, no matter what technique was employed. This view still has considerable force. Even today, after 25 years of research and clinical practice, a substantial percentage of the chronic patients who come to the UAB CI therapy clinic for treatment have been told by their physicians and therapists that there is nothing that can be done to improve their motor deficit.

Naming the Treatment

The movement-restriction and training situations share a common feature: They both are powerful means of inducing use of the more affected arm. One procedure physically restrains the less affected arm so that the individual, whether monkey or human, must use the more affected extremity to avoid being rendered helpless and thereby subject to multiple sources of punishment. The other method, training, induces use of the more affected arm by altering the contingencies of reinforcement so that it must be used in order to obtain reinforcement or, in monkeys, to avoid punishment. Thus, both procedures constitute constraints that promote use of the more affected arm by a major alteration of the contingencies of reinforcement. Although the name is accurate, the use of the term *constraint* in the title of the therapy has turned out to be confusing. The rehabilitation field was not used to thinking of training as imposing a constraint on behavior. Instead, the large majority of professionals interpreted the focal word in the name of the therapy as being an alternate way of saying "restraint," so that the general impression arose that restraint of the less affected arm was the central and most important feature of the therapy. As indicated below, that is very far from being true; physical restraint of the less

affected arm can be dispersed with entirely in achieving a maximal result if the training conditions are arranged appropriately. Recently, the field has begun to accept that the word *constraint* is meant to include training. The use of this term is consistent with Timberlake's analysis (1993) of reinforcement as constituting "constraint of a functional *causal system* comprised of multiple interrelated causal sequences, complex linkages between causes and effects and a set of initial conditions" (p. 105).

COMPONENTS OF CI THERAPY

As noted, the CI therapy protocol incorporates a number of procedures that are commonly used in behavioral approaches to modifying behavior. First, shaping is used in the laboratory so that movement of the more impaired extremity is brought to more closely approximate that of individuals who have not suffered a neurological injury. In addition, and perhaps most important, a set of behavioral techniques (the TP) is used to increase the frequency with which the more affected extremity is used spontaneously in the performance of activities in the real-world environment. The objective of the TP is to effect transfer or generalization of gains that are made in the laboratory to the life situation and to then make them habitual. For the interested reader, further description of the methods employed in the CI therapy protocol may be found in the following papers: Taub et al. (1994); Morris and Taub (2008); Taub, Uswatte, Mark, et al. (2006). An extended case study is attached to Morris and Taub (2008) as an appendix.

Training of the More Affected Extremity: Shaping

A standard approach to shaping is employed in which a behavioral objective is approached in small steps by successive approximations (Morgan, 1974; Panyan, 1980; Skinner,

1938, 1968). A task is made more difficult in accordance with a patient's progressively increasing motor capabilities; alternatively, the requirement for speed of performance is incrementally increased (Taub et al., 1994). A battery of over 100 shaping tasks has been developed with a preliminary written shaping plan for each. (See Appendix B for an enumeration of the principles used in shaping and a description of sample shaping tasks and generic shaping plans for each.) Each subject's program is individualized by selecting approximately 12 tasks from the larger battery and creating new ones when it seems that they would be advantageous for that individual. The selection of tasks for each person depends on (a) specific joint movements that exhibit the most prominent deficit; (b) joint movements that project staff believe have the greatest potential for improvement; and (c) the subject's preference among tasks that have a similar potential for producing specific improvements. Prior to treatment, a patient's functional movement capacity and the nature of his or her impairment are determined on an individual joint movement basis during a systematic evaluation and are recorded on a standardized form.

In developing the battery, care was taken to select tasks that can be broken down into subtasks and can be objectively measured even when only small improvements occur. Each activity is usually practiced for a set of 10 trials (30 s each) and explicit, immediate feedback is provided regarding the subject's performance on each trial. When the level of difficulty of a shaping task is increased, the parameter selected for change relates to the participant's movement problems, as determined in the course of training by the therapist. For example, if the participant's most significant movement deficits are with thumb and finger dexterity and an object-flipping task is used, the diffi-

culty of the task would be increased by making the object progressively smaller if the movement problem is in thumb adduction and finger flexion (i.e., making a pincer grasp); in contrast, if the movement problem involves thumb abduction and finger extension (i.e., releasing a pincer grasp), the difficulty of the task would be increased by making the object progressively larger. As another example, if there is a significant deficit in elbow extension and a pointing or reaching task is used, the shaping progression might involve placing the target object at increasing distances from the participant.

In the shaping progression, the amount of task-difficulty increase is such that it is likely that the participant will at each step be able to accomplish the task, although with effort. This incremental increase in difficulty often makes it possible to achieve a given objective that might not be attainable if several large increments in motor performance were required. Coaching is provided liberally throughout all shaping procedures, including the usual techniques of cuing and prompting. Modeling is also employed as needed. Verbal reinforcement is provided enthusiastically at frequent intervals (e.g., "that's excellent," "first class," "keep trying"). Criticism is never made; poor performance is generally ignored and further efforts at improvement are encouraged.

The Transfer Package

One of the overriding goals of CI therapy is to achieve transfer of therapeutic gains made in the research or clinical setting to the participant's real-world environment. It could almost be said that if what patients learn in the clinic is not generalized to the life situation, then rehabilitation is not really being accomplished. When CI therapy research was begun, there were no methods or tests being used to assess

how or whether a patient was using a stroke-affected extremity in the life situation. However, a behavior-analytic approach made it intuitively obvious that a primary goal of rehabilitation treatment had to be the development of methods to induce use of the more affected arm in the life situation and then monitoring that use. This was the case independent of considerations relating to LNU, although these certainly reinforced the need for real-world monitoring of behavior; hence, the development of the Motor Activity Log (MAL; Taub et al., 1993; Uswatte, Taub, Morris, Light, & Thompson, 2006; Uswatte, Taub, Morris, Vignolo, & McCulloch, 2005). The MAL results have been confirmed by accelerometer data from transducers worn on both arms for 3 days before and 3 days after the end of treatment (Uswatte, Miltner, et al., 1997, 1998; Uswatte, Spraggins, Walker, Calhoun, & Taub, 1997). The TP consists of the following techniques.

Behavioral contract. At the outset of treatment, the therapist negotiates a contract with the patient (and separately with the caregiver, if one is available) in which agreement is reached that the patient will use his or her more impaired extremity as much as possible outside the laboratory. Specific activities during which the patient will practice using the more impaired extremity are discussed, agreed on, and written down. At the end of this process, the negotiated document is signed by the patient (or caregiver), the therapist, and a witness to emphasize the character of the document as a contract.

Daily home diary. During treatment, the patients catalogue on a daily diary form how much they have used the more affected arm for the activities specified in the behavioral contract. The diary is kept for the part of the day spent outside the laboratory and is reviewed in detail each morning with the therapist.

