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Speed-accuracy trade-off in a trajectory-constrained self-feeding task: a quantitative index of unsuppressed motor noise in children with dystonia

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Abstract

Motor speed and accuracy are both affected in childhood dystonia. Thus, deriving a speed-accuracy function is an important metric for assessing motor impairments in dystonia. Previous

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work in dystonia studied the speed-accuracy trade-off during point-to-point tasks. To achieve a more relevant measurement of functional abilities in dystonia, the present study investigates upper-limb kinematics and electromyographic activity of 8 children with dystonia and 8 healthy children during a trajectory-constrained child-relevant task that emulates self-feeding with a spoon and requires continuous monitoring of accuracy. The speed-accuracy trade-off is examined by changing the spoon size to create different accuracy demands. Results demonstrate that the trajectory-constrained speed-accuracy relation is present in both groups, but it is altered in dystonia in terms of increased slope and offset towards longer movement times. Findings are consistent with the hypothesis of increased signal-dependent noise in dystonia, which may partially explain the slow and variable movements observed in dystonia.

Keywords

childhood dystonia; speed-accuracy relation; kinematics; electromyography; signal-dependent noise

INTRODUCTION

Dystonia in children is defined as “a movement disorder in which involuntary sustained or intermittent muscle contractions cause twisting and repetitive movements, abnormal postures, or both”¹. Features of dystonia include excessive co-contraction during voluntary movement and overflow of activity to muscles that would not normally be active in the task.^{2,3} Voluntary arm movements in dystonia are both slower and exhibit greater variability than in healthy subjects^{4,5,6,7,8}, resulting in severely impaired quality of movement.

Previous studies have hypothesized that the abnormal features of dystonia can be partially explained by increased random and uncontrollable noise⁹, although the origin of this noise is not clear. The noise in the neural control signals increases with the mean level of the signals because of its signal-dependent nature.¹⁰ In the presence of such signal-dependent noise, moving as fast as possible requires large control signals, which would increase the variability of movement, thus resulting in a decreased endpoint accuracy. Therefore, symptoms of dystonia are consistent with the hypothesis of an increase in the amount of signal-dependent noise, since such an increase will result in a decrease in the maximum speed achievable for movements of any specified accuracy, and this may partially explain slower and variable movements in dystonia.¹¹

The importance of investigating the nature of the relationship between speed and accuracy in childhood dystonia is twofold. First, the hypothesis of signal-dependent noise implies that accuracy in a task can be improved by having low control signals, which means slowing down the speed of movement, thus imposing a trade-off between speed and accuracy of movement.¹⁰ Therefore, an increase in the amount of signal-dependent noise in dystonia would be reflected in an altered speed-accuracy trade-off during task execution. Secondly, since moving fast and accurately can be considered a central goal of motor performance, deriving a speed-accuracy trade-off function is considered a crucial metric for execution assessment.¹² This measure is particularly suitable for dystonia, in which motor speed and accuracy are both affected, because the speed-accuracy trade-off quantifies motor

performance while characterizing the motor impairments peculiar to this movement disorder.

Previous studies on children with dystonia investigated the nature of the relationship between speed and accuracy during point-to-point reaching movements toward end points of fixed size.^{11,13} However, for many tasks performed in everyday life, the quality of the motor performance goes beyond the accuracy of the final target, as is evident when transporting a glass of water or eating with a spoon. Compared to point-to-point reaching tasks with constrained end points, in which accuracy is required only at the end of the task, transporting substances with a spoon, for example, constrains the trajectory and requires the continuous monitoring of accuracy as the movement unfolds. Additionally, the mechanics of such a task directly penalize large accelerations as this leads to dropping the substances transported. To achieve a more complete and relevant measurement of the effect of the speed-accuracy trade-off on functional ability, we must examine trajectory-constrained tasks requiring accurate execution throughout the entire movement. Recent work in healthy adults has investigated motor performance during tasks that are constrained along the entire trajectory.^{14,15} Our goal, here, is to investigate the continuous speed-accuracy relation in children with dystonia and healthy children using a child-relevant task. For this reason, we have defined a task mimicking components of self-feeding, where subjects are asked to transport a marble in a spoon back and forth between two targets as fast as possible and without letting the marble fall. In order to avoid dropping the marble, the accuracy is constrained along the entire trajectory. It is not known whether there is a speed-accuracy trade-off for this task, therefore we will investigate the speed-accuracy trade-off by changing the spoon size to create four different accuracy demands. This laboratory-based task is intended to emulate the requirement of transport of solid or liquid food between plate and the child's mouth. Eating with a spoon is complex when we consider the precise coordination of movements of the trunk, arm, and hand that is required to complete the task successfully, especially for children who have to cope with a movement disorder.

The purpose of this study is, firstly, to demonstrate the presence of a speed-accuracy trade-off in a trajectory-constrained task in children with dystonia and in healthy children. Secondly, if such a tradeoff is present, it will be used to quantitatively assess and compare the motor performance of children with dystonia and healthy children, with the twofold purpose of characterizing movement abnormalities in dystonia, and shedding light on the still unclear underlying mechanisms of this highly disabling movement disorder.

