

# Changes in Movement Characteristics of the Spastic Upper Extremity After Botulinum Toxin Injection

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**ABSTRACT.** Hurvitz EA, Conti GE, Brown SH. Changes in movement characteristics of the spastic upper extremity after botulinum toxin injection. *Arch Phys Med Rehabil* 2003;84:444-54.

**Objective:** To examine the longitudinal effects of botulinum toxin injection on movement characteristics of the spastic upper extremity in children by using motor control testing (MCT) techniques and standard clinical measures.

**Design:** Open-label clinical trial.

**Setting:** Motor control laboratory at an academic medical center.

**Participants:** A convenience sample of 9 subjects (5 boys, 4 girls; age range, 7–16y) with cerebral injury (stroke or cerebral palsy) and asymmetric upper-extremity function because of spasticity. Eight subjects had right-sided involvement.

**Interventions:** Botulinum toxin injection to the involved upper extremity, involving elbow, wrist, and finger flexors, depending on clinical presentation.

**Main Outcome Measures:** Clinical measures included range of motion (ROM), the Ashworth Scale, FIM™ instrument, Pediatric Evaluation of Disability Inventory, portions of the Bruininks-Oseretsky Test of Motor Proficiency, and the Purdue pegboard. MCT consisted of visually guided reaching, bilateral finger-to-nose movements, hand tapping, and isometric pinch force tasks. Kinematic assessments were made before and at 2, 4, 6, 12, 18, and 24 weeks after botulinum toxin injection.

**Results:** All subjects had increased ROM and decreased Ashworth values throughout the testing period. In motor control tasks, improvement typically occurred earlier in the least complex movements, such as hand tapping, with 6 of 9 subjects showing a maximum, although transient, unilateral tapping speed by 6 weeks. A similar time course was observed for pinch force tasks. Improvement in more complex, forward-reaching tasks occurred much later (week 12 or later) or did not occur at all. As with the hand tasks, improved reach performance declined toward the end of the testing period. All subject showed minimal or no improvement in bilateral finger-to-nose movements. Neither maximum changes in ROM or

Ashworth values correlated with improvements in functional elbow extension during sit and reach tasks, with 3 subjects with normal active ROM showing late onset or no change in reach.

**Conclusions:** Although botulinum toxin reduced tone and increased ROM of the spastic upper extremity, the time course and degree of motor improvement appears to depend on the complexity of the task. Future research should focus on the value of adjunct therapy, such as task-specific training, in addition to botulinum toxin treatments to facilitate functional improvement of the spastic upper extremity.

**Key Words:** Arm; Botulinum toxin; Kinematics; Rehabilitation; Spasticity.

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**I**N THE PAST DECADE, botulinum toxin has been an important addition in the management of spasticity in children, offering localized reduction in tone with minimal side effects.<sup>1-3</sup> Within days of injection, patients typically show improved range of motion (ROM) and decreased tone. This improvement lasts for approximately 4 months.<sup>3,4</sup> Although improvement in upper- and lower-limb function has been reported in several of studies, the application of quantitative motor assessment procedures has been largely restricted to gait analysis, in which increased knee extension, decreased plantarflexion, and improved stride have been reported.<sup>5-9</sup>

Several studies<sup>10-12</sup> have documented changes in upper-limb function after injection with botulinum toxin. However, these studies focused primarily on subjective evaluation of spasticity, ROM, and/or functional improvement. Functional changes after upper-extremity botulinum toxin injection have been measured, for example, by task inventory, when there was improvement in several functional activities such as nail clipping and clearing the palm.<sup>13</sup> Other studies<sup>4,6,14,15</sup> used a combination of subject reports and activities of daily living (ADLs) to assess functional gains. For example, Smith et al<sup>14</sup> found no change in upper-extremity dressing time, but did record subjective impressions of improvement in significantly more of their test subjects than in their controls. Others<sup>14,16-18</sup> have used videotaped assessments that were evaluated by blinded raters. A recent study by Fehlings et al<sup>19</sup> found that the Quality of Upper Extremity Skills Test was a useful tool with which to assess changes in upper-limb function after botulinum toxin injection.

However, these studies—although they provided valuable information—did not address the direct effects of the treatment on motor function. Improvements observed with passive testing, such as ROM and spasticity measures, do not always correlate well with improvements in function.<sup>20</sup> Changes in skills and task performance are theoretically related to improvements in movement characteristics based on the intervention, but other factors can play a role, including cognitive and visual skills and motivation. Moreover, the upper extremity performs a wide variety of movements, ranging from simple, single joint tasks to bilateral or multijoint motor tasks. A complete assessment of motor function must, therefore, ade-

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Table 1: Subjects and Injection Sites

Subject	Gender/Age (y)	Diagnosis	Initial FIM Score*	Injection Site (dosage in units)
1	M/15	Right hemiparetic CP	126	Biceps (100), FCR (50), FCU (50)
2	M/16	Right hemiparetic CP	121	Biceps (100), FCR (50), FCU (50)
3	F/7	Right hemiparetic CP	123	Biceps (100), pron teres (30), FCR (35), FCU (35)
4	F/11	Left hemiparetic CP	114	Triceps (65), biceps (60), pectoralis (75)
5	M/8	Right hemiparetic CP	99	Biceps (100), FCR (50), FCU (50)
6	F/16	Right hemiparesis, CVA at age 6	126	FCR (50), FCU (50), FDP (100)
7	F/14	Right hemiparetic CP	75	Biceps (100), brachialis (50), FCR (50), FCU (50), FDP (50)
8	M/11	Right hemiparetic CP	107	Biceps (100), brachialis (100), brachioradialis (100)
9	M/12	Right hemiparetic CP	116	Pron teres (50), FCR (50), FCU (50), FDP (50)

Abbreviations: M, male; F, female; CP, cerebral palsy; CVA, cerebrovascular accident; FCR, flexor carpi radialis; FCU, flexor carpi ulnaris; FDP, flexor digitorum profundus; Pron teres, pronator teres.

\* No change was seen in FIM scores throughout the testing period for any patient.

quately assess several aspects of upper-limb performance. Because of the complexity of the upper limb, from both a functional and central nervous system (CNS) control perspective, it is important for rehabilitation specialists to understand what aspects of a child's motor repertoire are most responsive to an intervention such as botulinum toxin injections.

The ability to quantify subtle but potentially important changes in movement characteristics with motor control testing (MCT) methods is a useful adjunct to more clinically oriented assessment procedures. MCT can further provide important insights into the general organizing principles used by the CNS during the programming and execution of goal-directed movement.<sup>21-23</sup> Kinematic analyses of upper-limb movements, as measured by MCT, have been particularly useful in understanding altered motor performance in a different pediatric conditions, such as Friedreich's ataxia,<sup>24</sup> spasticity,<sup>25,26</sup> and developmental coordination disorder.<sup>27</sup> A recent case study<sup>28</sup> that used MCT showed that changes in upper-limb function after botulinum toxin injections may be transient and variable in onset, depending on motor task complexity. The purpose of our study was to examine the effects of spasticity reduction through botulinum toxin injection on motor control of the upper arm in children with cerebral spasticity.

