

Application of Combined Botulinum Toxin Type A and Modified Constraint-Induced Movement Therapy for an Individual With Chronic Upper-Extremity Spasticity After Stroke

Background and Purpose. Constraint-induced movement therapy (CIMT) is a promising intervention for retraining upper-extremity function after a stroke. The purpose of this case report is to describe the use of a combination of botulinum toxin type A (BtxA) and a modified CIMT program for a patient with severe spasticity who was unable to use his right upper extremity. **Case Description.** The 52-year-old patient, who had a stroke 4 years ago, did not meet the minimum motor criteria for CIMT benefit. After receiving BtxA injections targeting the elbow, wrist, and finger flexors, he completed a 4-week program of modified CIMT followed by a 5-month home exercise program. **Outcomes.** The patient exhibited improvement in muscle tone (the velocity-dependent resistance to stretch that muscle exhibits) and in scores on several upper-extremity function tests (Modified Ashworth Scale, Motor Activity Log, Wolf Motor Function Test, Action Research Arm Test, and Fugl-Meyer Assessment of Motor Recovery). He also reported making much progress in the functional use of the involved upper extremity. **Discussion.** In a patient with severe flexor spasticity and nonuse of the dominant upper extremity after a stroke, a combined treatment of BtxA and modified CIMT may have resulted in improved upper-extremity use. [Sun SF, Hsu CW, Hwang CW, et al. Application of combined botulinum toxin type A and modified constraint-induced movement therapy for an individual with chronic upper-extremity spasticity after stroke. *Phys Ther.* 2006;86:1387–1397.]

Key Words: *Botulinum toxin, Constraint-induced movement therapy, Spasticity, Stroke.*

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This case report is a baseline description of combined botulinum toxin type A and modified constraint-induced movement therapy for a patient with stroke and disabling upper-extremity spasticity.

Constraint-induced movement therapy (CIMT) has been shown to produce lasting improvements in upper-extremity movement following a stroke.¹⁻¹⁶ The basic components of CIMT involve restraint of the unaffected arm for 90% of the person's waking hours for a 2-week period in conjunction with repetitive training of the more-affected upper extremity.^{1,4-9} The less-affected extremity is restrained with a mitt, sling, or glove. During the 2-week period, patients typically participate in 6-hour activity sessions each weekday. The minimum motor criteria of patients who show benefit from CIMT include at least 20 degrees of wrist extension and 10 degrees of extension at each metacarpophalangeal and interphalangeal joint of the affected upper extremity.^{5-8,16} Participants in these studies demonstrated improvements in the amount of use and quality of movement in the more-involved upper extremity as well as carryover of skills from the hospital to the real world.^{4-9,17}

It is estimated that approximately 20% to 25% of people with chronic stroke with residual motor deficit meet the minimum motor criteria.² Most studies of CIMT excluded patients with severe upper-limb spasticity. Severe spasticity of the upper extremity is a common complication after stroke, and it is usually a major contributor to the motor function disability.¹⁸ *Spasticity*, defined as "a velocity-dependent increase of tonic stretch reflexes with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex,"¹⁹ is a condition that results from a number of neurological disorders such as spinal cord injury, traumatic brain injury, and stroke.²⁰ Untreated spasticity can result in a net imbalance of force, leading to deformity across the joints.²¹

Management of spasticity is considered essential to prevent deformities, to improve function, and to relieve distressing symptoms; optimal medical treatment often requires multiple interventions.²²⁻²⁴

In recent years, botulinum toxin type A (BtxA) has been shown to be effective in reducing poststroke spasticity and its complications.²⁵⁻²⁸ However, controversy exists about improvement in motor function relative to improvement in spasticity. Botulinum toxin type A injected into the skeletal muscle belly prevents the release of acetylcholine from the presynaptic axon of the motor endplate and blocks signal transmission at the neuromuscular junction.²⁹

Because the evidence indicates that minimum motor criteria are necessary to optimize the benefit from CIMT in people after a stroke, those people who do not meet these initial criteria may not benefit from CIMT.¹² The purpose of this case report is to describe the use of a combination of BtxA (Dysport)* injections and a modified CIMT program for a man who did not meet the

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minimum motor criteria for CIMT and had nonuse of the right upper extremity 4 years after a stroke. This patient's initial motor abilities compared with his ultimate gains after CIMT and BtxA warrant reporting the combined program and the outcomes.

Case Description

History, Diagnosis, and Prognosis

The patient was a 52-year-old man who had a stroke 4 years previously, with resultant hemiparesis in his dominant right hand and arm. Computed tomography revealed low density over the left temporoparietal region. Before the stroke, he worked as a manager in an international trading company. He had a 5-year history of hypertension. After participating in inpatient rehabilitation for 6 weeks, he could ambulate slowly without an assistive device. After discharge, he had received an average of 3 outpatient physical therapy and occupational therapy sessions per week continuously for 1 year. Subsequently, he was able to walk at least 2 km. He learned to drive one-handed and went back to work occasionally as a consultant 1 year after the stroke.

Since the stroke, he used his left upper extremity almost exclusively to perform daily activities. The patient reported that he did not use his right arm or hand to write, eat, or dress. He could not open doors or drawers, turn on lights, or answer the telephone with his right hand. His doctor and therapists told him that his motor recovery had plateaued and that additional recovery was doubtful. He responded to information about an ongoing stroke research project on a combination of BtxA injections and a modified CIMT program at our institution. When we saw him, the patient appeared motivated and excited about the combined interventions, and his goal for the program was to increase function in his right upper extremity. After completing the screening process, he gave written informed consent to participate in the program.

Examination and Evaluation

The patient met the screening criteria for entry: (1) more than 1 year after stroke with disabling spasticity and residual hand function with some active movement in wrist and fingers; (2) no obvious fixed contractures of the upper-limb joints; (3) no medical complications or other pre-existing neurological conditions (eg, myasthenia gravis, Eaton-Lambert syndrome, or motor neuron disease); (4) evidence of preserved cognitive function (Mini-Mental Status Examination score of at least 24/30)³⁰; (5) no previous treatment with BtxA or neurolytic or surgical procedures in the affected limb and no concomitant oral antispastic medication during this study; and (6) not currently participating in any experimental rehabilitation or drug studies.

