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Motor sequence awareness in impaired in dystonia despite normal performance

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Abstract

OBJECTIVE—Dystonia is a movement disorder that has been associated with impaired motor learning and sequence recognition. However, despite evidence that patients with dystonia have a reduced sense of agency, it is unclear whether dystonia is specifically associated with impaired recognition of a *movement* sequence. We have shown previously that performance consistency in the temporal and kinematic domains predicts awareness of underlying motor patterns in a finger tapping task. Because movements in dystonia are characterized by high variability, we predicted that subjects with dystonia would have decreased motor sequence awareness.

METHODS—Subjects with dystonia (n= 20) and healthy control adults (n= 30) performed finger tapping sequences with a common motor pattern and changing stimulus-to-response mappings. Subjects were said to be “aware” of the motor pattern if they recognized their fingers moved in the same order during each stimulus-to-response remapping.

RESULTS—Subjects with dystonia had decreased motor pattern awareness, but those differences were not due to greater performance variability. Subjects with dystonia tapped sequences as series of discrete movements, rather than as a combined series.

INTERPRETATION—Dystonia is associated with impaired recognition of a repeating movement pattern. This difference may result from a strategy to separate sequential elements and attend to them individually.

INTRODUCTION

Dystonia is a movement disorder characterized by involuntary movements and abnormal postures. The range of clinical manifestations in dystonia is highly heterogeneous. On one

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AUTHOR CONTRIBUTIONS

Both authors contributed to the conception and design of the study, the acquisition and analysis of data, and drafting the text and preparing the figures.”

POTENTIAL CONFLICTS OF INTEREST

Nothing to report.

extreme, the involuntary movements may affect multiple body parts and be present at rest. On the other, the movements may be isolated to a single body part and appear only during specific tasks, as in musician's focal hand dystonia. Dystonia has been associated with impaired motor sequence learning with evidence that this impairment is caused by underlying abnormalities in sequence cognition.^{1,2}

Sequence learning has mostly been studied in dystonia through paradigms similar to the serial reaction time task,³ in which subjects respond to individual stimuli that are cyclical (i.e., the stimuli appear in a either nonrandom or fixed order). For example, manifesting and non-manifesting carriers of the DYT1 gene mutation, but not the DYT6 mutation, lack the ability to predict the target location in a sequential radial target task.^{1,2} Performance with random stimuli is normal in people with dystonia, indicating that the differences are not due to impaired ability to perform the task. Sequence learning in dystonia does not seem to be caused by the dystonic movements themselves.

There are two main components to the serial reaction time task – the stimulus and the response. That subjects with dystonia have difficulty predicting upcoming target locations does not distinguish whether learning impairment exists at the level of the stimulus or the level of the response. In other words, beyond unawareness of a pattern in the stimulus, are people with dystonia also unaware of that they are *moving* in a pattern? It has been shown that subjects with dystonia have difficulty reporting a sequence even outside of motor performance (i.e., with only observation of the stimulus).¹ We wanted to know if subjects with dystonia have abnormal knowledge of patterns in the motor *response* in addition to the stimulus.

We predicted that awareness of patterns in the motor response would be abnormal in people with dystonia. Dystonia is associated with a reduced sense of agency, meaning that people with dystonia are not always aware that they are controlling their own movements.⁴ This is likely related to the well-described impairment in sensorimotor integration,^{5,6} with specific deficits in spatial and temporal discrimination⁷ or proprioception.⁸ There is evidence that performance monitoring is abnormal in dystonia.⁹ We tested our hypothesis that subjects with dystonia would have reduced motor awareness with a common motor pattern prompted by changing stimulus-to-response mappings.

Using a finger sequence tapping task designed to separate motor performance from awareness of the motor pattern, we have shown in healthy subjects that awareness of the underlying motor pattern is predicted by tapping consistency in the temporal and kinematic domains.¹⁰ In the present study, we used this task to explore motor awareness in individuals with dystonia. Since movement variability is a hallmark of dystonia, we hypothesized that subjects with dystonia would have decreased motor awareness due to decreased temporal and kinematic consistency. Our results show that subjects with dystonia have decreased motor awareness, but that those differences are not due to greater performance variability.