METHODS

Participants

Inclusion criteria for this study were: I) primary or secondary dystonia; II) pediatric age (10–21 years); III) upper limb control impairment that does not prevent the spoon task execution; IV) no cognitive impairment that prevents understanding of instructions; V) absence of upper-limb spasticity. Participants (Table 1) consisted of 8 children with dystonia (2 girls, 6 boys; ages 11–21 years, mean 16.1 ± 3.8 years; 2 primary dystonia, 6 secondary dystonia; 1 subject (d2) with Deep Brain Stimulation (DBS)) recruited from the Children's Hospital Los Angeles Movement Disorders Clinic and diagnosed by a pediatric neurologist (TDS), and a

control group with 8 healthy children (2 girls, 6 boys; ages 10–21 years, mean 15.6 ± 3.7 years). The age distributions of the two groups were not statistically different. The University of Southern California Institutional Review Board approved the study protocol. All parents gave informed written consent for participation and authorization for use of protected health information, and all children gave written assent. The study was performed in accordance with the Declaration of Helsinki.

Experimental Task

Subjects were unrestrained seated upright at a height-adjustable desk, with their back against the back of the chair. A board with two targets was positioned on the desk. The distance between the centers of the two targets was 20 cm along the sagittal axis (X-axis). Each target was bounded by two plastic blocks (positioned 7 cm apart) to prevent subjects from sliding with the spoon between the two targets (Figure 1). The plastic blocks were attached to the board.

Subjects were instructed to hold the spoon in a power grip so that the handle of the spoon was parallel to the front edge of the table (Y-axis). At the start of each trial, the experimenter positioned the spoon on the target closest to the participants (target 1) with the marble in it, and asked the subjects to grasp the spoon. After the experimenter had given a verbal go-signal, the subjects had to transport the marble in the spoon to the furthest target (target 2) (outward movement). Subsequently, they were asked to transport the marble in the spoon back to target 1 (inward movement). The subjects were instructed to reach the targets as fast as possible, without dropping the marble. They were also told to pause on the targets as long as desired before starting the following movement, and not to move the trunk. Subjects were asked to perform a block of 15 successful back and forth movements for each spoon size (30 one-way movements: 15 outward + 15 inward). In case the marble fell from the spoon, subjects were instructed to start the sequence from the beginning. Each subject performed the task with 4 spoons of different sizes (Table 2), resulting in a grand total of 120 trials (30 one-way movements $\times$ 4 sets; 1 set for each spoon) per participant. The order of the spoons was randomized. The marble size was constant across the trials (diameter = 2.61 cm). Participants took a short break between each set and could always indicate when they needed extra rest. Before each block, each participant performed 6 practice trials. The total experiment took approximately 1 hour.

When only one side was affected by dystonia, patients performed the task with the impaired arm. If dystonia was present on both sides, subjects were asked to use their most affected arm, as long as the severity of symptoms was compatible with the task execution. The dominant arm, assessed with a modified Edinburgh Handedness Inventory¹⁷, was used for control children. The other hand rested on the tabletop.

Apparatus

A 3-D motion-tracking device (Flock of Birds® (FOB), Ascension, Burlington, VT USA; 100 Hz sample frequency) was used for movement recording. Three sensors were attached using medical-grade adhesive placed on the handle of the spoon (SPO), elbow (ELB), and acromion (ACR) of the side used to perform the task. The system was synchronized to an

EMG device (DataLOG MWX8, Biometrics Ltd, Newport, UK; 1000 Hz sample frequency; 15–450 Hz band-pass). The bipolar surface EMG electrodes were positioned on 5 muscles of the upper limb: Biceps (BIC), Triceps (TRIC), Anterior Deltoid (AD), Lateral Deltoid (LD), and Posterior Deltoid (PD). The actual testing was also videotaped.

Data analysis and Statistics

Data analysis was executed with Matlab® R2011b (Mathworks®, Natick, MA USA). Statistical analysis was performed using RStudio® Version 0.98.981 (RStudio Inc.®, Boston, MA, USA) and the R-package ‘lme4’ Version 1.1–7.¹⁸

Kinematic analysis—Before performing the kinematic analysis, kinematic data were processed with a low-pass Butterworth filter (5th order, 5 Hz). Each sequence of movements was then cut into 30 individual one-way movements. The beginning (t_{ONSET}) and end (t_{OFFSET}) of each movement were identified by the first and last time points at which the velocity values exceeded the sum of the mean value and twice the standard deviation of a 200 ms segment selected before the onset of the movement. Four different accuracy requirements were achieved by changing the spoon size (Table 2). The difficulty of the task is related to the depth of the spoon, and we define the Index of Difficulty (ID) as the ratio of the marble size to the depth of the spoon.

The Movement Time (MT) was defined as the duration of each one-way movement.

Velocity and acceleration curves were obtained by differentiating the kinematic filtered data of SPO over the trajectory. Peak Velocity (V_{max}) and Peak Acceleration (A_{max}) were defined as the maxima of the velocity and acceleration curves respectively and were calculated for each one-way movement. Smoothness is regarded as a hallmark of skilled and coordinated movements and it is typically estimated using jerk, the time-derivative of acceleration.¹⁹ To quantify smoothness properly, it is important that the jerk-based measure is independent of duration and amplitude of movement.²⁰ Thus, for each one-way movement, we calculated a dimensionless measure of *Jerk* as:

$$Jerk = \left(\int_{t_{ONSET}}^{t_{OFFSET}} [\ddot{x}(t) + \ddot{y}(t) + \ddot{z}(t)] dt \right) \cdot \frac{(t_{OFFSET} - t_{ONSET})^5}{L^2},$$

where L is the length of the trajectory of the one-way movement.²¹

Trajectories of SPO, ELB, and ACR in the 3D space of every one-way movement were time-normalized by resampling them to the mean duration of the one-way movements for the group. For each subject, for each spoon size, the 30 (resampled) trajectories of SPO, ELB, and ACR were separated in 15 inward and 15 outward movements. For each group of 15 movements, mean and standard deviation of these trajectories were computed for each time frame. The average over time frames of these standard deviations was computed and the mean value between outward and inward movements was taken as an index of intra-subject trajectory variability (*Trial-to-trial Variability*) for SPO, ELB, and ACR separately.