During the physical examination, he had difficulty extending his fingers and his elbow. He could not open his hand widely after making a fist and could not release his grasp on a tennis ball. Although he was able to elicit finger movement into synergy patterns, only minimal active extension movement was noted in his right wrist and fingers. He did not meet the minimum motor criteria for CIMT because he had only approximately 8 degrees of active wrist extension and minimal finger extension of less than 10 degrees (motor criteria were tested with the forearm supported on the edge of a table and the wrist in a passively flexed position over the edge of the table). He had dysesthesia to light touch on the right upper arm and palm of the hand. To test joint position sense, the patient's joints of the right upper extremity were grasped laterally and passively moved. While keeping the eyes closed, he was able to indicate the direction of movement and final position of the shoulder and elbow, but joint position sense was impaired at the wrist and thumb.

He was able to actively flex and abduct his shoulder to approximately 90 degrees, but not without elbow flexion, indicating a flexor synergy. He reported pain in the shoulder with passive flexion, abduction, and external rotation and pain in the elbow with passive extension. He had intermittent right shoulder pain when he attempted to move his right upper extremity. When he attempted to perform activities that required right shoulder movement, he used trunk substitution or scapular elevation to move his right arm.

Baseline Testing

Prior to the combined interventions, the patient completed baseline testing, which consisted of the following tests and measures:

Mini-Mental State Examination (MMSE). The MMSE is a brief cognitive screening instrument with scores ranging from 0 to 30. We used the MMSE to detect any gross cognitive changes that may have occurred during the study period. Concurrent validity (r) has been reported as .78 and .66 for the MMSE versus the Verbal IQ and the Performance IQ portions of the Wechsler Adult Intelligence Scale, respectively.³¹ Test-rest reliability (r) has been reported as .89.³¹ Intertester reliability (r) has been reported as .83.³¹

Modified Ashworth Scale (MAS). The MAS has been shown to yield reliable data in the assessment of upper-limb spasticity. The reliability (kappa) of the MAS scores was reported to be .84 and .83 for interrater and intrarater comparisons, respectively.³² Muscle tone (the velocity-dependent resistance to stretch that muscle exhibits) was assessed separately at the elbow, wrist, and fingers. The degree of resistance to the passive muscle

stretch that was felt by the examiner was scored on a 6-point ordinal scale ranging from 0 (no increase in muscle tone) to 4 (the affected part is rigid in flexion and extension). A supplementary level "1+" between the scores of "1" and "2" was used to indicate slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the range of motion.

Motor Activity Log (MAL). Real-world outcome is assessed by the MAL, which consists of a semi-structured interview measuring how patients use their affected limbs for activities of daily living (ADL).³³ The patient rated how much and how well he used the affected arm for ADL during the past week using a 6-point Amount Scale and a 6-point How Well Scale (Appendix 1).¹³ Examples of items on the questionnaire include opening an envelope, combing hair, pouring coffee or tea, cutting fingernails, and donning and doffing shoes.

Wolf Motor Function Test (WMFT). The WMFT was developed for people with mild to moderate stroke.^{1,34} It incorporates 15 upper-extremity functional tasks to assess movement components required for daily tasks. The time required for each task (up to 120 seconds) is measured, and the median time score is reported. Quality of movement scoring is assessed using a 6-point Functional Ability Scale, with scores ranging from 0 (not attempted) to 5 (normal movement) (Appendix 2). The mean Functional Ability Scale score is reported. Interrater reliability (r) of the WMFT was reported to be .97 or greater for performance time and .88 or greater for functional ability.³⁴ Intrarater reliability (r) was reported to be .90 for performance time and .95 for functional ability. Wolf et al³⁵ reported interrater reliability (r) of WMFT scores ranging from .97 to .99.

Action Research Arm Test (ARAT). The ARAT is a functional assessment of upper-extremity strength (force-generating capacity of a muscle), dexterity, and coordination.³⁶ Derived from the Fugl-Meyer Scale, the ARAT consists of 19 items divided into 4 subscales: grasp, grip, pinch, and gross movement. The performance of each motor task is rated on a 4-point ordinal scale, ranging from 0 (no movement possible) to 3 (movement performed normally). Scores on individual items are added, with a maximum score of 57 per arm. The concurrent validity has been supported by comparison with the Brunnström-Fugl-Meyer test.³⁷ Scores for the ARAT has been reported to have interrater reliability (r) of .99 and test-retest reliability (r) of .98,^{36,38} and the test has been shown to be responsive.³⁹

Fugl-Meyer Assessment of Motor Recovery (FMA). The FMA is an accurate method of assessing function in patients with hemiparesis based on the natural progres-

sion of functional return.⁴⁰ It is a cumulative assessment that measures motor skill, coordination, speed of the upper extremity, balance, sensation, and some joint function in people with hemiparesis. We used the Upper Extremity Motor Score (0–66 points) and an overall total Comprehensive Score consisting of the Upper Extremity, Sensation, Joint Range of Motion, and Pain scale scores (0–126 points). Test-retest reliability has been reported to be high for the total scores of upper- and lower-extremity motor performance (at least $r = .984$ and $r = .886$, respectively).⁴¹

The MAS is an accepted measure for evaluating muscle tone and spasticity in clinical trials.⁴² All of the other tests were selected because they have commonly been used in CIMT and modified CIMT research,^{1,3,7–9,14,17} and were shown to be responsive to changes in function after CIMT.³⁸ Before the intervention period began, the ARAT and FMA were administered on 2 occasions 1 week apart, and the WMFT and MAL were administered once. The 2 baseline ARAT and FMA scores were averaged for subsequent analyses.