METHODS

Participants

Twenty-one adults with dystonia ($n=21$) participated in this study. The dystonia group contained musicians with task-specific focal hand dystonia ($n=9$) and non-musicians with other forms of dystonia ($n=12$). Healthy adults ($n=30$) participated as a control group. The participants with dystonia performed the finger tapping with the more affected hand or, if dystonia prevented task performance, with the less affected hand. It was not always the case that the dominant hand was the most affected hand. The healthy control participants performed finger tapping with the dominant hand as assessed by the Edinburgh Handedness Inventory.¹¹ We assessed digit span with a custom-written program that presented single numbers on a computer screen every second. We used years of regular daily music practice as an index of musical experience. A year was defined as 10 to 12 months and daily was defined as 5 to 7 times per week.¹²

For subjects with dystonia, we assessed dystonia severity and disability with the Burke-Fahn-Marsden dystonia rating scale.¹³ Dystonia subjects held dystonia medications for the morning of the study visit. Subjects with deep brain stimulators (DBS) had their stimulators turned OFF for the duration of the tapping tasks. All subjects provided informed written consent prior to participating. The University of Rochester Research Subjects Review Board approved the study.

Setup

Subjects sat at a table with feet flat on the floor, facing a computer monitor. Five capacitance switches were arranged so that each finger on the tested hand could comfortably reach a switch. We labeled the switches with the numbers 1 through 5. Tapping prompts were presented on the computer monitor in front of the subject, and the subject could view his or her hands throughout the entire experiment. Correct taps were indicated with high pitched tones and incorrect taps were indicated with low pitched tones. There was no external pacing. In each experiment, we told subjects to “tap the sequence as quickly and accurately as possible.”

We performed data collection as previously described in detail.¹⁰ Subjects wore a CyberGlove (Virtual Technologies, Palo Alto, CA) during tapping to measure finger movements. Finger position data were digitally sampled from the Cyberglove at 91 Hz and stored to disk. Contact of a finger with a capacitance switch was detected electronically, time stamped, and stored to disk. Data collection was controlled by a Power 1401 device and Spike2 Version 6 software (Cambridge Electronic Design, Cambridge, UK) with a custom written script.

We determined temporal consistency with Kendall's Coefficient of Concordance.¹⁴ This procedure ranks the mean inter-key-interval (IKI) across each tap position (1–7) and compares the rank agreement across blocks. The Coefficient of Concordance ranges from 0 (no agreement) to 1 (complete agreement). We calculated the Coefficient of Concordance across all nine blocks over the entire experiment.

We measured kinematic consistency with a Generalized Procrustes Analysis (GPA) of the velocity-acceleration curve for the 200ms before each tap of each finger within an Experiment.^{15,16} GPA is a shape-matching process that translates, rotates, and resizes data to minimize differences and finds the root mean square of the distance of all the transformed shapes to the mean (or consensus) shape. We subtracted this number from 1 to obtain a Procrustes metric that ranges from 0 (no similarity) to 1 (maximum similarity in finger trajectory across taps). We used the statistical package “shapes”¹⁷ in R software (R Development Core Team 2015) for GPA analysis. For all experiments, we calculated the Procrustes metric for each finger for all taps (e.g., across all 9 blocks in Experiment 1). We averaged the Procrustes metric from each of the five fingers to give one measure per subject.

We examined several other motor performance variables in addition to the consistency measures. We considered a tap correct when the instructed switch was tapped without contact with other switches. We defined Error Rate as the number of substitution errors (i.e., an index finger tap where a middle finger tap is instructed) per tap. We performed all other performance analyses only for correct taps followed by another correct tap. In each experiment, we used time stamp information from the capacitance switches to determine the IKI between taps, or the time from contact with one switch until the time from contact with the next switch. We found IKI Improvement by subtracting the mean IKI from the last three repetitions from the mean IKI of the first three repetitions in each block. Negative values indicate a decrease in IKI over the course of the block.

Fingertip position was determined from the CyberGlove recordings as previously described¹⁰. We found velocity and acceleration by taking the first and second derivatives of the position data. The time of movement start for each tap was the point at which the finger exceeded 10% of maximum velocity for that tap, and the end of movement time for each tap was the point at which the finger velocity returned to less than 10% of the maximum velocity after the tap.¹⁸ We measured tapping symmetry as the ratio of time spent in flexion (time from movement start to 0 velocity) to time spent in extension (time from 0 velocity to movement stop). Inter-movement-interval (IMI) was the time from the end of a tap movement to the start of the next tap movement. Figure 1 demonstrates the relationship between IMI and IKI.

