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RESEARCH ARTICLE

Does dystonia always include co-contraction? A study of unconstrained reaching in children with primary and secondary dystonia

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Abstract Dystonia is a movement disorder in which involuntary or intermittent muscle contractions cause twisting and repetitive movements, abnormal postures, or both. 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 and reduced speed of movement is often attributed to involuntary activation of antagonist muscles about a joint. In the present study we describe muscle activity during unconstrained multi-joint reaching movements. Children diagnosed with arm dystonia due to cerebral palsy (CP) or primary dystonia (n = 7, 4–16 years, 4 with CP, 3 primary) and similar age healthy subjects pointed alternately to two targets as fast as possible. The children with dystonia showed decreased speed, greater variability, and pauses at targets compared with controls. Decreased speed was mostly due to difficulty in reversing reaching direction, and increased variability was associated with large fluctuations in the duration of the pauses at targets, rather than with variations in the flexion/extension velocity profiles. Surface electromyographic (EMG) activities were examined to assess if the abnormalities observed in the children with dystonia could be explained in terms of increased levels of co-contraction. Unexpectedly, we found that the children with dystonia showed lower levels of co-contraction than the controls during movement, and the pauses at targets were associated with reduced levels of activation rather than with excessive activity in antagonist groups of muscles. Therefore reduced speed of movement during unconstrained reaching may not be due to involuntary activation of the antagonist muscle, and co-contraction of opposing muscles about a joint is not an obligatory feature of multi-joint movement in children with dystonia.

Keywords Dystonia · Childhood · Pediatric · Co-contraction · EMG · Reaching

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Introduction

Dystonia in children has been defined as "a movement disorder in which involuntary sustained or intermittent muscle contractions cause twisting and repetitive movements, abnormal postures, or both" (Fahn et al. 1987; Sanger et al. 2003). Dystonia is considered to be "primary" when it is the dominant manifestation of a defined or presumed genetic disorder, otherwise it is considered to be "secondary". Dystonia is thought to be associated with three physiological phenomena; co-contraction of antagonist muscles, overflow of electromyographic (EMG) activity onto uninvolved muscles during voluntary movement, and involuntary activation of muscles during passive shortening (Marsden 1984). The hypothesis that in dystonia abnormal motor patterns arise as a consequence of dysfunction in the basal ganglia (Berardelli et al. 1998) has received empirical as well as theoretical support (see Sanger 2003, for review). According to one model of basal ganglia function, dystonia arises from a net decrease in the firing of inhibitory neurons projecting

from the internal segment of the globus pallidus (GPi) to the ventral lateral thalamus, thus increasing the activity of excitatory thalamocortical projections to motor and premotor regions of the frontal cortex (Vitek 2002). Consequently, dystonia is sometimes considered to result from excessive motor cortical outflow with involuntary activation of muscles not normally involved in the desired movement or posture, and it is thus assumed that the result of the basal ganglia abnormality is an increase in activation of muscles.

Dystonia is an abnormality of both movement and posture (Marsden 1984; Sanger et al. 2003). The effect of dystonia on active movement has been difficult to characterize. While fixed dystonic postures are frequently observed and movements are slow, inaccurate, variable, and awkward (Sanger et al. 2005), the relation between dystonic postures that are seen at rest and abnormalities of movement has not been investigated. It is tempting to hypothesize that dystonic postures intrude during movement and are reflected by involuntary and inappropriate muscle activation. Co-contraction of opposing muscles and overflow onto muscles that antagonize movement may be a cause of the abnormalities in trajectory and the reduced speed of movement. However, these hypotheses have not been tested.

Most studies of the kinematics of children with motor disorders have focused on the lower extremities in order to understand and improve ambulatory function (Damiano and Abel 1996; O'Byrne et al. 1998; Thelen et al. 2003). With few exceptions (McPherson et al. 1991; Fetters and Kluzik 1996; Utley and Sugden 1998; Chang et al. 2005; van der Heide et al. 2005a) studies of upper extremity function have mostly been limited to constrained single-joint movement (Harris 1991; Duque et al. 2003). Therefore, impairment in the upper limbs has not yet been well described. In the present study, we examined abnormalities in elbow joint kinematics observed during unconstrained multi-joint reaching movements in children with either primary or secondary dystonia. In agreement with previous clinical and experimental observations, we expected to observe decreased speed of movement and increased variability in the joint kinematics (Sanger et al. 2005; Van Der Heide et al. 2005b). Our goal was to describe the nature of these two characteristic features in relation to the EMG activity recorded in the antagonist biceps/triceps muscle groups. In particular, we wanted to determine if movement slowness could be attributed to abnormal patterns of co-contraction and involuntary activation of muscles opposing movement.