Speed-accuracy trade-off—According to Fitts²², the speed-accuracy relationship that characterizes the motor performance is due to a limitation of information transmission in the human motor system. Therefore the Index of Performance (*IP*), expressed by the inverse of the linear equation slope, represents the information processing capacity, and it is regarded as a measure of performance.²² The *IP* for this trajectory-constrained task was calculated as the inverse of the slope of the linear function between *MT* and *ID* for each subject.

EMG analysis—Before performing the analysis, each EMG signal was processed with a stop-band Butterworth filter (5th order, 60 Hz). Stop-band filtering was applied at the acquisition frequency and multiples (Butterworth, 5th order, 100, 200, 300 Hz) to cancel electrical interference introduced by the recording system. Signals of the subject with dystonia implanted with DBS electrodes were also stop-band filtered (Butterworth, 5th order) in correspondence to the DBS stimulation frequency and multiples. To extract the linear envelopes, EMG signals were full-wave rectified and low-pass filtered (Butterworth, 5th order, 15 Hz). The envelopes were then normalized to the muscle's maximum rectified and filtered EMG amplitude observed during the Maximum Voluntary Contraction (MVC) recordings, thus obtaining signals ranging from 0 to 1. As a consequence of the synchronization between EMG and kinematics, it was possible to cut the EMG signals into single one-way movements.

For each one-way movement, the root mean square EMG activation was used as an index of the force exerted by each muscle (*Muscle Force*).

Co-contraction of antagonist muscles is a typical parameter of interest in dystonia, since excessive co-contraction and abnormalities in the time course of reciprocal inhibition between antagonist groups of muscles are considered to be cardinal features of some types of dystonia.^{1,2} For this reason, the levels of co-contraction (*CC*) between BIC and TRIC and between AD and PD were investigated. For each pair of antagonist muscles, *CC* was computed as the minimum value of the EMG (normalized envelopes) between the two muscles of each time sample, averaged over each one-way movement.²³

Statistical analysis—The aim of the statistical analysis applied was to express the relationships in our data in terms of a function. The design of our experiment had multiple measures for each subject, which violates the independence assumption. This assumption is necessary to run the linear regression analysis that is usually applied for this purpose. Instead of averaging data for each subject, which implies a loss of information, we applied a more robust linear mixed effects analysis, which resolves non-independence by assuming different random intercepts for each subject.

In particular, we performed a linear mixed effects analysis on *MT*. As fixed effects, we entered *ID* (4 levels) and *Group* (2 levels) into the model. As random effects, we had intercepts for subjects, as well as by-subject random slopes for the effect of *ID*.

$$MT \sim ID + Group + (1 + ID | Subject)$$

The inverse of this random slope for each subject was the subject's *IP*. Then, to investigate a possible difference in *IP* between the two groups (Dystonia and Control), we applied an Independent Samples t-test ($p\text{-value} < 0.05$).

The linear mixed effects analyses on V_{max} , A_{max} , *Jerk*, and *Trajectory Variability* (SPO, ELB, and ACR) comprised ID (4 levels) and Group (2 levels) as fixed effects, and intercepts for subjects as a random effect.

$$Dependent\ variable \sim ID + Group + (1|Subject)$$

For the linear mixed effects analyses on *Muscle Force* we entered ID (4 levels), Group (2 levels), and Muscle (5 levels) as fixed effects. As random effect, we had intercepts for subjects.

$$Muscle\ Force \sim ID + Group + Muscle + (1|Subject)$$

The linear mixed effects analysis on *CC* comprised ID (4 levels), Group (2 levels), and Muscle Pair (2 levels) as fixed effects, and intercepts for subjects as a random effect.

$$CC \sim ID + Group + Muscle\ Pair + (1|Subject)$$

Once we had created the models, in order to test if the fixed effects significantly affected the dependent variable, we compared the model including all the factors (Full) against a reduced model without the effect in question (Null), for each dependent variable and for each factor. Similarly, in order to test interaction, that is inter-dependence between two fixed effects, we compared the model that takes into account the interaction between fixed effects (Full) against the model without the interaction (Null), for each dependent variable. For all comparisons, p -values and Akaike's Information Criterion values²⁴ (AIC) were obtained by likelihood ratio tests of the Full model with the Null model. If the factor in question significantly affects the dependent variable, then the comparison will report a significant p -value (< 0.05) and an AIC value lower for the Full model (AIC_{Full}). Similarly, a significant interaction between factors will result in a significant difference between the Full and the Null models ($p\text{-value} < 0.05$), with the Full model characterized by a lower AIC.