## METHODS

### Participants

Subjects included a convenience sample of children and adolescents, ages 7 to 18 years, with a diagnosis of spasticity of cerebral origin and asymmetric upper-extremity motor function. The subjects were selected from a pediatric rehabilitation clinic population at a university medical center. Exclusion criteria included (1) a history of botulinum toxin injections, surgery, or significant injury to the upper extremities; (2) inability to attend to and/or to cooperate with motor control testing; (3) joint contractures limiting elbow, wrist, or finger mobility by more than 25%; and (4) inability to attend all testing sessions.

Of 15 subjects originally recruited for the study, 6 were excluded because they failed to complete the protocol. Nine subjects (5 boys, 4 girls; age range, 7-16y) completed the study. Six were ambulatory without aids, 1 used a walker, and 2 used wheelchairs for mobility. Subject data are presented in table 1.

### Procedures

Before the intervention, subjects' parents signed an informed consent document that followed guidelines established by the University of Michigan's institutional review board. The intervention in this study was the injection of selected muscles with botulinum toxin, followed by serial clinical and motor control testing. No other clinical intervention occurred during the study period. All patients were evaluated by a physician experienced in botulinum toxin injection technique (EAH). He made a clinical evaluation about which upper-extremity muscles would benefit most from injection. Botulinum toxin (Botox) was obtained in a frozen, crystallized form and reconstituted with 2mL of 0.9% sterile saline. Table 1 lists dosages and muscles injected. Each muscle received between 50 and 100U, depending on the subject's weight and the size of the muscle. Motor point locations of the targeted muscles were identified visually and used to determine injection sites. Each muscle was injected in a single site. A topical anesthetic cream was applied to the injection sites approximately 45 minutes before the injection. None of the subjects or their family members reported adverse effects immediately after injection or at any time during the study.

The testing protocol used both clinical and motor control tests in the 6 months after injection. Testing occurred in the late afternoon immediately preinjection, and at 2, 4, 6, 12, 18, and 24 weeks postinjection. Motor control testing was done at all testing sessions, whereas clinical assessments were performed at 2, 6, and 18 or 24 weeks.

Clinical tests provided information on the degree of upper-limb spasticity, active and passive ROM, and function, for comparison with MCT findings. The Modified Ashworth Scale<sup>29</sup> (MAS) was used to measure spasticity. The scale has good reliability for many muscle groups, including the muscles we involved in this study. Functional ability was measured by using the ADL domain of the Pediatric Evaluation of Disability Inventory<sup>30</sup> (PEDI), and the FIM<sup>TM</sup> instrument.<sup>31</sup> An experienced occupational therapist (GEC) measured active and passive ROM of the elbow, wrist, and fingers by using standardized techniques.<sup>32</sup> Upper-limb goniometry has high reliability coefficients among experienced raters by using an increase of 10° as a valid change that was not subject to intratester variability.<sup>33,34</sup> Coordination was assessed by using the Purdue pegboard<sup>35,36</sup> and selected subtests from the Bruininks-Oseretsky Test of Motor Proficiency.<sup>37</sup> Several subtests were

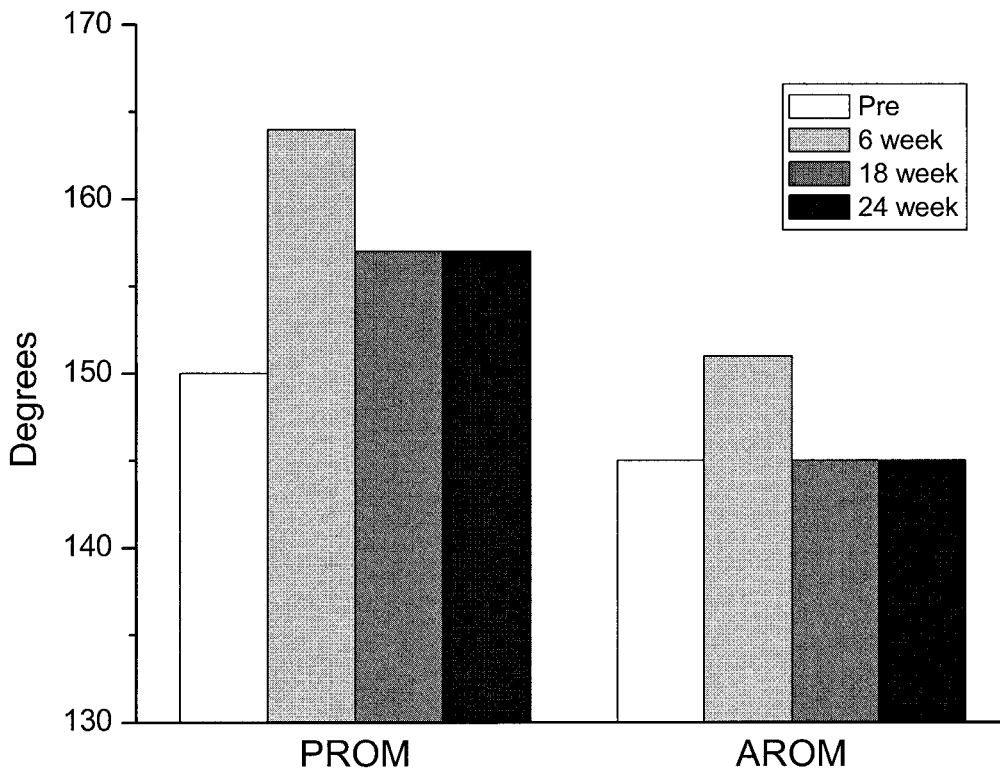


Fig 1. Mean elbow ROM. Values are shown for preinjection, 6 weeks, 18 weeks, and 24 weeks postinjection. Bar groupings represent passive ROM (PROM) and active ROM (AROM).

compared with MCT findings, including the bilateral finger-to-nose test and synchronized tapping of foot and finger on the same and opposite sides of the body. The Bruininks-Oseretsky test has good validity and reliability, and raw scores have been shown to be sensitive to change over time.<sup>38</sup> The subjects also performed maximal isometric grasp and pinch by using a calibrated dynamometer (Jamar™) and pinch gauge.<sup>a</sup>

Subjects performed several motor control tasks to assess multijoint upper-limb movement, bilateral coordination, hand tapping, and isometric force production. These included the following.

**Forward reach.** In response to an auditory tone, the subject was asked to reach forward from a seated position and touch a wall-mounted switch that was located at approximately shoulder height. The subjects were instructed to move as fast and accurately as possible and to touch the switch with any part of the hand. Ten trials were performed unilaterally and bilaterally.