Methods

Subjects

Seven children aged 4–16 years (mean 11.1) diagnosed with dystonia by an experienced child neurologist (TDS) were recruited from the Stanford Pediatric Movement Disorders Clinic. (an eighth child was also recruited but was not able to perform a sufficient number of trials to be included in the analyses.) Subjects with dystonia were included only if they exhibited abnormal dystonic postures of the arm during forward reaching movements. Three subjects (2, 5, and 6) were classified as "primary" dystonia due to lack of an identified cause, normal early development with subsequent appearance of dystonia, and normal MRI findings (all were negative on testing for the DYT1 gene). The remaining four subjects (1, 3, 4, and 7) were classified as "secondary" and carry a diagnosis of cerebral palsy (CP) due to known prenatal or peri-natal injury (see Table 1). None of the subjects showed evidence of spasticity (a spastic catch or elevated tendon reflexes) in the elbow flexors or extensors. Seven control subjects aged 5–16 years (mean 10.6) without motor disorders were recruited from a convenience sample of children. All healthy children were right hand dominant by parent report. Informed consent was obtained from parents consistent with a protocol approved by the Stanford University Institutional Review Board. Authorization for analysis, storage, and publication of protected health information was obtained from parents according to the Health Information Portability and Accountability Act (HIPAA). All subjects were rated at the time of testing on the Gross Motor Function Classification System (GMFCS) (Palisano et al. 1997), the upper extremity subscale of the Burke–Fahn–Marsden dystonia rating scale (BFM) (Burke et al. 1985), the Barry–Albright dystonia rating scale (BAD) (Barry et al. 1999), and the Unified Dystonia Rating Scale (UDRS) (Comella et al. 2003). At the time of testing, subject 4 was taking trihexyphenidyl and baclofen. The remaining subjects were on no medications. This information is summarized in Table 1.

Experimental task

Subjects were seated comfortably and unrestrained in a non-metallic chair. Subjects were asked to perform a task directly derived from the "finger-to-nose" reaching task commonly used in routine neurological evaluation; specifically subjects were required to point alternately to a target located at arm's length in front

Table 1 Clinical characteristics and testing results for all subjects

ID	Age	Sex	BFM		UDRS		BAD		GMFCS	Diagnosis	Symptoms	Pause duration mean ± SD (s)	Co-contraction 'MIN' mean ± SD
			R	L	R	L	R	L					
1	4	F	2	2	2	2	1	1	2	Prematurity with perinatal intraventricular hemorrhage	Bilateral arm dystonia and leg spasticity	0.207 ± 0.177	0.055 ± 0.057
2	8	F	2	0	1.5	0	2	0	2	Primary hemidystonia	Right foot and hand dystonia	0.163 ± 0.273	0.077 ± 0.038
3	9	M	4	9	6	10	2	3	5	Prematurity with perinatal intraventricular hemorrhage	Left > right arm dystonia and leg spasticity	0.434 ± 0.324	0.045 ± 0.035
4	13	F	9	9	13	12	4	3	5	Perinatal hypoxic injury	Generalized dystonia and chorcoathetosis	1.0474 ± 0.753	0.061 ± 0.054
5	13	M	4	2	1.5	1.5	1	1	2	Primary dystonia	Bilateral arm dystonia and writer's cramp	0.247 ± 0.255	0.044 ± 0.028
6	15	F	4	9	3	10	2	3	3	Primary dystonia	Generalized dystonia	0.226 ± 0.174	0.096 ± 0.026
7	16	M	9	9	6	8.5	3	3	4	Perinatal hypoxic injury	Generalized dystonia and chorcoathetosis	0.667 ± 0.520	0.072 ± 0.022

of them in the sagittal plane and their nose. Location of the target was adjusted for each subject such that it was situated at the same height as the nose of the subject and at full arms-length distance. Children were asked to perform the task "as fast as possible without missing". Each child performed two series of 20 complete flexion/extension cycles with each arm. Most of the children with dystonia had difficulty maintaining continuous movement for 20 trials in a row. For the analyses, we selected series of at least five cycles of movements that were executed without interruption (interruption was defined as any pause that lasted more than 3 s). This criterion resulted in a rejection of 28% of the movement cycles for the subjects with dystonia and less than 1% for the controls. For several subjects with dystonia the proportion of rejected cycles was close to 50%. Therefore in order to include a comparable number of movements for both groups of subjects, for each subject we analyzed only the first 20 movement cycles that satisfied the criterion (for one child with dystonia (subject 1) only 18 trials could be included). The preferred arm (less impaired, for the children with dystonia and dominant for the controls) was always tested first. Subject 4 was able to complete the task only on the left arm due to severe dystonia on the right side. Series of trials were self-initiated starting at the distal target.

Signal recording

Kinematic data were recorded using magnetic position sensors (Polhemus Inc.) attached using either Velcro™ straps or medical-grade adhesive to eight points on the body: the mid-shaft of each upper arm, the dorsum of each distal forearm between the radius and ulna, the dorsum of each hand over the mid-shaft of the third metacarpal bone, the back over the first or second thoracic vertebra, and the forehead 1–3 cm above the nose in the midline. The location of joint axes relative to each sensor was measured using one of the sensors as a marker, in accordance with the "digitizing" procedure of commercially available kinematics analysis software (Skill Technologies, Inc.).

EMG activity of four groups of muscles in each arm was recorded using surface electrodes (DE2.3, Delsys Inc.). Each active electrode has two parallel bar contacts of length 1 cm and width 1 mm, with inter-electrode spacing of 1 cm. Internal electronics in the electrodes provide 1000 ± 2% amplification and analog filtering with half-height cutoff between 20 ± 5 and 450 ± 50 Hz and roll-off of 12 dB per octave. Common-mode rejection ratio (CMRR) is greater than 80 dB at 60 Hz. Electrodes were placed over the belly of the biceps brachii and triceps brachii. Electrodes were also placed over the flexor carpi radialis and extensor carpi radialis longus, but data from the forearm electrodes was not used in this experiment since the forearm electrodes were not placed over muscles that contribute to elbow motion. EMG signals were sampled at 1,000 Hz and digitized with 16-bit precision (CED Power 1401; Cambridge Electronic Design, Cambridge, UK).

