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Tremor and Other Hyperkinetic Movements

Articles

Predicting Improvement in Writer's Cramp Symptoms following Botulinum Neurotoxin Injection Therapy

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Abstract

Introduction: Writer's cramp is a specific focal hand dystonia causing abnormal posturing and tremor in the upper limb. The most popular medical intervention, botulinum neurotoxin type A (BoNT-A) therapy, is variably effective for 50–70% of patients. BoNT-A non-responders undergo ineffective treatment and may experience significant side effects. Various assessments have been used to determine response prediction to BoNT-A, but not in the same population of patients.

Methods: A comprehensive assessment was employed to measure various symptom aspects. Clinical scales, full upper-limb kinematic measures, self-report, and task performance measures were assessed for nine writer's cramp patients at baseline. Patients received two BoNT-A injections then were classified as responders or non-responders based on a quantified self-report measure. Baseline scores were compared between groups, across all measures, to determine which scores predicted a positive BoNT-A response.

Results: Five of nine patients were responders. No kinematic measures were predictably different between groups. Analyses revealed three features that predicted a favorable response and separated the two groups: higher than average cramp severity and cramp frequency, and below average cramp latency.

Discussion: Non-kinematic measures appear to be superior in making such predictions. Specifically, measures of cramp severity, frequency, and latency during performance of a specific set of writing and drawing tasks were predictive factors. Since kinematic was not used to determine the injection pattern and the injections were visually guided, it may still be possible to use individual patient kinematics for better outcomes.

Keywords: Writer's cramp, focal hand dystonia, botulinum toxin, kinematics

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Ethics Statement: This study was performed in accordance with the ethical standards detailed in the Declaration of Helsinki. The authors' institutional ethics committee has approved this study and all patients have provided written informed consent.

Introduction

Writer's cramp is a task-specific form of focal hand dystonia in which patients experience abnormal posturing and movement in the upper limb while performing repetitive or fine motor movements, specifically writing or drawing tasks.[1] Symptoms often include a combination of joint posturing, excessive pen grip force, and writing tremor.[2] These symptoms cause pain and discomfort in the upper limb, further inhibiting task performance. The impairments that writer's cramp patients experience often intrude on their abilities to complete professional work,[3] a factor that may relate to the higher incidence of depression and anxiety in this population.[4] Therefore, effective treatment is essential to improve quality of life and to allow patients to re-enter the work force.

The most popular medical intervention for treatment of writer's cramp is botulinum neurotoxin type A (BoNT-A) injection therapy.[5] Visual assessment of posturing of the upper limb is used to guide the injector to select appropriate muscles for injection. By temporarily weakening the injected muscles, BoNT-A reduces local muscle activity and directly alleviates symptoms.[6] As with most treatments, however, BoNT-A therapy is only effective for a certain percentage of the patient population. A review by Dashtipour and Pender[7] revealed that approximately 50–70% of patients with writer's cramp have variable benefit from this treatment. The remaining injected patients showed no efficacy but had the potential for substantial arm and hand weakness that may last from weeks to months.[8,9] Additionally, injections may cost patients up to 600 dollars per treatment for uninsured therapy.[10] As it regularly takes several 3-month injection cycles to determine the efficacy of treatment or lack thereof,[11] patients may spend thousands of dollars and endure more than a year of side-effects before being identified as a non-responder.

Unfortunately, there is currently no pre-injection method of identifying patients that may respond to BoNT-A therapy. Although Djebbari et al.[12] identified some independent motor characterizations that predicted BoNT-A response, they were unable to create a comprehensive response profile. The issue underlying this prediction attempt and the varied efficacy measures reported in the literature[7] may be a lack of application of multiple measurements within the same patient population. In the field of writer's cramp research, there are four main methods of assessing symptoms: clinical assessment, self-reports, performance assessments, and kinematic assessments, each with inherent limitations. Clinical assessments such as the Writer's Cramp Rating Scale (WCRS) are confined by a lack of consensus of which scale offers the most accurate results. In fact, it has been shown that these clinical scales each measure different aspects of motor impairment.[13] These scales are also confined by a lack of sensitivity. For example, only one of the 10 items on the commonly used Unified Dystonia Rating Scale (UDRS) pertains to hand dystonia. Kinematic measurement offers an objective method of assessing movement, but studies of biomechanical analyses to date have generally ignored the multi-segmental nature of the disorder,[14] focusing on specific joint angles or applied forces.[15,16] Despite the limitations of these assessments, there remains a tendency in the literature to employ only one scale from multiple categories,[12,17] or apply only one type of assessment.[15,18–20] This lack of comprehensive measurement, which has inhibited the development of a BoNT-A response profile for writer's cramp, may be overcome by implementing various measures from all assessment categories. Therefore, the aim of the present study is to utilize a comprehensive measurement paradigm, implemented at baseline, to create predictive profiles of BoNT-A responders and non-responders. The creation of such a response profile would allow injectors to use pre-treatment assessments to predict post-treatment improvement in writer's cramp symptoms after BoNT-A is injected into affected muscles based on the clinician's best visual judgment of the posturing of the limb.