**Bilateral rhythmic movements.** By using simultaneous movements of both arms, the subject was asked to make continuous rhythmic finger-to-nose movements from a position of 90° of shoulder abduction. Both muscle homologous (simultaneous elbow flexion or extension) and direction homologous (simultaneous elbow flexion and contralateral elbow extension) movements were examined. After an auditory tone, 2 trials were recorded, each lasting 8 seconds.

**Isometric pinch force production.** The subjects were instructed to perform a lateral pinch with maximal force on a strain gauge mounted on a vertical rod approximately 53cm above the table surface. Assistance was provided as needed in positioning the affected hand to maximize contact of the thumb and index finger. The mean of 3 repetitions was calculated for each hand.

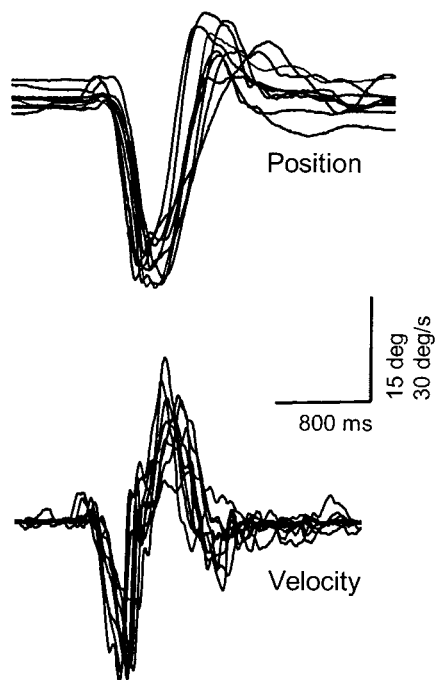
**Hand tapping.** The subject was seated at a horizontal surface and asked to tap for 6 seconds a microswitch mounted

on the table. He/she was asked to tap as quickly as possible in the unilateral right and left tasks. In the bilateral task, subjects were told to tap both hands simultaneously and as fast as possible.

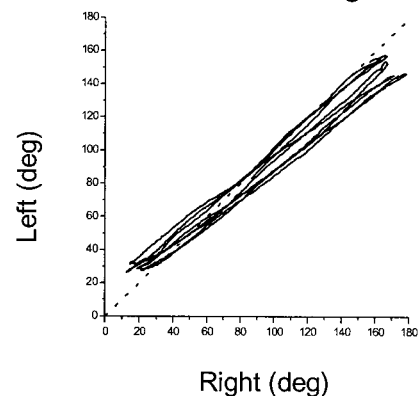
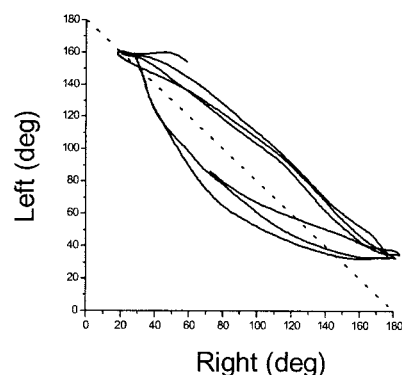
#### Data Acquisition and Analysis

MAS and ROM data were analyzed by the Student *t* test, comparing means of preinjection values to the most improved postinjection values. Mean hand dynamometer results were also analyzed by using the *t* test, comparing the results at each trial to the initial values. SPSS software<sup>b</sup> was used. Angular displacement of the elbow was recorded during forward-reach trials by using electrogoniometry.<sup>c</sup> Although this task involved multiple joints, it is well established in motor control literature that angular and tangential movement profiles are similar for multiple joints engaged in the same task.<sup>39,40</sup> Pinch tasks were quantified by using custom-designed strain gauges, with a range of 0 to 45kg (100lb). Each gauge had a transducer that was placed between 2 stainless steel bars, which were 1.5cm wide and 20cm long. Custom-designed microswitches recorded the number of hand taps. The switches had a raised keyboard-type key, which was placed in a plastic casing. The casing had a Velcro® base for stabilization on the desk surface. The switches were activated by a touch on any corner or any spot on top of the key, with any amount of depression. A debouncer chip was placed inside the switch to stabilize the signal.

All data were digitized at 250Hz, filtered by using a fourth-order Butterworth filter, and analyzed off line with a custom-designed analysis program using commercial software.<sup>d</sup> Data were then analyzed by visually comparing patterns of motor performance to known patterns of healthy individuals. Changes in performance between trials were noted and compared between subjects (see Results section and figs 2-7). The order of testing (forward reach, rhythmic bilateral, pinch, hand tapping)

**A Forward Reach**

**Fig 2.** (A) Typical elbow kinematic records associated with forward-reaching movements performed by a healthy 12-year-old child. Several consecutive records have been overplotted with downward deflections indicating elbow extension. Velocity was obtained by differentiation of the position signal. Angle-angle plots of (B) bilateral elbow displacement during muscle and (C) direction homologous movements for the same person. Dashed lines indicate perfectly coupled bilateral movements.

**B Muscle Homologous****C Direction Homologous**

remained constant for each testing session, which lasted approximately 30 minutes.

## RESULTS

### Clinical Results

In 8 of 9 subjects, spasticity decreased in at least 1 joint at some point during the 24 weeks. Mean elbow MAS  $\pm$  standard deviation decreased from  $2.7 \pm 1.4$  to  $1.1 \pm 1.2$ . Mean wrist MAS decreased from  $2.7 \pm 1.2$  to  $2.0 \pm 1.4$ . These changes were not statistically significant. Passive ROM at the elbow increased in the 6 subjects with initial range limitations in the elbow, but the changes were not significant (fig 1).

Mean changes in active elbow ROM were minimal (fig 1). Four subjects improved their active ROM by at least  $10^\circ$  within the first 6 weeks of testing, whereas the other 2 lost active ROM, according to goniometric measurements taken over the course of testing. Improvement in passive and active wrist extension was even more variable, in both extent and time of change. No significant changes in wrist extension were noted.

As expected, the unaffected hand generated forces with dynamometric testing that were generally within normal limits,<sup>34</sup> whereas the force generated by the affected hand was typically well below normal limits. Force generation in the affected hand improved at week 4, with further increases by week 6. Values between weeks 6 and 12 were still higher than initial values, but were less than at week 6 (table 2). Examination of the individual records revealed variable responses

after the injection, with no clear trends toward improved or decreased force production in the affected extremity. Four subjects had a decrease in maximum force production at week 2 compared with preinjection levels; 3 of the 4 had botulinum toxin injected into the wrist and finger muscles. Force produced by 5 subjects remained higher at week 24 compared with preinjection levels, with increases ranging from 20% to 179%.

The remaining clinical assessments were less sensitive to change. Assessments of functional ability (PEDI, FIM) were unchanged throughout the testing period. Only 3 subjects were able to grasp a peg in the Purdue pegboard task, and no change was apparent throughout the 6-month period. Subject scores also did not vary from initial scores on any of the subtests of the Bruininks-Oseretsky Test of Motor Proficiency. Four subjects achieved a pass rating for tapping foot and hand on the same and on opposite sides, whereas 4 others failed these subtests.