Data analysis

Kinematic data were recorded from each position sensor, sampled at 120 Hz, filtered with a digital low-pass filter (6 dB cutoff at 20 Hz), and numerically differentiated. In the present paper, analyses are restricted to elbow kinematics. For each movement cycle, onset and offset of flexion and extension were defined using the velocity profile zero-crossings. Each flexion or extension movement was then further divided into

acceleration and deceleration phases according to the zero-crossings of the acceleration. For the subjects with dystonia, two additional phases were defined that corresponded to pauses in the velocity and acceleration profiles that these subjects exhibited at both distal and proximal targets before initiating movement direction reversal. Such pauses were not seen in the control subjects. Therefore there were six phases for children with dystonia: acceleration during extension, deceleration during extension, pause at the distal target, acceleration during flexion, deceleration during flexion, and pause at the proximal target. Control subjects did not exhibit pauses, and therefore had only four phases. For each flexion/extension cycle, we computed the duration of the complete cycle and the duration of each movement phase, as well as the maximum joint angular velocity and maximum and minimum joint angles. To assess kinematic variability across trials for each subject, we also calculated the coefficient of variation (CV) of each measure: the standard deviation over the trials divided by the mean. The use of CV allows comparison of measures of variability between different performance conditions.

In accordance with standard practice for analysis of EMG signals (for example Hogan and Mann 1980; Clancy and Hogan 1994; Miscellaneous 1996), any constant DC offset was removed, and then the EMG signals were full-wave rectified and low-pass filtered at 20 Hz to extract the amplitude envelope. The resulting amplitude envelope reflects the temporal changes in power over the entire sampled spectrum. The choice of low pass filter at 20 Hz was determined by the low-pass cutoff of the kinematic measurements in order to allow comparison. Because the EMG activity levels observed during unconstrained reaching may be very different from those observed during isometric maximum voluntary contraction (MVC), rectified and filtered EMG for each muscle was normalized to the muscle's maximum rectified and filtered EMG amplitude observed during the entire experiment, rather than to MVC.

To compare average levels of co-contraction during each of the six phases of movement, we used two different methods of time binning. The first method used fixed 50 ms time bins. In this case, the final bin of each movement phase could be less than 50 ms long. The second method divided each movement phase into five-bins of equal length. This resulted in variable-length bins between 33 and 108 ms for the children with dystonia, and between 25 and 67 ms for the controls. Similar results were obtained with both methods, and in the results below we report data for variable-length bins. The rectified, low-pass filtered, and normalized EMG was averaged over each time bin.

There is no generally-accepted quantitative measure of co-contraction. We performed our analysis using two different methods, each of which produces a scalar value for each time bin. The first method ("DOT") calculates the dot product of the (filtered, rectified, normalized, and averaged) EMG between the biceps and triceps in each time bin, which is equivalent to computing the zero-time-lag covariance. Since rectified EMG is always positive, this measure will be zero if and only if at most one of the two muscles is active at the same time. The second method ("MIN") calculates the minimum value of the (filtered, rectified, normalized, and averaged) EMG between the agonist and antagonist muscles in each time bin. This measure will also be zero if and only if one of the two muscles is always zero. The principal difference between the two methods is that in DOT, the value of co-contraction depends on both the agonist and antagonist activation, while for MIN the value depends only on the antagonist. The DOT method represents a model of co-contraction as an abnormal correlation between opposing muscles, but it suffers from the fact that increasing agonist activity will increase the measure of co-contraction even if the antagonist remains unchanged. The MIN method represents a model of co-contraction as any activity in the normally-silent antagonist muscle. (Note that although MIN is related to the amount of agonist torque that is countered by the antagonist, we do not attempt to estimate the resulting torques since there are not yet widely accepted methods for determining the relation between surface EMG and torque during movement.) Since EMG is normalized by the maximum level observed during the testing, both methods take into account possible differences in electrode placement or muscle morphology.

There are other possible methods of quantifying co-contraction (Damiano et al. 2000). We chose not to use the ratio of antagonist to agonist activity since the magnitude of co-contraction could become very large if the agonist activity is low. We chose not to use the ratio of the lesser to the greater of the opposing muscles (which is equivalent to the MIN value normalized to the opposing muscle's activity) since this may underestimate co-contraction when agonist activity is large. Recently, a new co-contraction index has been proposed that (in the elbow) is related to the ratio of the difference in muscle activities to the sum of their activities (Yao et al. 2004, 2006). However, this index is not suitable for our purposes, since it can produce values indicating maximal co-activation even when total activation is very low, and it is undefined when both muscles are relaxed as we frequently observed during movement.

Due to variability in the velocity profile, it was difficult to compare EMG signals across different trials in the children with dystonia. For visualization purposes, we therefore used a temporal transformation process to realign the EMG by adjusting the time-scale of each movement so that peaks and zero crossings of the elbow velocity profile were aligned across trials. Specifically, we used a marker registration procedure in which the zero-crossings of the velocity and acceleration profiles for each subject are aligned by a piecewise non-linear transformation (using B-splines) of the time scale during each phase of movement (Bookstein 1991; Ramsay and Silverman 1997). The result of this procedure is illustrated in Fig. 1, where it is applied to the velocity traces of movements performed by a child with dystonia (subject 3). For most controls, this technique had only negligible effects, as these subjects tended to have very consistent velocity profiles—as can be seen in Fig. 2a showing velocity curves for a representative control subject. Note that although we use the time realignment procedure in order to be able to display the average co-contraction in the EMG signal and compute the

