

Motor Control Testing of Upper Limb Function After Botulinum Toxin Injection: A Case Study

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ABSTRACT. Hurvitz EA, Conti GE, Flansburg EL, Brown SH. Motor control testing of upper limb function after botulinum toxin injection: a case study. *Arch Phys Med Rehabil* 2000;81:1408-15.

Objective: To evaluate changes in upper extremity function in a hemiparetic patient after treatment with botulinum toxin (BTX) using motor-control testing (MCT) techniques.

Design: Interventional with longitudinal study, open label.

Setting: A children's hospital and a motor-control laboratory at a major academic center.

Participants: A 16-year-old male with right hemiparetic cerebral palsy and a healthy 12-year-old control subject.

Interventions: BTX injections to the elbow and wrist flexors.

Main Outcome Measures: MCT was used to examine 4 upper extremity movements: forward reach, bilateral rhythmic movements (both muscle homologous and direction homologous), isometric pinch, and hand tapping. The patient was tested before treatment and at 2, 4, 6, 12, 18, and 24 weeks after treatment. In addition, range of motion (ROM), the Ashworth scale of spasticity, Functional Independence Measure™, and the mobility and activities of daily living (ADL) sections of the Pediatric Evaluation of the Disability Inventory were performed.

Results: Forward reach demonstrated little change initially despite patient reports of "feeling looser." Improvement was noted after 18 weeks, but returned to baseline level at 24 weeks. Bilateral rhythmic movements also showed slight improvement at 18 weeks. Pinch force increased significantly after 2 weeks, but declined again at 6 weeks. Improvements occurred in ROM and the Ashworth rating of spasticity, but were not temporally associated with each other or with MCT results. Functional assessment data did not change during the study period.

Conclusions: Improvements in more complex motor tasks were noted after significant delay from the time of treatment, while simpler tasks demonstrated a more rapid improvement, followed by a rapid return to baseline levels. This case suggests that MCT techniques can provide quantitative and qualitative data, which can add new information about upper extremity motor disability and the outcome of treatment.

Key Words: Botulinum toxin type A; Muscle spasticity; Arm; Case report; Cerebral palsy; Functional assessment; Rehabilitation.

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THE MANAGEMENT OF SPASTICITY and its evaluation present challenges to the rehabilitation specialist. Over the past several years, treatment options for spasticity have expanded to include the use of neural depressants and nerve blocks,¹⁻⁵ and surgical interventions such as tendon transplants or lengthening,⁶⁻⁹ and selective dorsal rhizotomy.¹⁰⁻¹³

Assessment of treatment-related changes in spastic conditions using motor-control and biomechanic techniques has received increasing attention over the past few years. Most studies have focused on changes in locomotor function following various therapeutic interventions.¹⁴⁻¹⁶ Assessment of therapy-related changes in upper extremity motor function, however, is still largely confined to subjective, observational approaches or standardized measures of muscle tone, range of motion (ROM), and task performance. Because of limitations in methodology, it has been difficult to determine quantitatively movement speed, accuracy, or changes in dynamic movement characteristics. Movement dynamics can be of particular importance, because they are thought to reflect general organizing principles used by the central nervous system (CNS) during the programming and execution of goal-directed movement.^{17,18}

The effectiveness of motor control analytic methods in quantifying subtle but meaningful alterations in movement dynamics has been demonstrated for a variety of upper limb motor deficits. For example, individuals with mild cerebellar ataxia can show significant changes in trajectory kinematics, which are clinically undetectable.¹⁹⁻²¹ Similar techniques have been used to evaluate the effectiveness of different therapies in the treatment of neuromuscular disorders such as Lambert-Eaton syndrome and myasthenia gravis.²² These approaches have been widely used to study motor deficits in Parkinson's disease and other CNS disorders²³ and in elderly populations.²⁴ Upper limb kinematic quantification of functional disability is well tolerated by pediatric populations, as has been recently demonstrated in ataxic children as young as 6 years.²⁵

Botulinum toxin (BTX) is a powerful neuromuscular blocking agent that has been used to decrease muscle tone in lower limb muscles and thereby improve locomotor ability in spastic conditions such as cerebral palsy and stroke.^{14,26-28} BTX is uniquely suited for use in the spastic upper extremity, because the effects are localized and there is minimal risk of paresthesia and other unpleasant side effects. However, reports regarding the effectiveness of BTX in upper limb function have been largely restricted to subjective evaluation of functional improvement and onset of action.²⁹⁻³⁴ In terms of onset of action, results have varied from the first 12 hours to 6 weeks after injection. This variance results largely from different measurement techniques, ranging from changes in the compound muscle action potential to observed changes in gait patterns.^{27,35-37}

In this case report, motor control testing (MCT) was used to evaluate changes in upper limb function over a 6-month period after BTX injection. The results demonstrate that kinematic analysis of limb movement can reveal valuable information

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about the nature and time course of functional improvement, which may not be observable using more conventional functional assessment or electrophysiologic tools.

