

Effect of Baseline Spastic Hemiparesis on Recovery of Upper-Limb Function Following Botulinum Toxin Type A Injections and Postinjection Therapy

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ABSTRACT. Chang C-L, Munin MC, Skidmore ER, Niyonkuru C, Huber LM, Weber DJ. Effect of baseline spastic hemiparesis on recovery of upper-limb function following botulinum toxin type A injections and postinjection therapy. *Arch Phys Med Rehabil* 2009;90:1462-8.

Objective: To determine whether baseline hand spastic hemiparesis assessed by the Chedoke-McMaster Assessment influences functional improvement after botulinum toxin type A (BTX-A) injections and postinjection therapy.

Design: Prospective cohort study.

Setting: Outpatient spasticity clinic.

Participants: Participants (N=14) with spastic hemiparesis divided into 2 groups: Chedoke-McMaster Assessment Hand-Higher Function (stage \geq 4, n=5) and Chedoke-McMaster Assessment Hand-Lower Function (stage=2 or 3, n=9).

Interventions: Upper-limb BTX-A injections followed by 6 weeks of postinjection therapy.

Main Outcome Measures: Primary outcomes were Motor Activity Log-28 and Motor Activity Log items. Secondary outcomes were Action Research Arm Test (ARAT), Motor Activity Log-Self-Report, and Modified Ashworth Scale (MAS). Measures were assessed at baseline (preinjection), 6 weeks, 9 weeks, and 12 weeks postinjection.

Results: Primary and secondary outcomes improved significantly over time in both groups. Although no significant differences in ARAT or MAS change scores were noted between groups, Chedoke-McMaster Assessment Hand-Higher Function group demonstrated greater change on Motor Activity Log-28 ($P=.013$) from baseline to 6 weeks and Motor Activity Log items ($P=.006$) from baseline to 12 weeks compared to Chedoke-McMaster Assessment Hand-Lower Function group.

Conclusions: BTX-A injections and postinjection therapy improved hand function and reduced spasticity for both Chedoke-McMaster Assessment Hand-Higher Function and Chedoke-McMaster Assessment Hand-Lower Function groups.

Clinicians should expect to see larger gains for persons with less baseline impairment.

Key Words: Botulinum toxin type A; Electric stimulation therapy; Muscle spasticity; Recovery of function; Rehabilitation; Stroke; Upper extremity.

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SPASTIC HEMIPARESIS IS A common and severely disabling condition after stroke and traumatic brain injury. Approximately 55% to 85% of persons with acute or chronic hemiparesis have restricted upper-extremity function.^{1,2} Impaired hand function due to spastic hemiparesis limits functional use of the hand for critical tasks, such as drinking a glass of water, opening a door, and controlling the steering wheel while driving a car. Thus, quality of life is severely compromised by spastic hemiparesis.

Clinicians and researchers have effectively used activity-based rehabilitation interventions³⁻¹⁰ to promote motor improvement after central nervous system injury. However, severe spastic hemiparesis may prevent people from engaging in activity-based rehabilitation interventions that are necessary to restore motor function. As a result, these therapies have only been proven to be effective in persons with mild hemiparesis and generally little or no spasticity.¹¹

To enable people with severe symptoms to participate effectively in activity-based therapies, rehabilitation interventions should include additional treatments to reduce spasticity. BTX-A has been shown to relieve spasticity in persons with upper limb spasticity.¹²⁻¹⁶ Although BTX-A is effective in reducing severe spasticity, some investigators noted this reduction favors significant improvements in hand function, whereas others disagree.¹⁷⁻¹⁹ Nevertheless, our clinical experience suggests that BTX-A injections and postinjection therapy can improve hand function in many persons with spastic hemiparesis.