As a measure of how much other fingers moved during the tap of a given finger, we calculated the Individuation Index.¹⁹ The Individuation Index is a metric that quantifies the independence of each finger. For a given finger to be independent when tapping, other fingers should have minimal movement. We normalized each finger's range of motion within each Block by setting the maximum flexion point to 1 and the maximum extension point to 0. For each tap duration, we found the slope of the tapping finger's position plotted against each other finger's position. We found the absolute value of the average of this number for all 4 slopes (the tapping finger vs the four other fingers), and subtracted this value from 1. An individuation index of 1 signified a completely independent digit. An individuation index less than 0 signified greater movement in non-tapping fingers than the tapping finger.

We tested normality on each variable with the Shapiro-Wilk normality test and transformed the data where appropriate. Some variables were bounded. For example, the Procrustes metric and Coefficient of Concordance are bounded between 0 and 1. Preliminary analysis revealed that the majority of the data were near the middle of the range and passed the assumption of normality, so we continued with a linear analysis.

We compared all performance measures between musicians with dystonia (MD) to subjects with non-musician forms of dystonia (Non-MD) with a Mann Whitney U test with Bonferroni correction to adjust for multiple comparisons. We analyzed motor performance variables using Univariate and Multivariate Analysis of Covariance (ANCOVA, MANCOVA) with diagnosis as a between-subject variable. Since age is known to affect motor performance^{20,21} we included age as a covariate. All reported values are adjusted for age unless otherwise specified. We corrected post-hoc tests with the Bonferroni method.

The procedure is the same as described previously¹⁰ and summarized in Figure 2. Seven numbers appeared on the computer monitor. The background was black and all the numbers were white except the number to be tapped, which was yellow. After subjects tapped all seven numbers on the screen, the first number became yellow again, prompting the next repetition of the sequence. All subjects performed at least 10 repetitions of the tapping sequence.

Once each subject reached a performance plateau as determined by minimum inter-key-interval difference between repetitions, we shuffled the numbers on the finger buttons so that each finger now corresponded to a different number. We presented a new display sequence and, again, instructed the subject to “tap as quickly and accurately” as possible with the new finger-to-number mapping. We did not reveal to the subjects that they were tapping the same motor pattern (i.e., the same fingers were moving in the same order). There was a total of three motor patterns (sequences). Each sequence consisted of three blocks (A through C) of finger-to-number remapping.

At the conclusion of blocks B and C in each sequence, we verbally assessed the subjects’ subjective awareness that they had just tapped a motor pattern they had tapped before.^{22,23} We asked, “did you notice anything special about what you just tapped?” If the subject answered “yes” and was able to tap the sequence from memory, we considered this awareness of the common motor pattern. If the subject answered “no,” we asked if the sequence was “easier or harder than the one before” and recorded the response. Subjects had 6 opportunities in Experiment 1 (Blocks B and C in each of the three sequences) to verbalize awareness of the underlying motor pattern. We said a subject was “aware” if he or she attained awareness on at least one block.

RESULTS

Twenty-one subjects with dystonia and 30 control subjects completed this experiment. The clinical characteristics of the dystonia subjects are presented in Table 1. Data from one subject were excluded because of severe tremor that prevented completion of the tasks. All other subjects were able to perform the tapping tasks. One subject (subject #13) chose to

stop participation after sequence 2 because of fatigue. We included data from the first 6 blocks from this subject in our analyses. Subject #7 could not perform finger tapping with the most affected hand (left), so this subject performed tapping with the dominant right hand. Hand dominance is indicated by the Edinburgh Handedness Inventory, which ranges from 1 (completely right handed) to -1 (completely left handed).

The subjects with dystonia were older than control subjects (mean $\pm$ SD (yrs); Dystonia 52.6 ± 16.0 , Control 40.9 ± 18.6 , Mann-Whitney $U = 189.5$, $p = 0.03$) but had similar years of musical experience (Dystonia 11.4 ± 15.3 , Control 5.9 ± 5.2 , Mann-Whitney $U = 279$, $p = 0.7$). Non-MD subjects had a higher Burke Fahn Marsden Severity score and Disability score than did MD subjects (mean $\pm$ SD); Severity score, non-MD = 8.8 ± 6.7 , MD = 3.3 ± 1.2 , $U = 21.0$, $p = 0.03$; Disability score, non-MD = 4.2 ± 2.1 , MD = 0.9 ± 1.0 , $U = 7.0$, $p = 0.001$). This difference reflects the focal nature of the dystonia in MD. There was no difference in the subset Severity score on the upper extremity used for tapping between the two groups (non-MD = 1.5 ± 0.9 , MD = 1.8 ± 0.7).