Methods

Participants

Nine patients (three females, M = 60.2 years, SD = 7.1 years, range 51–70 years; see Table 1) diagnosed with writer's cramp were recruited from the London Movement Disorders Clinic at University Hospital, London, Canada. All participants were afflicted in their dominant hand; seven participants were right-hand dominant. Symptom duration ranged from 3 to 40 years (M = 12.3 years, SD = 11.2 years). All participants were toxin naïve at the start of the study. The study was approved by the local Health Sciences Research Ethics Board and all participants gave written informed consent. None of the participants were receiving any other form of treatment or therapy for their writer's cramp symptoms 6 months before enrollment in the study.

Procedure

Study timeline. Participants attended for a total of five visits over the course of 32 weeks. Visits occurred at weeks 0 (visit 1), 6 (visit 2), 16 (visit 3), 22 (visit 4), and 32 (visit 5). Seven participants completed all five visits, and two withdrew after completing the first three visits (see Table 1, Adverse Events). Injections were given at visits 1 and 3, at the end of the session. The two participants who withdrew from the study after visit 3 did not receive injections at the end of that visit. The current standard of care requires a minimum of 3 months between consecutive BoNT-A injections; [21] an extra month washout period was added between injections to minimize excess arm weakness. Each visit lasted approximately 2 hours. This study is part of a larger investigation, and therefore not all collected data are reported.

Clinical assessment. At the beginning of each visit, three clinical scales were administered: the UDRS, the Dystonia Movement and Disability Scale (DMDS) and the WCRS. All scales were administered by a movement disorders neurologist (MDN) or trained research personnel.

Kinematic sensors and assessment. Following clinical assessment, kinematic sensors were attached and writing/drawing tasks were completed. Four types of kinematic sensors were used to collect biomechanical information. One force sensor placed beneath the writing surface was used to measure the force applied down onto the page by the participant during writing (Multi-Axis Force Sensor – Gamma Transducer: ATI Industrial Automation Inc.). Two identical finger pressure sensors were placed underneath thin rubber pads on the pen. One pressure sensor was held beneath the thumb, the other held beneath the index finger (DTS A201 FlexiForce Sensor; TekScan Inc.). The pressure sensors were used to measure the grip force employed during the tasks. Three electrogoniometers were placed across the back of the wrist (Twin Axis SG150 Goniometer; Biometrics Ltd.), the outside of the elbow (Twin Axis SG150 Goniometer; Biometrics Ltd.) and along the top of the shoulder (Twin Axis SG150 Goniometer; Biometrics Ltd.), respectively, to measure joint angles. Finally, one torsiometer was placed across the forearm to measure

Table 1. **Patient Demographics and Injection Parameters.**

Patient Number	Gender	Age (years)	Affected Limb	Symptom Duration (years)	Adverse Events	Injection 1: Total Dose	Injection 1: No. of Muscles Injected	Injection 2: Total Dose	Injection 2: No. of Muscles Injected
01	M	52	R	3	N/A	100	4	135	4
03	M	70	R	11	*	50	4	N/A	N/A
07	F	55	R	2	N/A	40	4	40	4
15	M	58	R	45	N/A	50	4	70	4
18	M	70	R	15	N/A	40	4	50	4
24	M	64	L	3	N/A	50	4	50	4
29	M	55	L	7	*	60	2	N/A	N/A
32	F	55	R	7	N/A	60	6	50	6
50	F	60	R	3	N/A	90	7	135	7

*Severe weakness reported at visit 2, after first injection; patient still reporting debilitating weakness at visit 3, resulting in withdrawal from study.

forearm rotation during the tasks (Single Axis Q150 Torsiometer; Biometrics Ltd.). The kinematic sensors were attached to the affected arm using 3M hypoallergenic micropore paper tape. All kinematic sensors were connected to an electronic transmitter (TeleMyo™ 2400T G2 Transmitter; Noraxon Inc.) that wirelessly relayed all biomechanical measurements to a laptop computer, via a receiver system (TeleMyo™ 2400R G2 Mini Receiver; Noraxon Inc.). An associated software package (MyoResearch XP Master; Noraxon Inc.) was used to digitally record the three-dimensional kinematic measurements in real time during task completion.