One explanation for these varied results may be due to differences in severity of baseline hand impairment. Presently there are several thoughts as to whether baseline hand impairment impacts functional recovery during rehabilitation. One hypothesis is that persons with mild baseline hand impairment attain more functional recovery after targeted interventions compared to those with severe baseline hand impairment. Some have even suggested that intensive rehabilitation inter-

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List of Abbreviations

ARAT	Action Research Arm Test
BTX-A	botulinum toxin type A
CMA	Chedoke-McMaster Assessment
FES	functional electrical stimulation
MAS	Modified Ashworth Scale

Table 1: Chedoke McMaster Assessment Hand Impairment Scale: Stage 2 to 5 of Recovery of Hand

Stage	Chedoke McMaster Assessment
2	Positive Hoffman sign Resistance to passive wrist or finger extension Facilitated finger flexion
3	Wrist extension more than one-half range Finger/wrist flexion more than one-half range Supination, thumb in extension: thumb to index finger
4	Finger extension, then flexion Thumb extension more than one half range, then lateral prehension Finger flexion with lateral prehension
5	Finger flexion, then extension Pronation: finger abduction Hand unsupported: opposition of thumb to little finger

Data from: Gowland et al.²³

ventions for upper-limb impairment should not be offered to those with severe impairment because the possibility of recovery is low.²⁰ An alternative hypothesis is that persons with severe baseline hand impairment sustain greater functional recovery than persons with mild baseline hand impairment because persons with mild baseline hand impairment have less potential gain to achieve. A third hypothesis is that baseline hand impairment does not influence the amount of functional recovery after BTX-A injections and postinjection therapy.

The purpose of this study was to determine whether baseline hand impairment assessed by the CMA influences functional improvement after BTX-A injections and 6 weeks of standardized postinjection therapy. In contrast to focusing on impacts of severity of hand paresis after acute stroke in persons without spasticity (flaccid upper limb),²¹ we examined persons with severe spasticity after chronic stroke because they were less likely to show significant functional changes through traditional rehabilitation care. Understanding the role of baseline hand impairment that can be easily assessed in a clinical setting will be useful for predicting functional outcomes for people with spastic hemiparesis.

METHODS

Participants

A convenience sample was recruited from the Department of Physical Medicine and Rehabilitation Spasticity Clinic at the University of Pittsburgh. People who had unilateral spastic hemiparesis for a minimum of 6 months and had at least 2 prior sessions of BTX-A for spasticity treatment were eligible for participation. This prior exposure confirmed that participants tolerated injection therapy without adverse reactions with a predictable dosage. All participants had their most recent bot-

ulinum toxin injection at least 3 months before study participation. We selected a 3-month washout period based on the work of de Paiva et al,²² who reported that the motor endplate where botulinum toxin was injected regained its function fully after 3 months and was indistinguishable from endplates where toxin was not injected.

All participants had preinjection Modified Ashworth scores of 2 or more in at least one of the following muscle groups: elbow, wrist, or finger flexors. In addition, all participants had to attain at minimum a stage 2 on the CMA Hand Impairment Scale, plus demonstrate the ability to complete at least one of the tasks that met criteria for stage 3 (table 1). Stage 2 on the CMA includes at least 2 of 3 items: positive Hoffman sign, resistance to passive wrist or finger extension, and facilitated finger flexion. These criteria defined participants with minimal residual hand function and excluded those who had no voluntary motion. Participants with CMA scores of 3, 4, and 5 were also included. All participants were able to answer questions and follow instructions; they did not have severe, fixed joint contracture in the affected arm. Persons who met the screening criteria were provided additional information regarding the study, and, if they were interested, they provided informed consent. All procedures were approved by the university's institutional review board.

Measures

Baseline hand impairment was assessed with the 7-point CMA.²³ The CMA is reliable and valid²³; it determines the presence and severity of physical impairments in the hand. For the purposes of this study, we divided the cohort into 2 groups based on their CMA Hand Impairment Scale score (table 2). Participants with a CMA score of stage 4 or higher were classified as high functioning (CMA Hand-Higher Function) and participants with a CMA Hand-Higher Function and score of stage 2 or 3 were classified as low functioning (CMA Hand-Lower Function).