Subjects with dystonia had reduced awareness

Fewer dystonia subjects than control subjects attained awareness. Of the 20 subjects with dystonia who completed the experiment, only 2 subjects (subjects #7 and #10) attained awareness of the underlying motor pattern. Each of those 2 subjects attained awareness in only 1 block of 1 sequence. Thirteen control subjects (43%) attained awareness.¹⁰ Both aware subjects with dystonia only attained awareness on 1 of 6 potential blocks. Eleven of the 13 control subjects with awareness had awareness on 2 or more blocks.

Subjects with dystonia did not tap with more variability than controls

The main performance variables for control subjects were reported previously.¹⁰ There were no differences in the main measures of performance between MD and non-MD groups (Table 2), so the two groups were combined into a single “dystonia” group for further analysis. There was no difference between dystonia and control subjects in temporal consistency (adjusted mean control: 0.49, dystonia: 0.38, $F(1, 47) = 4.0$, $p = 0.05$) or kinematic consistency (adjusted mean control: 0.53, dystonia: 0.51, $F(1, 47) = 1.0$, $p = 0.3$).

Subjects with dystonia still improved

To determine whether decreased awareness in control subjects was related to decreased performance, we compared IKI and IKI improvement across Blocks and Sequences (Figure 3). We used a repeated-measures ANOVA with Diagnosis and Age as between-subject factors and Sequence and Block as within-subject factors for IKI improvement. We used Diagnosis, Age, Sequence, Block, and Tap position as factors for IKI. There was no significant effect of diagnosis on IKI improvement ($F(1, 46) = 0.02$, $p = 0.9$) but there was a significant effect of sequence ($F(2, 92) = 4.2$, $p = 0.02$). There was also no significant main effect of diagnosis on IKI ($F(1, 46) = 1.7$, $p = 0.2$). However, there was a significant Diagnosis x Block interaction ($F(2, 92) = 7.6$, $p < 0.001$), and a significant Diagnosis x Sequence interaction ($F(2, 92) = 3.4$, $p = 0.04$). Post-hoc tests revealed that subjects with dystonia had longer IKIs on Block 2 ($p < 0.001$) and Block 3 ($p < 0.05$) and Sequences 1 and 2

than controls ($p < 0.05$). Overall, the difference in learning curves between dystonia and controls became smaller with each subsequent block.

Subjects with Dystonia tapped with more discrete movements

We ran an exploratory multivariate analysis of variance (MANOVA) to find performance differences between dystonia and control groups that might explain the differences in awareness. We included IMI, peak velocity, individuation, tap symmetry, and error rate into the MANOVA. There was a significant MANOVA effect of diagnosis ($F(5, 43) = 2.8$, $p = 0.03$, Wilks lambda = 0.8). Post hoc tests revealed that subjects with dystonia made more errors ($p = 0.004$) and had a longer IMI ($p < 0.001$) than control subjects. This pattern held when we excluded subjects with myoclonus-dystonia (subjects 19 and 20) from the analysis.

DISCUSSION

Subjects with dystonia had significantly reduced awareness of underlying motor patterns in this finger tapping task. We have previously shown that motor awareness in this task is predicted by kinematic and temporal consistency in control subjects. Surprisingly, subjects with dystonia tapped with similar consistency to control subjects, suggesting that the difference in awareness is due to factors other than performance variability. Exploratory analysis revealed that subjects with dystonia tapped the sequence with longer pauses between finger movements. This experiment expands on previous research suggesting that subjects with dystonia have an impairment of pattern recognition in a sequence stimulus. Reduced knowledge of patterns in both the stimulus and the motor response indicates a fundamental difference in the cognition of a sequence in people with dystonia.