Experimental tasks. After sensor attachment, participants completed a set of simple writing and drawing tasks. Participants were seated on a height-adjustable chair in front of a standard desk. All tasks were completed on printed sheets fixed on the pressure-sensitive writing surface. Participants performed a set of 16 tasks, summarized and listed in order in Table 2. Tasks were chosen to provide the sensors with the most comprehensive information possible, allowing for accurate characterization of motor abnormalities. Hovering the pen above a fixed point on the paper provided a baseline for cramping occurring in the absence of writing. Writing of a standard sentence was chosen to induce cramping most representative of the original symptom. All other tasks are standardized drawing tasks used to break down movements made during writing into simpler components. Kinematic assessment of these components allowed for collection of detailed information about individual motor abnormalities. Spiral drawing effectively localizes wrist and hand movements while minimizing elbow and shoulder involvement. Similarly, connecting two dots with a straight line isolates movement to the elbow joint. The more complex sinusoid tracing tasks provide information about full arm motions, as they tend to recruit full upper-limb joint involvement.

Non-kinematic assessment. During task completion, a timer was run continuously. Start and end times for each task were recorded. While the participants completed each task, they were asked to state when their cramping sensations began; this time was also recorded. Owing to differences in individual symptomatology, "cramping" was defined as "the sensation you experience that interferes with your ability to write normally." After each individual task, participants were asked to rate the level of cramp intensity on a numerical scale from 0 (no cramp) to 4 (most severe cramping: maximal pain/discomfort). At the end of each visit, writing quality (task performance) was assessed for each task on a scale from 0 (normal writing quality) to 3 (severely abnormal writing quality to completely illegible or unable to complete task). The task performance scale was adapted from the Fahn–Tolosa–Marin Tremor Rating Scale Section C, which is used to assess similar writing and drawing tasks to those used in the present study.

BoNT-A injections. At the end of visits 1 and 3, participants received injections with BoNT-A (Botox®; Allergan Inc.: Irvine, CA; 50 units per vial). Based on the visual clinical assessment during the writing task performed that day and prior clinical experience, the MDN determined which muscles to inject and the toxin dose. BoNT-A was then reconstituted (1:1 saline dilution) and injected locally into the affected muscles by the MDN under electromyographic guidance (Dantec Clavis™ and Bo-ject® Needle Electrodes; Natus Medical Inc.). As per clinical standards, muscle selection and dosing were adjusted as

Table 2. **Task Descriptions. Tasks were completed in order from 1 to 16.**

Task No.	Task Description
1	Hovering pen over fixed dot for 30 seconds
2	Spiral drawing (1): large, counterclockwise
3	Spiral drawing (2): small, counterclockwise
4	Spiral drawing (3): large, clockwise
5	Spiral drawing (4): small, clockwise
6	Writing standard sentence: "Today is a bright and sunny day"
7	Connect two dots: left to right
8	Connect two dots: right to left
9	Sinusoid tracing (1): low frequency, high amplitude, left to right
10	Sinusoid tracing (2): high frequency, high amplitude, left to right
11	Sinusoid tracing (3): low frequency, low amplitude, left to right
12	Sinusoid tracing (4): high frequency, low amplitude, left to right
13	Sinusoid tracing (5): low frequency, high amplitude, right to left
14	Sinusoid tracing (6): high frequency, high amplitude, right to left
15	Sinusoid tracing (7): low frequency, low amplitude, right to left
16	Sinusoid tracing (8): high frequency, low amplitude, right to left

necessary for the second injection. Adjustments were based upon self-reports of injection efficacy by the patient, reported side effects, and clinical experience of the MDN.

Statistical analysis

All statistical analyses were performed using SPSS software, version 20.0 (SPSS Inc., Chicago, IL). Missing data are a common part of clinical data collection.[22] This study design contains two visits during peak injection efficacy (visits 2 and 4) and three visits in which little to no drug effects are present[21] (visits 1, 3, and 5). Therefore, missing data were replaced with data from a compatible visit. These compatible data were used for all statistical analyses.

Response classification. Scores from the handwriting item of the DMDS (of the Fahn–Marsden Dystonia Scales) were used to classify patients as responders or non-responders. All item scores (0–4) on the DMDS were multiplied by a provoking factor score (0–4) to get a total item score from 0 to 16. The full DMDS score was not used, as other scale items did not pertain specifically to focal hand dystonia. Handwriting DMDS scores were compared between visits 1 (baseline) and 4 (peak efficacy, injection 2): patients whose scores had decreased by 50% or more between visits 1 and 4 were classified as responders; patients whose scores had decreased by less than 50% were classified as non-responders. Scores from visit 2 (peak efficacy, injection 1) were used for comparison for the two patients who completed only one injection cycle. Session notes were used to confirm whether patients had felt they were responders or non-responders. All DMDS classifications aligned with patients' self-reports.