Primary outcomes were upper-extremity function during activities of daily living assessed observationally by Motor Activity Log-28 and Motor Activity Log-5 items (wash hands, dry hands, pick up a phone, operate a doorknob, and pick up a glass). The Motor Activity Log-28²⁴ is a tool that assesses hand function with daily tasks. For the purpose of this study, we used the "How Well Scale" of the Motor Activity Log-28. The 5 items were selected before participants enrolled in the study and were based on our expectations that the interventions would show improvement in at least these tasks. We selected 5 activities that focused specifically on hand function (compared with arm function) because we focused on testing the changes in hand function. The 5 items were selected from 28 items in the Motor Activity Log, which has reliability and validity. Secondary outcomes were (1) dexterous hand function as measured by the ARAT,^{25,26} (2) participant's perception of self-performance in activities of daily living assessed with the

Table 2: Participant Demographics and Clinical Characteristics

Group	CMA Hand-Lower Function (n=9)	CMA Hand-Higher Function (n=5)
Age (y)	44.4±13.3	45.6±12.2
Type of stroke	Thrombotic (n=4; 45%), TBI (n=3; 33%), other (n=2; 22%)	Thrombotic (n=3; 60%), other (n=2; 40%)
Side of lesion	Left (n=6; 67%), right (n=3; 33%)	Left (n=2; 40%), right (n=3; 60%)
Area of stroke	Cortical (n=9; 100%)	Cortical (n=4; 80%), subcortical (n=1; 20%)
Years since onset	5.9±1.9	15.2±9.1
Total BTX-A dose (units)	303.9±121.0	290.3±117.0

NOTE: Values are mean ± SD or as otherwise indicated. Abbreviation: TBI, traumatic brain injury.

Motor Activity Log—Self Report,²⁴ and (3) clinical spasticity assessed by the MAS.^{27,28} Reliability and validity of these outcome measures have been reported elsewhere.²⁴⁻²⁹ Brashear et al³⁰ also reported good intra- and interrater reliability of the Ashworth Scale for elbow, wrist, finger, and thumb flexion tones. The Motor Activity Log-28 and Motor Activity Log-5 were laboratory-based measures, in contrast with the Motor Activity Log-Self Report. All measures were evaluated in the outpatient clinics.

Procedure

All participants received BTX-A treatment as a routine component of their clinical care for spasticity management (within 2wk of baseline assessment) before receiving postinjection interventions (within the next 7d after BTX-A treatment), including repetitive task practice³ and FES (Ness H200 system^a) (fig 1). The postinjection intervention provided six 1-hour visits and an activity-based repetitive task practice home exercise program (a total of 60min each day) for 12 weeks using a standardized protocol.^{3,11} The activity-based therapy (without restraint of the intact arm) was not constraint-induced therapy but simply a repetitive task practice intervention program that required participants to practice 4 to 5 selected functional tasks representative of hand function tasks completed in daily routines. Examples of the tasks included stacking canned goods, dealing cards, placing pennies in coin sleeves, wiping down counters, and washing mirrors. The therapist educated the participants on the use of FES system and programmed it to be used in conjunction with the repetitive task practice tasks. The tasks were included in the home-exercise program (60min/d) for 12 weeks. We recorded outcome measures (without using the FES system) at 4 time points: baseline (preinjection), and 6 weeks, 9 weeks, and 12 weeks postinjection. We collected data on adherence through home activity logs; the CMA high group had similar attended sessions and home compliance when compared with the low group.