The MMSE, MAS, and FMA were administered by the same physician. All administrations of the MAL, WMFT, and ARAT were done by the same occupational therapist who had 10 years of experience with examination and intervention for people with neurological deficits. The MAL and WMFT instructions included detailed descriptions and scripts for test administration. The WMFT and ARAT were administered in the same room, using the same equipment and the same chair and table position and with the same verbal directions at each administration. In the present case, the r values for test-retest reliability on the WMFT, ARAT, and FMA were between .75 and .90. Test-retest reliability of these scores was determined by the same observer and by repeat videotape assessment of 10 randomly selected subjects with chronic hemiplegia (1 year), showing moderate motor impairment. To standardize the assessment environment, the same chair, testing equipment, and testing procedures were used for every subject and at each evaluation point.

Intervention

Botulinum toxin type A (Dysport), supplied as vacuum-dried powder in a 500-unit vial, was reconstituted with sterile normal saline (0.9%) to reach a total volume of 2.5 mL per vial. Muscles chosen for injection were based on previous experience with BtxA in upper-limb spasticity.²⁸ About 400 units of BtxA were injected into the muscle belly of the biceps brachii muscle at 2 sites (each site received 200 units). The flexor digitorum superficialis, flexor digitorum profundus, flexor carpi ulnaris, and flexor carpi radialis muscles were injected with 150 units each at 1 site per muscle. The injections were placed in

the muscle belly using anatomical landmarks as in routine electromyography.

After receiving 1,000 units of Dysport injection in the spastic muscles of right upper extremity, the patient received a 4-week modified CIMT program consisting of 2 hours of training each day 3 times weekly at our rehabilitation center. During this period, he restrained his less affected upper extremity with a soft mitt attached around the wrist. He was told to wear the restraint as long as possible and for at least 5 hours of his waking hours per day during the study period. We employed a less intense, modified CIMT program because a traditional CIMT protocol might be problematic, given the required practice intensity and the duration of the restraint schedule.¹⁴ In addition, traditional CIMT might impose substantial demands on the therapists and the resources of a rehabilitation unit.

The training approaches implemented in this program included massed practice, shaping, a home treatment agreement, and a daily treatment diary. Massed practice for this client involved repeatedly attempting to move and use his affected arm and hand, while restraining his less-affected side for at least 5 hours each day of the week for a period of 4 weeks. Massed practice is thought to be the driving force behind the use-dependent cortical reorganization described in neuroimaging studies involving CIMT.^{5,6,43}

Shaping is a behavior technique, and it is particularly important in the management of patients with less movement ability.¹¹ Taub and colleagues² defined *shaping* as: (1) selecting tasks tailored to address the motor deficits of the individual patient, (2) helping the patient to carry out parts of a movement sequence if they could not complete the movement at first, and (3) providing positive verbal feedback for small improvements in task performance. The therapist progressively increases the challenge of the task according to the patient's improvement in task performance.

The home treatment agreement and daily treatment diary are essential behavioral components in a CIMT program.⁴⁴ A home treatment agreement is a contract that details what activities will be done with the restraint on, when the restraint will be worn in the community or in social situations, and when the restraint should be removed for potentially unsafe situations. The treatment diary is a detailed daily log to track use of the affected arm when away from the hospital. The diary was kept to document device use time, as well as activities performed during restraint hours. The patient used this diary for daily documentation and included as much detail and description as possible. For example, the patient might have reported that for the previous day's dinner he ate

Table 1.
A Typical Treatment Day

7:00 AM	The patient awoke, performed morning hygiene and dressing tasks, and had breakfast with both hands (using the right upper extremity as much as possible and documenting how much it was used).
8:00 AM	He applied the restraint, got his newspaper, performed household chores, then he drove to the hospital.
9:30 AM	He reviewed the treatment diary and discussed the previous day's events with the therapist.
9:50 AM	Right upper-extremity training, implementing the concepts of massed practice and shaping: activities focusing on eliciting and strengthening his ability to move and functionally use his right upper extremity. Tasks were modified to increase difficulty when appropriate (each task was performed for 30 to 40 minutes, with appropriate rest periods interspersed with movement attempts).
11:50 AM	We reviewed the day's happenings and assigned practice tasks for the evening and the following day. In the treatment diary, a homework log listed the tasks to be completed and included space for the patient to comment on his performance. He was encouraged to perform activities of daily living with his right arm as much as possible.
12:00 PM	He left the hospital and continued with home practice activities and functional tasks using the involved upper extremity as much as possible. He bought lunch and ate it with the restraint on. The restraint was worn on the left upper extremity for most of the day. Events were documented in detail until he arrived at the hospital.
2:30 PM	He drove to his company and worked as a consultant.
6:00 PM	He prepared, ate, and cleaned up after dinner with both hands (using the right upper extremity as much as possible). He ate dinner with the restraint on. He chose foods that could be cut into chunks and more easily speared with a fork.
Weekends: He continued to wear the restraint and used the affected upper extremity for exercises and functional tasks as much as possible. Assigned repetitive exercise tasks, similar to what was done in the hospital, were detailed for each Saturday and Sunday.	

80% of a meatball with a built-up spoon. The patient also might report how much time it took to perform an activity, such as 8 minutes to open the door using only the affected upper extremity. The diary assists with ongoing evaluation of program adherence. Table 1 shows a typical treatment day for the patient.

One of the main focuses of the intervention was to teach the patient about learned nonuse and cortical reorganization after stroke. We expected that this program would increase awareness of the needs and benefits in using his affected arm and that he would continue to carry out a modified CIMT program at home over the following 5 months. We gave specific instructions for repetitive home exercises and how to progress tasks as he gained movement at home. The postintervention program included practicing functional tasks using the affected upper extremity with activities such as picking up pen-

cils, tossing a ring, typing on a computer, and moving blocks or cans. A daily activity log was kept to record what tasks had been attempted and how the tasks were progressed. As he improved in performance, the complexity and difficulty of the tasks were increased (such as by adding a time component, increasing the degrees of freedom, increasing the height or distance, or increasing the pattern complexity) to challenge him. We suggested that he should wear the restraint at home as much as possible when it did not compromise his safety.

Posttreatment and Follow-up Testing

At the end of the 4-week modified CIMT program and 3 months and 6 months after injection, the patient completed posttreatment assessment consisting of the MMSE, MAS, MAL, WMFT, ARAT, and FMA instruments. We also elicited feedback and patient's satisfaction and comments about the program through a questionnaire and discussion (Appendix 3).