It is possible that reduced awareness in the motor response is a separate phenomenon than that of awareness of the stimulus. Reduced awareness of the motor response in dystonia may be related to abnormal proprioception.⁸ Abnormal proprioception can manifest as abnormalities in a sense of agency (i.e., awareness of initiating and controlling movements),⁴ tactile discrimination,^{24–27} impaired cognition of hand movements,^{28,29} and enlargement and overlap of cortical receptive fields.²⁶ Proprioception plays an important role in motor learning and sequence performance.^{30,31} Aberrant proprioceptive feedback from the motor system would likely provide less or unclear information about what the fingers are doing, and this could lead to difficulty in discovering underlying patterns.

Notwithstanding the importance of the motor system in this experiment, awareness of underlying motor patterns may rely most on perceptual mechanisms. In the present study and previous studies of sequence learning in dystonia, patterns are embedded in a spatial structure: symbolic stimuli (i.e., numbers on a screen) prompted a spatial response (i.e., five spatially organized capacitance switches).² The consensus is that the perceptual system, consisting of the frontoparietal cortices and associative regions of the basal ganglia and cerebellum, primarily drives spatial sequence learning and is heavily involved at the beginning of the learning process.³² In a series of experiments manipulating the spatial and symbolic mappings of the stimulus and response, Koch and Hoffman demonstrated that motor learning is based primarily on spatial elements and occurs most readily in whichever domain – the stimulus or the response – is organized spatially.³³

Given that learning happens most readily in spatial domains, it is striking that so few subjects with dystonia became aware of the motor pattern. However, we find it unlikely that our findings represent spatial processing difficulty since spatial span and spatial working memory are normal in subjects with primary dystonia.³⁴ Dystonia is likely associated with an underlying abnormality in sequence cognition which stems from a performance strategy involving isolated, discrete movements.

Despite all seven numbers of the sequence prompt appearing on the computer screen, subjects with dystonia tapped as if responding to each number individually. It is not unprecedented that dystonia is associated with more discrete movements: patients with dystonia pause more between sequential zigzag movements of the fingertip,³⁵ oppositional thumb-finger movements,³⁶ radial movements to and from a central target,³⁷ and sequential arm movements tracing a shape on the table.³⁸ Furthermore, when subjects with dystonia perform a sequence of arm movements, they perform the individual movements faster in isolation than in a continuous series.³⁸ Indeed, finger movements are initiated sooner if there is knowledge of upcoming stimuli.³⁹ This suggests that subjects with dystonia did not preplan finger movements, despite having the entire sequence prompt displayed on the computer screen.

Discrete movements may prevent motor pattern awareness through a combination of attentional demands and reduced internal representation. Discrete movements invoke greater activity in frontal cortical regions and demand more attention than continuous or rhythmic movements.⁴⁰ It has been shown previously that people with dystonia require more attentional resources toward finger movements to achieve similar tapping speed as controls.⁴¹ Greater attentional demands may also explain the relative slowing in Blocks B and C - during the remappings of the finger numbers - in dystonia compared to control subjects with the increase in cognitive load. Subjects with dystonia would have limited cognitive resources available to attend to the *contents* of the sequence, thereby reducing the probability of pattern awareness. In other words, it is less likely that subjects with dystonia formed a representation of the entire motor pattern that could be revisited in subsequent blocks.

There are some potential limitations to our study that warrant discussion. All control subjects performed the experiment with the dominant hand, but this was not always the case in the subjects with dystonia. All subjects with dystonia tested as right handed on the Edinburgh Handedness Inventory, but three subjects (#1, #5, #6) with dystonia performed finger tapping with the most affected left hand. Additionally, one subject (#7) performed with the dominant right hand since the affected left hand could not perform the task. Both subjects with dystonia (#7 and #10) who attained awareness tapped with the dominant hand. We believe dominance was not a factor in determining awareness since sequence learning has been shown in the non-dominant hand left hand, and even recruits more cognitive-related regions than learning with the dominant hand.⁴² Furthermore, awareness in both subjects with dystonia was weak since it was only attained on one block of one sequence. Thus, it is unlikely that these differences in group characteristics contributed significantly.

Since we found no difference in any performance variables between musicians with focal hand dystonia and people with non-musician dystonia, we combined the data for these two

groups to increase statistical power. There is debate whether musician's dystonia shares etiology with non-musician specific dystonias.^{43,44} Although they are both characterized by involuntary movements, non-focal non-musician dystonia tends to appear earlier and be stable in presentation, while musician dystonia tends to appear later and is more likely to spread. Other than a smaller IKI attributable to greater musical experience in musicians with dystonia, there was no difference in performance. One musician with dystonia and one non-musician with dystonia attained motor pattern awareness in this task, and neither aware subject had a marked difference in dystonia severity from the rest of the subjects. This suggests that the interaction between dystonia and motor pattern awareness is independent of etiology. Future studies with more subjects should confirm this conclusion.