METHODS

Case Report

Upper limb function was assessed in a 16-year-old man with right spastic hemiparetic cerebral palsy, which was diagnosed at 9 months of age. He was independent in most activities of daily living (ADL), typically using his left hand, and was active in sports such as soccer and in-line skating. He presented to the clinic with a desire to dribble a basketball, improve handgrip, and tie his shoes. At the time of testing, he was not receiving any antispasticity medications, nor was he involved in a regular therapy regimen, although previously he had intermittently worn bracing on his right upper and lower extremities. Clinical evaluation of the right upper limb revealed increased flexor tone and limited elbow and wrist passive ROM (PROM) (table 1). Right-sided grip was weak but improved slightly when the wrist was passively extended.

Clinical Assessment

Active ROM (AROM) and PROM measurements of the elbow and wrist were performed by a single experienced occupational therapist using a standardized technique. Upper limb goniometry has been shown to have good intratester reliability, with higher reliability coefficients found among experienced raters.^{38,39} Spasticity was measured using the modified Ashworth scale.⁴⁰ Functional ability was measured by the physiatrist using the Pediatric Evaluation of the Disability Inventory (PEDI)⁴¹ and the Functional Independence Measure™ (FIM).⁴² Clinical assessments were performed before injection and at 6, 18, and 24 weeks after injection.

Motor Control Tasks

All MCT was performed in the late afternoon before BTX injection, and at 2, 4, 6, 12, 18, and 24 weeks after injection. Injection occurred immediately after the first testing session. Four motor tasks were examined to assess upper limb function and bilateral coordination (forward reach, rhythmic bilateral tasks), as well as the ability to produce simple hand movements such as hand tapping and isometric force contractions.

Forward reach. In response to an auditory tone, the subject was asked to touch a wall-mounted switch that was located at approximately shoulder level. Movements were made from a seated position with the subject positioned to minimize trunk

flexion during the reaching task. The subject was instructed to move as fast and accurately as possible and to touch the switch with his hand. Both arms were tested independently (unilateral condition) and simultaneously (bilateral).

Bilateral rhythmic. Using both arms, the subject was asked to make rhythmic “finger-to-nose” movements from a 90° shoulder abduction position. Both in-phase (muscle homologous-simultaneous flexion or extension of both arms) and anti-phase (direction homologous-simultaneous flexion and extension of both arms) movements were examined. All movements were made from a standing position.

Isometric pinch grip. The subject performed maximal isometric force contractions by gripping a strain gauge mounted on a vertical rod in front of him. For the affected hand, the experimenter assisted in positioning the hand to maximize contact of the thumb and fingers with the strain gauge. The task was performed from a seated position, and 3 repetitions for each hand were recorded.

Hand tapping. The subject was seated with both forearms resting on a horizontal surface positioned at waist level. Using the hand, the subject tapped the switch as fast as possible for 6 seconds. Both hands were tested independently (unilateral condition) and simultaneously (bilateral).

Injection Technique

Before baseline testing and injection, the subject’s parents signed an informed consent document following the guidelines established by the University of Michigan’s institutional review board. BTX (Botox^a) was obtained in a frozen, crystallized form and reconstituted with 2mL of 0.9% sterile saline. The toxin was injected into the biceps brachii (100U), flexor carpi radialis (50U), and flexor carpi ulnaris (50U) muscles. Motor point locations of the targeted muscles were identified visually and used to determine injection sites. A topical anesthetic cream was applied to the injection sites approximately 45 minutes before injection. No adverse effects were reported by the subject or family members.

Data Recording and Analysis

Assessment of forward reach movements was restricted to an analysis of elbow displacement. While this task can be considered multijoint, it is well established in the motor-control literature that joint angular and tangential movement profiles share similar kinematic features.^{43,44} More recently, single-joint elbow analysis associated with a forward-reach task in ataxic children revealed subtle changes in motor performance that were undetectable using clinical evaluation procedures.²⁵ For both the forward-reach and rhythmic bilateral tasks, elbow displacement was recorded using electrogoniometers^b mounted across the elbow joint of both arms. For the hand-tapping task, custom-designed microswitches recorded the number of taps. Isometric grip force was recorded using custom-designed strain gauges mounted on a vertical rod.

All data were digitized at 250Hz and analyzed off-line using commercial software.^c Order of testing (forward reach, rhythmic bilateral, hand tapping) remained constant for each testing session. The duration of each testing session was approximately 30 to 40 minutes.