Daily administration of the MAL. The MAL collects information about use of the more affected extremity in 30 important activities of daily living (ADL) in all major domains of everyday life. The daily repetition of this detailed report, which is probed and verified in a number of ways, serves to keep the patient's attention on the use of the more affected extremity outside the laboratory or clinic.

Problem solving. During administration of the MAL, the therapist helps patients analyze, circumvent, or overcome any barriers to using the more impaired arm in the life situation. For example, if the patient is concerned about spilling liquid from a glass, the therapist may suggest filling the glass only half way. If patients use the less affected arm for manipulating eating utensils in a restaurant because they are embarrassed by dropping food from a utensil onto a table, the therapist may suggest not going to a restaurant during the course of the treatment.

Home skill assignments. During treatment, subjects are asked to carry out at home five difficult (for them) ADL tasks and five easy tasks using the more affected arm, selected daily from a list of approximately 200 (e.g., brush teeth, wash hands, use TV remote). In addition, patients are asked to spend 15 to 30 min at home on a daily basis repetitively performing with their more affected arm specific upper extremity tasks that are similar to those performed in the laboratory or clinic. The tasks are chosen for practice to improve the most significant movement deficits. Subjects check off the ADL activities and exercises carried out on a form provided to them each day.

Weekly telephone contacts with patients. For the first month after the end of treatment, the MAL is administered by phone, and problem solving is carried out.

Posttreatment practice. Toward the end of treatment, an individualized

posttreatment home practice program of approximately 100 tasks is developed and given to the patients. They are encouraged to perform two or three tasks for 10 min daily after the treatment period, but to also continually focus attention on using the more affected arm in ADL whenever possible.

In most physical rehabilitation regimens, there is a passive element; the patient is responsible for carrying out the therapist's instructions primarily or only during treatment sessions. 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 sessions but also at home during the treatment period and for the first month after laboratory therapy has been completed (and afterward, although this is not monitored). The TP makes patients responsible for adhering to the requirements of the therapy, and therefore in effect they become responsible for their own improvement.

The TP is the main way in which CI therapy differs from other rehabilitation procedures. Its critical importance in producing a large treatment effect was recently demonstrated (Gauthier et al., 2008). Twenty subjects were given the full CI therapy protocol including the TP. A second group received the same treatment in the laboratory, but none of the TP techniques were administered. Both groups showed a significant increase in the amount of spontaneous use of the more affected arm in the life situation, but the improvement of the CI therapy TP group was approximately 2.5 times as great as the improvement recorded for the non-TP group.

Less Affected Limb Restraint

In initial experiments, limb restraint was achieved using a rigid resting hand splint and a sling (Taub et al., 1993). However, this level of restraint was found to be unnecessary, and currently a mitt with a

heavily padded palmar surface is employed. It prevents the use of the fingers and hand for a target of 90% of waking hours and gives as good results as the resting hand splint and sling arrangement. This was, and still is, generally considered to be the signature if not the differential component of CI therapy. This is unfortunate, because there is evidence that less affected limb restraint is not necessary or even important for producing a maximal treatment effect (Taub et al., 1999; Uswatte, Taub, Morris, Barman, & Crago, 2006). However, although less affected limb restraint is not necessary with adult humans, it is important for monkeys and young children (pediatric CI therapy), who have less capacity for self-suppression of behavior and deferral of reinforcement. Even in adult humans, when restraint of the less affected arm is used, it may make some contribution to promoting a long-lasting increase in use of the more affected arm in the home. This is a clinical opinion not based on a controlled study, but it is thought to be a sufficiently real possibility that use of the restraining mitt during the treatment period is still retained in the UAB laboratory and clinic.

CI THERAPY IN OTHER LABORATORIES

In the UAB laboratory, over 400 patients with stroke have been given one variant or another of CI therapy and all but three of these patients have demonstrated substantial improvement in motor ability. There have also been over 300 papers from other laboratories on adult and pediatric CI therapy published to date. To our knowledge all but two of the studies have reported positive results. In particular, CI therapy was the subject of a multisite randomized controlled trial (Wolf et al., 2006), the gold standard of proof of efficacy in medical fields. The results were positive.

With respect to magnitude of the treatment effect, this laboratory's results have been replicated with patients with chronic stroke in published studies from four laboratories in which therapists were trained in this laboratory and monitored twice yearly (Dettmers et al., 2005; Kunkel et al., 1999; Miltner, Bauder, Sommer, Dettmers, & Taub, 1999; Sterr et al., 2002). Some of the other papers report outcomes as large as those obtained in this and related laboratories; however, many studies report results that are significant but only one half to one third as large as those obtained here. The likely reasons for this disparity are twofold: (a) There was incomplete or complete lack of use of the procedures of the transfer package, which, although reported in the papers from this laboratory, had been largely ignored. As noted above, we have replicated the reduced treatment effect obtained by others by duplicating everything that is normally done in treatment here except implementation of the TP (Gauthier et al., 2008). (b) A protocol with attenuated intensity (tasks or movements per unit time) was used, such as in a study by van der Lee, Beckerman, Lankhorst, and Bouter (1999).

The techniques of the TP have often been used separately by individual therapists, but rarely systematically and never combined together in an attempt to make patients' compliance with the protocol outside the laboratory critical so that they become responsible for their own improvement. Even when the behavioral techniques of the TP and intensive training are used, CI therapy does not constitute a "cure" for the motor deficit following stroke. On a group basis, patients in studies from this laboratory with mild or moderate deficits regain approximately 50% of the amount of use of the more affected arm they had before stroke from an initial level of approximately 10%. This is a five

times difference and a substantial improvement, but it is not a cure. There is still considerable room for further improvement. CI therapy can also produce a large treatment effect (although not as large) in patients with more severe motor deficits than those in the mild or moderate deficit category treated in most CI therapy studies, including patients with initially plegic hands (see below).

APPLICATIONS OF CI THERAPY

The LNU formulation predicts that any substantial damage to the CNS may lead to LNU. Thus, CI therapy, which initially had been found to be helpful in overcoming LNU in stroke patients with mild or moderate motor deficits, should be applicable to motor limitations more severe than those originally worked with, to deficits other than motor impairment of the upper extremity, and to other types of neurological conditions.