Outcomes

The patient wore the restraint for an average of 80% of his waking hours for the 4-week program and for approximately 60% of his waking hours for the postintervention home program. Comparisons of scores on the MAL, MAS, WMFT, ARAT, and FMA at baseline, week 4, and the 3-month and 6-month follow-ups are shown in the Figure and Tables 2, 3, 4, and 5.

MMSE

The patient's MMSE score remained relatively constant (27 at baseline, 28 at week 4 and at the 3-month and 6-month follow-ups), suggesting that he had no cognitive changes throughout the intervention and follow-up period that might have affected test performance or carryover of the program.

MAS

Before the intervention, the patient did not have sufficient volitional control of his upper-extremity extensor muscles to overcome predominantly flexor synergies. At week 4, his MAS score was reduced significantly at the elbow, wrist, and fingers, with the effect most prominent at the elbow (Tab. 2). He could voluntarily extend his wrist to 30 degrees and open his hand halfway after making a fist. Although MAS scores increased at the

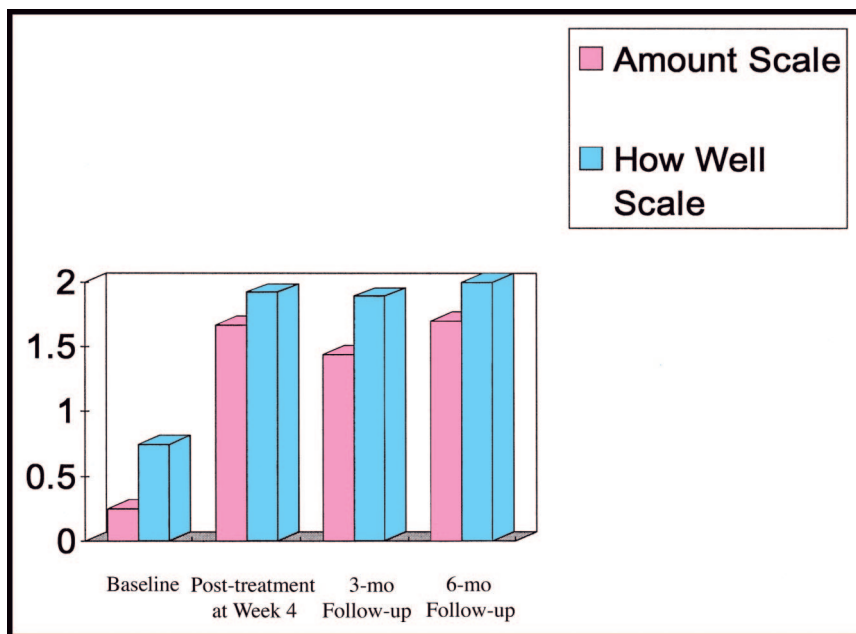


Figure.

Motor Activity Log results. The patient rated how much and how well he used the affected arm for activities of daily living during the past week using a 6-point Amount Scale and a 6-point How Well Scale. For the Amount Scale: 0=never use affected arm for this activity; 1=occasionally use; 2=sometimes use; 3=use affected arm about half as much as before the stroke; 4=use almost as much as before stroke (3/4 prestroke); 5=always use affected arm (same as prestroke). For the How Well Scale: 0=did not attempt task with affected arm (never); 1=affected arm was moved, but unable to perform task (very poor); 2=perform task very slowly or with difficulty, needed some help from the stronger arm (poor); 3=perform task for the purpose indicated, but movements were slow or were made with only some effort (fair); 4=almost normal, just not as fast or accurate; 5=appears normal.

3-month and 6-month follow-ups, they still remained lower than at baseline level (Tab. 2).

MAL

The client scored higher on the MAL after the combined interventions (Figure). On the Amount Scale, he changed from 0.25 at baseline to 1.67 at week 4. This finding suggested that he had never, or only occasionally, used his affected arm for ADL before treatment. He progressed to some use of the right upper extremity, but he was still primarily dependent on the left upper extremity at week 4. The score decreased slightly to 1.44 at the 3-month follow-up, but it further increased to 1.7 at the 6-month follow-up.

On the How Well Scale, his score changed from 0.75 at baseline to 1.92 at week 4. This finding indicated that his right arm was not really helpful. The score slightly decreased to 1.89 at the 3-month follow-up, but it further increased to 2 at the 6-month follow-up. Both subscale scores of the MAL appeared to increase greatly at the 6-month follow-up, which suggested that he did increase the use of his more-affected limb for ADL (Figure).

Table 2.
Modified Ashworth Scale (MAS) Scores^a

	Elbow	Wrist	Fingers
Baseline	3	2	2
Posttreatment at week 4	1	1	1
3-mo follow-up	1+	1+	1
6-mo follow-up	2	1+	1+

^aThe MAS is scored on a 6-point ordinal scale ranging from 0 to 4. 0=no increase in muscle tone; 1=slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of motion when the affected part is moved in flexion or extension; 1+=slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the range of motion (ROM); 2=more marked increase in muscle tone through most of the ROM, but affected part(s) easily moved; 3=considerable increase in muscle tone, passive movement difficult; 4=affected part(s) rigid in flexion or extension.

Table 3.
Wolf Motor Function Test (WMFT) Scores^a

	Median Time Score (s)	Mean Function Ability Scale Score
Baseline	104.07	2.15
Posttreatment at week 4	88.21	3.4
3-mo follow-up	90.56	3.4
6-mo follow-up	100.12	3.47

^aThe WMFT incorporates 15 upper-extremity functional tasks to assess movement components required for daily tasks. The time required to perform each task (up to 120 seconds) is measured. A low time score is optimal. Quality of movement scoring is assessed using a 6-point Functional Ability Scale, with scores ranging from 0 to 5. 0=not attempted; 1=attempt made, but affected arm not participating functionally; 2=arm does participate, but needs more than 2 attempts, needs assistance from the stronger arm, needs compensatory movements, or accomplishes very slowly; 3=arm does participate, but movement influenced by synergy or performs task slowly or with effort; 4=movement close to normal, but slightly slower, lack precision or fine coordination; 5=normal movement.