RESULTS

Clinical Assessments

Physical findings and functional assessment scores at the time of injection are given in table 1. Spasticity, as measured by the modified Ashworth scale, showed a slight decline at 6

Table 1: Physical Findings and Functional Assessment

Assessment	Preinjection	6 Weeks	18 Weeks	24 Weeks
Full elbow extension (AROM)	140	145	135	150
Full elbow extension (PROM)	150	155	150	165
Elbow Ashworth	2	1+	2	2
Wrist AROM (deg from neutral)	-50	-45	-45	-25
Wrist PROM (deg from neutral)	45	45	45	65
Wrist Ashworth	1+	1	2	2
PEDI Self-Care	72/123	No change	No change	No change
PEDI Caregiver				
ADL	38	No change	No change	No change
FIM	118	No change	No change	No change

weeks, but increased again at 18 weeks. A variation of at least 5° was used to identify change in ROM between assessment sessions.³⁸ Both elbow and wrist AROM and PROM increased, with maximal active and passive elbow and wrist extension occurring at week 24. No changes were noted in the PEDI or FIM.

Motor Control Assessments

For purposes of comparison, typical elbow extension profiles associated with forward reaching in a healthy 12-year-old control subject are shown in figure 1. As can be seen, extension of the elbow occurred in a smooth and continuous fashion. Elbow velocity was characterized by a typical bell-shaped, symmetric time course, indicating approximately equal amounts of time spent in acceleration and deceleration. Movements were highly consistent over repeated trials, resulting in minimal temporal and spatial variability from 1 trial to the next.

Baseline MCT of the subject revealed an inability to reach forward with the affected right arm. This is evident in the first set of elbow position and velocity records in figure 2 (preinjection). Despite self-reports of a reduction in muscle tone within days following injection, testing at 2 weeks postinjection showed continued impairment in reaching ability. This is

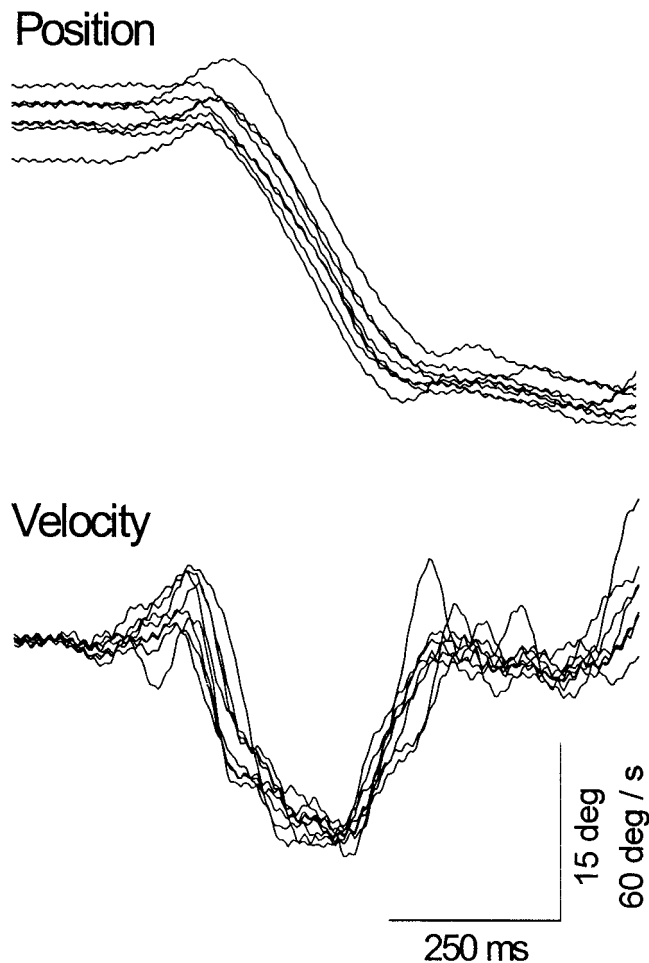


Fig 1. Typical elbow kinematic records associated with forward reaching movements made by the dominant arm in a healthy 12-year-old. Records are plotted so that downward position deflections indicate elbow extension. Angular velocity records were obtained by differentiation of the position signal.

demonstrated in figure 2 by the limited elbow extension and the high degree of variability seen across repeated movements. No consistent pattern of movement was observed at 4, 6, or 12 weeks after injection. It was not until 18 weeks' postinjection that a more stereotyped and consistent pattern of elbow extension emerged. At that time, a significant increase in elbow extension occurred that was characterized by relatively time-symmetric velocity profiles. Movement trajectories were relatively smooth from 1 trial to the next, which resulted in a considerable reduction in overall variability compared with earlier testing sessions. However, subsequent testing at 24 weeks revealed an almost complete loss of active elbow extension.