DISCUSSION

We have shown that, compared to controls, subjects with dystonia have reduced awareness of underlying motor patterns in finger tapping sequences. This finding expands previous research suggesting an abnormality in pattern recognition in a sequence stimulus in people with dystonia.^{1,2} Recognition of sequential patterns in both a visual stimulus and a motor response suggest a general impairment of sequence recognition in people with dystonia. This difference may result from a strategy to separate sequential elements and attend to them individually.

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References

1. Carbon M, et al. Impaired sequence learning in dystonia mutation carriers: A genotypic effect. *Brain*. 2011; 134:1416–1427. [PubMed: 21515903]
2. Ghilardi MF, et al. Impaired sequence learning in carriers of the DYT1 dystonia mutation. *Ann Neurol*. 2003; 54:102–9. [PubMed: 12838525]
3. Nissen MJ, Bullemer P. Attentional requirements of learning: Evidence from performance measures. *Cogn Psychol*. 1987; 19:1–32.
4. Delorme C, et al. Explicit Agency in Patients with Cervical Dystonia: Altered Recognition of Temporal Discrepancies between Motor Actions and Their Feedback. *PLoS One*. 2016; 11:e0162191. [PubMed: 27575487]
5. Wu CC, et al. Impaired sensorimotor integration in focal hand dystonia patients in the absence of symptoms. *J Neurol Neurosurg Psychiatry*. 2010; 81:659–665. [PubMed: 19965853]
6. Abbruzzese G, Berardelli A. Sensorimotor integration in movement disorders. *Mov Disord*. 2003; 18:231–40. [PubMed: 12621626]
7. Tinazzi M, et al. Deficits of temporal discrimination in dystonia are independent from the spatial distance between the loci of tactile stimulation. *Mov Disord*. 2002; 17:333–338. [PubMed: 11921120]
8. Avanzino L, Fiorio M. Proprioceptive dysfunction in focal dystonia: from experimental evidence to rehabilitation strategies. *Front Hum Neurosci*. 2014; 8:1000. [PubMed: 25538612]
9. Ruiz MH, Strübing F, Jabusch HC, Altenmüller E. EEG oscillatory patterns are associated with error prediction during music performance and are altered in musician's dystonia. *Neuroimage*. 2011; 55:1791–1803. [PubMed: 21195188]