Kinematic variables. A computer software program (Matlab R2014b: MathWorks Inc.) was used to analyze the data recorded by the kinematic sensors during testing. Nine kinematic measures were extracted for each of the 16 experimental tasks completed during visit 1: thumb force (N), index force (N), hand force (N), wrist flexion–extension (°), wrist ulnar–radial deviation (°), forearm pronation–supination (°), elbow flexion–extension (°), shoulder flexion–extension (°), and shoulder abduction–adduction (°). All angular measurements were recorded in degrees with negative numbers representing the following movement directions: wrist/elbow/shoulder extension, wrist radial deviation, wrist supination, and shoulder adduction. The values for each kinematic measure were averaged across all writing and drawing tasks, giving nine kinematic scores for each participant. The visit 1 kinematic scores for the responder and non-responder groups were compared using separate Mann–Whitney *U* tests. Any kinematic score found to be significantly different for responders versus non-responders indicated a discrete biomechanical marker that could be used to predict whether or not a patient would experience improvement in his or her writer's cramp symptoms following BoNT-A injection therapy.

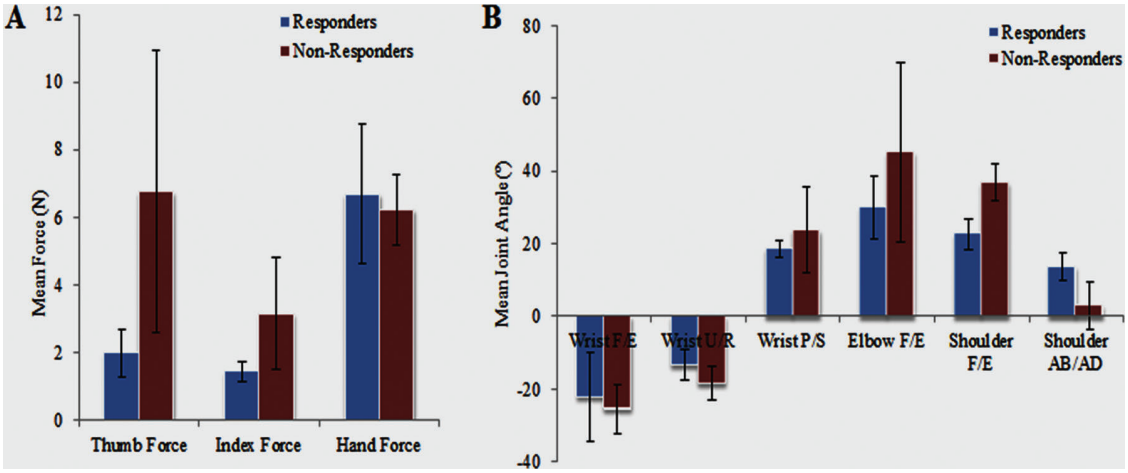

Figure 1. **Kinematic Results.** (A) Mean (±standard error [SE]) finger and hand forces across all tasks. (B) Mean (±SE) joint angles across all tasks. Positive values represent (respectively): wrist flexion, wrist radial deviation, wrist pronation, elbow flexion, shoulder flexion, shoulder adduction.

Clinical and non-kinematic variables. UDRS score (units) and WCRS score (units) refer to the total scale scores. Cramp frequency (units) was calculated by dividing the number of tasks during which a participant experienced cramping by the total number of tasks. Cramp latency (seconds) was calculated by subtracting task start time (seconds) from cramp start time (seconds); latency scores were then averaged across all tasks. Cramp severity (units) and task performance (units) scores were averaged across all tasks. All clinical and non-kinematic scores were compared across responders and non-responders using separate Mann–Whitney *U* tests. Any clinical or non-kinematic score found to be significantly different for responders versus non-responders indicated a predictive factor that could be used to predict improvement in writer's cramp symptoms following BoNT-A injection therapy.

z-Score calculation and profile creation. For measures that showed a significant difference (or a difference trending towards significance) between responders and non-responders, z-scores were calculated. These z-scores were used to determine relative levels of "high" and "low" scores on the predictive measures, as no literature basis for such average scores exists to our knowledge.