The ability to produce coordinated, rhythmic, bilateral elbow movements was severely limited before injection as shown in the angle-angle plots in figures 3 and 4 (preinjection). Typically, movements of both arms show a tight spatial coupling in which angular displacement is matched throughout the time course of the movement whether or not similar or opposite muscle groups are simultaneously activated. Perfectly matched coupling of both elbows results in a straight-line excursion, as indicated by the dashed lines in figures 3 and 4. Angle-angle plots from muscle homologous movements made by the subject showed marked deviations from a straight line as a result of both a reduction in right elbow extension, most noticeable before injection, and a tendency toward sequential rather than simultaneous movement of both elbows. A transient improvement was noted at week 2, as identified by electrogoniometry and shown in figure 3. This improvement in bilateral coordination was seen again at week 18, persisting through week 24.

A complete loss of interlimb coordination was observed during direction homologous movements in which elbow flexion of one arm was coupled with elbow extension of the other arm (fig 4). As reflected in the multiple vertical and horizontal components comprising each angle-angle plot, bilateral elbow movement occurred sequentially rather than simultaneously. No improvement was observed across testing sessions.

Changes in isometric lateral pinch grip are shown in table 2. Before the injection, pinch grip produced by the affected hand was 80% less than that of the unaffected hand. At 2 weeks after injection, pinch force on the affected side increased over fourfold as compared with preinjection values ($t = .0006$). However, this was followed by a reduction to preinjection values at 6 weeks. Subsequent testing at 12, 18, and 24 weeks revealed slight but statistically insignificant increases in pinch force.

Before BTX injection, the subject was unable to produce hand-tapping movements with the affected right hand under either unilateral or bilateral conditions. In contrast, left-hand unilateral performance remained relatively constant at approximately 27 taps per 6 seconds across the testing period (fig 5). At 2 weeks, the subject was able to produce unilateral tapping movements with the affected hand, albeit it at a much slower rate (7 taps per 6sec) than the unaffected hand. At 4 and 6 weeks, tapping rate increased slightly to 11 taps per 6 seconds, which was then followed by a decrease to 6 taps per 6 seconds which persisted for the remainder of the testing period. Interestingly, bilateral tapping resulted in a significant reduction in tapping rate of the unaffected hand while facilitating tapping performance of the affected hand. This was most obvious at 2, 4, and 6 weeks, with maximal tapping rates occurring at 4 weeks. From 6 weeks onward, tapping rates were virtually identical for both hands during the bilateral tapping task.