Lower Functioning Patients

Most of the patients treated at the UAB laboratory could be characterized as having deficits that were mild or moderate, defined as having the ability to extend 20° at the wrist and 10° at each of the fingers. Experiments have also been carried out with patients with moderate and moderately severe deficits (Taub et al., 1999). Their treatment change was somewhat less than for higher functioning patients (e.g., increases of approximately 400% and 350% for patients with moderate and moderately severe deficits, respectively, compared to approximately 500% for patients with mild or moderate deficits), but the treatment changes were nevertheless very large. Most recently, work has been carried out with patients with useless, plegic hands that were initially fisted. Conventional physical rehabilitation procedures, including some from neurodevelopmental treatment (NDT) and

functional electrical stimulation (FES) were used to maintain the fingers in a sufficiently extended and aligned position so that CI therapy training procedures could be carried out. At the end of treatment, the patients exhibited a 186% improvement in the real-world use of the more affected arm. This arm had been converted into a useful “helper” in the life situation (e.g., keeping a piece of paper in place while writing with the less affected hand, holding a toothpaste tube while unscrewing the cap, bearing body weight for bed mobility).

We estimate that CI therapy is applicable to at least 50% of the chronic stroke population with motor deficit, perhaps more. This is a very large group of individuals; an estimated 4,000,000 people in this country have had strokes in previous years, and in addition, there are more than 3,000,000 people who have had had traumatic brain injuries. Very few of the more than 50% of these individuals with persisting motor deficit are given any rehabilitation treatment. Thus, CI therapy could potentially improve the quality of life and increase the independence of a large number of currently untreated persons with brain damage.

Lower Extremity

An obvious target for transfer of the CI therapy techniques developed for the upper extremity was the more affected lower extremity of stroke patients. The 38 chronic stroke patients treated to date have had a wide range of disability extending from being close to nonambulatory to having moderately impaired coordination (Taub et al., 1999). The treatment (lower extremity CI therapy) consists of massed or repetitive practice of lower extremity tasks (e.g., overground walking, treadmill walking with and without a partial body weight support harness, sit-to-stand, lie-to-sit, step climbing, walk-

ing over obstacles, various balance and support exercises) for at first 6 and then 3 hr per day with interspersed rest intervals as needed over 3 weeks and 0.5 hr per day devoted to TP procedures. Task performance is shaped as in the upper extremity protocol. Training is enhanced through the use of force feedback (limb load monitor) and limb displacement (joint angle/electric goniometer) feedback devices. No restraining device is placed on the less affected leg. The lower extremity procedure is considered to be a form of CI therapy because of the use of the TP, the strong massed practice and shaping element, and because the reinforcement of adaptive patterns of ambulation over maladaptive patterns in our training procedure constitutes a significant general form of constraint. Control data were provided by a general fitness control group that received the same battery of lower extremity tests as the treatment subjects. The ES of the change in real-world performance due to the treatment was very large, but not quite as large as for the upper extremity. The improved lower extremity use was retained without any decrement for the 2 years that were tested.

Conditions Other Than Stroke

The CI therapy protocol has been applied with success, as noted at the beginning of the article, to traumatic brain injury (Shaw, Morris, Uswatte, McKay, & Taub, 2003), upper and lower extremity in multiple sclerosis (Mark, Taub, Bashir, et al., 2008; Mark, Taub, Uswatte, et al., 2008), cerebral palsy and pediatric motor disorders of neurological origin across the full range of age from 1 year old through the teenage years (Taub, Griffin, et al., 2006; Taub et al., 2007, 2011; Taub, Ramey, DeLuca, & Echols, 2004), focal hand dystonia in musicians (Candia et al., 1999, 2002), and, though not a motor

disorder, phantom limb pain after amputation (Weiss, Miltner, Adler, Bruckner, & Taub, 1999).

Aphasia. The application of CI therapy that is probably of greatest interest from a behavior-analytic point of view is to aphasia, especially the work being done currently. Aphasia arises as a consequence of focal brain damage, often in association with stroke. There is as much LNU after stroke associated with the verbal behavior of aphasics as there is with motor deficit. Because of halting and slow verbal production and incomplete understanding, speech becomes very effortful and often embarrassing. The person compensates by greatly reducing attempts to speak or remaining silent entirely and by using gestures and other nonverbal means of communication. In addition, when there is difficulty in understanding speech, many aphasics with receptive problems (Wernicke's aphasia, fluent aphasia) simply tune out. Thus, the demonstration that motor deficits are modifiable in chronic stroke raised the possibility that verbal impairment could also be rehabilitated by an appropriate modification of the CI therapy protocol. The LNU formulation predicted that this was a strong possibility. In the first studies by Pulvermüller, Taub, and coworkers (Pulvermüller et al., 2001; Taub, 2002), aphasic patients with chronic stroke who had previously received extensive conventional speech therapy and had reached an apparent maximum in recovery of language function were induced to talk and improve their verbal skills for 3 hr each weekday over a 2-week period. The intervention was termed constraint-induced aphasia therapy (CIAT I). The constraint was imposed by the contingencies of reinforcement in the shaping paradigm that was used; there was no physical restraint, although as noted, physical restraint is not necessary to obtain a good result with CIMT. Groups of three patients and

a therapist participated in a language card game (Pulvermüller, 1990; Pulvermüller & Schonle, 1993). The exercise resembles the child's card game "Go Fish." A participant asks one of the other players if they have in their hand a card with a specific pictured object to match one in their own. If they do, the requester can meld those cards. Participants win the game if they meld each of the cards they were dealt so that none are left. The difficulty of the required request by each patient is progressively increased in small steps (i.e., shaped) along several dimensions: number of words in the request (or response to it), number of formulas of politeness, precision of patient's card description (animal, pet, dog), complexity of card depiction (dog, two dogs, one red and one blue dog), and grammatical correctness.

CIAT I patients in the initial RCT improved much more than patients who received conventional aphasia therapy. This study has since been replicated (Bhogal, Teasell, & Speechley, 2003; Kirmess & Maher, 2010; Maher et al., 2006; Meinzer et al., 2004, 2007). Following a positive evaluation of a committee appointed by the American Speech and Hearing Association (Raymer et al., 2008), CIAT I is now beginning to spread. The results of the CIAT I protocol have been positive; however, the intervention was only an incomplete translation of CIMT. CIMT produced an improvement of approximately 500% in real-world use of the more affected extremity of chronic stroke patients with mild to moderate motor deficit in one experiment (Taub, Uswatte, King, et al., 2006). Other experiments from this laboratory have reported treatment effects of similar size. Aphasic patients given CIAT I showed an improvement of 30% in real-world verbal behavior. This is a large treatment effect compared to conventional speech language therapies, but it is very small compared to the results produced by

CIMT. Consequently, to determine whether this large difference was the result of an incomplete translation of the CI therapy protocol employed in the UAB laboratory with motor deficits to the treatment of language impairment, the initial aphasia treatment protocol (CIAT I) was modified to more closely resemble the CIMT protocol.