Results

BoNT-A response

Consistent with rates reported in literature, statistical analysis revealed a 56% response rate; the following five patients exhibited 50% or greater rectification of their writer's cramp symptoms, as determined by a decreased in DMDS handwriting scores between visits 1 and 4: WC-01 (67% reduction), WC-07 (100% reduction), WC-18 (50% reduction), WC-32 (100% reduction), and WC-50 (50% reduction). These patients were thus classified as BoNT-A responders. The remaining four patients exhibited symptom reduction of less than 50%, or symptom worsening between visits 1 and 4: WC-03 (50% worsening), WC-15 (0% reduction), WC-24 (33% reduction), and WC-29 (200% worsening). These patients were therefore categorized as BoNT-A non-responders. Patients who experienced symptom worsening reported that their increased handwriting difficulties were due to excessive weakness. Session notes indicated that regardless of weakness, these patients were not satisfied with the symptom reduction achieved by BoNT-A therapy.

Kinematic predictors

Statistical analyses (Mann–Whitney *U* tests) revealed no significant difference between groups for any of the nine recorded kinematic measures. None of the three measured forces was found to be significantly different between BoNT-A responders and non-responders (see Figure 1A): thumb force (U [7]=8.0, p=0.624), index finger force (U [7]=9.0, p=0.806), and hand force (U [7]=8.0, p=0.624). Thus none of these forces were biomechanical indicators of BoNT-A therapy response. Likewise, none of the six measured joint angles was found to be significantly different between responders and non-responders (see Figure 1B): wrist flexion/extension (U [7]=9.0, p=0.806), wrist radial/ulnar deviation (U [7]=7.0, p=0.462), wrist pronation/supination (U [7]=7.0, p=0.462), elbow flexion/extension (U [7]= 9.0, p=0.806), shoulder flexion/extension (U [7] = 4.0, p = 0.142), and shoulder abduction/adduction (U [7]=7.0, p=0.462). Therefore, the measured joint angles also did not reveal any kinematic predictors.

Clinical and non-kinematic predictors

For the clinical scales, self-reports and task performance measures, statistical analyses (Mann–Whitney *U* tests) revealed a significant difference in cramp severity scores (U [7]=0.0, p=0.014] (Figure 2A) and in cramp frequency scores (U [7]=1.0, p = 0.026) (Figure 2B) between BoNT-A responders and non-responders. Both cramp severity and frequency represent predictive factors. Although statistical analyses revealed a non-significant difference in cramp latency scores (U [7]=4.0, p=0.124) (Figure 2C) between responders and non-responders, this assessment score was trending towards significance. Therefore, cramp latency scores were also used as predictive factors in