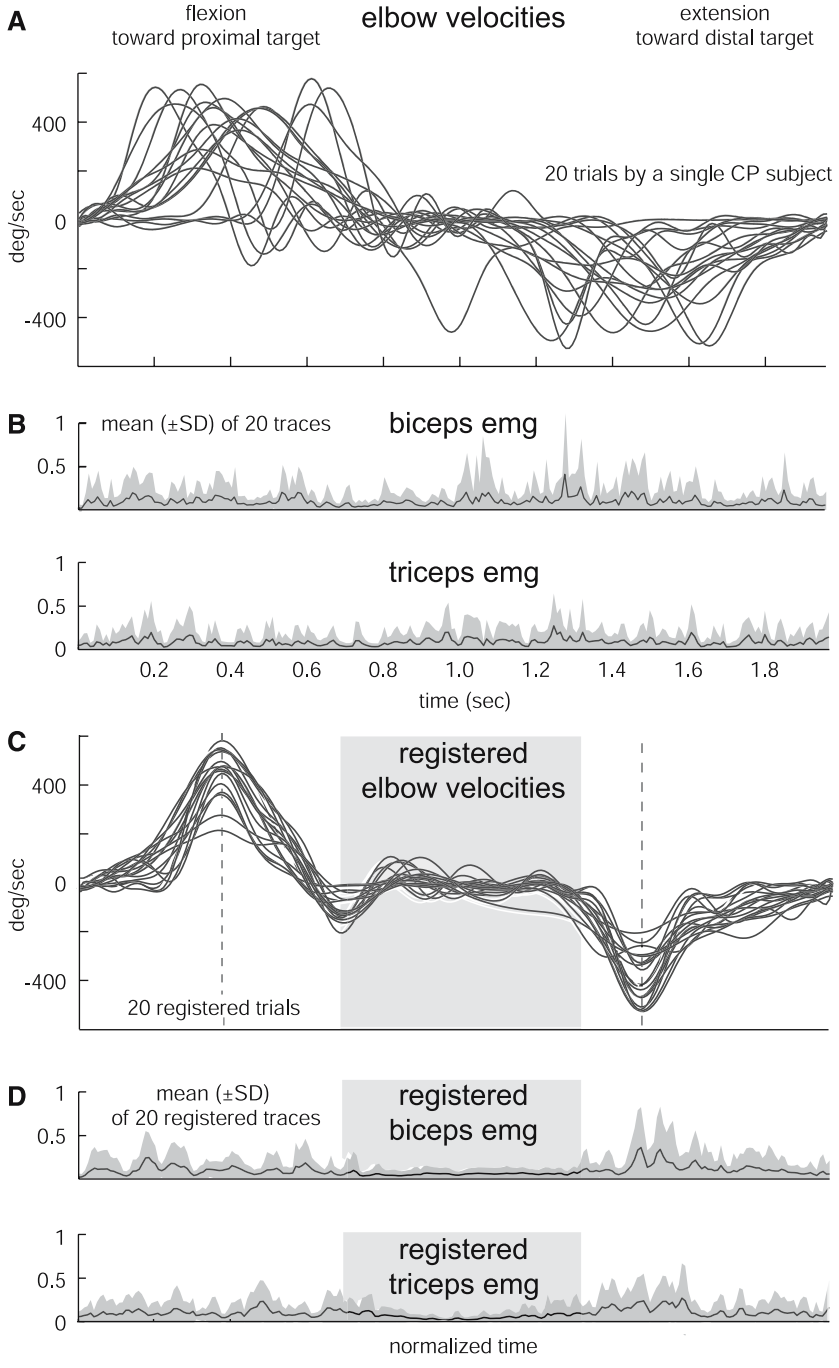

Fig. 1 Elbow kinematics and muscle activation pattern for a single subject with dystonia; extensive pauses at targets—at time of movement reversal—were typically observed in the children with dystonia. **a** Elbow velocity curves for individual trials. **b** Means (± SD) of the EMG activity amplitudes for the biceps (*top*) and the triceps (*bottom*) muscles for the same trials as in **a**. **c** Same elbow velocity traces as in **a** after application of the registration procedure; i.e. transformation of the time axis of each trial in order to align the different movement phases (acceleration, deceleration and pauses). **d** Means (± SD) of the same EMG activity amplitudes as in **b** using the same time axis transformations as in **c**

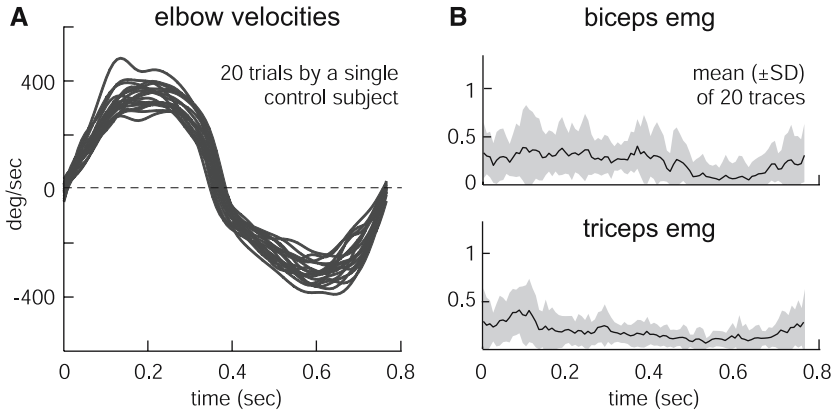

Fig. 2 Elbow kinematics and muscle activation pattern for a single control subject; smooth transition between the flexion and extension phases was typically observed in the controls. Some controls exhibited very high levels of antagonist muscle coactivation. **a** Elbow velocity profiles for individual trials. **b** Means (± SD) of the EMG activity amplitudes for the biceps (*top*) and the triceps (*bottom*) muscles corresponding to the trials shown in **a**

variable bin widths for EMG analysis, analysis of the velocity profile for variability, speed, and pauses was done without modification of the time scale.