In the restructured and enhanced protocol (CIAT II), use of behavior-analytic procedures was increased and emphasized. Revisions involved addition of new exercises, including the final exercise, considered to be the most important, in which everyday verbal interactions are simulated and modeled. In addition, a TP parallel to that used in CIMT was introduced, there was increased emphasis on the shaping of responses, and the primary caregiver was trained as an alternate therapist so that the training begun in the laboratory could be continued at home, both during and after formal training.

To date, only four patients have been treated with the new protocol. However, their results have far exceeded those obtained with CIAT I and are comparable to the results obtained with CIMT. With CIAT I, as noted, there was a 30% improvement in real-world verbal behavior; for the recent patients, the mean improvement was 537%, which is approximately 18 times greater than for CIAT I and roughly equivalent to the treatment effect for CIMT. Of additional interest is the fact that at 6-month follow-up, the patients showed no loss in retention; instead, the verbal behavior scores increased substantially to a 643% improvement over pretreatment scores. This increase appears to be attributable to the continuation of training by the caregivers in the real-world environment.

CI THERAPY AND BRAIN PLASTICITY

As noted, overcoming LNU is one of the mechanisms by which CI therapy achieves its therapeutic ef-

fect. Another important mechanism relates to the fact that CI therapy produces large plastic changes in the structure and function of the brain.

Starting in the 1980s, Merzenich and collaborators showed in monkeys that a decrease or increase in the amount of use of a body part or a sensory function decreased or increased the size of the brain region that represented that function (e.g., Jenkins, Merzenich, Ochs, Allard, & Guic-Robles, 1990; Merzenich et al., 1983). This phenomenon was originally termed *cortical reorganization* and is now called *brain plasticity* or *neuroplasticity*. In the 1990s, Taub and collaborators in Germany showed that neuroplastic cortical reorganization occurred in humans, and that it had functional significance in that it could affect movement, behavior, and the quality of sensory experience (e.g., Elbert, Pantev, Wienbruch, Rockstroh, & Taub, 1995; Flor et al., 1995).

A substantial number of studies have now shown that CI therapy produces a large neuroplastic cortical reorganization in humans with stroke-related paresis of an upper limb. This was first demonstrated by Nudo, Wise, SiFuentes, and Milliken (1996) in an animal model of CI therapy. Subsequently, Liepert, Bauder, Miltner, Taub, and Weiller (2000) used focal transcranial magnetic stimulation (TMS) to map the area of the motor cortex that controls an important muscle of the hand (abductor pollicis brevis) in 15 patients with a chronic upper extremity 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 patients' amount of arm use in the home over a 2-week treatment period. Over the same interval, the cortical region from which electromyography responses of the abductor pollicis brevis muscle could be elicited by TMS was greatly increased, and both the clinical effect and the alteration in

brain function persisted for the 6 months tested. CI therapy had led to an increase in the excitability and recruitment of a large number of neurons in the innervation of movements of the more affected limb adjacent to those originally involved in control of the extremity prior to treatment. The effect was sufficiently large that it represented a return to normal size of the motor output area of the abductor pollicis brevis muscle on the infarcted side of the brain, although it was the size of excitable cortical area that had become normal, not its function; the affected hand, though much improved after CI therapy, was not normal in function. In another study, Kopp et al. (1999) carried out dipole modeling of steady-state movement-related cortical potentials (EEG) of patients before and after CI therapy. We found that 3 months after treatment the undamaged motor cortex ipsilateral to the affected arm, which normally controls movements of the contralateral (less affected) 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 the sustained increase in more affected arm use in the life situation produced by CI therapy over the 3-month follow-up period. This experimental evidence that CI therapy is associated with substantial changes in brain activity has been confirmed by convergent data from two other neurophysiological studies that used two additional techniques in association with the administration of CI therapy. Bauder, Sommer, Taub, and Miltner (1999) showed that there is a large increase in the amplitude of the late components of the Bereitschaftspotential (a movement-related cortical potential) after CI therapy, suggesting that an enhanced neuronal excitability is induced in the damaged hemisphere; this is consistent with the results of Liepert et al. (2000). We also found that after CI therapy there was a large

increase in the activation of the usually weakly active healthy, ipsilateral hemisphere with more affected hand movement in confirmation of the findings of Kopp et al. (1999). In addition, Wittenberg et al. (2003) found in a positron emission tomography study that before CI therapy there was a larger activation in multiple areas of the brain with more affected arm movement than in healthy control subjects. This excessive activation diminished after CI therapy. The preliminary interpretation of this result is that less effort is required to produce movements after CI therapy than before treatment.

Since these initial studies, there have been approximately 20 other studies that have demonstrated an alteration in brain function associated with a CI therapy-induced improvement in movement after CNS damage. By providing a physiological basis for the treatment effect reported for CI therapy, these results have tended to increase confidence in the clinical results.

The studies described to this point show that alterations in limb use can alter the function and organization of specific brain regions, but until recently there was no evidence that environmental stimuli could measurably alter brain structures in adult humans. It has now been shown that seasoned taxi drivers have significantly expanded hippocampi (Maguire et al., 2000), jugglers acquire significantly increased temporal lobe density (Draganski et al., 2004), and thalamic density significantly declines after limb amputation (Draganski et al., 2006). Moreover, in an animal model of stroke, CI therapy combined with exercise reduced brain tissue loss associated with stroke (DeBow, Davies, Clarke, & Colbourne, 2003). Accordingly, structural imaging studies became a logical next step toward understanding whether there are anatomical changes following the administration of CI therapy in humans and whether these

Figure 3. Cortical surface-rendered images of changes in gray matter. Gray matter increases displayed on a standard brain for (a) participants who received the CI therapy transfer package and (b) those who did not. Surface rendering was performed with a depth of 20 mm. Bar values indicate t statistics ranging from 2.2 to 6.7.

are correlated with clinical improvements. Moreover, anatomical studies that make use of structural MRI have advantages over fMRI studies, including the fact that no task is carried out during scanning so that there is no need to exercise experimental control over the topography and force of task-related movements.

Longitudinal (pre- vs. posttreatment) voxel-based morphometry was performed on the brain scans of subjects enrolled in our study of the contribution made by the TP to CI therapy outcome (Gauthier et al., 2008). It was found that structural brain changes paralleled changes in amount of use of the impaired extremity for activities of daily living. Groups receiving the TP showed profuse increases in gray matter tissue in sensorimotor areas on both sides of the brain (Figure 3) as well as in bilateral hippocampi. In contrast, the groups that did not receive the TP showed relatively small improvements in real-world arm use and failed to demonstrate gray matter increases.

The research just reviewed makes it clear that behavior and sensory experience are involved in a fundamental feedback loop that keeps remodeling the nervous system. The relation of the nervous system and behavior is not a one-way street; the nervous system is involved in a process of continual plastic change throughout the life span based on feedback from the environment and from a person's own behavior. In addition, CI therapy appears to harness this life-long plasticity of the nervous system to produce an improvement in movement and language after damage to the nervous system.