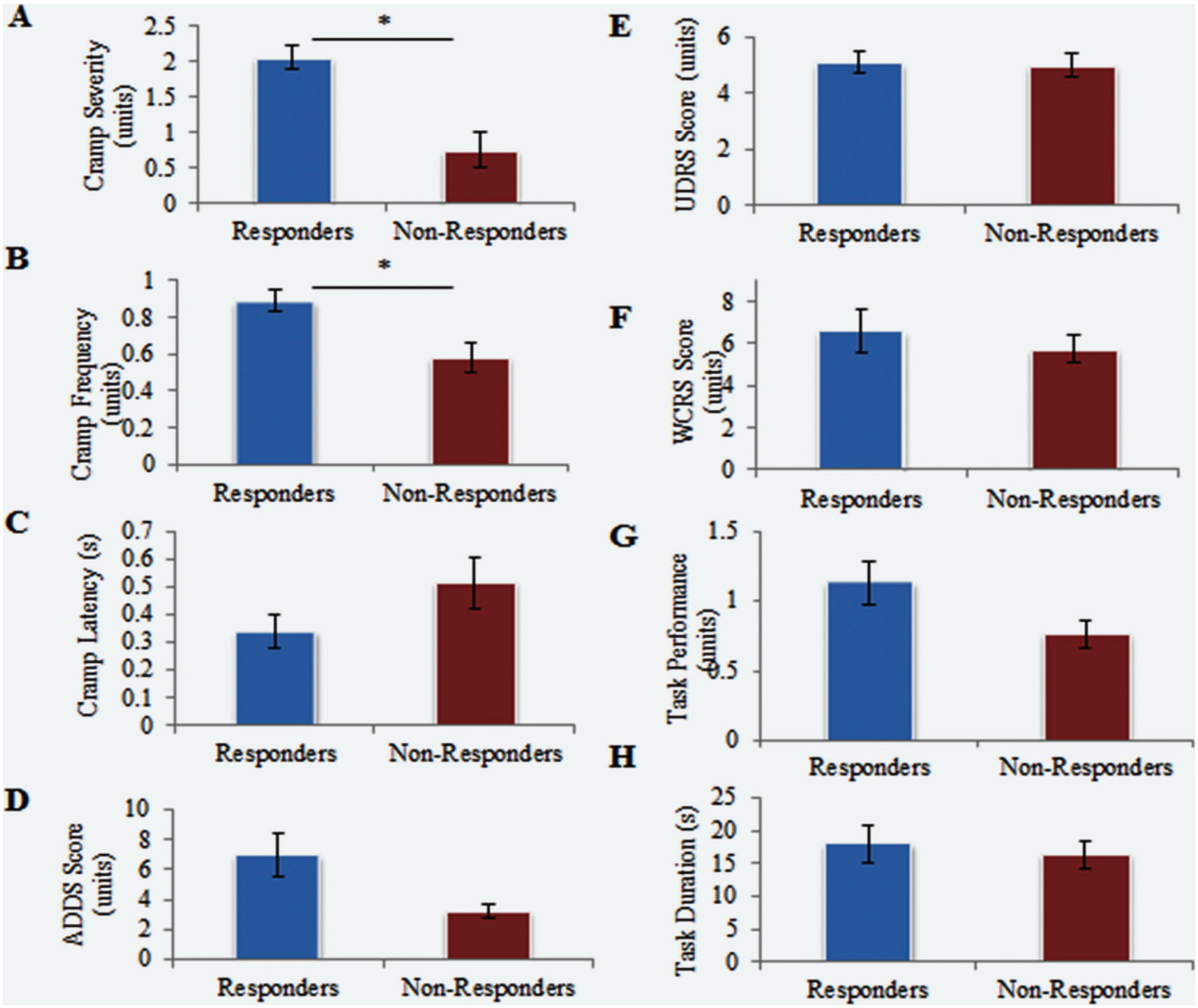

Figure 2. **Clinical and Non-kinematic Results.** Asterisks represent a significant difference between groups. (A) Mean (±standard error [SE]) cramp severity scores across all visit one tasks. (B) Total (±SE) cramp frequency score for visit one. (C) Mean (±SE) cramp latency scores across all visit one tasks. (D) Total (±SE) Unified Dystonia Rating Scale score from visit one. (E) Total (±SE) Writer's Cramp Rating Scale score from visit one. (F) Mean (±SE) task performance scores across all visit one tasks.

the subsequent response profile creation. Statistical analyses revealed no significant difference for the following clinical and non-kinematic assessment scores: UDRS scores (U [7]=7.5, p=0.521) (Figure 2D), WCRS scores (U [7]=8.5, p=0.706) (Figure 2E), and task performance (U [7]=7.0, p = 0.462) (Figure 2F). Thus none of these scores was a predictor of BoNT-A therapy response and none was used in subsequent profile creation.

Response profile

Compared with non-responsive patients, BoNT-A responders tended to have high cramp frequency (Figure 3A), high cramp severity (Figure 3B), and low cramp latency (Figure 3C). Therefore, above-average (high) scores on cramp severity and cramp frequency as well as a below-average (low) score for cramp latency were considered predictors of improvement in writer's symptoms following BoNT-A therapy. High or low scores were those above or below the following averages, respectively: cramp severity (M=1.48 units, SD=0.80 units), cramp frequency (M=0.75 units, SD=0.21 units), and cramp latency (M=0.42 seconds, SD=0.17 seconds). z-Score results were used to determine whether individual participants fell into each of the predictive categories. z-Score results are represented in Figure 3. Coincidence of these three predictive categories for each patient is examined in Figure 4, giving a visual representation of how each patient fits into the BoNT-A response profile. The three patients who experienced the largest reduction in DMDS handwriting scores (WC-01, WC-32, and WC-50; data not shown) fit into all three