Data Analysis

We calculated average participant scores for the following outcome measures: Motor Activity Log-28 and Motor Activity

Log-5 items, ARAT, and Motor Activity Log-Self Report. Then the average scores across all participants for each outcome measure, including Motor Activity Log-28 and Motor Activity Log-5 items, ARAT, Motor Activity Log-Self Report, MAS-Wrist, MAS-Elbow, MAS-Finger, and MAS-Thumb, were calculated. We used 2 (group) × 4 (time) mixed-effects model analyses to evaluate the differences in outcome variables between the CMA Hand-Lower Function and CMA Hand-Higher Function groups over baseline and 6-, 9-, and 12-week measurements. We used “subject” as our random effect; fixed effects included group (CMA Hand-Lower Function and CMA Hand-Higher Function) and time (in weeks) so that participants are allowed to start at different levels. The mixed model takes baseline differences into account. We checked the distribution of the outcome variables and verified all assumptions, including compound symmetry and sphericity. In case the interaction between group and time yielded significance, we performed post hoc analysis by using the Benjamini-Hochberg method³¹ to control for multiple testing. A *P* value of .05 was used to establish significance.

RESULTS

Fourteen persons with spastic hemiparesis participated in this prospective cohort study. Table 2 shows participant demographics and clinical characteristics for CMA Hand-Higher Function and CMA Hand-Lower Function groups. The 2 (group) × 4 (time) mixed-effects model analyses showed significant group and time effects for most of the outcome measures. There were also significant group by time interaction effects on Motor Activity Log-5 items (*P*=.02), MAS-Elbow (*P*=.039), Motor Activity Log-28 (*P*=.093; a trend), and Motor Activity Log-Self Report (*P*=.069; a trend).

Differences Between Chedoke-McMaster Assessment Hand-Higher Function and Chedoke-McMaster Assessment Hand-Lower Function Groups in Average Scores of Outcome Measures

Figure 2 shows the average scores for each outcome measure from baseline to 12 weeks postinjection. The 2 (group) × 4

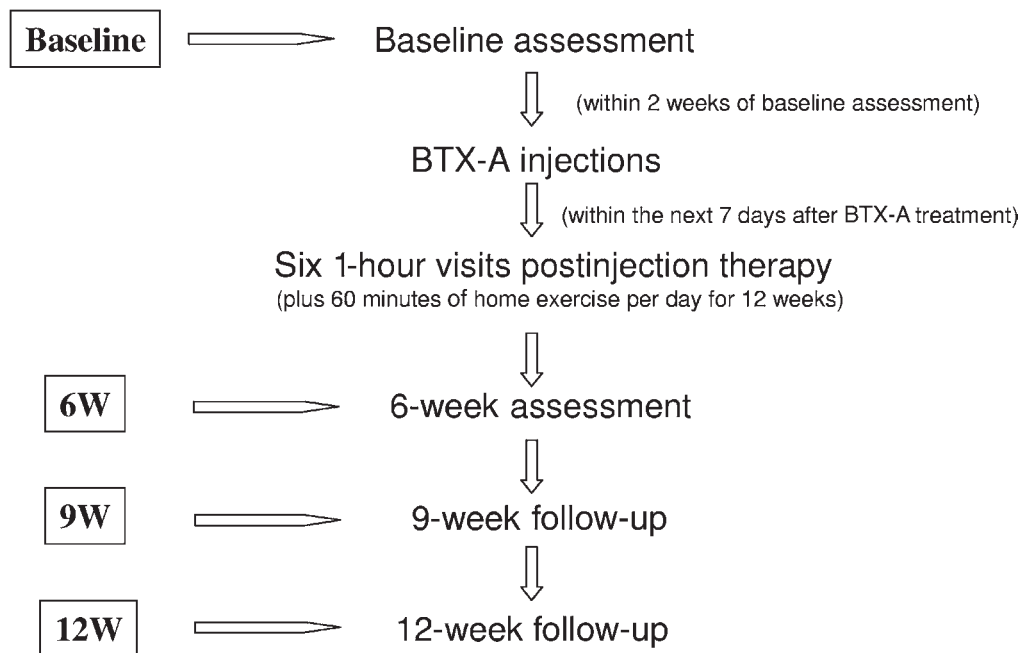


Fig 1. Experimental protocol time table.