WMFT

The patient's initial median time on the WMFT was 104.07 seconds, indicating inefficient movement or difficulty performing a majority of the tasks (Tab. 3). The time improved to 88.21 seconds at week 4. The time increased to 100.12 seconds at the 6-month follow-up, but it still remained lower than at baseline. His initial mean Function Ability Scale score was 2.15, suggesting that his right upper extremity was not used in some tasks or was used with assistance, multiple attempts, compensatory movements, or extra time. The score increased to 3.4 at week 4. The highest score was 3.47 at the 6-month follow-up, which suggested that the quality of his movement might have improved (Tab. 3).

ARAT and FMA

Baseline ARAT and FMA scores (which were taken on 2 occasions) were stable, suggesting that the patient was exhibiting stable motor deficits. Baseline total ARAT scores were 13 and 13. Baseline FMA Upper Extremity

Motor Scores were 24 and 22. His comprehensive scores were 67 and 65.

After the 4-week intervention, the patient displayed an improvement of 16 points on the ARAT (Tab. 4). The posttreatment subtest scores at week 4 were higher in the grasp, grip, and pinch subscales. At the 3-month and 6-month follow-ups, total ARAT scores further increased to 31 and 43, respectively (Tab. 4).

The patient also demonstrated higher scores on the FMA after the intervention period (Tab. 5). The greatest gain was noted at week 4 (from 23 to 29 on the Upper Extremity Motor Score and from 66 to 78 on the Comprehensive Score) (Tab. 5). The patient was able to perform more forearm supination, elbow extension, and wrist extension within the flexor synergy at week 4. Both subscale scores decreased slightly at the 3-month follow-up. The scores, however, still remained higher at the 6-month follow-up than at baseline.

Discussion

The patient, who had upper-extremity spasticity 4 years after a stroke, typically would not have been expected to make obvious improvement in his physical abilities. After the combination of BtxA and modified CIMT, he did achieve improvements on the MAL, WMFT, ARAT, and FMA scores from baseline to posttreatment testing at week 4. Although MAL and FMA scores decreased slightly at the 3-month follow-up from week 4, all tests improved at the 6-month follow-up compared with baseline testing.

These changes in test scores may be attributed to several factors. They could reflect improvement in strength and coordination in the affected upper extremity as a result of spasticity reduction and repetitive training, a change in learned nonuse behaviors, or use-dependent cortical changes after the combination of BtxA and modified CIMT. It is also possible that either CIMT or BtxA alone could have been the critical factor accounting for observed changes in this individual.

Upper-extremity spasticity interferes with ADL; it also may interfere with voluntary motor function in patients with residual muscle power.⁴⁵ Reduction in spasticity, however, does not necessarily translate into better functional abilities.^{46,47} Although the effectiveness of BtxA in reducing poststroke spasticity had been demonstrated in some large randomized controlled trials, no significant improvement in the functional outcomes was observed.²⁵⁻²⁹ Generally, functional gains usually involve the acquisition of new motor skills or the use of compensatory strategies with repeated practice over a period of time. It is plausible that a combination of modified CIMT using intensive practice of functional tasks with

Table 4.
Action Research Arm Test (ARAT) Scores^a

	Total ARAT	Grasp	Grip	Pinch	Gross Motor
Baseline ^b	13	6	0	0	7
Posttreatment at week 4	29	9	3	10	7
3-mo follow-up	31	10	4	10	7
6-mo follow-up	43	8	10	18	7

^aThe ARAT is a functional assessment of upper-extremity strength, dexterity, and coordination. The ARAT includes 19 items divided into 4 subscales: grasp, grip, pinch, and gross movement. The performance of each motor task is rated on a 4-point ordinal scale, ranging from 0 (no movement possible) to 3 (movement performed normally). Scores on individual items are added, with a maximum score per arm of 57.

^bThe ARAT was administered 2 times, 1 week apart, before intervention. Baseline measurements are displayed as an average of the 2 measurements.

Table 5.
Fugl-Meyer Assessment of Motor Recovery (FMA) Scores^a

	UE Motor Score (0-66)	Comprehensive Score (0-126)
Baseline ^b	23	66
Posttreatment at week 4	29	78
3-mo follow-up	26	76
6-mo follow-up	26	75

^aHigher scores represent better function. The Comprehensive score is a combination of the Upper Extremity, Sensation, Joint Range of Motion, and Pain scale scores.

^bThe FMA was administered 2 times, 1 week apart, before intervention. Baseline measurements are displayed as an average of the 2 measurements.

BtxA injection to reduce spasticity may result in better upper-extremity function after stroke.

Week 4 was chosen as the optimal time for the first outcome assessment because the clinical effect of BtxA peaks around this period.⁴⁸ Similarly, the timing of the subsequent assessments at 3 months was determined by the pharmacodynamic properties of BtxA because neurotransmission is restored in approximately 3 months by a process of neuronal sprouting.^{49,50} Some authors recently showed that the contractile activity of the injected muscles might enhance the BtxA effect.^{51,52} In our case, the patient continued using his injected upper extremity as much as possible, and thus increased the overall contractile activity of the affected upper extremity and possibly prolonged the BtxA effect to at least 6 months.

It is believed that patients who have had a stroke display greater motor disability on their more affected sides than actually exists.¹⁴ Over time, this movement suppression, or learned nonuse, becomes so habitual that patients use the less affected side for most ADL.² In our case, the patient might have unknowingly been capable of performing more movement with his right upper

extremity than he was doing prior to this intervention. With the restraint on and the intensive training directed toward his right upper extremity, he attempted to move and use his arm much more during the 4-week modified CIMT program than he had done previously. This was evidenced by his Amount Scale scores on the MAL as well as through clinical observation. It is appropriate to speculate that, with this patient, motivation and repeated, task-specific practice through modified CIMT might have overcome a learned nonuse behavior.