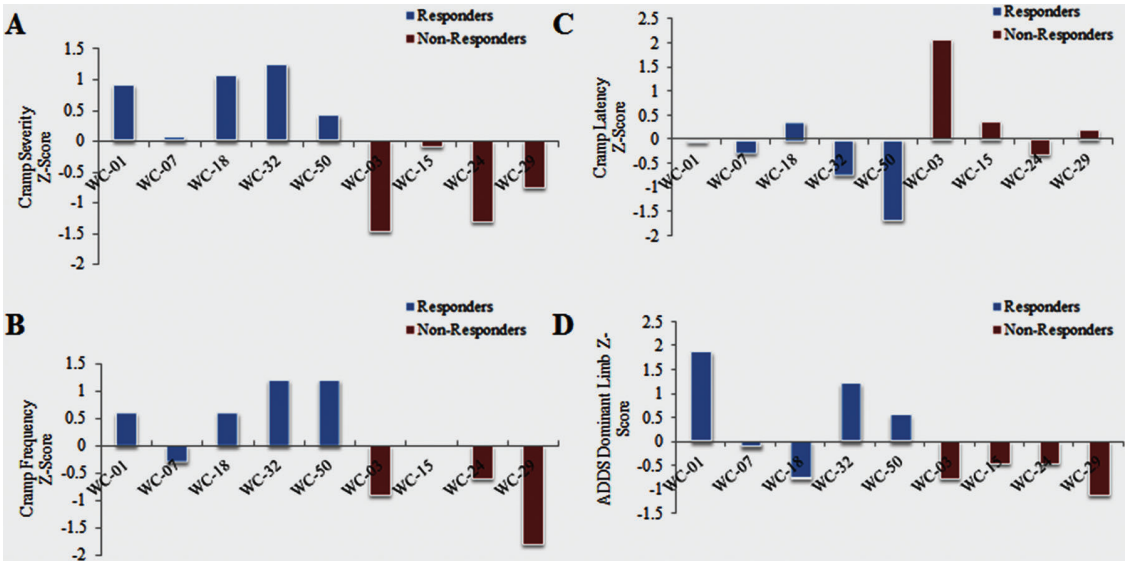

Figure 3. **z-Scores for Response Profile Measures.** Light-grey bars represent responders, and dark-grey bars represent non-responders. Positive values represent above average scores. (A) Cramp frequency (mean=0.75 units). (B) Cramp severity (mean=1.48 units). (C) Cramp latency (mean=0.42 seconds).

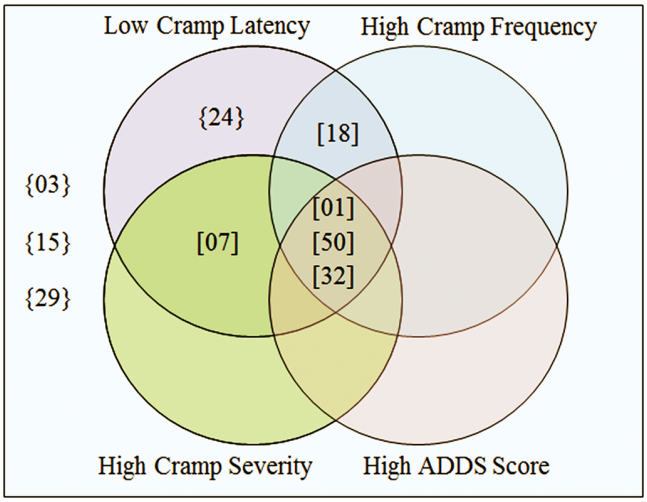

Figure 4. **Response Profile.** Patient numbers in brackets: square brackets indicate responders, curved brackets indicate non-responders. Three response predictors identified in previous analyses represented: high cramp severity, high cramp frequency, and low crap latency. Circle intersections represent co-occurrence of response predictors in patient assessment.

predictive categories. The remaining two responding patients (WC-07 and WC-18) each fit into two of the three predictive categories. Three non-responsive patients (WC-03, WC-15, and WC-29) exhibited no predictive response factors. The final non-responsive patient (WC-24) exhibited low latency in the absence of any other predictive factor.

Discussion

This investigation used a comprehensive assessment paradigm to determine which measurements were predictive of improvement in writer's cramp symptoms following BoNT-A injection therapy. As predicted, the response rates from the present study matched the literature-reported 50–70% efficacy rate,[7] with 56% of participants BoNT-A responsive.

Despite previous findings by Djebbari et al.[12] that increased wrist flexion and forearm pronation were kinematic predictive factors, the current study found no biomechanical predictors. The discrepancy in these results may be due to methodological differences. The present study employed a biomechanical assessment paradigm, but Djebbari et al.[12] utilized a visual assessment paradigm. More specifically, the lack of kinematic predictors identified in this study may be due to the small sample size and the large individual variation in biomechanical measurements (discussed below). Further, it is possible that a lack of explicit analysis of finger and thumb flexion and extension precluded kinematic predictive factors from being identified. Finally, the present study did not employ simultaneous needle electromyography recording alongside the kinematics, in an attempt to limit invasive study procedures. Such recordings may have helped guide kinematic analysis by identifying which muscles are the major generators of involuntary movements. Despite these biomechanical assessment limitations, the lack of kinematic significance may be a fortuitous finding in terms of clinical relevance. The kinematic system used in this study is relatively expensive, and the kinematic recordings take approximately 30 minutes to complete. It is therefore more realistic for an injector to adopt a short non-kinematic assessment routine as a BoNT-A therapy screening paradigm.