CONCLUSION

It might be a fitting end to this story of my journey into the world of clinical treatment to recount the events associated with a grand rounds I gave just before attempting the translation of the research with deafferented monkeys to humans after CNS damage. The talk was in a department of physical medicine

and rehabilitation. I described the work with primates in the context of a possible translation to humans, although the latter was implied and not specifically stated. The chairman of the department, who was a prominent clinician and rehabilitation investigator, sat quietly through my talk but with a frigid expression. After I was finished, he said with progressively increasing volume, "Are you trying to tell me that you have a *behavioral* intervention that you think will improve the symptoms of a *neurological* lesion?" I saw that I was on dangerous ground and so I said, "Well, no"; but that, of course, was what I had been implying for the past hour. I paused for a while and then said as mildly as I could, "But after all, isn't that what physical therapy is?" That was a mistake. He sputtered a few words, which I didn't catch, while his face quite literally began purpling. However, to his credit, after the first experiment was completed and the report appeared in print, he changed his opinion and became a strong and valuable supporter. This pretty well sums up the way in which the rehabilitation community has reacted to CI therapy. At first, there was a strong bias against a treatment based on behavior analysis; few members of the rehabilitation community had any familiarity with behavior analysis or had even heard of it. However, as the evidence began to mount and attempts at replication were successful, attitudes began to change. With the success of the multisite RCT cited above, and the fact that CI therapy produced substantial plastic structural changes in the brain, the case had essentially been made. Use of CI therapy is still not by any means universal, probably in part because of insurance reimbursement problems due to the duration and therefore expense of the treatment. However, even with that, the treatment is beginning to spread, especially in modified forms that are more readily reimbursed by insurance. In addition,

as I understand it, schools of physical and occupational therapy are beginning to teach CI therapy and at least some of the principles of behavior analysis. Behavior analysis has thus begun to make an appearance on the stage of neurorehabilitation.

REFERENCES

- Azrin, N. H., & Holz, W. C. (1966). Punishment. In W. K. Honig (Ed.), *Operant behavior: Areas of research and application* (pp. 380-447). New York, NY: Appleton-Century-Crofts.
- Bauder, H., Sommer, M., Taub, E., & Miltner, W. H. R. (1999). Effect of CI therapy on movement-related brain potentials [Abstract]. *Psychophysiology*, 36 (Suppl. 1), S31.
- Bhagal, S. K., Teasell, R., & Speechley, M. (2003). Intensity of aphasia therapy, impact on recovery. *Stroke*, 34, 987-993.
- Candia, V., Elbert, T., Altenmüller, E., Rau, H., Schäfer, T., & Taub, E. (1999). Constraint-induced movement therapy for focal hand dystonia in musicians. *Lancet*, 353, 42.
- Candia, V., Schafer, T., Taub, E., Rau, H., Altenmüller, E., Rockstroh, B., et al. (2002). Sensory motor retuning: A behavioral treatment for focal hand dystonia of pianists and guitarists. *Archives of Physical Medicine and Rehabilitation*, 83, 1342-1348.
- Catania, A. C. (1998). *Learning* (4th ed.). Upper Saddle River, NJ: Prentice Hall.
- Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Hillsdale, NJ: Erlbaum.
- DeBow, S. B., Davies, M. L. A., Clarke, H. L., & Colbourne, F. (2003). Constraint-induced movement therapy and rehabilitation exercises lessen motor deficits and volume of brain injury after striatal hemorrhagic stroke in rats. *Stroke*, 34, 1021-1026.
- Dettmers, C., Teske, U., Hamzei, F., Uswatte, G., Taub, E., & Weiller, C. (2005). Distributed form of constraint-induced movement therapy improves functional outcome and quality of life after stroke. *Archives of Physical Medicine and Rehabilitation*, 86, 204-209.
- Draganski, B., Gaser, C., Busch, V., Schuierer, G., Bogdahn, U., & May, A. (2004). Changes in grey matter induced by training. *Nature*, 427, 311-312.
- Draganski, B., Moser, T., Lummel, N., Gänssbauer, S., Bogdahn, U., Haas, F., et al. (2006). Decrease of thalamic gray matter following limb amputation. *Neuroimage*, 31, 951-957.
- Elbert, T., Pantev, C., Wienbruch, C., Rockstroh, B., & Taub, E. (1995). Increased cortical representation of the fingers of the left hand in string players. *Science*, 270, 305-307.