(time) mixed-effects model analyses showed significant group effect. CMA Hand-Higher Function group was superior to CMA Hand-Lower Function group for the average scores of the following measures: Motor Activity Log-28 ($F_{11}=3.367$, $P=.006$), Motor Activity Log-5 items ($F_{11}=2.066$, $P=.063$; a trend), ARAT ($F_{11}=2.946$, $P=.013$), and Motor Activity Log-Self Report ($F_{11}=2.108$, $P=.059$; a trend).

Entire Cohort Improves Over Time

The 2 (group) \times 4 (time) mixed-effects model results not only showed significant group effect but also time effect. We charted the time course of changes in functional recovery from baseline to 12 weeks postinjection in figure 2. It shows that the entire cohort improved significantly over time for primary outcomes (Motor Activity Log-28, $F_{37}=4.203$, $P<.001$; Motor Activity Log-5 items, $F_{37}=3.321$, $P=.002$), and so did most of secondary outcomes (ARAT, $F_{37}=2.823$, $P=.008$; Motor Activity Log-Self Report, $F_{37}=4.181$, $P<.001$; MAS-Elbow, $F_{37}=-2.077$, $P=.045$; MAS-Wrist, $F_{37}=-3.305$, $P=.002$; MAS-Finger, $F_{37}=-3.404$, $P=.002$). The significant time effect showed the Motor Activity Log-28, Motor Activity Log-5 items, ARAT, and Motor Activity Log-Self Report increased 25%, 25%, 19%, and 89% from baseline to 12 weeks postinjection, respectively, for the entire cohort. The significant time effect on spasticity indicated that BTX-A injections and postinjection therapy resulted in 19%, 41%, and 34% reduction in MAS-Elbow, MAS-Wrist, and MAS-Finger spasticity from baseline to 12 weeks postinjection, respectively.

Differences Between Chedoke-McMaster Assessment Hand-Higher Function and Chedoke-McMaster Assessment Hand-Lower Function Groups in Amount of Improvement over Time (Change Scores) of Primary Outcome Measures

There was a significant group by time interaction effect on MAS-Elbow ($F_{37}=-2.142$, $P=.039$). Although spasticity of the elbow joint for both CMA Hand-Lower Function and CMA Hand-Higher Function groups decreased from baseline to 6 weeks, this interaction effect indicates CMA Hand-Higher Function group showed less elbow spasticity than CMA Hand-Lower Function group after 6 weeks postinjection.

There were also significant group by time interaction effects on Motor Activity Log-5 items ($F_{37}=2.422$, $P=.02$), Motor Activity Log-28 ($F_{37}=1.725$, $P=.093$; a trend), and Motor Activity Log-Self Report ($F_{37}=1.872$, $P=.069$; a trend). Although both groups showed significant improvement over time, the amount of improvement over time (change score) was different between groups: CMA Hand-Higher Function group demonstrated greater change scores on Motor Activity Log-28 ($P=.013$) from baseline to 6 weeks (CMA Hand-Higher Function, .78; CMA Hand-Lower Function, .36) and Motor Activity Log-5 items ($P=.006$) from baseline to 12 weeks (CMA Hand-Higher Function, .83; CMA Hand-Lower Function, .02) compared with CMA Hand-Lower Function group (fig 3). The groups had no significant differences in change scores of Motor Activity Log-Self Report, ARAT, or MAS between baseline to 6 weeks and between baseline to 12 weeks.