### MCT Results

**Forward-reaching movements.** During the performance of discrete forward-reaching movements in healthy individuals, extension of the elbow was characterized by smooth, continuous trajectories and bell-shaped, time-symmetric velocity profiles. This is shown in figure 2A, where individual position and velocity records have been overplotted. In addition, movement trajectories were highly reproducible from 1 trial to the next, resulting in minimal spatiotemporal variability. Such consistency in reach performance was characteristic of healthy people

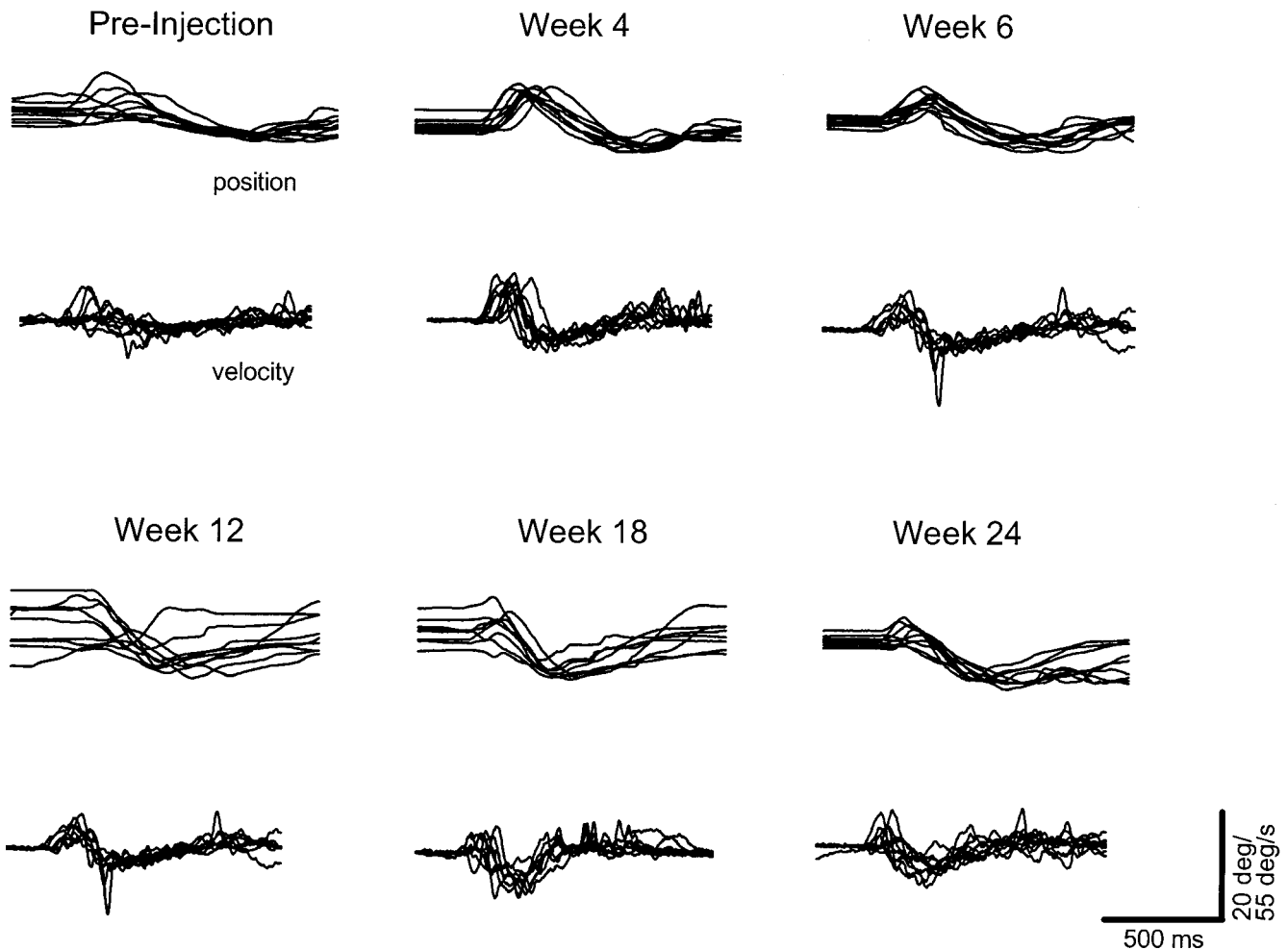


Fig 3. Overplots of elbow position and velocity associated with forward-reaching movements made before and after injection with botulinum toxin. Each data set is comprised of 6 to 10 consecutive extension movements. Data from week 2 (not displayed) were similar to preinjection data. Downward deflection of the tracings equals elbow extension, and upward deflection reflects elbow flexion.

across all motor tasks. Movements requiring simultaneous elbow flexion (muscle homologous) or simultaneous flexion and extension (direction homologous) were highly coupled in healthy subjects. As shown by the angle-angle records in figure 2B, this was particularly true for muscle homologous movements. Angular displacements of both elbows were tightly matched throughout the time course of the movement, showing little deviation from an ideal, straight-line excursion indicated by the dashed lines. Bilateral elbow movements requiring simultaneous activation of opposite muscle groups (eg, elbow flexion and contralateral elbow extension; fig 2C) were also coupled, although right-left differences in the degree of elbow displacement occasionally led to increased spatial variability. However, whether or not simultaneous activation of similar or opposite muscle groups was required, movement about both elbow joints occurred continuously.

None of the test subjects was able to produce goal-directed, forward-reaching movements with the affected arm before the injection of botulinum toxin. This is shown in figure 3 where overplotted records of elbow position and velocity are shown for the entire testing period (excluding week 2, which was similar to week 4) for a typical subject. At 4 weeks postinjection, an increase in elbow extension was observed that was

frequently preceded by a small amplitude, elbow flexion movement. This pattern of initial elbow flexion followed by limited elbow extension also was seen at week 6, and was observed in 7 other subjects after injection. At week 18, a more typical pattern of elbow extension associated with forward reaching was observed. As described for healthy individuals in figure 2A, elbow extension trajectories were characterized by smoother displacement curves, and were associated with relatively time-symmetric velocity profiles. Initial elbow flexion before the reach movement was minimal or nonexistent. Compared with previous testing sessions, movements were produced at higher speeds that resulted in shorter movement durations. Twenty-four weeks after injection, movement duration had increased, compared with the previous testing session. The emergence of a more typical movement profile at week 18 or later was characteristic of all test subjects, whereas the ability to maintain a more normal pattern of elbow extension at week 24 varied highly across the subject group.