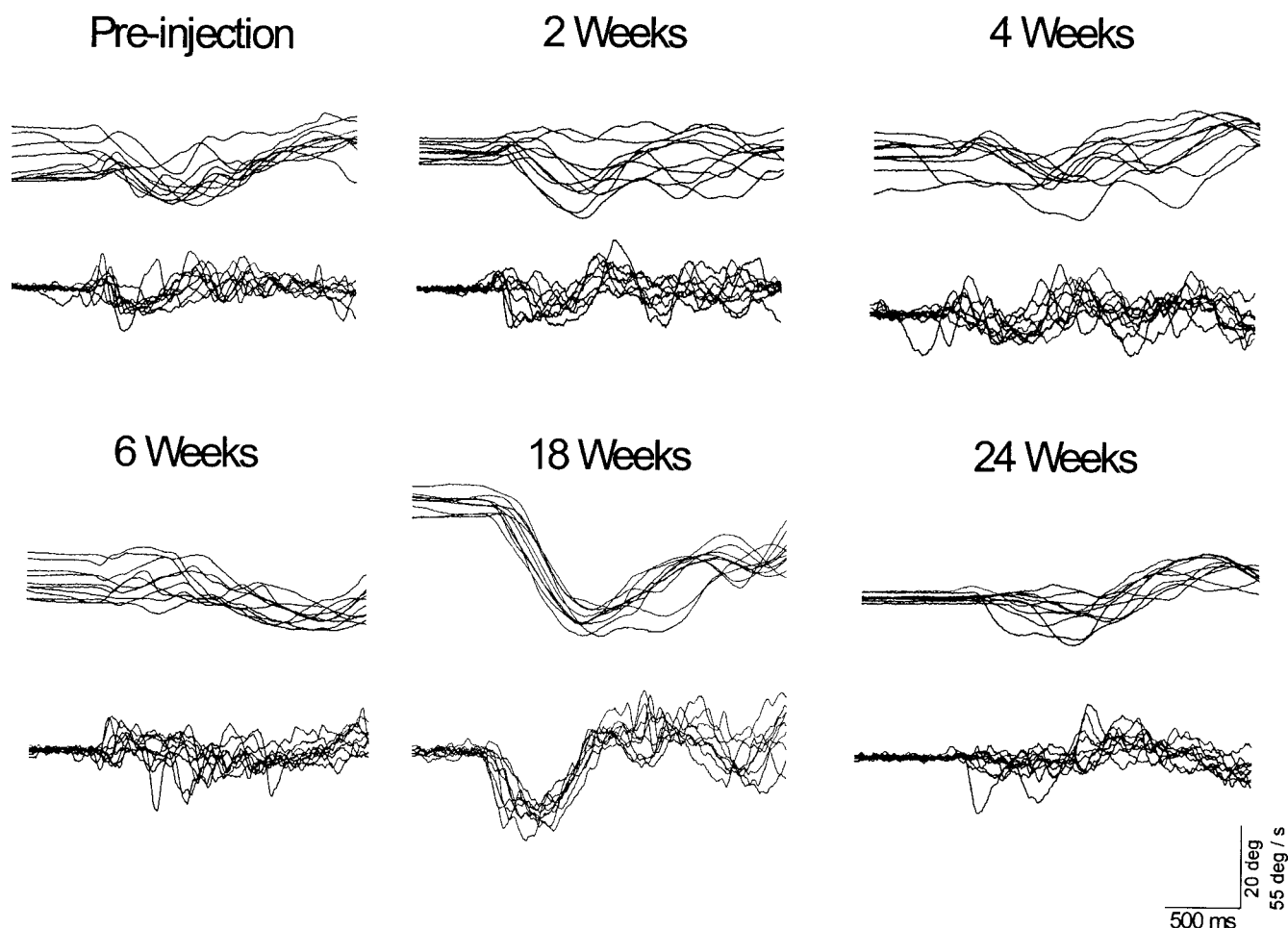


Fig 2. Overplots of elbow position and velocity associated with forward reaching movements before and following injection with BTX. Each data set (upper records, position; lower, velocity) is comprised of 6 to 10 consecutive extension movements. Data from 12 weeks were similar to 6 week data, and thus were omitted from this figure and figures 3 and 4 for purposes of clarity.

DISCUSSION

Several studies have documented the effectiveness of BTX in reducing lower limb spasticity, thereby improving locomotor function and balance in a variety of spastic conditions.^{14,27,28,35,45} In particular, kinematic analysis of gait parameters such as stride length, ankle dorsiflexion, and knee flexion has provided useful insights into the nature of locomotor improvement after BTX injection.^{14,27}

In contrast, few quantitative studies exist that have examined changes in motor function following BTX use in the upper extremity, with most reports relying on subjective assessment of muscle tone, ROM, and functional independence. For instance, Das and Park²⁹ injected the upper extremities of 6 individuals with stroke and noted improvement in ROM and the Oswestry spasticity scale, which rates tone and voluntary movement. Minor increases in functional outcome scores using the Barthel index were also found postinjection. Wall et al³⁰ measured grip strength, ROM, and took photos and videotapes of the hand in 5 hemiparetic children with cerebral palsy. The images were rated subjectively by a blinded panel. They noted a trend toward improvement in hand appearance and the performance of simple set tasks. Yablon and associates³³ observed improvements in the modified Ashworth scale and in ROM in 21 patients with traumatic brain injuries, but functional measures were not included. Similar improvements in tone were

found by Simpson et al³² in 37 stroke patients. However, no significant changes in the FIM and other standardized clinical assessment instruments were found. Bhakta et al³¹ developed a task inventory based on a 1-to-4 rating scale. It was noted that 14 of 17 persons with stroke demonstrated some functional benefit after BTX injections, with clearing the palm and cutting fingernails being common areas of improvement. A case study by Mall et al³⁴ reported decreased spasticity and improved function, but no details of functional measures were provided. In a recent double-blinded study, Corry et al⁴⁶ evaluated 2 simple functional tasks as well as ROM, Ashworth scale, and the carrying angle of the arm in 14 hemiparetic patients. Some improvement was seen in range and tone, but no change was measured in task performance.

While the above studies demonstrate the effectiveness of BTX in reducing muscle tone, documentation of functional improvement has been limited, due in part to a lack of sensitivity in current functional assessment tests. Such limitations have been noted by Bhakta et al³¹ in explaining the lack of upper limb improvement using standardized functional assessments after BTX injection. Using kinematic analysis techniques, the study presented here is the first to demonstrate systematic, task-dependent changes in the quality of upper limb movements after BTX injections. Of particular interest was the change in elbow kinematics associated with forward reaching.