RESULTS

Movement Time and Index of Performance

The likelihood ratio test reported a significant effect of ID on *MT* [AIC_{Full} = 587.74; AIC_{Null} = 606.26; $p < 0.0001$], meaning that this trajectory-constrained task effectively imposes a speed-accuracy trade-off. *MT* increases with ID by 0.4477 ± 0.0692 s (standard error). A significant effect on *MT* was reported also for the fixed effect Group [AIC_{Full} = 587.74; AIC_{Null} = 593.18; $p = 0.0064$]. *MT* of the control group was 0.6638 ± 0.1508 s

lower than MT of the group with dystonia. A significant interaction between the two fixed effects was reported [$AIC_{Full} = 578.52$; $AIC_{Null} = 587.74$; $p = 0.0008$], meaning that the effect of ID on the dependent variable *MT* was different for the two groups (Figure 2 – Panel a). The inverse of the by-subject random slopes extracted from the *MT* mixed model represents the subject-specific *IP* for this trajectory-constrained task. Statistics reported a significant difference in *IP* between healthy subjects and subjects with dystonia [Control: $4.1385 \pm 0.4300 \text{ s}^{-1}$; Dystonia: $2.1227 \pm 0.5809 \text{ s}^{-1}$; $p = 0.0154$] (Figure 2 – Panel b).

Peak Velocity

A significant effect of ID on V_{max} was observed [$AIC_{Full} = 12892$; $AIC_{Null} = 14512$; $p < 0.0001$]. V_{max} decreases with ID by $17.8088 \pm 0.3483 \text{ cm/s}$. A significant effect on V_{max} was reported also for the fixed effect Group [$AIC_{Full} = 12892$; $AIC_{Null} = 12906$; $p = 0.0001$]. The peak velocity of the control group was $21.8213 \pm 4.3540 \text{ cm/s}$ higher than the group with dystonia. The likelihood ratio reported a significant interaction between the two fixed effects [$AIC_{Full} = 12890$; $AIC_{Null} = 12892$; $p = 0.0301$]. The difficulty of the task affected the dynamics of motion in different ways for the two groups.

Peak Acceleration

A significant effect of ID on A_{max} was observed [$AIC_{Full} = 22156$; $AIC_{Null} = 23361$; $p < 0.0001$]. A_{max} decreases with ID by $178.928 \pm 4.325 \text{ cm/s}^2$. A significant effect on A_{max} was reported also for Group [$AIC_{Full} = 22156$; $AIC_{Null} = 22167$; $p = 0.0003$]. Compared to the group with dystonia, the peak acceleration of the control group was higher by $144.272 \pm 32.058 \text{ cm/s}^2$. The likelihood ratio reported a significant interaction between the two fixed effects [$AIC_{Full} = 22093$; $AIC_{Null} = 22156$; $p < 0.0001$]. The difficulty of the task affected the dynamics of motion in different ways for the two groups.

Jerk

Jerk was significantly affected by ID [$AIC_{Full} = 56027$; $AIC_{Null} = 56050$; $p < 0.0001$]. *Jerk* increased with ID by 217308 ± 42840 . A significant effect on *JERK* was reported also for Group [$AIC_{Full} = 56027$; $AIC_{Null} = 56030$; $p = 0.0273$]. *Jerk* was increased by a factor 321285 ± 134771 for the group with dystonia, meaning that movements in dystonia are less smooth and less coordinated compared to the control group. The likelihood ratio reported a significant interaction between the two fixed effects [$AIC_{Full} = 55998$; $AIC_{Null} = 56027$; $p < 0.0001$]. The difficulty of the task affected the smoothness of movement in different ways for the two groups.

Trial-to-trial Variability

ID affected only *Trial-to-trial Variability* of SPO [$AIC_{Full} = 15.544$; $AIC_{Null} = 18.727$; $p = 0.0228$], which increased with ID by $0.1169 \pm 0.0500 \text{ cm}$. No significant effect of ID was reported on *Trajectory Variability* of ELB and ACR [ELB: $AIC_{Full} = 179.54$; $AIC_{Null} = 179.70$ $p = 0.1415$; ACR: $AIC_{Full} = 157.70$; $AIC_{Null} = 157.98$; $p = 0.1311$]. Fixed effect Group significantly affected *Trajectory Variability* of SPO, ELB, and ACR [SPO: $AIC_{Full} = 15.544$; $AIC_{Null} = 24.069$; $p = 0.0012$; ELB: $AIC_{Full} = 179.54$; $AIC_{Null} = 184.87$; $p = 0.0068$; ACR: $AIC_{Full} = 157.70$; $AIC_{Null} = 163.08$; $p = 0.0066$]. For the group with

dystonia, *Trial-to-trial Variability* was increased by $0.3927 \text{ cm} \pm 0.1018$ for SPO, $0.7023 \pm 0.2303 \text{ cm}$ for ELB, and $1.0351 \pm 0.3380 \text{ cm}$ for ACR. No interaction between the two fixed effects was reported for SPO, ELB, and ACR [SPO: $\text{AIC}_{\text{Full}} = 17.495$; $\text{AIC}_{\text{Null}} = 15.544$; $p = 0.8252$; ELB: $\text{AIC}_{\text{Full}} = 179.89$; $\text{AIC}_{\text{Null}} = 179.54$; $p = 0.1985$; ACR: $\text{AIC}_{\text{Full}} = 159.0$; $\text{AIC}_{\text{Null}} = 157.7$; $p = 0.4028$]. *Trial-to-trial Variability* was increased in dystonia and, regardless of the group, it was affected by the difficulty of the task only at the end effector level.

