Arm Trajectories in Dyskinetic Cerebral Palsy Have Increased Random Variability
Terence D. Sanger

J Child Neurol 2006 21: 551
DOI: 10.1177/08830738060210070201

The online version of this article can be found at:
http://jcn.sagepub.com/content/21/7/551

Published by:
SAGE
http://www.sagepublications.com

Additional services and information for Journal of Child Neurology can be found at:

Email Alerts: http://jcn.sagepub.com/cgi/alerts

Subscriptions: http://jcn.sagepub.com/subscriptions

Reprints: http://www.sagepub.com/journalsReprints.nav

Permissions: http://www.sagepub.com/journalsPermissions.nav

Citations: http://jcn.sagepub.com/content/21/7/551.refs.html
Arm Trajectories in Dyskinetic Cerebral Palsy Have Increased Random Variability

Terence D. Sanger, MD, PhD

ABSTRACT

Dyskinetic cerebral palsy results from injury to the basal ganglia early in life. Symptoms can include hyperkinetic or dystonic arm movements that impair function. It is not known whether these movements comprise a small number of specific abnormal motor patterns or whether they are random and variable. We hypothesize that injury to the basal ganglia leads to impaired filtering and removal of undesired neural signals and that lack of appropriate removal of noisy or irrelevant neural signals leads to random and variable arm movements. To test this hypothesis, we quantified the variability in arm trajectories while seven children with dyskinetic cerebral palsy between the ages of 4 and 13 years old made repeated outward reaching movements. We compared the results with those of 21 healthy children between the ages of 5 and 16 years. The best-fit trajectory to the set of reaching movements for each child was taken as the predictable component of movement. We calculated the ratio of the power in the best-fit trajectory to the total variance. This measure is the signal-to-noise ratio, and it quantifies the extent to which trajectories are predictable. We found that children with dyskinetic cerebral palsy had a significantly reduced signal-to-noise ratio compared with healthy children at similar ages. This result shows that there is increased movement variability, and it is consistent with the hypothesis that inadequate removal of noisy signals could be a cause of the movement disorder in dyskinetic cerebral palsy. (J Child Neurol 2006;21:551–557; DOI 10.2310/7010.2006.00113).

Dyskinetic cerebral palsy accounts for approximately 10% of cases of cerebral palsy,\textsuperscript{1–3} therefore, dyskinetic cerebral palsy has a total incidence of 0.15 to 0.25 per 1000 in Western countries.\textsuperscript{4} Abnormal upper extremity movements are a disabling and poorly understood symptom of this disorder. A characteristic feature is excessive movement of multiple joints during attempts at reaching. Reaching can overshoot or undershoot the target, and the required hand shape and endpoint force can be poorly controlled.\textsuperscript{5,6} Distal hand or finger movements are often seen mirrored by the contralateral hand, and complex movements of one hand can accentuate dystonic posturing of the opposite arm.\textsuperscript{7,8}

Mink proposed that the basal ganglia can serve an important function in the selection of desired movements and inhibition of undesired movements.\textsuperscript{9} Based on this theory, we expect that basal ganglia dysfunction could lead to difficulty in selecting an appropriate movement or to an inability to suppress unwanted components of movement. We hypothesize that the latter dysfunction causes the abnormal movements in dyskinetic cerebral palsy. If this is the case, then we expect hyperkinetic movements to exhibit high variability owing to the lack of suppression of unwanted, varying, and irrelevant neural activity. On the other hand, if dyskinetic movements are due to planning or selection of an inappropriate movement pattern, then we would instead expect low variability with a consistent and predictably incorrect trajectory.

To test the hypothesis that dyskinetic movements are variable owing to unwanted and random movement components rather than to repeated and predictable abnormal trajectories, we recorded the joint angles of the upper extremity while 7 children with dyskinetic cerebral palsy and 21 control subjects of similar ages performed unconstrained outward reaching movements. We used principal component analysis to analyze the variability in the trajectories for each subject. Principal component analysis has been used to analyze predictable components of movements in healthy subjects,\textsuperscript{10} but it has not
been applied in dystonia. We calculated the signal-to-noise ratio as an indication of the repeatability of each child’s set of movements. The more predictable and repeatable the movements, the higher the signal-to-noise will be.

We compared the signal to noise ratio at different ages between children with dyskinetic cerebral palsy and healthy children. If the hypothesis is correct, then we predict a lower signal-to-noise ratio in children with dyskinetic cerebral palsy. If the hypothesis is incorrect, then the signal-to-noise ratio will not be different, indicating that there is no additional variability despite the abnormal patterns of movement.