Clinical and non-kinematic results indicated that BoNT-A-responsive patients exhibited all (or a selection of) the following response factors: higher than average cramp severities and cramp frequencies, and below-average cramp latencies. These three factors thus formed a simple yet comprehensive profile of BoNT-A response for writer's

cramp patients. By matching each patient's results to the response profile, it was shown that any patient whose results fit into two or more of the defined predictive categories is likely to be a responder, with a better degree of improvement for those falling into more predictive categories. On the other hand, patients exhibiting one or fewer response factors are most likely non-responders. The one non-responder who fit one predictive category had a DMDS score reduction rate only slightly below the level required to be classified as a responder. This may indicate that the response profile can be used to predict degree of responsiveness to BoNT-A therapy, rather than simply predicting binary response versus non-response categories. Importantly, all three predictive scores were related to completion of a set of 16 writing and drawing tasks designed specifically for this investigation. Taken together, these results suggest the creation of a short and inexpensive BoNT-A screening paradigm, discussed below, which may be implemented in a clinical setting.

Being an exploratory, proof of concept clinical investigation, this study did have limitations. The major drawbacks of this investigation were the small sample size and the lack of placebo control and blinding. The small sample undermined statistical power[23] and likely contributed to the lack of statistically significant kinematic findings. In addition, a larger sample size would provide more security for the calculated response rate matching the literature reported response rate, thus increasing generalizability of the results. It may be noted, however, that previous studies investigating this patient population have utilized comparably small sample sizes: Baur et al.,[24] (seven participants); Kimberley et al.,[25] (12 participants); Rosenkranz et al.[26] (two groups of six participants). The other major limitation was that all injections were carried out on the basis of visual assessment. Although visual determination of injection parameters is the clinical standard,[5] the subjective nature of this practice suggests that literature reported efficacy rates may be due to suboptimal injections by physicians. A more objective means of determining injection parameters could increase BoNT-A therapy efficacy, eliminating the need for predictive analyses. Regardless, such a method does not yet exist. Clinicians will likely continue to use visual assessment to determine injection parameters for the foreseeable future, necessitating a predictive profile.

Therefore, the results of the present study have important clinical relevance. As previously discussed, for the 30–50% of patients for whom BoNT-A therapy is ineffective,[7] these treatments can unnecessarily cost thousands of dollars and up to a year of life-altering arm and hand weakness. Although BoNT-A treatment professionals may be able to minimize severity or longevity of negative physical side effects of this treatment, the monetary limitations remain a likely barrier for many prospective patients. Clinicians could alleviate these issues by adopting a simple BoNT-A therapy screening paradigm, consisting of completion of the 16 writing and drawing tasks used in this study. Adoption of this simple paradigm by clinicians would take only approximately 10 minutes for task completion and score calculation, but would save patients large amounts of time, money, and quality of life alterations.

The next step in continuing this research is to utilize a larger sample size, in order to increase statistical power and generalizability.[23,27] The use of a larger sample size would result in generation of average response factor scores (cramp severity, frequency, and latency) that could be applied widely in a clinical setting. In the future, these response factors could be analyzed using a linear regression analysis to create a response algorithm. If predictive weights of the various scales and scores are determined and input into the regression, this algorithm may even have the power to predict to what degree the treatment will be effective for a given patient. Researchers may then consider applying this method of profile creation to other patient populations. For example, to essential tremor patients who receive BoNT-A therapy for tremor relief.[28] Additionally, recent research has shown that writer's cramp patients have unique, pre-treatment kinematic symptomatology profiles.[29] Therefore, a larger scale step for this line of research is to examine the relationship between writer's cramp symptom characteristics and treatment outcome. Future researchers may also investigate the role of mechanism of action of BoNT-A on variability of treatment outcomes for writer's cramp patients.

Although no biomechanical predictors of BoNT-A response were identified in this study, kinematic assessment has much to offer the field of writer's cramp research. Full upper-limb kinematic measurement remains a novel assessment tool for writer's cramp and should undoubtedly be investigated further. The large variability in the kinematic recordings taken during this study imply that writer's cramp patients each have unique profiles of motor abnormalities. This has implications for improving BoNT-A injection therapy by optimizing injection parameter determination. The use of objective kinematic sensors may allow for a more sensitive determination of which muscles are hyperactive, leading to more effective determinations of BoNT-A injection parameters.

In conclusion, this study implemented a novel, comprehensive assessment paradigm to predict improvement in writer's cramp symptoms following BoNT-A injection therapy. The results showed that responsive patients fit into two or more of the following predictive categories: high cramp severity, high cramp frequency, and low cramp latency. Although further investigation with increased sample size is required before this profile can be clinically utilized, proof of concept was shown for creation of a comprehensive profile that predicts BoNT-A therapy response.

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