- Estes, W. K. (1944). An experimental study of punishment. *Psychological Monographs*, 57(Serial No. 263).
- Flor, H., Elbert, T., Knecht, S., Wienbruch, C., Pantev, C., Birbaumer, N., et al. (1995). Phantom limb pain as a perceptual correlate of massive reorganization in upper limb amputees. *Nature*, 375, 482–484.
- Gauthier, L. V., Taub, E., Perkins, C., Ortmann, M., Mark, V. W., & Uswatte, G. (2008). Remodeling the brain: Plastic structural brain changes produced by different motor therapies after stroke. *Stroke*, 39, 1520–1525.
- Jenkins, W. M., Merzenich, M. M., Ochs, M. T., Allard, T., & Guic-Robles, E. (1990). Functional reorganization of primary somatosensory cortex in adult owl monkeys after behaviorally controlled tactile stimulation. *Journal of Neurophysiology*, 63, 82–104.
- Kirmess, M., & Maher, L. (2010). Constraint Induced language therapy in early aphasia rehabilitation. *Aphasiology*, 24, 725–736.
- Knapp, H. D., Taub, E., & Berman, A. J. (1959). Conditioned response following deafferentation in the monkey. *Transactions of the American Neurological Association*, 84, 185–187.
- Knapp, H. D., Taub, E., & Berman, A. J. (1963). Movements in monkeys with deafferented limbs. *Experimental Neurology*, 7, 305–315.
- Kopp, B., Kunkel, A., Mühlhnickel, W., Villringer, K., Taub, E., & Flor, H. (1999). Plasticity in the motor system related to therapy-induced improvement of movement after stroke. *NeuroReport*, 10, 807–810.
- Kunkel, A., Kopp, B., Müller, G., Villringer, K., Villringer, A., Taub, E., et al. (1999). Constraint-induced movement therapy for motor recovery in stroke patients. *Archives of Physical Medicine and Rehabilitation*, 80, 624–628.
- Lassek, A. M. (1953). Inactivation of voluntary motor function following rhizotomy. *Journal of Neuropathology and Experimental Neurology*, 3, 83–87.
- Liepert, J., Bauder, H., Miltner, W. H. R., Taub, E., & Weiller, C. (2000). Treatment-induced cortical reorganization after stroke in humans. *Stroke*, 31, 1210–1216.
- Maguire, E. A., Gadian, D. G., Johnsrude, I. S., Good, C. D., Ashburner, J., Frackowiak, R. S. J., et al. (2000). Navigation-related structural change in the hippocampi of taxi drivers. *Proceedings of the National Academy of Sciences, USA*, 97, 4398–4403.
- Maher, L. M., Kendall, D., Swearingin, J. A., Rodriguez, A., Leon, S. A., Pingel, K., et al. (2006). A pilot study of use-dependent learning in the context of constraint induced language therapy. *Journal of the International Neuropsychological Society*, 12, 843–852.
- Mark, V., Taub, E., Bashir, K., Uswatte, G., Delgado, A., Bowman, M., et al. (2008). Constraint-induced movement therapy can improve hemiparetic progressive multiple sclerosis. *Multiple Sclerosis*, 14(7), 992–994.
- Mark, V. W., Taub, E., Uswatte, G., Bashir, K., Bryson, C., Bowman, M., et al. (2008). Impaired gait in progressive multiple sclerosis improves with constraint-induced movement therapy [Abstract]. *Archives of Physical Medicine and Rehabilitation*, 89(10), E5.
- Meinzer, M., Elbert, T., Barthel, G., Djundja, D., Taub, E., & Rockstroh, B. (2007). Extending the constraint-induced movement therapy (CIMT) approach to cognitive functions: Constraint-induced aphasia therapy (CIAT) of chronic aphasia. *Neuro-Rehabilitation*, 22, 311–318.
- Meinzer, M., Elbert, T., Wienburch, C., Djundja, D., Barthel, G., & Rockstroh, B. (2004). Intensive language training enhances brain plasticity in chronic aphasia. *BMC Biology*, 2, 20–29.
- Merzenich, M. M., Kaas, J. H., Wall, J., Nelson, R. J., Sur, M., & Felleman, D. (1983). Topographic reorganization of somatosensory cortical areas 3b and 1 in adult monkeys following restricted deafferentation. *Neuroscience*, 8, 33–55.
- Miltner, W. H. R., Bauder, H., Sommer, M., Dettmers, C., & Taub, E. (1999). Effects of constraint-induced movement therapy on chronic stroke patients: A replication. *Stroke*, 30, 586–592.
- Morgan, W. G. (1974). The shaping game: A teaching technique. *Behavior Therapy*, 5, 271–272.
- Morris, D., & Taub, E. (2008). Constraint-induced movement therapy. In S. O'Sullivan & T. Schwartz (Eds.), *Guide to physical therapy practices* (pp. 232–245). Philadelphia, PA: American Physical Therapy Association.
- Mott, F. W., & Sherrington, C. S. (1895). Experiments upon the influence of sensory nerves upon movement and nutrition of the limbs. *Proceedings of the Royal Society of London*, 57, 481–488.
- Nudo, R. J., Wise, B. M., SiFuentes, F., & Milliken, G. W. (1996). Neural substrates for the effects of rehabilitative training on motor recovery after ischemic infarct. *Science*, 272, 1791–1794.
- Panyan, M. V. (1980). *How to use shaping*. Lawrence, KS: H & H Enterprises.
- Pulvermüller, F. (1990). *Aphasische kommunikation. Grundfragen ihrer analyse und therapie [Communication in aphasics. Basic questions and therapeutic approaches]*. Tuebingen, Germany: Gunter Narr Verlag.
- Pulvermüller, F., Neining, B., Elbert, T., Mohr, B., Rockstroh, B., Köbbel, P., et al. (2001). Constraint-induced therapy of

- chronic aphasia following stroke. *Stroke*, 32, 1621–1626.
- Pulvermüller, F., & Schonle, P. (1993). Behavioral and neuronal changes during treatment of mixed transcortical aphasia. *Cognition*, 48, 139–161.
- Raymer, A., Beeson, P., Holland, A., Kendall, D., Maher, L., Martin, N., et al. (2008). Translational research in aphasia: From neuroscience to neurorehabilitation. *Journal of Speech, Hearing, & Language Research*, 5(1), S259–S275.
- Shaw, S. E., Morris, D. M., Uswatte, G., McKay, S. B., & Taub, E. (2003). Adherence to constraint induced movement therapy procedures and outcome for persons with traumatic brain injury. *Journal of Neurologic Physical Therapy*, 27(4), 180.
- Sherrington, C. S. (1910). Remarks on the reflex mechanism of the step. *Brain*, 33, 1–25.
- Skinner, B. F. (1938). *The behavior of organisms*. New York, NY: Appleton-Century-Crofts.
- Skinner, B. F. (1968). *The technology of teaching*. New York, NY: Appleton-Century-Crofts.
- Sterr, A., Elbert, T., Berthold, I., Kölb, S., Rockstroh, B., & Taub, E. (2002). Longer versus shorter daily constraint-induced movement therapy of chronic hemiparesis: An exploratory study. *Archives of Physical Medicine and Rehabilitation*, 83, 1374–1377.
- Taub, E. (1977). Movement in nonhuman primates deprived of somatosensory feedback. *Exercise and sports science reviews* (Vol. 4, pp. 335–374). Santa Barbara, CA: Journal Publishing Affiliates.
- Taub, E. (1980). Somatosensory deafferentation research with monkeys: Implications for rehabilitation medicine. In L. P. Ince (Ed.), *Behavioral psychology in rehabilitation medicine: Clinical applications* (pp. 371–401). New York, NY: Williams & Wilkins.
- Taub, E. (2002). CI therapy: A new rehabilitation technique for aphasia and motor disability after neurological injury. *Klinik und Forschung*, 8, 48–49.
- Taub, E., & Berman, A. J. (1963). Avoidance conditioning in the absence of relevant proprioceptive and exteroceptive feedback. *Journal of Comparative and Physiological Psychology*, 56, 1012–1016.
- Taub, E., & Berman, A. J. (1968). Movement and learning in the absence of sensory feedback. In S. J. Freedman (Ed.), *The neuropsychology of spatially oriented behavior* (pp. 173–192). Homewood, IL: Dorsey.
- Taub, E., Crago, J. E., Burgio, L. D., Groomes, T. E., Cook, E. W., DeLuca, S. C., et al. (1994). An operant approach to rehabilitation medicine: Overcoming learned nonuse by shaping. *Journal of the Experimental Analysis of Behavior*, 61, 281–293.
- Taub, E., Ellman, S. J., & Berman, A. J. (1966). Deafferentation in monkeys: Effect on conditioned grasp response. *Science*, 151, 593–594.
- Taub, E., Goldberg, I. A., & Taub, P. B. (1975). Deafferentation in monkeys: Pointing at a target without visual feedback. *Experimental Neurology*, 46, 178–186.
- Taub, E., Griffin, A., Gammons, K., Nick, J., Uswatte, G., & Law, C. R. (2006). *CI therapy for young children with congenital hemiparesis*. Atlanta, GA: Society for Neuroscience.
- Taub, E., Griffin, A., Nick, J., Gammons, K., Uswatte, G., & Law, C. R. (2007). Pediatric CI therapy for stroke-induced hemiparesis in young children. *Developmental Neurorehabilitation*, 10, 1–16.
- Taub, E., Griffin, A., Uswatte, G., Gammons, K., Nick, J., & Law, C. R. (2011). Treatment of congenital hemiparesis with pediatric constraint-induced movement therapy. *Journal of Child Neurology*, 26, 1163–1173.
- Taub, E., Heitman, R., & Barro, G. (1977). Alertness and level of activity and purposive movement following deafferentation in the adult and developing monkey. In H. P. Zeigler & B. M. Wenzel (Eds.), *Tonic functions of sensory systems* (Vol. 290, pp. 348–365). Ann, NY: Academic Sciences.
- Taub, E., Miller, N. E., Novack, T., Cook, E. W., III., Fleming, W. C., Nepomuceno, C. S., et al. (1993). Technique to improve chronic motor deficit after stroke. *Archives of Physical Medicine and Rehabilitation*, 74, 347–354.
- Taub, E., Perrella, P. N., & Barro, G. (1973). Behavioral development following forelimb deafferentation on day of birth in monkeys with and without blinding. *Science*, 181, 959–960.
- Taub, E., Perrella, P. N., Miller, D., & Barro, G. (1975). Diminution of early environmental control through perinatal and prenatal somatosensory deafferentation. *Biological Psychiatry*, 10, 609–626.
- Taub, E., Ramey, S. L., DeLuca, S., & Echols, E. (2004). Efficacy of constraint-induced (CI) movement therapy for children with cerebral palsy with asymmetric motor impairment. *Pediatrics*, 113, 305–312.
- Taub, E., & Uswatte, G. (2009). Constraint-induced movement therapy: A paradigm for translating advances in behavioral neuroscience into rehabilitation treatments. In G. Berntson & J. Cacioppo (Eds.), *Handbook of neuroscience for the behavioral sciences* (Vol. 2, pp. 1296–1319). Hoboken, NJ: Wiley.
- Taub, E., Uswatte, G., King, D. K., Morris, D., Crago, J., & Chatterjee, A. (2006). A placebo controlled trial of constraint-induced movement therapy for upper extremity after stroke. *Stroke*, 37, 1045–1049.