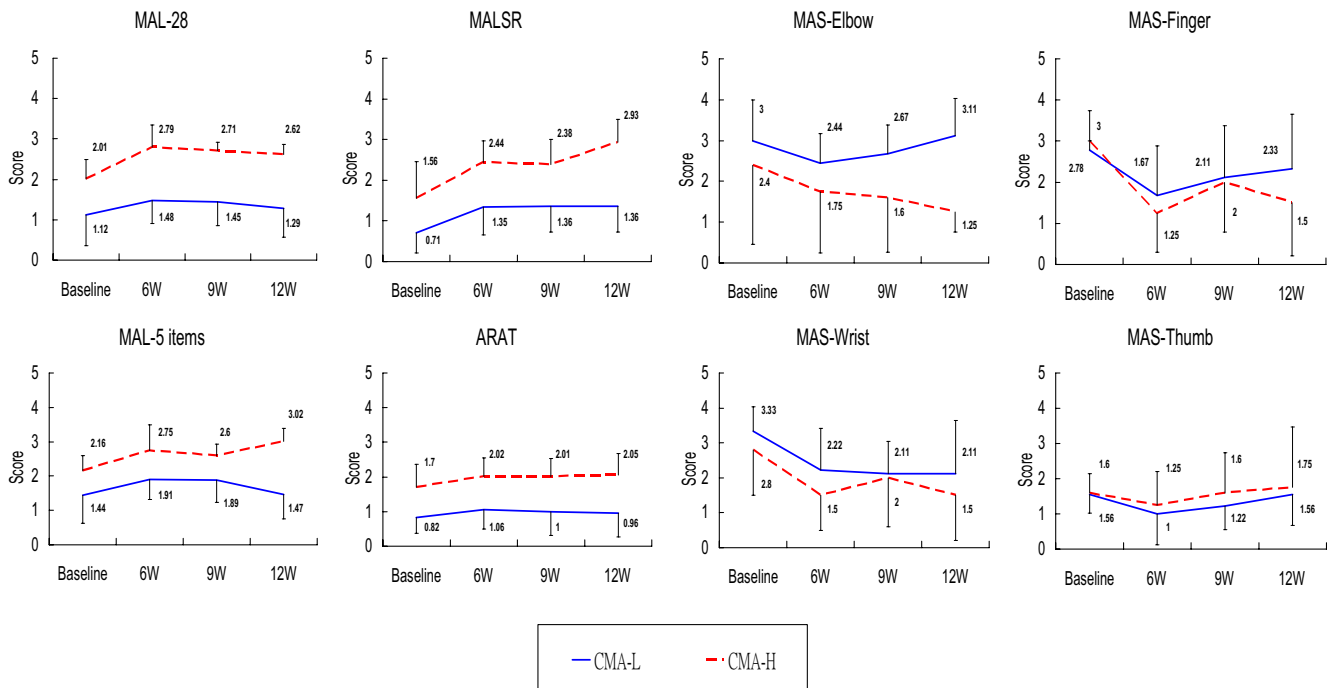


Fig 2. Outcome measures for Chedoke-McMaster Assessment Hand-Lower Function and Chedoke-McMaster Assessment Hand-Higher Function groups at baseline (preinjection), 6 weeks, 9 weeks, and 12 weeks postinjection. MAL-2); Motor Activity Log-5 items (wash hands, dry hands, pick up a phone, operate a door knob, and pick up a glass and take a drink); participant's perception of self-performance in activities of daily living assessed with the MALSR; ARAT; MAS. Abbreviations: CMA-L, Chedoke-McMaster Assessment Hand-Lower Function; CMA-H, Chedoke-McMaster Assessment Hand-Higher Function, MALSR, Motor Activity Log—Self Report; MAL, Motor Activity Log; MAL-28, Motor Activity Log-28.