In order to examine differences between groups on multiple potentially correlated measures, we ran multivariate analyses using the SAS GLM (Generalized Linear Model) procedure (SAS v8.02; SAS Institute, Cary, NC). Univariate repeated measures analyses of variance were run using the SAS MIXED procedure (in each case, the Akaike Information Criterion (AIC) statistic was used to choose the covariance matrix structure). For post hoc comparisons, P values were compared to levels adjusted by using a Bonferroni-Holm sequential procedure. The primary outcome measure was the average co-contraction over flexion and extension compared between children with dystonia and controls. Secondary measures included analysis of EMG activation levels during individual (acceleration/deceleration and pause) phases, the duration of complete movement cycles and of each phase, the flexion/extension velocity peaks, the maximum elbow rotation, and the coefficient of variation for each of these measures.

Results

Preliminary statistical tests

We performed a set of preliminary analyses to determine the significance of differences between the two arms (more vs. less impaired for the children with dystonia; dominant vs. non-dominant for the controls). Using observations on both arms, we ran a one way repeated measures MANOVA on the duration of the cycle of movement (flexion/extension) and its variability (CV) that included group and arm as between and within subject factors. For the children with dystonia, we opposed the less impaired to the most impaired limb, and for the healthy controls we contrasted the dominant to the non-dominant arm. (The subject with dystonia (subject 5) for whom data from only the right arm was available was excluded from this part of the analysis.) As expected, the children with dystonia showed longer and more variable cycle duration than the healthy subjects [Wilks' Lambda, $F(2,10) = 11.37$, $P = 0.0027$]. Associated univariate tests revealed that the two groups differed the most in their degree of variability [$F(1,11) = 23.34$, $P = 0.0005$, for CV of cycle duration; and $F(1,11) = 4.63$, $P = 0.0546$, for cycle duration]. There was an interaction between arm and group [Wilks' Lambda, $F(2,10) = 6.43$, $P = 0.0160$; univariate tests: $F(1,11) = 5.39$, $P = 0.0405$, for duration; and $F(1,11) = 8.36$, $P = 0.0147$, for CV], suggesting a different effect of changing the arm on performance of the subjects with and without dystonia. Complementary univariate repeated measures ANOVAs were run whose post-hoc comparisons showed that subjects with dystonia were significantly slower and more variable with the most impaired arm than with the less impaired one (for cycle duration: 1.991 ± 0.241 (mean ± SE) vs. 1.570 ± 0.246 s, $P = 0.0098$; for CV of cycle duration: 0.213 ± 0.01 vs. $0.134 \pm 0.01\%$; $P = 0.0010$) while the controls performed comparably well with the dominant and non-dominant arm (for cycle duration: 1.011 ± 0.147 vs. 1.020 ± 0.104 s, $P = 0.9416$; for CV of cycle duration: 0.087 ± 0.008 vs. $0.084 \pm 0.007\%$; $P = 0.8690$). In order to evaluate the effects of dystonic compared with unimpaired arms, analyses will focus on comparisons between data collected on the most impaired arm of the subjects with dystonia and observations on the dominant arm of the healthy subjects (for subject 5, we used the data collected on the less impaired arm). In this way we hope to accentuate the magnitude of any differences between dystonic and control subjects.

Given the fact that our subjects were seated unrestrained (which was necessitated by the abnormal truncal postures in some children with dystonia), and thus had the possibility to move their trunk toward the distal target, a necessary preliminary was to ensure that reaches by subjects of both groups involved comparable elbow excursions. Rotation amplitude was 87.78 ± 5.91° (mean ± SE) for the subjects with dystonia and 92.39 ± 4.79° for the controls, and rotation amplitude CV was 15.9 ± 2.8% for subjects with dystonia and 11.4 ± 2.7% for the healthy subjects; these values were not significantly different [mutivariate test: Wilks' Lambda, $F(2,11) = 0.61$, $P = 0.5632$; univariate tests: $F(1,12) = 0.37$, $P = 0.5552$, for amplitude; $F(1,12) = 1.31$, $P = 0.2741$, for CV of amplitude].

Analysis of kinematics

We compared the two groups of subjects on the duration of the movement cycles and the maximum angular elbow velocities reached during flexion and extension, whose means (± SE) are presented in Fig. 3a. A one way MANOVA on these three variables was not significant [Wilks' Lambda, $F(3,10) = 2.02$, $P = 0.1754$], but univariate analyses showed that while the subjects with dystonia performed movement cycles of longer duration than the controls [$F(1,12) = 5.85$, $P = 0.0323$], the maximum elbow velocities they reached during flexion and extension were not reliably lower [$F(1,12) = 3.06$, $P = 0.1056$, for flexion; $F(1,12) = 1.35$, $P = 0.2680$, for extension]. This is easily explained when one examines the velocity profiles that characterized the reaching cycles by the children with dystonia. As an example, Fig. 1a and c shows the elbow angular velocity traces for trials by a single subject with dystonia (subject 3); one may see how this subject pauses at targets before reversing movement direction. In contrast, smooth transition between flexion and extension was typically observed in the healthy children; as illustrated in Fig. 2a that shows velocity profiles for individual trials by a representative control subject. In fact, the difference in movement duration between groups did not remain significant after subtracting the pauses at the targets from the movement durations of the children with dystonia [$t(12) = 0.57$, $P = 0.577$]. Duration of the pauses was 0.358 ± 0.104 s (mean ± SE) at the distal and 0.336 ± 0.062 s at the proximal targets.