Muscle Force

Muscle Force was not affected by ID [$\text{AIC}_{\text{Full}} = -46329$; $\text{AIC}_{\text{Null}} = -46330$; $p = 0.2796$], while it was significantly affected both by Group [$\text{AIC}_{\text{Full}} = -46329$; $\text{AIC}_{\text{Null}} = -46326$; $p = 0.0207$] and Muscle [$\text{AIC}_{\text{Full}} = -46329$; $\text{AIC}_{\text{Null}} = -45656$; $p < 0.0001$]. The *Muscle Force* exerted during task execution by the group with dystonia was increased by a factor 0.0131 ± 0.0051 compared to the control group (Figure 3). The likelihood ratio reported a significant interaction between the two fixed effects Group and Muscle [$\text{AIC}_{\text{Full}} = -46719$; $\text{AIC}_{\text{Null}} = -46329$; $p < 0.0001$], meaning that the two groups adopted different muscular strategies and force distribution.

Co-contraction

CC was neither affected by ID [$\text{AIC}_{\text{Full}} = -19029$; $\text{AIC}_{\text{Null}} = -19030$; $p = 0.2777$] nor Group [$\text{AIC}_{\text{Full}} = -19029$; $\text{AIC}_{\text{Null}} = -19031$; $p = 0.3957$], while it was significantly affected by Muscle Pair [$\text{AIC}_{\text{Full}} = -19029$; $\text{AIC}_{\text{Null}} = -18896$; $p < 0.0001$]. *CC* between AD and PD was increased by a factor 0.0070 ± 0.0006 compared to BIC and TRIC. The likelihood ratio reported a significant interaction between the two fixed effects ID and Group [$\text{AIC}_{\text{Full}} = -19046$; $\text{AIC}_{\text{Null}} = -19029$; $p < 0.0001$], as well as between the two fixed effects Group and Muscle Pair [$\text{AIC}_{\text{Full}} = -19039$; $\text{AIC}_{\text{Null}} = -19029$; $p = 0.0008$]. This means that, for the two groups, *CC* is modulated in different ways according to the difficulty of the task and the muscle pair, consistent with the findings on *Muscle Force* that report different muscular involvement between the two groups.

DISCUSSION

In the present study we propose a simple task that is related to daily life and imposes a speed-accuracy trade-off on the entire trajectory.

Results showed that the trajectory-constrained speed-accuracy relation is present in children with dystonia and in healthy children. Indeed, movement time was related to the difficulty of the task. This feature allowed us to easily and quantitatively measure the motor performance in a trajectory-constrained functional motor task. The Index of Performance reflects the efficiency of the motor system to deal with tasks of increasing difficulty²⁵ and it is a common measure of performance in the literature, but it is usually extracted in tasks with constrained end points accuracy.^{26,27,28,29} The Index of Performance proposed in the present study represents a more complete and informative measure because, since the task accuracy is constrained along the whole trajectory, the index summarizes and quantifies the motor performance as a whole. In this study, children with dystonia had an Index of Performance

that was significantly decreased compared to control subjects, showing an overall reduced ability to perform the task. The time required to move from one target to the other was significantly higher in children affected by dystonia than in control children. In other words, our results show that children with dystonia do present a speed-accuracy trade-off in continuous accuracy constrained daily tasks, but that the nature of this trade-off is altered both in terms of increased slope and offset towards longer movement times, confirming the results reported for point-to-point reaching movements, during which children with dystonia required significantly larger targets to achieve speed comparable with that of control children.^{11,13} This means that, for patients with dystonia, the speed of movement is more sensitive to accuracy requirements, and that the speed to accomplish a certain level of accuracy is decreased compared to healthy subjects. Our finding is consistent with the hypothesis of an increase in the amount of signal-dependent noise in dystonia. If the variance of the noise increases with the control signal, fast movements requiring large control signals are characterized by increased variability, resulting in inaccuracy of motion.⁹ For this reason, accuracy can be improved only by slowing down the speed of movement. The slower movements observed in dystonia, characterized by decreased peak velocity and acceleration, can at least partially be explained as a compensatory strategy for the increased variability due to increased signal-dependent noise. Indeed, the increased amount of noise affecting the sensorimotor system in dystonia is reflected in the abnormal kinematics of these children, characterized by jerky, poorly-coordinated and variable movements.

Both primary and secondary dystonia are associated with dysfunction or injury to the basal ganglia.^{30,31,32} Neurophysiological studies support the theory that, when voluntary movement is generated, the basal ganglia are responsible for the focused selection of the desired motor patterns and for the inhibition of undesired and competing motor mechanisms that would otherwise interfere with the planned movement.^{33,34,35} According to several motor control theories, the process of generating voluntary movement can be divided into two steps: a planning stage and an execution stage. Since the speed-accuracy trade-off has been reported also in the absence of overt movement^{36,37,38}, the presence of a trade-off between speed and accuracy can be considered the consequence of a proper motor planning stage. While performing our task, children with dystonia show a speed-accuracy trade-off, which suggest a successful motor planning. Thus, movement abnormalities arising from dysfunction of the basal ganglia in dystonia may be related to the inability to remove unwanted movement components thus affecting the execution step, rather than to the inability to select the desired movement during the planning stage. Previous studies suggested that this inability to suppress noisy and unwanted movement components may result in the impaired kinematics⁹ and in the aberrant EMG activity peculiar to dystonia. In accordance with this hypothesis, our results reported abnormalities both in the kinematics and in the EMGs of children with dystonia. In particular, EMG results showed that children with dystonia exerted an aberrant increased amount of muscle force during task execution. We also observed that, compared to control children, children with dystonia adopted different muscle strategies and faced the increasing difficulty of the task by modulating the relative recruitment of antagonist muscles in different ways. It is worth noting that, in accordance with previous studies²³, children with dystonia do not present increased levels of co-contraction, compared to control subjects. This suggests that patients modulate co-

contraction in a different way compared to control subjects as a strategy to compensate for the uncontrollable force production.