10. Jaynes MJ, Schieber MH, Mink JW. Temporal and kinematic consistency predict sequence awareness. *Exp Brain Res*. 2016; :1–12. DOI: 10.1007/s00221-016-4704-7
11. Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia*. 1971; 9:97–113. [PubMed: 5146491]
12. Ollen, J. A criterion-related validity test of selected indicators of musical sophistication using expert ratings. The Ohio State University; 2006.
13. Burke RE, et al. Validity and reliability of a rating scale for the primary torsion dystonias. *Neurology*. 1985; 35:73–73. [PubMed: 3966004]
14. Povel DJ, Collard R. Structural factors in patterned finger tapping. *Acta Psychol (Amst)*. 1982; 52:107–123. [PubMed: 7164844]
15. Dryden, I., Mardia, K. Statistical Shape Analysis. John Wiley & Sons Ltd; 1998.
16. Loehr J, Palmer C. Sequential and biomechanical factors constrain timing and motion in tapping. *J Mot Behav*. 2009; 41:128–136. [PubMed: 19201683]
17. Dryden I. Shapes: Statistical Shape Analysis. 2015
18. Friedman J, Korman M. Kinematic Strategies Underlying Improvement in the Acquisition of a Sequential Finger Task with Self-Generated vs. Cued Repetition Training. *PLoS One*. 2012; 7:e52063. [PubMed: 23272210]
19. Hager-Ross C, Schieber MH. Quantifying the Independence of Human Finger Movements: Comparisons of Digits, Hands, and Movement Frequencies. *J Neurosci*. 2000; 20:8542–8550. [PubMed: 11069962]
20. Howard D, Howard J. When it does hurt to try: adult age differences in the effects of instructions on implicit pattern learning. *Psychon Bull Rev*. 2001; 8:798–805. [PubMed: 11848602]
21. Cousins MS, Corrow C, Finn M, Salamone JD. Temporal measures of human finger tapping: Effects of age. *Pharmacol Biochem Behav*. 1998; 59:445–449. [PubMed: 9476994]
22. Honda M, et al. Dynamic cortical involvement in implicit and explicit motor sequence learning. A PET study. *Brain*. 1998; 121:2159–73. [PubMed: 9827775]
23. Moisello C, et al. Motor sequence learning: Acquisition of explicit knowledge is concomitant to changes in motor strategy of finger opposition movements. *Brain Res Bull*. 2011; 85:104–108. [PubMed: 21459132]
24. Fiorio M, Tinazzi M, Bertolasi L, Aglioti SM. Temporal processing of visuotactile and tactile stimuli in writer's cramp. *Ann Neurol*. 2003; 53:630–5. [PubMed: 12730997]
25. Aglioti SM, Fiorio M, Forster B, Tinazzi M. Temporal discrimination of cross-modal and unimodal stimuli in generalized dystonia. *Neurology*. 2003; 60:782–5. [PubMed: 12629233]
26. Sanger TD, Tarsy D, Pascual-Leone A. Abnormalities of spatial and temporal sensory discrimination in writer's cramp. *Mov Disord Off J Mov Disord Soc*. 2001; 16:94–99.
27. Tinazzi M, Fiorio M, Bertolasi L, Aglioti SM. Timing of tactile and visuo-tactile events is impaired in patients with cervical dystonia. *J Neurol*. 2004; 251:85–90. [PubMed: 14999494]
28. Fiorio M. Selective impairment of hand mental rotation in patients with focal hand dystonia. *Brain*. 2005; 129:47–54. [PubMed: 16150847]
29. Fiorio M, et al. Impaired body movement representation in DYT1 mutation carriers. *Clin Neurophysiol*. 2008; 119:1864–1869. [PubMed: 18571468]
30. Adams JA, Gopher D, Lintern G. The Effects of Visual and Proprioceptive Feedback on Motor Learning. *Proc Hum Factors Ergon Soc Annu Meet*. 1975; 19:162–165.
31. Verwey WB, Shea CH, Wright DL. A cognitive framework for explaining serial processing and sequence execution strategies. *Psychon Bull Rev*. 2014; 22:54–77.
32. Hikosaka O, Nakamura K, Sakai K, Nakahara H. Central mechanisms of motor skill learning. *Curr Opin Neurobiol*. 2002; 12:217–222. [PubMed: 12015240]
33. Koch I, Hoffmann J. The role of stimulus-based and response-based spatial information in sequence learning. *J Exp Psychol Learn Mem Cogn*. 2000; 26:863–882. [PubMed: 10946368]
34. Scott RB, et al. Executive cognitive deficits in primary dystonia. *Mov Disord*. 2004; 19:116–7. author reply 117. [PubMed: 14743375]
35. Currà A, et al. Movement cueing and motor execution in patients with dystonia: A kinematic study. *Mov Disord*. 2000; 15:103–112. [PubMed: 10634248]

36. Currà A, et al. Impairment of individual finger movements in patients with hand dystonia. *Mov Disord.* 2004; 19:1351–1357. [PubMed: 15389995]
37. Pelosin E, Bove M, Marinelli L, Abbruzzese G, Ghilardi MF. Cervical dystonia affects aimed movements of nondystonic segments. *Mov Disord.* 2009; 24:1955–1961. [PubMed: 19609907]
38. Agostino R, Berardelli A, Formica A, Accornero N, Manfredi M. Sequential arm movements in patients with Parkinson's Disease, Huntington's Disease and Dystonia. *Brain.* 1992; 115:1481–1495. [PubMed: 1422799]
39. Herbert O, Butz MV. Anticipatory planning of sequential hand and finger movements. *J Mot Behav.* 2009; 41:561–9. [PubMed: 19892660]
40. Schaal S, Sternad D, Osu R, Kawato M. Rhythmic arm movement is not discrete. *Nat Neurosci.* 2004; 7:1136–1143. [PubMed: 15452580]
41. Jahanshahi M, Rowe J, Fuller R. Cognitive executive function in dystonia. *Mov Disord.* 2003; 18:1470–1481. [PubMed: 14673884]
42. Grafton ST, Hazeltine E, Ivry RB. Motor sequence learning with the nondominant left hand. *Exp Brain Res.* 2002; 146:369–378. [PubMed: 12232693]
43. Defazio G, Berardelli A, Hallett M. Do primary adult-onset focal dystonias share aetiological factors? *Brain a J Neurol.* 2007; 130:1183–93.
44. Rosenkranz K, et al. Pathophysiological differences between musician's dystonia and writer's cramp. *Brain.* 2005; 128:918–31. [PubMed: 15677703]

Figure 1.