Analysis of kinematic variability

The mean values (± SE) of the CV for the duration of the movement cycles as well as for the maximum angular elbow velocities reached during flexion and extension are shown in Fig. 3b. A one way MANOVA on these variables showed that the subjects with dystonia exhibited substantially increased variability relative to

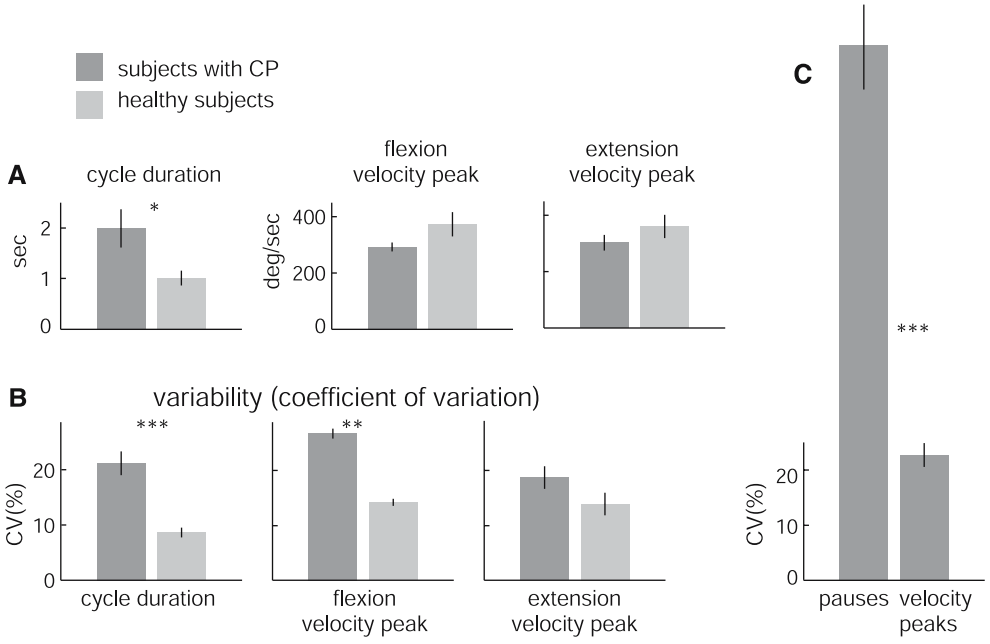

Fig. 3 Kinematic and kinematic variability measures for the two groups of subjects. **a** From left to right, means (± SE) across subjects for duration of the complete flexion/extension movement cycles, and flexion and extension velocity peaks. **b** From *left to right*, coefficients of variation (*CV*) for complete movement duration and for flexion and extension velocity peaks. **c** CV for the duration of pauses and the magnitude of velocity peaks during flexion and extension (*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$)

the controls [Wilks' Lambda, $F(3,10) = 8.30$, $P = 0.0046$]. Univariate tests revealed further that this group effect was mostly due to differences in cycle duration variability [$F(1,12) = 28.90$, $P = 0.0002$]. In fact, while the velocities reached by the subjects with dystonia were more variable than those reached by the controls during the flexion phase [$F(1,12) = 11.93$, $P = 0.0048$], both groups exhibited comparable level of variability during the extension phase [$F(1,12) = 2.75$, $P = 0.1230$]. For the children with dystonia, a comparison between CV of pauses and CV of velocity peaks—whose mean values are presented in Fig. 3c—showed that these subjects were substantially more variable in the duration of the pauses they observed at targets than in the velocity peaks they reached [repeated measures ANOVA, $F(1,6) = 39.96$, $P = 0.0007$], suggesting that much of the variability in cycle duration was due to variability in the duration of pauses at the targets.

Analysis of EMG

The patterns of EMG activities underlying the differences between subjects with dystonia and controls were examined using three different measures. To assess the level of antagonist muscle co-activation, we used DOT and MIN (see Methods); and to describe EMG activity modulation across reaching cycles, we used the average EMG amplitude observed for each muscle during each movement phase.

Unexpectedly, reaches by the children with dystonia were associated with lower levels of co-contraction than those executed by the healthy subjects. This occurred despite the visual observation of dystonia during reaching in all subjects with dystonia. Figure 4 presents the average level of co-contraction (MIN measure) for flexion and extension phases for both dystonia and control groups. Repeated measures MANOVA performed separately on the DOT and MIN measures of co-contraction as dependent variables, with group (dystonia vs. control; between subject variable) and direction of elbow rotation (flexion vs. extension; within subject variable) as independent variables, showed that the lower level of co-contraction in the subjects with dystonia was significant for both measures of co-contraction [Wilks' Lambda, $F(2,11) = 4.72$, $P = 0.0332$, univariate tests: $F(1,12) = 9.85$, $P = 0.0085$ for DOT; $F(1,12) = 7.84$, $P = 0.0161$ for MIN]. There was no significant main effect of rotation direction [Wilks' Lambda, $F(2,11) = 1.38$, $P = 0.2911$] nor a significant interaction effect [Wilks' Lambda, $F(2,11) = 0.13$, $P = 0.8787$].