**Bilateral arm movements.** The ability to produce coordinated, bilateral elbow movements was compromised in all subjects. Some subjects improved in performance of muscle homologous tasks after the injection. This is shown in figure 4, in which angular displacement of both elbow joints is plotted

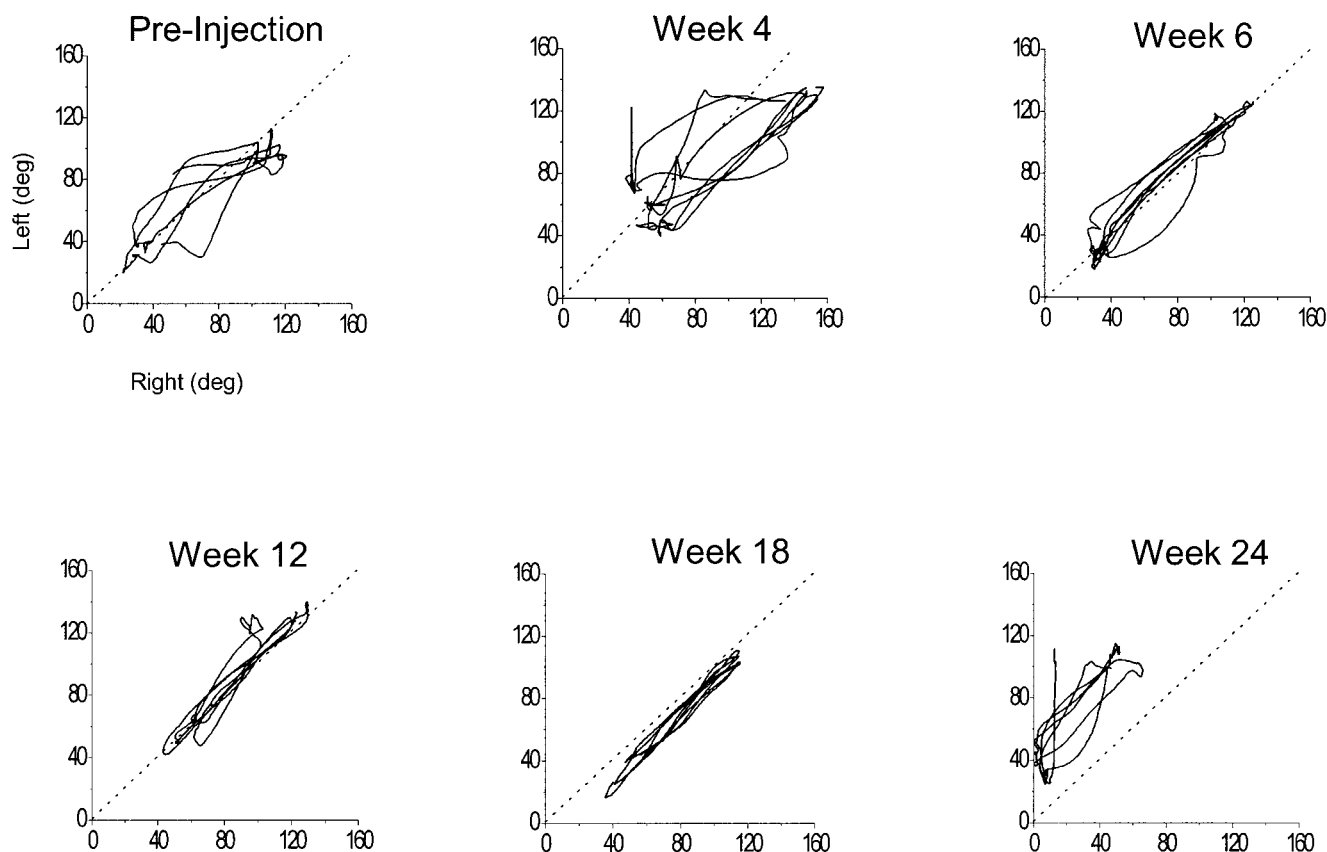


Fig 4. Elbow angle-angle plots associated with bilateral, muscle homologous movements. Extension of right (affected) elbow is plotted on the x axis; left (less affected) elbow extension on the y axis. Dashed lines indicate optimal excursion paths for tightly coupled bilateral movements.

for 1 subject across testing sessions. In comparison to tightly coupled excursion trajectories characteristic of normal muscle homologous movements (dashed lines), most subjects showed marked disruptions in interlimb coordination at baseline testing, which persisted at weeks 2 (not shown) and 4. Onset of improvement in spatial coupling was variable, with 4 subjects showing maximal improvement at week 12 or later, and 2 subjects showing maximal improvement during the first 6 weeks. In all cases, improvement was transient and typically was not seen during later testing sessions. This is shown in figure 3, which shows that improved spatial coupling was noted at week 18. By week 24, however, a loss in bilateral coordination was seen again.

At the time of injection, none of the subjects was able to produce direction homologous movements that required simultaneous elbow flexion of 1 arm with elbow extension of the opposite arm. Movements were made sequentially rather than simultaneously, as evidenced by the numerous horizontal and vertical components comprising the angle-angle plots (fig 5). In this particular subject, a slight improvement was noted at week 12 and again at week 18, but the degree of improvement was marginal compared with the performance of healthy individuals (dashed lines). In other subjects, however, no improvement was observed over the entire testing period.

**Hand-tapping performance.** Changes in tapping rates are shown for 4 representative subjects in figure 6. Five of the 9 subjects showed a 30% to 150% increase (mean, 82.4%) in hand-tapping rates for the affected hand, with maximal im-

provement occurring between 2 and 6 weeks after injection. This result contrasted with the delayed improvement noted with more complex upper-limb motor tasks. Marked differences in tapping rates between the affected and unaffected hand were observed in all subjects when the task was performed with only 1 hand (unilateral). In contrast, bilateral tapping led to a significant reduction in tapping rates for the unaffected hand that, in some subjects (fig 6B), reflected an overall decrease of 80% compared with unilateral tapping rates. Simultaneous tapping with both hands also led to smaller decreases in tapping rates for the affected hand.

**Isometric pinch force.** Changes in isometric pinch force produced by the affected hand were variable across subjects and throughout the testing period. Of the 9 subjects, 5 showed a relatively small decrease in force after injection compared with baseline values, as measured by the strain gauge force transducer. Data from 4 of these 5 subjects are shown in figures 7A–D. Although these 4 subjects showed decreased pinch force, clinical examination showed improved hand and finger function. Two of the 4 subjects could produce active index finger extension, 1 was observed spontaneously using the affected hand, and 1 improved in manipulation skills during Purdue pegboard testing. The remaining 5 subjects showed a marked increase in force with peak values generally occurring by 6 weeks postinjection (figs 7E–H). Furthermore, in subjects who exhibited improved pinch grip strength, the overall degree of improvement was several hundred times greater than the decrease in pinch grip strength observed in the other subjects.