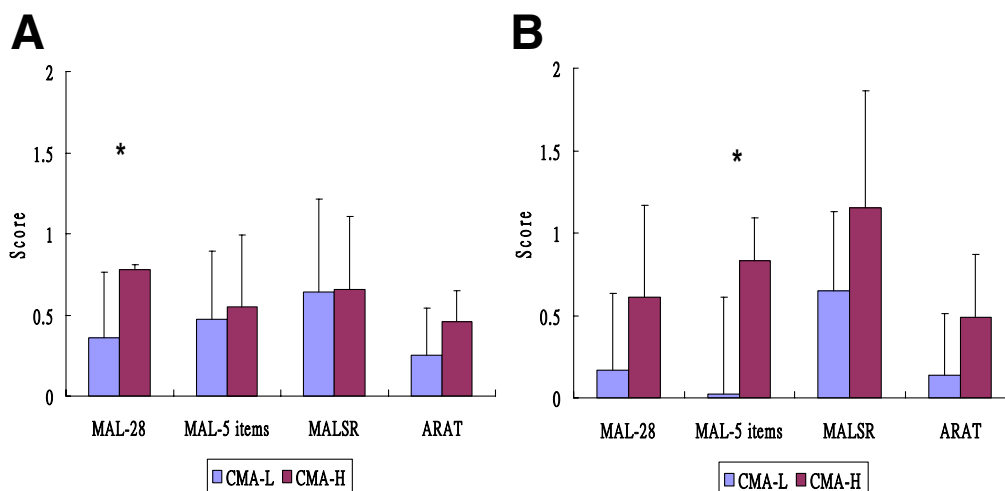


Fig 3. (A) Changes between baseline and 6 weeks after postinjection therapy (B) changes between baseline and 12 weeks postinjection. Abbreviations: CMA-L, Chedoke-McMaster Assessment Hand-Lower Function; CMA-H, Chedoke-McMaster Assessment Hand-Higher Function; MALSRS, Motor Activity Log—Self Report; MAL, Motor Activity Log; MAL-28, Motor Activity Log-28.

Differences Between Clinician's Evaluation (Motor Activity Log-28) and Patient's Perception (Motor Activity Log-Self Report)

Our results also showed that patients perceived greater functional improvement than observed by clinicians. For the entire cohort, Motor Activity Log-28 was objectively scored 1.57 at baseline and increased to 1.96 at 12 weeks postinjection. In contrast, Motor Activity Log-Self Report, which was assessed based on patient's perception, increased from 1.14 at baseline and improved to 2.15 at 12 weeks postinjection. Specifically, while Motor Activity Log-28 increased 25% from baseline to 12 weeks postinjection, Motor Activity Log-Self Report increased 89% over time.

DISCUSSION

We used simple evaluation of hand impairment as measured by CMA to test differences in the outcomes of functional recovery induced by BTX-A injection and postinjection therapy. Our results implied that hand impairment greatly influences the functional improvement after BTX-A injection and postinjection therapy.

The significant group effects suggest that baseline hand impairment assessed by CMA scores can distinguish group differences in other outcome measures, including Motor Activity Log-28, Motor Activity Log-5 items, ARAT, and Motor Activity Log-Self Report. These results might be due to the relation between hand impairment and upper-extremity function. For example, hand impairment has been associated with dexterous arm function as measured with ARAT.²¹ The significant time effects imply that combined BTX-A injections and postinjection therapy can improve hand function in persons with moderate to severe spastic hemiparesis for at least 12 weeks.

To answer the question about whether baseline hand impairment impacts functional recovery during rehabilitation, we further tested differences between CMA Hand-Higher Function and CMA Hand-Lower Function groups in amount of improvement over time (change scores) of primary outcome measures. Our results suggest that persons with less baseline hand impairment gain larger functional improvements than those with more impairment. However, one recent study proposed that persons with less baseline impairment as evaluated with Fugl-

Meyer Assessment had limited chances of recovery (relative to their initial state).³² Two factors may contribute to this difference. First, although participants in the Mirbagheri and Rymer³² study received traditional physical and occupational therapies, we used a novel intervention combined with BTX-A injections and postinjection therapy. Second, participants in the Mirbagheri and Rymer study were recruited within 4 weeks after a stroke, whereas the average years of stroke onset for CMA Hand-Lower Function and CMA Hand-Higher Function in this study were 5.9 and 15.2 years, respectively.