In order to obtain a better understanding of the patterns of muscle activation that characterized the subjects of the two groups, we examined the average level of EMG of each muscle for each reaching phase. Figure 5a and b show the means (± SE) for the children with dystonia and the healthy controls, respectively. We performed separate repeated measures ANOVA on biceps and triceps EMG with group and movement phase as between and within subject factors. For the biceps muscles, there was a significant main effect of group: control subjects exhibited globally higher level of EMG activities than subjects with dystonia [$F(1,12) = 13.96$, $P = 0.0028$]. However, there was also a significant main effect of movement phase $F(3,12) = 5.43$, $P = 0.0136$) and a reliable effect of interaction between group and movement phase [$F(3,12) = 3.66$, $P = 0.0442$]. Post-hoc contrasts revealed that the differences between groups were reliable during extension only; that is, when the biceps acts as antagonist ($P > 0.05$ for flexion acceleration and deceleration; $P = 0.0031$, and 0.0123, for extension acceleration and deceleration). For the triceps muscles, controls and subjects with dystonia exhibited levels of EMG activity that were globally comparable [No significant main effect of group; $F(1,12) = 0.27$, $P = 0.6149$], but again a significant effect of interaction was present [$F(3,12) = 5.42$, $P = 0.0137$]; post-hoc comparisons showed reliably higher activation in healthy subjects during flexion deceleration [$P = 0.0005$ for flexion acceleration; $P > 0.05$ for all other contrasts] when triceps muscles intervene to brake the movement. Therefore the pattern of muscle activation during flexion and extension was different between subjects with dystonia and controls. We can gain further insight by examination of Fig. 5. While for the control subjects activity in the agonist muscles starts high to initiate movement and then drops down during the deceleration phase ($P = 0.0037$, for biceps; this tendency did not reach statistical significance for the triceps muscle), for subjects with dystonia the EMG activities in biceps (during flexion) and triceps (during

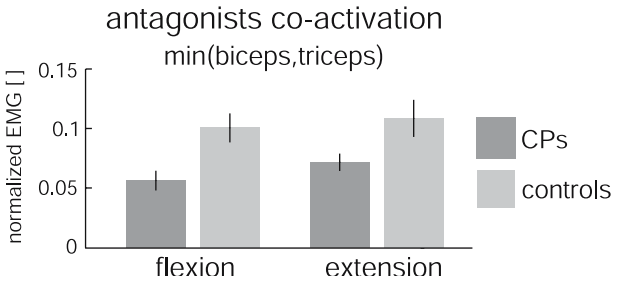

Fig. 4 For both groups, means (± SE) across subjects of biceps and triceps muscle co-activation levels (MIN measure, see Methods) during the flexion (*left*) and extension (*right*) movement phases

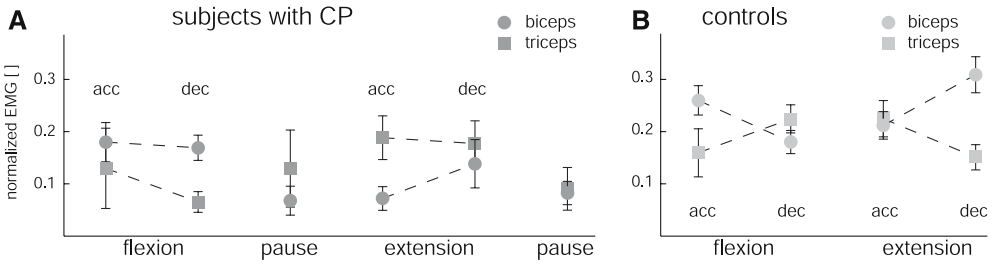

Fig. 5 EMG activity levels throughout the different movement phases for both groups of subjects; clearly different muscle activation patterns were observed for the two groups of subjects. **a**, **b** Means (± SE) of the EMG activity levels for the children with dystonia and the control subjects, respectively

extension) stay essentially at the same level throughout the acceleration and deceleration phases ($P > 0.05$, for both muscles). Thus subjects with dystonia did not exhibit the same degree of modulation of muscle activity as seen in the controls.

Note that—in contrast to the control subjects—in children with dystonia the relative activity of the biceps and triceps muscles was different at the end of flexion and the beginning of extension, as well as at the end of extension and the beginning of flexion. Thus the subjects with dystonia did not demonstrate a smooth transition from the end of the extension phase to the beginning of the flexion phase. We conjecture that the pause may in part be necessary in order to "reset" the muscle activities prior to the next movement.

Finally, we looked at the relation between our kinematic and EMG measures and the severity of symptoms for the children with dystonia. As expected from the finding that co-contraction is greater in the control subjects, there was no significant correlation in the subjects with dystonia between co-contraction and severity of dystonia (MIN measure against BFM: corr = 0.2008, $P = 0.6659$; UDRS: corr = 0.2312, $P = 0.6179$; BAD: corr = 0.4376, $P = 0.3260$). Correlations were much higher with the duration of the pauses, and approached but did not reach significance (duration of pauses and BFM: corr = 0.6378, $P = 0.1232$; UDRS: corr = 0.7100, $P = 0.0738$; BAD: corr = 0.5743, $P = 0.1774$). We suspect that with a larger number of subjects this latter correlation would achieve significance.

Discussion

We examined unconstrained reaching movements by children with primary and secondary dystonia. We described the kinematics of elbow movement and the surface EMG activity in the biceps and triceps. As expected, the analysis of kinematics showed increased movement duration and increased variability in movement duration in the children with dystonia compared to control subjects. However, the increased duration of the reaching cycles by the children with dystonia was mostly due to extensive pauses that these subjects exhibited at targets, rather than to reduced elbow rotation velocities. The increased variability was mostly due to variability in the duration of the pauses.