The fact that the patient received no other therapeutic intervention for the study duration might help explain that the improvement was the result of combined BtxA injection and modified CIMT. Data from our case further refute the notion that patients who have had a stroke can only exhibit gains up to 1 year after their stroke.^{53,54} The changes, however, also could be the result of the attention the patient received or the almost constant attention given by the physicians and therapists who were involved in moving his right upper extremity. We do not know whether actual changes occurred at the cortical level, because neuroimaging techniques were not included in our case. Currently, it is unknown whether use-dependent cortical reorganization can occur in people who have had a stroke and who have moderately severe spasticity.

Page and colleagues¹⁴ reported mean improvements of 18.4 and 11.4 points on the FMA and ARAT in patients with a subacute stroke after a 10-week course of modified CIMT. In our case, the patient exhibited a change score of 3 on the FMA and 18 on the ARAT at the 3-month follow-up. It is important to note that the severity of upper-extremity motor impairment in our case was greater than those of the subjects in other studies,^{4,7-9,14} lending support to the suggestion of Taub and Morris¹¹ that CIMT may be of some benefit for people who have had a stroke and have relatively severe motor impairment. Although our patient showed improvements in MAL, WMFT, ARAT, and FMA scores after intervention, these findings did not suggest that the combined program restored motor ability to prestroke level. It was not clear how increases in scores on any of these measures translate to real-world functional abilities. Further controlled study with more subjects and a longer period of observation would help to address this question.

A traditional CIMT protocol can be difficult and frustrating. The intensity of the practice schedule and the duration of the restraint schedule in CIMT could make

patient adherence and motivation, as well as the ability to engage in 6 hours training, problematic. Schaumburg et al⁵⁵ reported only 32% adherence to the CIMT restriction schedule. A recent survey administered to patients who have had a stroke and therapists showed that most patients with stroke would not want to participate in CIMT, but would prefer a therapy protocol lasting for more weeks with shorter activity sessions or fewer hours of wearing the restrictive devices.⁵⁶ We preferred a less-intense modified CIMT program because considerable evidence suggested that various practice schedules emphasizing repeated limb use could elicit cortical reorganization and subsequent functional improvement.^{57–60} In addition, the persistent program beyond the 4 weeks at home is a novel component and may be an important element as alternative means of CIMT delivery are explored. A patient who is adherent and self-directed may be able to work more independently or with family support. Although the patient demonstrated gains according to the assessment tools, at the 6-month follow-up visit, he said that wearing restraint did influence his cosmesis, affective state, and self-esteem. His motivation diminished over time, and he grew tired of wearing the restraint.

Conclusion

This is the first case report that describes the application of a combined program of BtxA and modified CIMT in an individual who had upper-extremity spasticity and only minimal volitional extension movement in his wrist and fingers 4 years after his stroke. His test scores improved immediately following the 4-week program and these increased scores were maintained at the 6-month follow-up.

This case report was meant to serve as a baseline descriptive effort of combined BtxA and modified CIMT for a patient with stroke and disabling upper-extremity spasticity. The results of this case were promising enough to justify further clinical studies. Additional studies with a larger sample size and a longer follow-up period would help to determine whether this combination would provide long-term and clinically significant benefits compared with traditional therapies for patients with spasticity. The cost/benefit ratio also should be addressed. Further research combining BtxA with other intense therapies, electrical stimulation, cycle training, or other motor recovery therapy is warranted to ascertain the optimal interventions for patients with chronic upper-limb spasticity and limited motor ability.

References

1 Wolf SL, Lecraw DE, Barton LA, Jann BB. Forced use of hemiplegic upper extremities to reverse the effect of learned nonuse among chronic stroke and head-injured patients. *Exp Neurol*. 1989;104:125–132.

2 Taub E, Uswatte G, Pidikiti R. Constraint-induced movement therapy: a new family of techniques with broad application to physical rehabilitation—a clinical review. *J Rehabil Res Dev*. 1999;36:237–251.

3 van der Lee JH, Wagenaar RC, Lankhorst GJ, et al. Forced use of the upper extremity in chronic stroke patients: results from a single-blind randomized clinical trial. *Stroke*. 1999;30:2369–2375.

4 Morris DM, Crago JE, DeLuca SC, et al. Constraint-induced movement therapy for motor recovery after stroke. *Neurorehabilitation*. 1997;9:29–43.

5 Liepert J, Miltner WH, Bauder H, et al. Motor cortex plasticity during constraint-induced movement therapy in stroke patients. *Neurosci Lett*. 1998;250:5–8.

6 Liepert J, Bauder H, Wolfgang HR, et al. Treatment-induced cortical reorganization after stroke in humans. *Stroke*. 2000;31:1210–1216.

7 Kunkel A, Kopp B, Muller G, et al. Constraint-induced movement therapy for motor recovery in chronic stroke patients. *Arch Phys Med Rehabil*. 1999;80:624–628.

8 Taub E, Miller NE, Novack TA, et al. Technique to improve chronic motor deficit after stroke. *Arch Phys Med Rehabil*. 1993;74:347–354.

9 Miltner WH, Bauder H, Sommer M, et al. Effects of constraint-induced movement therapy on patients with chronic motor deficits after stroke: a replication. *Stroke*. 1999;30:586–592.

10 Page SJ, Elovic E, Levine P, Sisto SA. Modified constraint-induced therapy and botulinum toxin A: a promising combination. *Am J Phys Med Rehabil*. 2003;82:76–80.

11 Taub E, Morris DM. Constraint-induced movement therapy to enhance recovery after stroke. *Curr Atheroscler Rep*. 2001;3:279–286.

12 Taub E, Crago JE, Uswatte G. Constraint-induced movement therapy: a new approach to treatment in physical rehabilitation. *Rehabil Psychol*. 1998;43:152–170.

13 Uswatte G, Taub E. Constraint-induced movement therapy: new approaches to outcome measurement in rehabilitation. In: Struss DT, Winocur G, Robertson IH, eds. *Cognitive Neurorehabilitation: A Comprehensive Approach*. New York, NY: Cambridge University Press; 1999: 215–222.