The speed-accuracy operator has been previously investigated in other movement disorders involving basal ganglia dysfunctions.^{39,40,41} Similar results were reported for Parkinson's Disease (PD) patients, whose speed-accuracy trade-off in point-to-point tasks was less efficient than in healthy subjects.^{40,42,43} In particular, Sheridan and Flowers⁴⁴ hypothesized that bradykinesia in PD might be a strategy actively adopted by patients to improve their accuracy. Another study⁴⁵ tested Huntington's Disease (HD) patients and healthy controls in a task that stressed accuracy. HD patients showed increased movement time and higher intra-subject variability compared to controls. The slowness of movement in HD and PD is similar to that seen in dystonia. However, the mechanisms in these conditions are probably different. Indeed, bradykinesia in PD usually co-exists with hypokinesia or akinesia, while HD is more reminiscent of dystonia, with bradykinesia occurring in conjunction with hyperkinesia.⁴⁶ Notwithstanding different complex mechanisms underlying the basal ganglia dysfunctions in these motor disturbances, a common hypothesis about basal ganglia pathophysiology is that disease may make the basal ganglia output noisy.⁴⁶ It is likely that this noise is reflected in the altered speed-accuracy trade-off observed in these movement disorders.

To conclude, we have proposed a simple but relevant daily life task that imposes a continuous speed-accuracy trade-off. Our results further characterize the kinematic and EMG abnormalities of upper-extremity movements in childhood dystonia. We have shown that the Index of Performance reflects quality and efficiency of the motor performance and it can be used to assess and compare the sensorimotor abilities between children with dystonia and healthy subjects. Children with dystonia showed a significantly lower Index of Performance and increased Movement Time compared to healthy children, consistent with the hypothesis of increased signal-dependent noise in dystonia. Notwithstanding increased noise, children with dystonia showed the ability to calibrate task velocity according to the accuracy demand. Since a change in the speed-accuracy trade-off is expected to reflect learning¹⁵, the Index of Performance proposed in the present study can have practical and useful implications in motor learning studies for children with dystonia. Importantly, we have developed a method for precisely quantifying the ability to perform a task relevant to daily life. In the future, this task may help reveal subtle yet relevant changes (possibly due to rehabilitation methods or changes in disease state) that otherwise may have been overlooked or difficult to quantify.

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References

1. Sanger TD, Delgado MR, Gaebler-Spira D, et al. Classification and Definition of Disorders Causing Hypertonia in Childhood. *Pediatrics*. 2003; 111:89–97.

2. Sanger TD. Toward a definition of childhood dystonia. *Curr Opin Pediatr.* 2004; 16:623–627. [PubMed: 15548923]
3. Marsden CD, Rothwell JC. The physiology of idiopathic dystonia. *Can J Neurol Sci.* 1987; 14(3 Suppl):521–7. [PubMed: 3315155]
4. Albanese A. The clinical expression of primary dystonia. *J Neurol.* 2003; 250:1145–1151. [PubMed: 14586593]
5. Berardelli A, Hallett M, Rothwell JC, et al. Single-joint rapid arm movements in normal subjects and in patients with motor disorders. *Brain.* 1996; 119(Pt 2):661–674. [PubMed: 8800955]
6. Casellato C, Zorzi G, Pedrocchi A, et al. Reaching and writing movements: sensitive and reliable tools to measure genetic dystonia in children. *J Child Neurol.* 2011; 26:822–9. [PubMed: 21421904]
7. Currà A, Berardelli A, Agostino R, et al. Movement cueing and motor execution in patients with dystonia: A kinematic study. *Mov Disord.* 2000; 15:103–112. [PubMed: 10634248]
8. Fahn S. Concept and classification of dystonia. *Adv Neurol.* 1988; 50:1–8. [PubMed: 3041755]
9. Sanger TD. Arm Trajectories in Dyskinetic Cerebral Palsy Have Increased Random Variability. *J Child Neurol.* 2006; 21:551–557. [PubMed: 16970842]
10. Harris CM, Wolpert DM. Signal-dependent noise determines motor planning. *Nature.* 1998; 394:780–784. [PubMed: 9723616]
11. Sanger TD, Kaiser J, Placek B. Reaching Movements in Childhood Dystonia Contain Signal-Dependent Noise. *J Child Neurol.* 2005; 20:489–496. [PubMed: 15996397]
12. Wickelgren WA. Speed–accuracy tradeoff and information-processing dynamics. *Acta Psychol.* 1977; 41:67–85.
13. Bertuccio M, Sanger TD. Speed-Accuracy Testing on the Apple iPad® Provides a Quantitative Test of Upper Extremity Motor Performance in Children with Dystonia. *J Child Neurol.* Epub 2013 Aug 21.
14. Hasson CJ, Shen T, Sternad D. Energy margins in dynamic object manipulation. *J Neurophysiol.* 2012; 108(5):1349–65. Epub 2012 May 16. 10.1152/jn.00019.2012 [PubMed: 22592302]
15. Shmuelof L, Krakauer JW, Mazzoni P. How is a motor skill learned? Change and invariance at the levels of task success and trajectory control. *J Neurophysiol.* 2012; 108(2):578–94. Epub 2012 Apr 18. 10.1152/jn.00856.2011 [PubMed: 22514286]
16. Barry MJ, VanSwearingen JM, Albright AL. Reliability and responsiveness of the Barry–Albright Dystonia Scale. *Dev Med Child Neurol.* 1999; 41:404–411. [PubMed: 10400175]
17. Oldfield RC. The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia.* 1971; 9(1):97–113. [PubMed: 5146491]
18. Bates DM, Maechler M, Bolker B. lme4: Linear mixed-effects models using S4 classes. R package version 0.999999–0. 2012
19. Flash T, Hogan N. The coordination of arm movements: an experimentally confirmed mathematical model. *J Neurosci.* 1985; 5(7):1688–703. [PubMed: 4020415]
20. Hogan N, Sternad D. Sensitivity of smoothness measures to movement duration, amplitude, and arrests. *J Mot Behav.* 2009; 41(6):529–34. 10.3200/35-09-004-RC [PubMed: 19892658]
21. Takada K, Yashiro K, Takagi M. Reliability and sensitivity of jerk-cost measurement for evaluating irregularity of chewing jaw movements. *Physiol Meas.* 2006; 27(7):609–22. Epub 2006 Apr 27. [PubMed: 16705259]
22. Fitts PM. The information capacity of the human motor system in controlling the amplitude of movement. *J Exp Psychol.* 1954; 47:381–391. [PubMed: 13174710]
23. Malfait N, Sanger TD. Does dystonia always include co-contraction? A study of unconstrained reaching in children with primary and secondary dystonia. *Exp Brain Res.* 2007; 176(2):206–16. [PubMed: 16850323]
24. Akaike, H. Information Theory and an Extension of the Maximum Likelihood Principle. In: Kotz, S.; Johnson, NL., editors. *Breakthroughs in Statistics. Vol. 1.* New York, NY: Springer-Verlag; 1992. p. 610–624. Springer Series in Statistics, Perspectives in Statistics
25. Smits-Engelsman BC, Sugden D, Duysens J. Developmental trends in speed accuracy trade-off in 6–10-year-old children performing rapid reciprocal and discrete aiming movements. *Hum Mov Sci.* 2006; 25:37–49. [PubMed: 16442174]