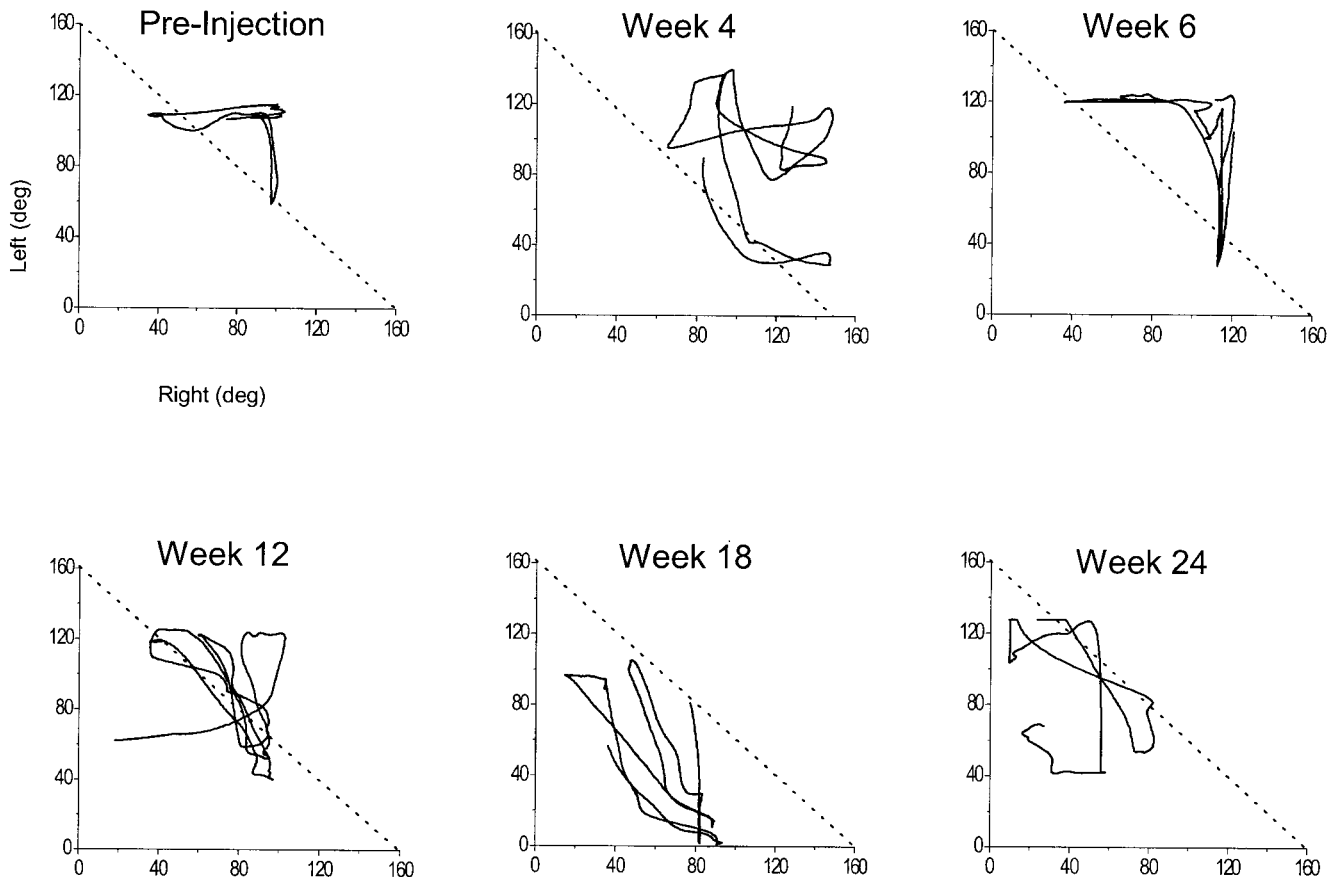


Fig 5. Elbow angle-angle plots associated with bilateral, direction homologous movements. Data are plotted as in figure 4.

No other improvement in hand or finger function was clinically observed for those subjects with increased pinch force production. Seven of the 9 subjects received wrist and/or finger injections; of the other 2, 1 showed a slight decrease and 1 an increase in pinch force production.

### DISCUSSION

As was true in other studies, our subjects generally had better MAS scores and ROM. The lack of correlation between clinical changes and improved motor patterns observed with MCT is notable. It would be expected, for example, that the greatest improvements in forward reach would occur at the same time that passive and active elbow extension was maximal. No such correlation was observed. In fact, 2 subjects showed improved reach performance at least 6 weeks before maximal improvement in ROM was seen, whereas others showed no improvement until several weeks after maximal improvement in ROM. Three subjects who had full active ROM despite spasticity at the time of injection showed an improvement in their reach pattern, but not until week 18 of testing. Similarly, there was no apparent correlation between changes in MAS and improved reach. These findings support the idea that assessment of improved motor outcomes requires more qualitative measures than ROM and MAS.

Ideally, it would be desirable to know the effects of an upper-extremity intervention on ADLs. However, the PEDI and FIM were insensitive to any change resulting from botulinum toxin injections. It is likely that the functional measures

we used were ineffective in detecting upper-limb improvement because most hemiparetic subjects use their less affected extremity in achieving independence in self-care skills. Even for those subjects who had difficulties with specific skills, as measured by the PEDI or FIM, it would seem unlikely that spasticity reduction alone would lead to improvement without focused training in that skill. The performance measures (Bruininks-Oseretsky test, Purdue pegboard) were difficult for most subjects to complete with their affected extremity, and were generally insensitive, despite changes seen with MCT.

Our initial report<sup>28</sup> noted a differential time course of improvements in motor function between hand tasks (pinch strength, tapping) and forward reach. This pattern was observed to a large degree in the subject group. These findings must be considered in light of the reported onset of action of the botulinum toxin; electrodiagnostic studies<sup>41,42</sup> have reported changes in the compound action potential within 12 hours after an injection. Most clinical studies, however, have found onset of changes within 2 to 4 weeks after treatment. In this study, a similar time course was observed for hand tapping and pinch strength, in which maximal improvement typically occurred by week 6 after the injection.