14 Page SJ, Sisto S, Levine P, McGrath RE. Efficacy of modified constraint-induced movement therapy in chronic stroke: a single-blinded randomized controlled trial. *Arch Phys Med Rehabil*. 2004;85: 14–18.

15 Blanton S, Wolf SL. An application of upper-extremity constraint-induced movement therapy in a patient with subacute stroke. *Phys Ther*. 1999;79:847–853.

16 Morris DM, Taub E. Constraint-induced therapy approach to restoring function after neurological injury. *Top Stroke Rehabil*. 2001;8:16–30.

17 Ostendorf CG, Wolf SL. Effect of forced use of the upper extremity of a hemiplegic patient on changes in function: a single-case design. *Phys Ther*. 1981;61:1022–1028.

18 Nakayama H, Jorgensen HS, Raaschou AO, Olsen TS. Recovery of upper extremity function in stroke patients: the Copenhagen Stroke Study. *Arch Phys Med Rehabil*. 1994;75:394–398.

19 Katz RT. Spasticity. In: Braddom RL, ed. *Physical Medicine and Rehabilitation*. 2nd ed. Philadelphia, Pa: WB Saunders Co; 2000:592.

20 Lance JW. Symposium synopsis. In: Feldman RG, Young RR, Koella WP, eds. *Spasticity, Disordered Motor Control*. Chicago, Ill: Year Book Medical Publishers; 1980:485–494.

21 Botte MJ, Nickel VL, Akeson WH. Spasticity and contracture: physiologic aspects of formation. *Clin Orthop Relat Res*. 1988;233:7–18.

22 Barnes MP. Management of spasticity. *Age Aging*. 1998;27:239–245.

- 23 Bhakta BB, Cozens JA, Bamford JM, Chamberlain MA. Use of botulinum toxin in stroke patients with severe upper limb spasticity. *J Neurol Neurosurg Psychiatry*. 1996;61:30–35.
- 24 O'Brien CF, Seeberger LC, Smith DB. Spasticity after stroke: epidemiology and optimal treatment. *Drugs Aging*. 1996;9:332–340.
- 25 Simpson DM, Alexander DN, O'Brien CF, et al. Botulinum toxin type A in the treatment of upper extremity spasticity: a randomized, double-blind, placebo-controlled trial. *Neurology*. 1996;46:1306–1310.
- 26 Bakheit AM, Thilmann AF, Ward AB, et al. A randomized, double-blind, placebo-controlled, dose-ranging study to compare the efficacy and safety of three doses of botulinum toxin type A (Dysport) with placebo in upper limb muscle spasticity after stroke. *Stroke*. 2000;31:2402–2406.
- 27 Bakhta BB, Cozens JA, Chamberlain MA, Bamford JM. Impact of botulinum toxin type A on disability and carer burden due to arm spasticity after stroke: a randomized double blind placebo controlled trial. *J Neurol Neurosurg Psychiatry*. 2000;69:217–221.
- 28 Brashear A, Gordon MF, Elovic E, et al. Intramuscular injection of botulinum toxin for the treatment of wrist and finger spasticity after a stroke. *N Engl J Med*. 2002;347:395–400.
- 29 Dolly O. Synaptic transmission: inhibition of neurotransmitter release by botulinum toxins. *Headache*. 2003;43(suppl 1):S16–S24.
- 30 Bleecker ML, Bolla-Wilson K, Kawas C, Agnew J. Age-specific norms for the Mini-Mental State Exam. *Neurology*. 1988;38:1565–1568.
- 31 Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12:189–198.
- 32 Gregson JM, Leathley M, Moore AP, et al. Reliability of the Tone Assessment Scale and the Modified Ashworth Scale as clinical tools for assessing poststroke spasticity. *Arch Phys Med Rehabil*. 1999;80:1013–1016.
- 33 Constraint-Induced Movement Therapy Research Group. *Manual: Upper Extremity Motor Activity Log (UE/MAL)*. Birmingham, Ala: University of Alabama at Birmingham and Birmingham Veteran's Administration Center; August 2000.
- 34 Morris DM, Uswatte G, Crago JE, et al. The reliability of the Wolf Motor Function Test for assessing upper extremity function after stroke. *Arch Phys Med Rehabil*. 2001;82:750–755.
- 35 Wolf SL, Catlin PA, Ellis M, et al. Assessing Wolf Motor Function Test as outcome measure for research in patients after stroke. *Stroke*. 2001;32:1635–1639.
- 36 Lyle RC. A performance test for assessment of upper limb function in physical rehabilitation treatment and research. *Int J Rehabil Res*. 1981;4:483–492.
- 37 de Weerd W, Harrison MA. Measuring recovery of arm-hand function in stroke patients: a comparison of the Brunnström–Fugl-Meyer test and the Action Research Arm Test. *Physiother Can*. 1985;37:65–70.
- 38 van der Lee JH, De Groot V, Beckerman H, et al. The intra- and interrater reliability of the Action Research Arm Test: a practical test of upper extremity function in patients with stroke. *Arch Phys Med Rehabil*. 2001;82:14–19.
- 39 van der Lee JH, Beckerman H, Lankhorst GJ, Bouter LM. The responsiveness of the Action Research Arm Test and the Fugl-Meyer Assessment scale in chronic stroke patients. *J Rehabil Med*. 2001;33:110–113.
- 40 Fugl-Meyer AR, Jaasko L, Leyman I, et al. The post-stroke hemiplegic patient, 1: a method for evaluation of physical performance. *Scand J Rehabil Med*. 1975;7:13–31.
- 41 Duncan PW, Propst M, Nelson SG. Reliability of the Fugl-Meyer assessment of sensorimotor recovery following cerebrovascular accident. *Phys Ther*. 1983;63:1606–1610.
- 42 Bakheit AM, Severa S, Cosgrove A, et al. Safety profile and efficacy of botulinum toxin A (Dysport) in children with muscle spasticity. *Dev Med Child Neurol*. 2001;43:234–238.
- 43 Kopp B, Kunkel A, Muhn timer W, et al. Plasticity in the motor system related to therapy-induced improvement of movement after stroke. *Neuroreport*. 1999;10:807–810.
- 44 Morris DM, Crago JE, Uswatte G, Taub E. Behavioral components of constraint-induced movement therapy [poster presentation]. *Neurology Report*. 2000;24:201.
- 45 Mizrahi EM, Angel RW. Impairment of voluntary movement by spasticity. *Ann Neurol*. 1979;5:494–495.
- 46 Sahrman SA, Norton BJ. The relationship of voluntary movement to spasticity in the upper motor neuron syndrome. *Trans Am Neurol Assoc*. 1977;102:108–112.
- 47 Knutsson E, Martensson A. Dynamic motor capacity in spastic paresis and its relation to prime mover dysfunction, spastic reflexes and antagonist co-activation. *Scand J Rehabil Med*. 1980;12:93–106.
- 48 Jankovic J, Schwartz K. Botulinum toxin injections for cervical dystonia. *Neurology*. 1990;40:277–280.
- 49 Borodic GE, Ferrante RJ, Pearce LB, Alderson K. Pharmacology and histology of the therapeutic application of botulinum toxin. In: Jankovic J, Hallett M, eds. *Therapy With Botulinum Toxin*. New York, NY: Marcel Dekker; 1994:119–157.
- 50 de Paiva A, Meunier FA, Molgo J, et al. Functional repair of motor endplates after botulinum toxin type A poisoning: biphasic switch of synaptic activity between nerve sprouts and their parent terminals. *Proc Natl Acad Sci U S A*. 1999;96:3200–3205.
- 51 Hesse S, Jahnke MT, Luecke D, Mauritz KH. Short-term electrical stimulation enhances the effectiveness of botulinum toxin in the treatment of lower limb spasticity in hemiparetic patients. *Neurosci Lett*. 1995;201:37–40.
- 52 Eleopra R, Tugnoli V, De Grandis D. The variability in the clinical effect induced by botulinum toxin type A: the role of muscle activity in humans. *Mov Disord*. 1997;12:89–94.
- 53 Parker VM, Wade DT, Langton Hewer R. Loss of arm function after stroke: measurement, frequency, and recovery. *Int Rehabil Med*. 1986;8:69–73.
- 54 Jorgensen HS, Nakayama H, Raaschou HO, et al. Outcome and time course of recovery in stroke, part II: time course of recovery, the Copenhagen Stroke Study. *Arch Phys Med Rehabil*. 1995;76:406–412.
- 55 Schaumburg S, Pierce S, Gaffney K, Gershkoff A. Constraint-induced therapy: moving research into practice. Paper presented at: American Congress of Rehabilitation Medicine Annual Meeting; October 16, 1999; Orlando, Fla.
- 56 Page SJ, Levine P, Sisto S, et al. Stroke patients' and therapists' opinions of constraint-induced movement therapy. *Clin Rehabil*. 2002;16:55–60.
- 57 Classen J, Liepert J, Wise SP, et al. Rapid plasticity of human cortical movement representation induced by practice. *J Neurophysiol*. 1998;79:1117–1123.
- 58 Liepert J, Terborg C, Weiller C. Motor plasticity induced by synchronized thumb and foot movements. *Exp Brain Res*. 1999;125:435–439.
- 59 Butefisch C, Hummelsheim H, Denzler P, Mauritz KH. Repetitive training of isolated movements improves the outcome of motor rehabilitation of the centrally paretic hand. *J Neurol Sci*. 1995;130:59–68.
- 60 Winstein CJ, Rose DK. Recovery and rehabilitation of arm use after stroke. *J Stroke Cerebrovasc Dis*. 2001;10:197.