Despite self-reports of a reduction in elbow flexor spasticity within days of the injection and an improved Ashworth rating at 6 weeks' postinjection, no improvement in reaching behavior was observed until 18 weeks, well past the time when BTX is considered to have its onset of effect.^{27,35-37} At 18 weeks, the subject was able to reach the target with smooth elbow extension trajectories and relatively time-symmetric velocity profiles. In other words, equal amounts of time were spent accelerating and decelerating the limb. Such velocity characteristics are considered an important invariant characteristic of upper limb reaching movements that may reflect a basic organizational strategy used by the CNS to minimize energy expenditure.¹⁷ Surprisingly, measures of both PROM and AROM and spasticity at 18 weeks revealed no improvement over preinjection values. Thus, the ability to produce a "normal" reaching pattern at 18 weeks occurred absent any improvement in clinical assessment measures.

The ability to produce coordinated, bilateral arm movements followed a similar time course, but only for bilateral tasks requiring simultaneous activation of homologous muscle groups.

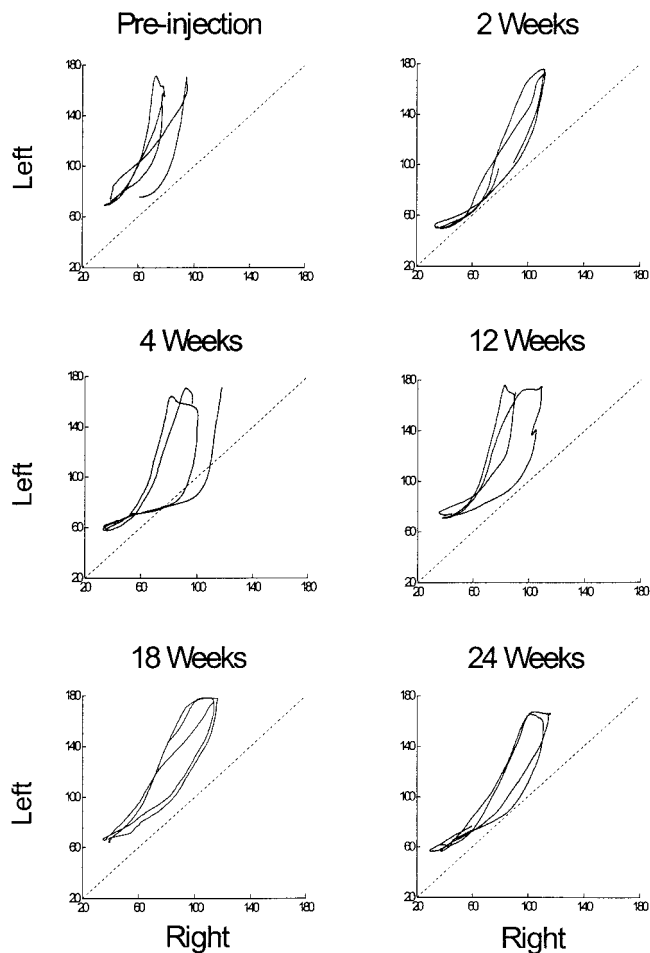


Fig 3. Elbow angle-angle plots associated with bilateral, muscle homologous movements. Right (affected) elbow position (in degrees) is plotted on the x axis; left (unaffected) elbow position on the y axis. *Dashed lines* indicate normal excursion paths for movements, which are tightly coupled throughout the range of angular displacement. In each graph, data from repetitive movements are shown. Increasing path length away from the origin reflects increasing elbow extension.