Figure 2.

Figure 3.

Table 1

Subject Characteristics

Subject	Age (yrs.)	M/F	Diagnosis	BFM Severity	BFM Disability	Duration(yrs.)	Etiology	DBS	Instrument	Edinburgh	Hand Tested	Awareness
1	19	F	Musician FHD LUE	3.5	0	unknown	Idiopathic	-	Violin	0.67	L	NO
2	74	F	Musician FHD RUE	2	0	2	Idiopathic	-	Violin	0.53	R	NO
3	66	F	Musician FHD RUE + WC	2	1	29	Idiopathic	-	Guitar	1.00	R	NO
4	22	M	Musician FHD LUE	2	0	<1	Idiopathic	-	Guitar	0.60	R	NO
5	64	M	Musician FHD LUE	4	1	9	Idiopathic	-	Piano	0.80	L	NO
6	64	M	Musician FHD LUE	4	2	38	Idiopathic	-	Guitar	1.00	L	NO
7	45	M	Musician FHD LUE	3	0	20	Idiopathic	-	Drums	1.00	R	YES
8	55	M	Musician FHD RUE + tremor	4	1	22	Idiopathic	-	Harp	0.75	R	NO
9	49	F	Musician FHD RUE + CD	5.5	3	4	Idiopathic	-	Organ	0.80	R	NO
10	36	M	Generalized Dystonia	13.5	5	30	DYT1	OFF	-	0.38	R	YES
11	72	M	Dystonia RUE + dysphonia	3.5	3	42	Idiopathic	-	-	1.00	R	NO
12	39	F	Dystonia of RUE, LLE	3	1	20	DYT1	-	-	0.30	R	NO
13	69	F	Dystonia of RUE	6	3	57	DYT1	-	-	0.20	R	NO *
14	50	F	Generalized Dystonia	21	6	46	Idiopathic	-	-	0.38	R	NO
15	52	M	Generalized Dystonia	16	8	45	Idiopathic	-	-	0.37	R	NO
16	70	F	WC + spasmodic dysphonia	4	3	10	Idiopathic	-	-	1.00	R	NO
17	62	F	Limb Dystonia	2	3	11	Idiopathic	-	-	0.90	R	NO
18	35	M	Generalized Dystonia	6	6	26	Idiopathic	-	-	0.40	R	NO
19	56	M	Myoclonus-Dystonia	16.5	6	50	Idiopathic, Familial	OFF	-	0.80	R	NO
20	52	F	Myoclonus-Dystonia	5	2	7	Idiopathic, Familial	-	-	0.80	R	NO

* subject only performed first two sequences

FHD = focal hand dystonia, LUE = left upper extremity, RUE = right upper extremity, WC = writer's cramp, CD = cervical dystonia, BFM = Burke Fahn Marsden, DBS = deep brain stimulation.

Table 2
Comparison of performance in musicians and non-musicians with dystonia. Raw Mean (SD)

Measure	MD (n=9)	Non-MD (n=11)	U	p-value*
Coefficient of Concordance	0.32 (0.17)	0.41 (0.14)	29.0	0.1
Procrustes Metric	0.51 (0.09)	0.47 (0.07)	37.0	0.4
Improvement (ms)	-224 (109)	-177 (71)	35.0	0.3
Mean IKI (ms)	862 (282)	999 (290)	90.0	0.1
IMI (ms)	306 (211)	368 (226)	41.0	0.5
Peak Velocity (cm/s)	18.4 (8.7)	13.2 (5.3)	29.0	0.1
Individuation Index	0.64 (0.09)	0.66 (0.09)	42.0	0.6
Tap Symmetry	2.52 (0.68)	2.62 (1.10)	46.0	0.8
Log Error Rate	-3.27 (0.878)	2.97(0.472)	39.0	0.5

* not corrected for multiple comparisons