Appendix 1.

Motor Activity Log Rating Scale^a

Amount Scale

- 0—Did not use weaker arm (never).
- 1—Occasionally used weaker arm, but only very rarely (very rarely).
- 2—Sometimes used weaker arm but did the activity most of the time with stronger arm (rarely).
- 3—Used weaker arm about half as much as before the stroke (half prestroke).
- 4—Used weaker arm almost as much as before the stroke (¾ prestroke).
- 5—Used weaker arm as often as before the stroke (same as prestroke).

How Well Scale

- 0—The weaker arm was not used at all for that activity (never).
- 1—The weaker arm was moved during that activity but was not helpful (very poor).
- 2—The weaker arm was of some use during that activity but needed some help from the stronger arm or moved very slowly or with difficulty (poor).
- 3—The weaker arm was used for the purpose indicated, but movements were slow or were made with only some effort (fair).
- 4—The movements made by the weaker arm were almost normal but not quite as fast or accurate as normal (almost normal).
- 5—The ability to use the weaker arm for that activity was as good as before the stroke (normal).

^aReprinted with permission of Williams & Wilkins from: Uswatte G, Taub E, Morris D, et al. Reliability and validity of the Upper-Extremity Motor Activity Log-14 for measuring real-world arm use. *Stroke*. 2005;36:2493–2496. Available online at: <http://www.strokeaha.org>.

Appendix 2.

Wolf Motor Function Test Functional Ability Scale^a

- 0 Does not attempt with involved arm.
- 1 Involved arm does not participate functionally; however, an attempt is made to use the arm. In unilateral tasks, the uninvolved extremity may be used to move the involved extremity.
- 2 Arm does participate, but requires assistance of uninvolved extremity for minor readjustments or change of position, or requires more than 2 attempts to complete, or accomplishes very slowly. In bilateral tasks, the involved extremity may serve only as a helper or stabilizer.
- 3 Arm does participate, but movement is influenced to some degree by synergy or is performed slowly and/or with effort.
- 4 Arm does participate; movement is close to normal, but slightly slower; may lack precision, fine coordination or fluidity.
- 5 Arm does participate; movement appears to be normal.

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Appendix 3.

Questionnaire on Constraint-Induced Movement Therapy (CIMT)

Please reply to the questionnaire about CIMT

1. Was the program beneficial? _____
2. Did you make any improvement with affected arm? _____
3. Did you try and use your affected arm more? _____
4. Did the program increase your awareness of need/benefits of trying to use your affected arm? _____
5. Other comments: _____