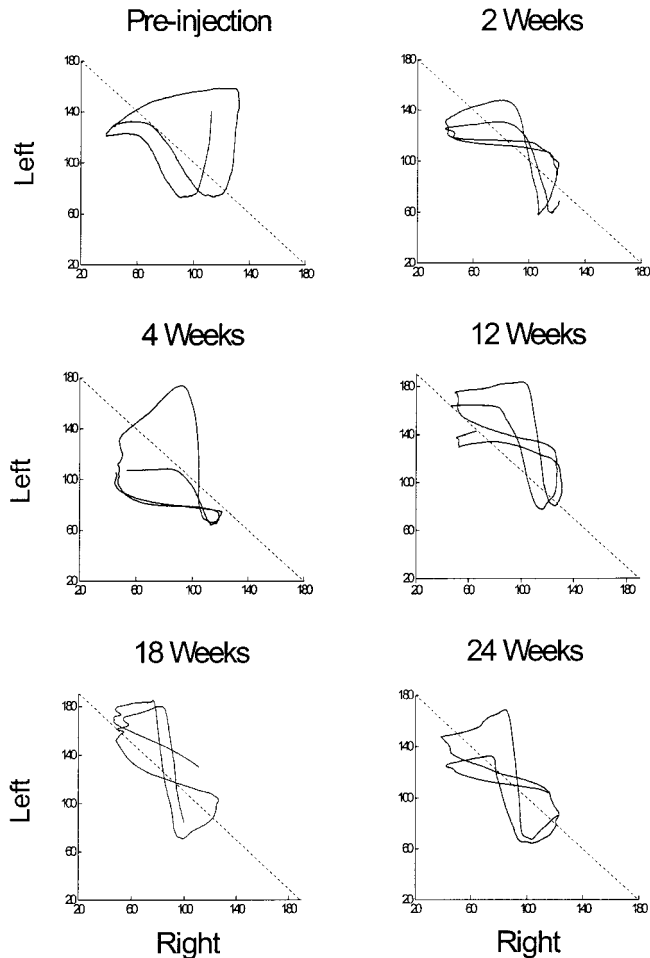


Fig 4. Elbow angle-angle plots associated with bilateral, direction homologous movements. Data are plotted using the same conventions as in figure 3. *Dashed lines* indicate normal excursion paths for movements in which elbow flexion of 1 limb is tightly coupled to elbow extension of the other limb.

In marked contrast, the subject remained unable to coordinate simultaneous flexion and extension elbow movements. Bilateral movements that require nonhomologous muscle activation are considered more difficult in terms of central motor programming and typically show more moment-to-moment variability than do muscle homologous movements.^{47,48} However, the ability to move both limbs simultaneously is preserved. In our study, both limbs moved independently rather than as a coordinated unit, suggesting impairment in central motor programming, impaired reciprocal activation of opposing motoneuron pools, or both.

The above motor tasks can be considered relatively complex in terms of central programming and execution.

Table 2: Mean Maximal Pinch Forces for the Right and Left Hands

	Preinjection	2 Weeks	6 Weeks	12 Weeks	18 Weeks	24 Weeks
Right	13.4	74.6	18.9	30.4	19.5	16.2
(SD)	(5.4)	(12.0)	(2.0)	(6.4)	(1.2)	(7.5)
Left	66.6	321.0	61.2	167.5	80.2	82.9
(SD)	(4.0)	(0.6)	(8.4)	(6.5)	(3.2)	(0.4)

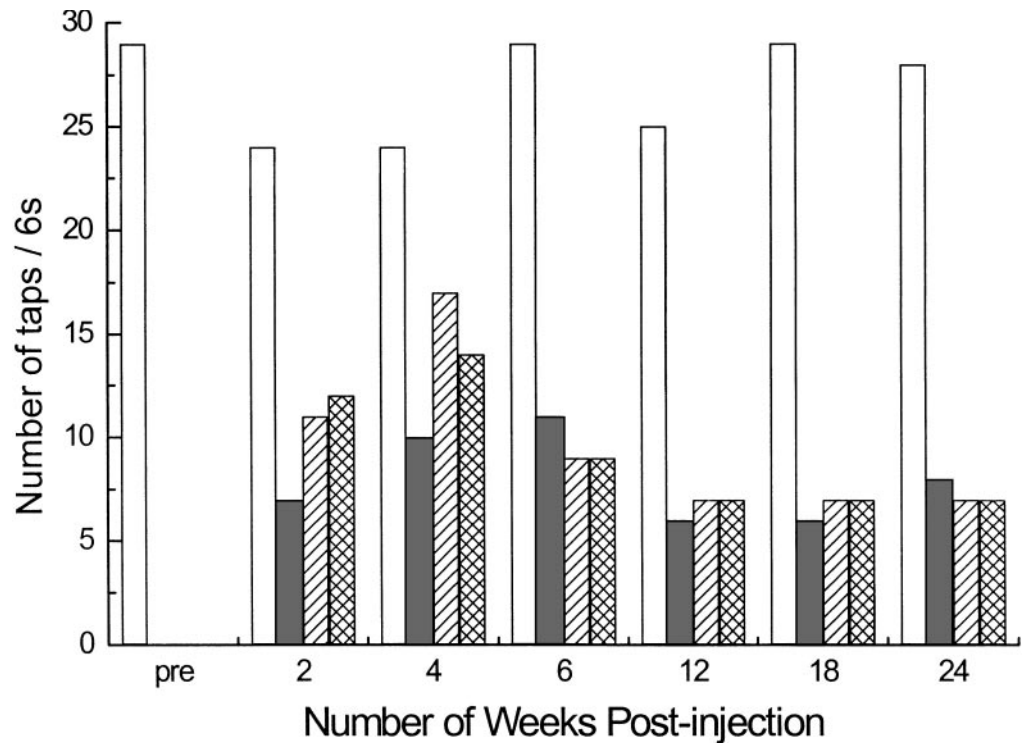


Fig 5. Hand-tapping performance before and after BTX injection. In each recording session, movements were made independently by the unaffected (□, left-hand unilateral) and affected (■, right-hand unilateral) hands, and simultaneously (▨, left-hand bilateral; ▩, right-hand bilateral). Before injection, the subject was able to produce tapping movements with the left hand but only in the unilateral condition. Each bar represents the number of taps per 6 seconds.