In contrast, the late onset of improved reach performance may be partially explained on the basis of central control processes. From a control perspective, forward-reaching movements are more complex than simple hand-tapping or isometric pinch tasks. The increased degrees of freedom associated with forward-reach tasks, as well as eye-hand coordination, place

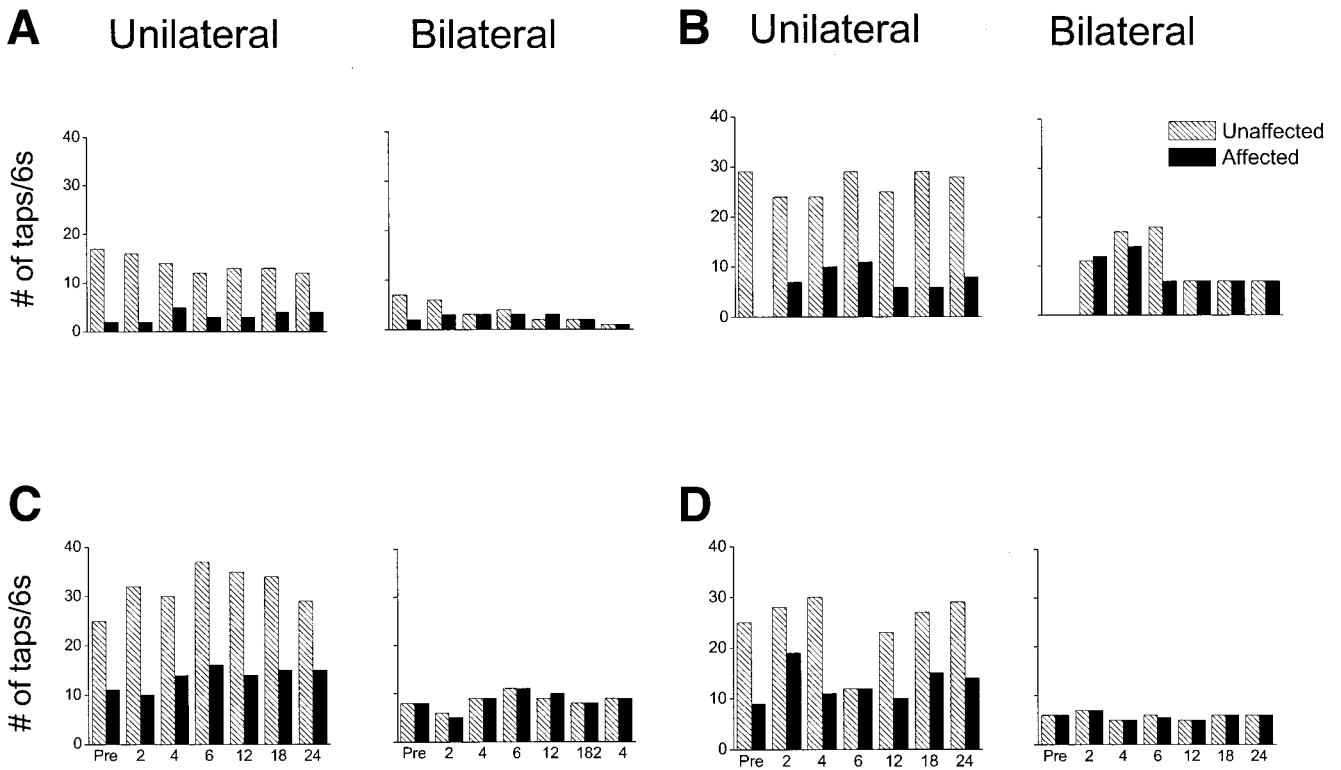


Fig 6. Hand-tapping performance before and after botulinum toxin injection for 4 subjects (A-D). Each histogram shows the number of hand taps per 6 seconds for unilateral and bilateral tasks made by the unaffected and affected hands.

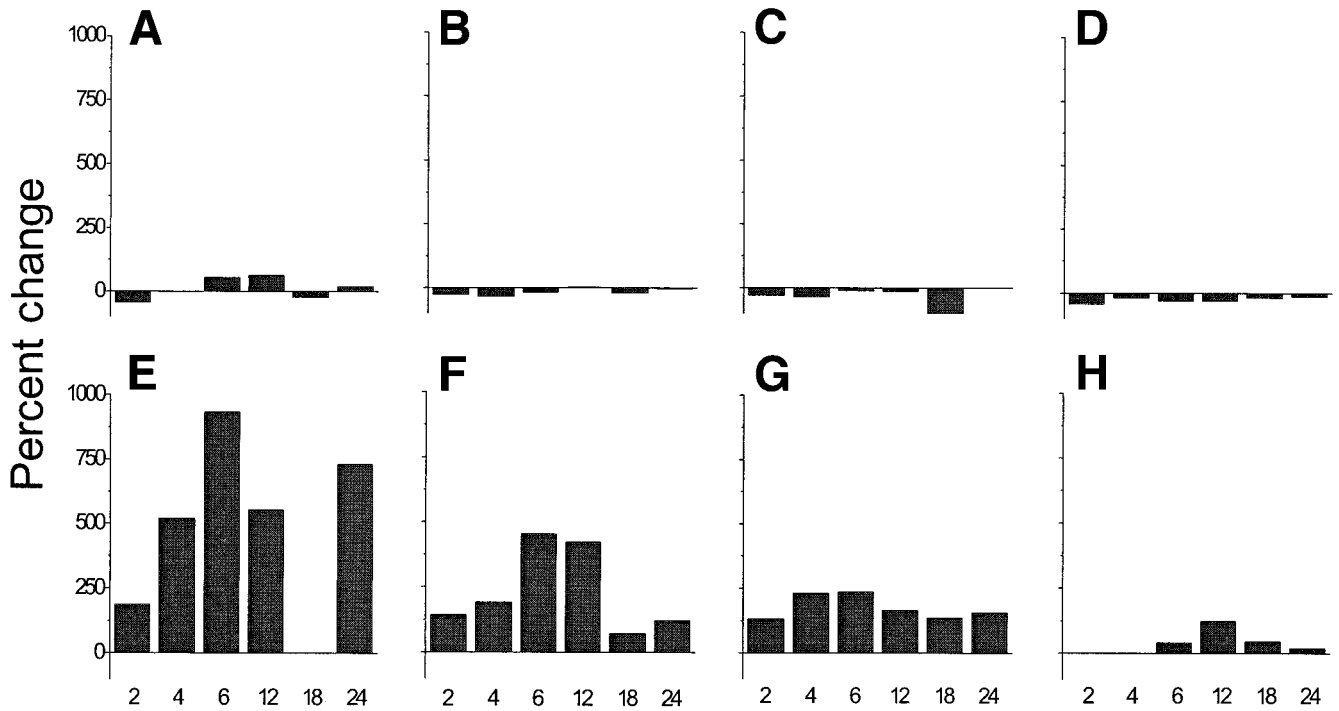


Fig 7. Change in isometric grasp force after botulinum toxin injection for 8 subjects. For each testing session, force values are expressed as a percentage change from preinjection values.