- Taub, E., Uswatte, G., Mark, V., & Morris, D. (2006). The learned nonuse phenomenon: Implications for rehabilitation. *Europa Medicophysica*, 42(2), 241–255.
- Taub, E., Uswatte, G., & Pidikiti, R. (1999). Constraint-induced movement therapy: A new family of techniques with broad application to physical rehabilitation—a clinical review. *Journal of Rehabilitation Research and Development*, 36, 237–251.
- Taub, E., Williams, E., Barro, G., & Steiner, S. S. (1978). Comparison of the performance of deafferented and intact monkeys on continuous and fixed ratio schedules of reinforcement. *Experimental Neurology*, 58, 1–13.
- Timberlake, W. (1993). Behavior systems and reinforcement: An integrative approach. *Journal of the Experimental Analysis of Behavior*, 60, 105–128.
- Twitchell, T. E. (1954). Sensory factors in purposive movement. *Journal of Neurophysiology*, 17, 239–254.
- Uswatte, G., Miltner, W. H. R., Varma, M., Moran, S., Sharma, V., Foo, B., et al. (1998). *Accelerometry: An objective approach to real-world outcome measurement in physical rehabilitation*. Paper presented at the inaugural meeting of the Program in Cognitive Rehabilitation of the James S. McDonnell Foundation, St. Louis, MO.
- Uswatte, G., Miltner, W., Walker, H., Spraggins, S., Moran, S., Calhoun, J., et al. (1997). Accelerometers in rehabilitation: Objective measurement of extremity use at home [Abstract]. *Rehabilitation Psychology*, 42, 139.
- Uswatte, G., Spraggins, S., Walker, H., Calhoun, J., & Taub, E. (1997). Validity and reliability of accelerometry as an objective measure of upper extremity use at home [Abstract]. *Archives of Physical Medicine and Rehabilitation*, 78, 896.
- Uswatte, G., Taub, E., Morris, D., Barman, J., & Crago, J. (2006). Contribution of the shaping and restraint components of constraint-induced movement therapy to treatment outcome. *NeuroRehabilitation*, 21(2), 147–156.
- Uswatte, G., Taub, E., Morris, D., Light, K., & Thompson, P. (2006). The motor activity Log-28: Assessing daily use of the hemiparetic arm after stroke. *Neurology*, 67, 1189–1194.
- Uswatte, G., Taub, E., Morris, D., Vignolo, M., & McCulloch, K. (2005). Reliability and validity of the upper-extremity motor activity Log-14 for measuring real-world arm use. *Stroke*, 36, 2493–2496.
- van der Lee, J., Beckerman, H., Lankhorst, G., & Bouter, L. (1999). Constraint-induced movement therapy [Letter to the Editor]. *Archives of Physical Medicine and Rehabilitation*, 80, 1606.
- Weiss, T., Miltner, W. H. R., Adler, T., Bruckner, L., & Taub, E. (1999). Decrease in phantom limb pain associated with prosthesis-induced increased use of an amputation stump in humans. *Neuroscience Letters*, 272, 131–134.
- Wittenberg, G. F., Chen, R., Ishii, K., Bushara, K. O., Taub, E., Gerber, L. H., et al. (2003). Constraint-induced therapy in stroke: Magnetic-stimulation motor maps and cerebral activation. *Neurorehabilitation and Neural Repair*, 17, 48–57.
- Wolf, S., Winstein, C., Miller, J., Taub, E., Uswatte, G., Morris, D., et al. (2006). Effect of constraint-induced movement therapy on upper extremity function 3–9 months after stroke: The EXCITE randomized clinical trial. *Journal of the American Medical Association*, 296, 2095–2104.

APPENDIX A

Steps Involved in the Shaping Progression from Total Absence of the Target Behavior to Thumb-Forefinger Grasp of a Food Object in Juvenile Monkeys Deafferented Prenatally or on Day of Birth

The steps in shaping were as follows:

1. Showing the juvenile a desirable food object (e.g. small apple cube, peanuts) and reinforcing any movement of the arm, whether in the correct direction or not, by food in the mouth.
2. Requiring arm movements of progressively greater excursion and more accurate direction for placement of food in the mouth.
3. Requiring that the food object be touched for food to be placed in hand so that it could be returned by the animal to its mouth.
4. Requiring that fingers be opened so that hand could be baited with a food object; wrist supported by experimenter at end of arm trajectory; fingers opened, first by passive manipulation by experimenter and subsequently with progressively more active finger extension required.
5. Grasping of food object by the animal at end of arm trajectory with no support of wrist.
6. Picking food object up from experimenter's palm, which was molded and moved to make prehension easier; any type of grasp permitted.