26. Bhushan N, Shadmehr R. Computational nature of human adaptive control during learning of reaching movements in force fields. *Biol Cybern.* 1999; 81:39–60. [PubMed: 10434390]
27. Meyer DE, Abrams RA, Kornblum S, et al. Optimality in human motor performance: Ideal control of rapid aimed movements. *Psychol Rev.* 1988; 95:340. [PubMed: 3406245]
28. Schmidt RA, Zelaznik H, Hawkins B, et al. Motor-output variability: a theory for the accuracy of rapid motor acts. *Psychol Rev.* 1979; 86:415. [PubMed: 504536]
29. Smits-Engelsman BC, Rameckers EA, Duysens J. Children with congenital spastic hemiplegia obey Fitts' Law in a visually guided tapping task. *Exp Brain Res.* 2007; 177(4):431–9. Epub 2006 Sep 22. [PubMed: 17019607]
30. Berardelli A, Rothwell JC, Hallett M, et al. The pathophysiology of primary dystonia. *Brain.* 1998; 121:1195–1212. [PubMed: 9679773]
31. Bhatia KP, Marsden CD. The behavioral and motor consequences of focal lesions of the basal ganglia in man. *Brain.* 1994; 117:859–876. [PubMed: 7922471]
32. Marsden CD, Obeso JA, Zarranz JJ, Lang AE. The anatomical basis of symptomatic hemidystonia. *Brain.* 1985; 108:463–483. [PubMed: 4005532]
33. Hallett M, Khoshbin S. A physiological mechanism of bradykinesia. *Brain.* 1980; 103:301–14. [PubMed: 7397480]
34. Mink JW. The basal ganglia: focused selection and inhibition of competing motor programs. *Prog Neurobiol.* 1996; 50:381–425. [PubMed: 9004351]
35. Nambu A, Tokuno H, Takada M. Functional significance of the cortico-subthalamo-pallidal 'hyperdirect' pathway. *Neurosci Res.* 2002; 43:111–117. [PubMed: 12067746]
36. Bertucco M, Cesari P. Does movement planning follow Fitts' law? Scaling anticipatory postural adjustments with movement speed and accuracy. *Neuroscience.* 2010; 171(1):205–13. Epub 2010 Sep 9. 10.1016/j.neuroscience.2010.08.023 [PubMed: 20804822]
37. Bertucco M, Cesari P, Latash ML. Fitts' Law in early postural adjustments. *Neuroscience.* 2013; 231:61–9. Epub 2012 Dec 2. 10.1016/j.neuroscience.2012.11.043 [PubMed: 23211560]
38. Decety J, Jeannerod M. Mentally simulated movements in virtual reality: Does Fitts's law hold in motor imagery? *Behav Brain Res.* 1995; 72:127–134. [PubMed: 8788865]
39. Hefter H, Hömberg V, Lange HW, Freund HJ. Impairment of rapid movement in Huntington's disease. *Brain.* 1987; 110 (Pt 3):585–612. [PubMed: 2953406]
40. Mazzoni P, Hristova A, Krakauer JW. Why don't we move faster? Parkinson's disease, movement vigor, and implicit motivation. *J Neurosci.* 2007; 27(27):7105–16. [PubMed: 17611263]
41. Wylie SA, van den Wildenberg WP, Ridderinkhof KR, et al. The effect of speed-accuracy strategy on response interference control in Parkinson's disease. *Neuropsychologia.* 2009; 47(8–9):1844–53. Epub 2009 Feb 28. 10.1016/j.neuropsychologia.2009.02.025 [PubMed: 19428416]
42. Montgomery EB, Nuessen J. The movement speed/accuracy operator in Parkinson's disease. *Neurology.* 1990; 40(2):269–72. [PubMed: 2300247]
43. Phillips JG, Martin KE, Bradshaw JL, Iansek R. Could bradykinesia in Parkinson's disease simply be compensation? *J Neurol.* 1994; 241(7):439–47. [PubMed: 7931446]
44. Sheridan MR, Flowers KA. Movement variability and bradykinesia in Parkinson's disease. *Brain.* 1990; 113 (Pt 4):1149–61. [PubMed: 2397387]
45. Carella F, Bressanelli M, Piacentini S, et al. A study of arm movements in Huntington's disease under visually controlled and blindfolded conditions. *Neurol Sci.* 2003; 23(6):287–93. [PubMed: 12624715]
46. Berardelli A, Rothwell JC, Thompson PD, Hallett M. Pathophysiology of bradykinesia in Parkinson's disease. *Brain.* 2001; 124(Pt 11):2131–46. [PubMed: 11673316]