Multiple joints are involved, and, in the case of forward reaching, end-point accuracy and joint interaction forces must be considered. In contrast, hand tapping performed from a stable forearm position requires minimal activation of opposing muscles. Thus, the relative simplicity of this task probably explains the early improvement seen at 2 weeks postinjection.

Bilateral hand tapping illustrated the profound influence of the affected limb on the clinically unaffected limb. Before injection, the subject was unable to produce tapping movements with either hand when required to tap simultaneously. After the injection, bilateral tapping actually led to an improvement in tapping rates for the affected hand but was associated with a significant decrease in tapping performance of the unaffected hand. Thus, motor performance in hemiparetic conditions can be enhanced during bilateral tasks but at a cost in performance of the uninvolved limb. This phenomenon has been also demonstrated for both acute and progressive motor dysfunction conditions such as cerebellar neoplasms and Friedreich's ataxia,²⁵ stroke,⁴⁹ and children with cerebral palsy.⁵⁰

Perhaps the most striking observation seen in our study was the delayed onset in improvement of reaching movements as determined by the appearance of typical kinematic profiles. If a reduction in spasticity was adequate to allow for efficient execution of descending motor commands, then it would be expected that an improvement in the quality of movement would parallel changes in clinical measures such as tone and ROM. In this subject, there were limited changes in these measures. In fact, it is questionable if the change in Ashworth score can be said to represent a true difference in tone based on treatment effect. It is, therefore, interesting to speculate as to why motor-control changes were seen in with what appeared to be either very slight or even possibly no change in ROM or spasticity. It is possible that these measures lack sensitivity in a patient with relatively mild spasticity. The levels of change in the Ashworth scale may be too large to pick up smaller changes

that have functional significance. Alternatively, changes in these measures noted during passive evaluations may correlate poorly with improvements in motor function. In view of these findings, a suggested hypothesis would be that improved motor function is also dependent on more long-term changes at the supraspinal level. There is convincing evidence that alterations in sensory feedback from tactile stimulation,⁵¹ deafferentation,⁵² immobilization,⁵³ brain injury such as stroke,^{54,55} and induced focal dystonia⁵⁶ can lead to reorganization of sensorimotor cortical areas. Thus, it is reasonable to speculate that, in the rehabilitation of spastic conditions in which there has been long-term nonusage of a limb, a reduction in muscle tone is a necessary but insufficient condition for motor improvement. Rather, the development of new motor commands following reorganization of sensorimotor-related cortical areas must occur, which, in the absence of a functionally specific treatment plan, may take several months. While it is reasonable to assume that the duration of functional impairment may affect the time course of recovery, it is clear from this case study that despite a long-standing disability the development of a more consistent and presumably more efficient movement pattern was possible, albeit for a brief time.

It is interesting to note that, in comparison with upper limb function, improvement in locomotion after BTX injection occurs earlier and persists for a longer period.^{27,28,35} This may be related to differences in central programming demands and motor pathways responsible for locomotor versus goal-directed upper limb movements. It is well accepted that central pattern generators located at the spinal level provide the basic circuitry for reciprocal activation of opposing muscles involved in locomotion. In contrast, multiple parallel circuits are thought to contribute to the generation of upper limb movements, including corticocerebellar and corticostriatal internal feedback pathways. Last, reinforcement of motor commands may be easier to accomplish for gait than for upper limb reaching tasks, because,

in the case of the lower limbs, motor function is primarily related to locomotion and postural control.

CONCLUSION

The data presented here suggest the value of kinematic analyses in documenting changes in motor function after BTX injection. Augmentation of current clinical evaluation procedures with motor control assessment techniques provides the rehabilitation specialist with a long-sought "quality-of-movement" measure, which is of particular importance in functional recovery of the upper limb. Because the ability to produce "normal" motor patterns may be limited or influenced by a variety of factors such as limb-posture interactions and sensory or cognitive factors, flexibility in determining what constitutes maximal recovery must be considered. Despite this caveat, however, qualitative evaluation of kinematic "snapshots" and quantification of subtle yet potentially significant changes in dynamic motor performance provide a powerful tool in the development and modification of treatment protocols.

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Suppliers

- a. Allergan, Inc, 2525 Dupont Dr, Irvine, CA 92612.
- b. Penny and Giles Model LS-100; Biometrics, Ltd, 547 Lake Caroline Dr, Ruther Glen, VA 22546.
- c. Labview, National Instruments, 11500 N Mopac Expwy, Austin, TX 78759-3504.