Traditionally, people with moderate to severe spasticity at baseline may be less likely to be referred for activity-based therapy. For example, persons who do not meet minimum motor criteria, which are 20° of volitional extension of the wrist and 10° volitional extension of each finger, are considered less likely to benefit from activity-based therapy.⁸ This may be because they have limited voluntary motion due to spastic hemiparesis. Our findings suggest that combined BTX-A injections and postinjection therapy can reduce challenges of motor control due to spasticity and facilitate functional recovery for persons with significant baseline impairment. Both CMA Hand-Higher Function and CMA Hand-Lower Function groups exhibited improved hand function and less spasticity after BTX-A injections and postinjection therapy. The effects after BTX-A injections and postinjection therapy were sustained for at least 12 weeks. Furthermore, although the reductions in spasticity as measured by MAS for both groups were similar, subjects in the CMA Hand-Higher Function group had a greater degree of upper-limb functional improvement than the CMA Hand-Lower Function group. Indeed, reduction of spasticity alone may not significantly improve function. With combined effects of spastic reduction and activity-based training, both groups improved upper-limb function. Overall, these results reveal the pretreatment impairment level greatly affects posttreatment improvement.

Differences Between Clinician's Evaluation (Motor Activity Log-28) and Patient's Perception (Motor Activity Log-Self Report)

Our findings indicated that patients perceived greater functional improvement than clinicians evaluated after BTX-A

injections and postinjection therapy. Two factors may contribute to the difference between clinician-based and patient-based evaluations. First, the task performance in an office setting may be different from what patients generally performed during daily life. Second, patients may expect to improve because they commit time to the study protocol. Although clinician-based evaluations (Motor Activity Log-28) are clearly needed to accurately and reliably characterize task performance, patient's perceptions on daily life activity (Motor Activity Log-Self Report) often drive the motivation for home exercises and intervention. Because clinician-based and patient-based evaluations may differ and contain important perspectives from clinicians and patients, use of both evaluations should be considered essential to a complete assessment of upper-extremity use during activities of daily living.

Possible Mechanisms Related to Differences Between Chedoke-McMaster Assessment Hand-Higher Function and Chedoke-McMaster Assessment Hand-Lower Function Groups in Amount of Improvement (Change Score) of Outcome Measures

Our findings suggest that persons with less baseline hand impairment can achieve greater improvement compared to those with more hand impairment. Baseline hand impairment may be related to available motor neuron pool because persons with less hand impairment may have more motor units available in their physiologic system. With inhibited spasticity and increased activity-based practices due to BTX-A injection and postinjection therapy, persons with less hand impairment may be able to recruit more motor units and rewire more neural networks than those with more hand impairment. Thus, they can make use of agonists and generate larger muscle force after spasticity reduction by BTX-A injection and control their hands better after postinjection training. Furthermore, persons with less hand impairment are able to practice various kinds of activity with a higher quality, participate more in their daily activity, and generalize what they learn from interventions to improve their daily life function. From the dynamic system theory perspective, a large amount of variable practice may facilitate exploration, selection, and self-organization of neural network and physiologic system.³³ Thus, newly developed neural network can emerge and compensate for impaired old neural network.

Study Limitations

Our study has a relatively small sample size (N=14) that may limit generalizability. To examine potential confounding factors, we ran univariate analyses between the outcome variables and the variables in table 2, but there were no significant relationships. We did not include all potential confounding factors, such as aphasia and sensory deficits, into our data analysis because of the small sample size. Although the Motor Activity Log-5 is a laboratory-based measure that uses 5 questions without modification from the Motor Activity Log-28 (which has reliability and validity), the reliability and validity of the Motor Activity Log-5 requires further evaluation. Reliability for MAS has been demonstrated for elbow and wrist joints.^{27,34} Although Brashear³⁰ reported good intra- and inter-rater reliability of the Ashworth scale for elbow, wrist, finger, and thumb flexion, the finger and thumb have not been validated for the MAS. Neurophysiology-related data, such as blood-oxygen-level dependent functional magnetic resonance imaging, will be needed to understand the underlying mechanisms that promote clinical improvement.

CONCLUSIONS

Hand impairment from spastic hemiplegia can be improved with targeted interventions that lessen spasticity and improve motor learning. Botulinum toxin injections and postinjection therapy can improve hand function for persons with either high or low baseline impairment. Clinicians should expect to see larger gains for persons with less baseline impairment.

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