Figure 1. Set-up

Subjects were seated at a desk. A board with two targets (Target 1 and Target 2) was positioned on the desk. The distance between the centers of the two targets was 20 cm along the sagittal axis (X-axis). Each target was bounded by two plastic blocks attached to the board.

Figure 2. Speed-accuracy Trade-off and Index of Performance

Panel a: Linear regression between Movement Time (MT) (seconds) and Index of Difficulty (ID) for Control (gray) and Dystonia (black). For each group, for each ID, mean values and standard error bars are presented. The trajectory-constrained speed-accuracy trade-off is present in both groups. In dystonia, the trade-off is characterized by increased slope and offset toward longer MT.

Panel b: Index of Performance (IP) (1/seconds) for Control (gray) and Dystonia (black). For each group, mean (box) and standard error (whiskers) are presented. IP is significantly decreased in dystonia (asterisk to describe statistical significance).

Figure 3. Muscle Force

Mean (bold lines) and standard deviation (areas) values of the *Muscle Force* of the five muscles (Rows: biceps (BIC), triceps (TRIC), anterior deltoid (AD), lateral deltoid (LD), posterior deltoid (PD)) exerted over 15 one-way outward movements. Plots report data from one control subject (c2: gray. Columns 1 and 3) and one child with dystonia (d3: black. Columns 2 and 4) during the execution of the task with two spoons, the one that imposes the lowest ID (S1) and the one that imposes the highest ID (S4). Horizontal axes show the time expressed as percentage of movement duration (the 15 movements are time-normalized to the mean duration). Vertical axes amplitude scales are different between the two subjects for clarity purpose. The figure shows that the child with dystonia exerts more *Muscle Force* compared to the healthy child. It is worth noting that the noise that affects the EMG increases with the difficulty of the task, and that this trend is more accentuated for the child with dystonia.

Table 1

Clinical Characteristics of Participants

Table A: Children with dystonia. Subject ID; Sex [M: Male; F: Female]; Age [years]; Diagnosis; Deep Brain Stimulation (DBS) [Y: yes; N: no]; Severity of Right Arm (R Arm), Left Arm (L Arm), Trunk, and Total Score (scores are based on the Barry-Albright Dystonia Scale¹⁶; for each segment the score ranges from 0 - absence of dystonia - to 4 - severe dystonia); Dominant arm (Dom. Arm); Medications.

Table B: Control children. Subject ID; Sex; Age; Dominant arm.

A)									
ID	SEX	AGE	DIAGNOSIS	DBS	BAD SCALE SCORE				MEDICATIONS
					R Arm	L Arm	Trunk	Total	
d1	M	16	Secondary dystonia, Cerebral Palsy	N	1	1	0	2	No Medication
d2	F	15	Primary dystonia, DYT1-	Y	1	1	2	12	Trihexyphenidyl
d3	M	11	Secondary dystonia, Cerebral Palsy	N	2	2	1	12	Clonazepam
d4	F	19	Generalized secondary dystonia	N	3	3	0	10	Carbidopa-Levodopa
d5	M	21	Secondary dystonia, Traumatic Brain Injury (TBI)	N	3	0	0	8	No Medication
d6	M	16	Generalized secondary dystonia	N	1	1	0	3	Trihexyphenidyl
d7	M	20	Primary dystonia	N	2	2	0	8	Vitamine E, Botulinum toxin injection 3 months prior the study
d8	M	11	Secondary dystonia, Cerebral Palsy	N	3	3	2	14	Trihexyphenidyl / Carbidopa-Levodopa

B)			
ID	SEX	AGE	DOM. ARM
c1	M	17	R
c2	M	15	R
c3	F	10	R
c4	M	19	R
c5	F	21	R
c6	M	17	R
c7	M	15	R
c8	M	11	R

Table 2

Dimensions and IDs of the four spoons

Spoon	Depth	Width	Length	ID
S1	1.3945 cm	2.9845 cm	4.5212 cm	1.8718
S2	1.2751 cm	3.9649 cm	5.1562 cm	2.0470
S3	1.0287 cm	3.5433 cm	5.0241 cm	2.5373
S4	0.8001 cm	2.5857 cm	3.6068 cm	3.2623