Table 2: Hand-Held Dynamometer Force Production for the Affected Hand

	Initial	2 Weeks	4 Weeks	6 Weeks	12 Weeks	24 Weeks
Mean (pounds of pressure)	21.9	25.4	25.5	30.6	23.8	25.5
Standard deviation	21.9	21.2	15.0	9.4	13.4	16.5
Comparison to initial value		NS	$P < .01$	$P < .01$	$P < .01$	$P < .01$

Abbreviation: NS, not significant.

greater programming demands on the CNS. Such movements must be actively controlled in terms of end-point accuracy. In addition, the multijoint nature of the task requires active control of joint interactional forces, including anticipatory control of limb-induced trunk movement. The development of more efficient, albeit complex, descending signals, as reflected in the eventual production of relatively time symmetric velocity profiles, may depend on more than just peripheral reduction in spasticity. For instance, the concept of cortical reorganization after injury or long-standing nonuse has become an increasingly attractive model for rehabilitation specialists, particularly as a rationale for the development of intensive treatment programs.<sup>43-46</sup> In this study, our subjects did not receive additional therapy apart from botulinum toxin injections. Thus, the prolonged time course of improvement for complex reaching movements may possibly be explained by a reduction in cortical areas dedicated to control of the affected limb. In the absence of task-specific training programs as adjunct therapy, for example, improvement of certain motor tasks after botulinum toxin injection might be expected to be slow to develop, or not to develop at all. This might account for the near total lack of improvement in bilateral limb movements involving simultaneous activation of nonhomologous motoneuron pools, whereas simple, single-joint movements such as hand tapping may show a more rapid pattern of improvement. The potential need for task-based retraining of the upper limb after botulinum toxin injection may also explain the transient nature of improvement that we found in this study.

As shown previously,<sup>28</sup> the ability to produce coordinated bilateral arm movements was compromised to varying degrees, depending on task complexity. Although bilateral movements requiring simultaneous activation of similar muscle groups showed a transient improvement in spatiotemporal coupling in some subjects, none were able to smoothly coordinate elbow flexion of 1 arm with elbow extension of the other. In terms of central motor programming, the simultaneous activation of nonhomologous muscles is considered to be a more complex task because trajectory variability is typically greater in such coupled movements compared with muscle homologous movements.<sup>47</sup> In healthy subjects, regardless of their age, such movements are still highly coupled, with both joints moving together as a single unit. We observed that bilateral movements requiring activation of nonhomologous muscles tend to be produced sequentially rather than simultaneously. It could be argued that this is because of a central programming deficit. Nevertheless, interactions between opposing spinal motoneuronal circuitry cannot be dismissed as a contributing factor.

Interlimb interactions during bilateral movements were also clearly evident during the performance of simple hand-tapping tasks. Of particular interest were the deleterious effects on the clinically less affected limb, in which movement frequency was markedly reduced during bilateral tapping, compared with unilateral tapping. This resulted in relatively symmetric tapping rates for both the affected and unaffected hands, a phenomenon previously reported during bilateral reaching movements in spastic hemiparesis<sup>28,48,49</sup> and cerebellar ataxia.<sup>24</sup>

Such coupling of homologous limb movements is thought to reflect programming constraints imposed by the CNS to minimize the number of degrees of freedom, and thereby to simplify control parameters.<sup>50</sup> However, in contrast to previous reports of a bilateral facilitation during coupled limb movements,<sup>28,48</sup> subjects frequently exhibited a reduction in tapping rates when the affected hand was coupled with movements of the less affected hand. We observed that bilateral tapping led to a general degradation in the performance of both hands despite obvious clinical asymmetries. This is likely because of differences in task requirements, including attentional factors as well as pathophysiologic differences across subject groups.

The most common adverse effect associated with botulinum toxin as a treatment for spasticity is muscle weakness.<sup>51</sup> Such weakness is usually minimal and, for the typical drug dose (150–200U) used to treat upper-limb spasticity, has not been thought to impact functional improvement.<sup>13</sup> Recently, however, Rodriguez et al<sup>16</sup> found a small but significant decrease in hand strength 3 days after botulinum injection into finger flexor muscles. Whether this was a transient or persistent change was not explored. Generalized, although transient, weakness confirmed by abnormal electromyographic findings has also been reported in a small number of patients who received focal botulinum toxin for dystonia.<sup>52</sup>

Two distinct patterns in pinch grip strength behavior were observed. In approximately 50% of the subjects, pinch force minimally decreased compared with preinjection values, despite improvement in active finger extension ROM. In contrast, other subjects showed a marked improvement in pinch force. In the latter instances, maximum improvement was not seen immediately but peaked at approximately 6 weeks after the injection. Although there was no obvious correlation between Ashworth Scale measures, ROM, or site of injection, it is difficult to explain such a clear difference in pinch force performance in this subject group. It is possible that hand positioning at the time of testing may have contributed to variable measurements, but it is unlikely that such errors would be repeated consistently by any particular subject over the entire testing period. An alternative and plausible explanation relates to the degree to which each subject may have spontaneously used his/her hand after the injection, with more active hand usage leading to improved pinch force. This argues, again, for the need to investigate combined pharmacologic and movement therapies to maximize functional improvement in spasticity conditions.

The conclusions that can be drawn from this study are limited by the small number of subjects. This is particularly true when the lack of significant changes in MAS and ROM is considered. However, the trends noted in this group provide a basis for further study. Large time gaps between testing periods present an additional problem. In designing the study, we expected that the most significant changes would occur in the first 6 weeks after injection, based on clinical studies of onset action.<sup>3,4</sup> The later testing periods were included to track the maintenance or loss of functional change. We did not expect that improvements in forward reach would occur after the

12-week point, as it did in 5 of the 6 patients who showed significant change. The lack of testing between 12 and 18 weeks makes it difficult to give accurate estimates of the true onset of functional change. However, it is clear that the change occurred some time late in the course of the treatment, and later than the changes seen in the simple hand task assessments. Limitations in the study design also led to an inability to make a definitive statement about the correlation between spasticity reduction and functional change. Limitations in the MAS, combined with limited numbers of measurement over the 24-week course, made such correlations difficult. ROM data are more robust, but do not necessarily correlate with spasticity because of limitations in range caused by shortening of the fibroelastic components of the muscle. Future studies may benefit from use of improved spasticity measures, such as the Tardieu scale,<sup>1</sup> or the use of biomechanical measurement techniques.

### CONCLUSION

Transient improvements in upper-extremity movement characteristics were seen after botulinum toxin injections in children and adolescents with spasticity. Less complex tasks generally improved earlier, within 6 to 12 weeks after the injection, whereas more complex movements showed improvement either later or not at all. Bilateral tasks were particularly challenging, with subjects having difficulty coordinating simultaneous movements. There was also evidence that bilateral tasks led to degradation of function of the less affected extremity. Spasticity and ROM also improved, but correlated poorly with kinematic changes. These findings suggest that botulinum toxin can be useful in improving motor function impaired by spasticity, but it would be most effective as an adjunct to a therapy program designed to overcome central programming deficits. The exact nature of such a program and the role of interventions to facilitate it are important for future research.

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#### Suppliers

- a. B&L Engineering, 3002 Dow Ave, Ste 416, Tustin, CA 92780.
- b. SPSS for Windows, version 9.0; SPSS Inc, 233 S Wacker Dr, Chicago, IL 60606.
- c. Penny & Giles Model LS-100; Biometrics Ltd, 547 Lake Caroline Dr, Ruther Glen, VA 22546.
- d. LabVIEW; National Instruments, 11500 N Mopac Expwy, Austin, TX 78759-3504.