We assessed if the abnormalities observed in the children with dystonia could be explained in terms of inappropriate antagonist muscle activation. Unexpectedly, we found that children with dystonia showed lower levels of co-contraction than healthy controls during movement. Moreover, the pauses at the targets that characterized the reaching cycles by the subjects with dystonia were associated with low levels of muscle activation, rather than co-contraction. Examination of the EMG patterns throughout the complete movement cycle indicated that the delays observed by subjects with dystonia between movements in opposite directions seem to arise as a consequence of deficient patterns of agonist/antagonist muscle activation. Specifically, in these children activation of the agonist muscle remained inappropriately constant throughout elbow displacement, and EMG activity in the antagonist muscle was not properly built up in order to slow elbow rotation and prepare for smooth movement reversal. As a consequence, erratic elbow trajectories were observed at the end of movement and the pauses at targets could be explained by a necessity for the system to "reset" EMG activity prior to reversal of movement direction.

Since basal ganglia have been implicated in deficits of timing and muscle activation as well as in abnormalities of motor pattern, our results are consistent with the hypothesis of deficits of basal ganglia function in children with dystonia. However, brain injury in secondary dystonia may be widespread, and we cannot exclude the possibility that our findings are due to a combination of motor deficits, including dystonia, bradykinesia, choreoathetosis, weakness, or spasticity. Extensive pauses have been described in adult patients with hand

dystonia performing repetitive finger flexion/extension movements (Curra et al. 2004). But in contrast to what we observed in children with dystonia (for whom the peak velocity during movement was not significantly different from controls), the adult patients also showed bradykinesia (Curra et al. 2000). Movement "fragmentation" is not a feature that is specific to dystonia and can also be observed, for instance, in developing infants (von Hofsten 1991) or in patients following stroke (Krebs et al. 1999). Furthermore, the gradual blending of submovements observed during development or during stroke recovery has been interpreted as evidence that complex movements are composed of discrete ballistic movements (Rohrer et al. 2002).

In contrast with this hypothesis, other recent findings point to the idea that rhythmic arm movement may be fundamentally different from discrete arm movements (Schaal et al. 2004). In the present context, further work would be needed to determine if the pauses exhibited by the subjects with dystonia are symptomatic of complex movement fragmentation or whether they reveal fundamental differences in the movement strategy adopted by the children with dystonia relative to healthy subjects. For example, children with dystonia might select (perhaps involuntarily) a strategy that includes sequential discrete reaching movements rather than smooth rhythmic movements. Since the subjects with dystonia and the control subjects used a fundamentally different type of trajectory of movement, our results need to be interpreted with caution since the differences in EMG may be partly explained by differences in the type of movement. This possibility does not weaken our main finding of decreased co-contraction in dystonia, but it does suggest that decreased co-contraction could be at least partly due to differences in the choice of trajectory rather than to differences in the activation of muscles for the same trajectory. Further study of this question will require experiments in which both groups of subjects are required to perform point-to-point movements with similar movement trajectories, in order to match the kinematic and dynamic properties of the movements as well as possible.

In agreement with the reduced co-contraction shown in our results, MacKinnon and co-workers (2004) reported that in ballistic wrist movements, prolonged agonist activation with co-contraction of the antagonist muscle could also be observed in healthy controls and therefore was not a feature specific to their adult patients with primary dystonia (who in fact exhibited deficits in muscle activation after movement onset rather than increased EMG activity). In the present study, the high levels of co-contraction that could be observed in controls—as illustrated in Fig. 2a—may have been a consequence of the biomechanical requirements of the task we used. In order to achieve smooth and rapid transitions between elbow rotations in opposite directions, the healthy subjects maintained high levels of activation in both agonist and antagonist groups of muscles throughout the series of repetitive reaching movements. The function of muscles controlling the elbow may have been to stabilize against interaction torques, while it is possible that shoulder muscles were the primary drivers of movement. When one examines Fig. 5, this seems to be especially true for the extension phase where rotation of the elbow might have been mostly determined by shoulder muscle contraction, while the biceps may have intervened essentially in order to achieve stabilization of the limb at the endpoint.

This study has several important weaknesses. In an attempt to characterize movement abnormalities in both primary and secondary dystonia, we included children from both groups and a large range of ages. However, the small total number of subjects does not allow comparison between groups, nor do we have adequate subjects to determine the effects of age. The study subjects were homogeneous in the sense of having the *symptom* of dystonia, but they were heterogeneous in terms of etiology. Although there was no significant difference in peak velocity between children with dystonia and control subjects, we did not attempt to match other features of the trajectory such as acceleration profiles or hand path, and it is thus possible that the increased co-contraction in the controls was due to the details of their movement trajectories. (For example, since children with dystonia moved more slowly, it is possible that this reduced the need to counteract elbow interaction torque generated by shoulder movement.) This possibility does not weaken our conclusion (that co-contraction was *not* significant in the children with dystonia) but it suggests that future studies should attempt to match the kinematic features of movement as much as possible. Despite these weaknesses, we feel that this study yields an important initial insight into the control of muscles during movement in children with dystonia. Although co-contraction may be present in certain adult dystonias and it may be present during static postures in children with dystonia, it may not be a dominant feature of active movement in children with dystonia.

In summary, in the present study, much of the variability in the elbow kinematics in the children with dystonia could be explained by abnormalities of the timing of sub-movements. Further, movement timing variability was mostly unrelated to variability in the transport phase, but instead was related to difficulty in reversing movement direction. The prolonged pauses observed

at targets did not appear to be associated with inappropriate co-contraction of antagonistic groups of muscles. Children with dystonia did not show higher levels of co-contraction relative to the healthy children. Therefore we conclude that co-contraction may not be a major cause of movement abnormality during unconstrained reaching in childhood dystonia.

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