7. Picking food object up from a flat wooden board. Lateral thumb-forefinger grasp (a monkey's normal mode of prehension) developed spontaneously over sessions, as did approaching the food object from above rather than accomplishing the grasp while the ulnar surface of wrist and lower forearm were supported by the board.

8. Placement of food objects (approximately 1-cm³ apple cubes) in shallow (0.5 mm) wells on a Klüver board (a board with multiple wells from which monkeys extract pieces of food) to promote more accurate thumb-finger approximation.

9. Placement of apple cubes on a Klüver board with deeper (1 cm) wells to promote pincer grasp (approximation of the palmar tips of the thumb and forefinger).

10. Use of smaller food objects, first peanuts, then raisins.

The terminal behavior achieved was retrieval of raisins from wells on the first attempt by pincer grasp on approximately 50% of trials. Sometimes, after two or more attempts failed, the monkeys would move the food object out of a well with the forefinger so that it could be grasped on the flat surface between wells.

APPENDIX B

Shaping Guidelines

Shaping is a training method in which a motor or behavioral objective is approached in small steps by successive approximations, or a task is gradually made more difficult in accordance with a subject's motor capabilities. The following guidelines employed in the UAB laboratory should be followed when using shaping for inducing recovery of motor function.

Specific shaping tasks should be selected for patients by considering (a) specific joint movements that exhibit the most pronounced deficits,

(b) the joint movements that trainers believe have the greatest potential for improvement, and (c) patient preference among tasks that have similar potential for producing specific improvements.

Shaping tasks should be modeled for the patient and encouragement and coaching (verbal prompts) provided liberally.

The level of difficulty of the shaping task should be slightly beyond what the patient can accomplish easily (e.g., encouraging him or her to do a little better than the previous performance).

In the shaping progression, moving to the next higher level of difficulty should be carried out when the patient has reached a relative plateau with regard to performance. For the present purposes, when a patient has performed five trials in a row with no improvement evidenced in their score, the next level of difficulty should be attempted. If subjects are permitted to achieve greater mastery, they frequently have a tendency to become "locked in" at that level. Subsequently, improvement becomes more difficult to achieve. (This is a guideline only. If the patient is "on a roll," progressing rapidly, he or she should be shifted to the next performance difficulty level as rapidly as the trainer feels the performance will keep improving at a maximal level.)

The shaping task is made progressively more difficult only as the patient improves in performance.

Any of the shaping progression parameters can be changed to increase the difficulty of the task (e.g., time, number of repetitions, height, placement, etc.).

When increasing the level of difficulty of an activity, the shaping progression parameters selected should relate to the subject's movement problems (i.e., in the flipping dominoes task, if the subject's most significant deficits are in thumb and forefinger

dexterity, the task progression should involve using, depending on the nature of the deficit, either larger or smaller dominoes. If the subject's most significant movement deficits are at the shoulder, the task progression should involve moving the dominoes farther away).

Shaping tasks are made more difficult when it is clear that, for the most part, the patient will be able to accomplish the task, though with effort.

Positive reinforcement or reward should be provided visually (i.e., keeping the shaping data form in plain view of the patient so that he or she can see performance history and "personal best"; task performance becomes like an arcade game). Task performance information should also be given verbally at frequent intervals.

An important function of the trainer is to act as a cheerleader, continuously encouraging the subject on a moment-to-moment basis to keep improving the performance.

Performance regressions are never punished and are usually ignored.

If a patient is experiencing excessive difficulty with a task, a simpler task involving similar movements can be substituted.

Rest intervals should be allowed during each shaping session. The rest period is usually the same length as the trial period, although longer intervals are sometimes needed to prevent fatigue.

Trainers should rate the performance of each shaping task trial using the quality-of-movement scale attached.

The results of each shaping task trial, including quality-of-movement rating, should be recorded on the shaping data form.

Encouragement and quality-of-movement ratings should be given to the subject verbally on at least 50% of the trials.

Placement of equipment used in shaping tasks should be recorded on the shaping data form so that the

task can be duplicated. Adhesive markers on the task performance table can be used for this purpose. Also, note any placement changes on the data sheet when a shaping task is made more difficult.

Only one shaping progression parameter at a time should be allowed to vary. For example, on an elbow extension task, there would be three parameters: time, number of repetitions, and distance. The time and number of the repetitions can be held constant and the distance can be slowly increased until the subject can no longer perform a specified number of extensions in a given period of time (e.g., 10 extensions in 30 s). Alternatively, distance can be held constant (e.g., 10 in.) and the subject would be encouraged to progressively increase the number of repetitions in a set period of time (e.g., 30 s). For a given task, more than one parameter should not be varied at the same time (e.g., both distance and number of repetitions). If the trainer feels that the subject would benefit from varying a second parameter, that is permissible. However, it should be understood that this training now must be quantified as a new entity on separate data sheets.

Example of Shaping Tasks: Flipping Dominoes

Activity description:

Approximately 25 dominoes are placed in front of the subject. The subject is asked to reach forward and flip the dominoes using either forearm pronation or supination. The correct movement can be best isolated by asking the subject to rest his or her forearm on the table during the task.

Potential shaping progression:

Placing the dominoes farther away to challenge elbow extension.

Using larger or smaller dominoes to challenge wrist and finger control.

Placing dominoes on a box to challenge shoulder flexion.

Potential feedback variables:

Number of dominoes flipped in a set period of time.

Time required to flip a set number of dominoes.

Movements emphasized:

Lateral pincer grasp.

Wrist extension.

Forearm supination or pronation (depending on direction of flip).

Shoulder flexion (if placed on a box).

Example of Shaping Tasks: Turning Magazine Pages

Activity description:

Place a magazine on the table. Ask the subject to turn the pages. Have the subject

concentrate on turning pages by either pronating or supinating.

Potential shaping progression:

The position of the magazine can be changed (moved farther away from the subject) to challenge elbow extension.

Increase the amount of time for the subject to turn the pages or increase the number of pages that the subject must turn to challenge the subject's endurance.

Potential feedback variables:

Number of pages turned in a set amount of time.

Time required to turn a set number of pages.

Movements emphasized:

Forearm supination.

Forearm pronation.

Pincer or lateral pincer grasp.

Shoulder internal and external rotation.