There have been no previous studies of the kinematics of arm movements in dyskinetic cerebral palsy. Most studies of the kinematics of children with cerebral palsy have been performed in the lower extremity with the intent of understanding and improving ambulatory function. With few exceptions, studies of upper extremity function have mostly been limited to constrained single-joint movement. In general, healthy children increase the smoothness of movements with training, and patterns of reaching movements become more stereotyped and increasingly energetically efficient for a particular task. Previous work has shown that measurement of total jerk (the third derivative of position), average curvature, variability, endpoint accuracy, interjoint coordination, prehension, and prediction of joint interaction torques can be used to differentiate between control subjects and adults or children with a variety of neurologic disabilities, including cerebral palsy. Down syndrome, cerebellar ataxia, and hemiplegia.

METHODS

Seven children aged 4 to 13 years (mean 9.7 years, SD 3.1 years) with dyskinetic cerebral palsy were recruited from the child movement disorders clinic at our institution. Twenty-one control subjects aged 5 to 16 years (mean 10.2 years, SD 3.1 years) without motor disorders were recruited from a convenience sample of children known to the investigator. Informed consent was obtained from parents according to the Health Information Portability and Accountability Act. The clinical features of the children with dyskinetic cerebral palsy are summarized in Table 1. All subjects were rated at the time of testing on the upper extremity subscales of the Burke-Fahn-Marsden Dystonia Rating Scale (BFM), the Barry-Albright Dystonia Scale (BAD), and the Unified Dystonia Rating Scale (UDRS). The mean product of the provoking and severity factors on the Burke-Fahn Marsden scale was 6.8 (SD 5.1), on the mean Barry-Albright dystonia scale was 2.5 (SD 1.3), and on the mean Unified Dystonia Rating Scale was 7.5 (SD 5.0). At the time of testing, subject 3 was taking trihexyphenidyl and baclofen, subject 4 was taking carbachol, and subject 6 was taking trihexyphenidyl and levodopa. The remaining subjects were on no medications.

Subjects were seated comfortably and unrestrained in a nonmetallic chair. Magnetic position sensors (Polhemus Inc., Colchester VT) were attached using either Velcro straps or medical-grade adhesive to 8 points on the body: the midshaft of each upper arm, the dorsum of each distal forearm between the radius and ulna, the dorsum of each hand over the midshaft of the third metacarpal bone, the back over the first or second thoracic vertebra, and the forehead 1 to 3 cm above the nasion 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., Phoenix AZ). Movement data were recorded from each sensor sampled at 120 Hz and filtered with a digital low-pass filter (6 dB cutoff at 20 Hz) and then stored in a microcomputer for later off-line analysis. Subsequent reconstruction using inverse kinematics algorithms in the commercial software yielded measurements of angular velocities for seven axes of rotation about three joints for each arm: three components of shoulder movement (extension/flexion, abduction/adduction, and rotation), one component of elbow movement (extension/flexion), and three components of wrist movement (extension/flexion, rotation, medial/lateral deviation).

During data acquisition, movements were videotaped and the output from the video camera was fed to a microcomputer for real-time digitization and image compression. Video and kinematic data were synchronized through the use of a commercial timecode generator (Horita Inc., Mission Viejo, CA), and synchronization was confirmed using a custom-built digital counter whose display was visible to the video camera.

During preliminary testing, it became apparent that the more severely affected subjects were unable to make accurate reaching movements that resulted in reliable contact with a fixed target, and not all subjects could reach to full extension of their arm. Attempts to contact a small target or to reach to full extension significantly worsened dyskinesia in some subjects. From related experiments, we found that

<table>
<thead>
<tr>
<th>ID</th>
<th>Age</th>
<th>Sex</th>
<th>Right</th>
<th>Left</th>
<th>Right</th>
<th>Left</th>
<th>Right</th>
<th>Left</th>
<th>Diagnosis</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>F</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>Prematurity with perinatal intraventricular hemorrhage</td>
<td>Bilateral arm dystonia and leg spasticity</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>F</td>
<td>2</td>
<td>0</td>
<td>1.5</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>Nonprogressive hemidystonia</td>
<td>Right foot and hand dystonia</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>M</td>
<td>4</td>
<td>9</td>
<td>6</td>
<td>10</td>
<td>2</td>
<td>3</td>
<td>Prematurity with perinatal intraventricular hemorrhage</td>
<td>Left &gt; right arm dystonia and leg spasticity</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>F</td>
<td>9</td>
<td>16</td>
<td>11</td>
<td>15</td>
<td>3</td>
<td>4</td>
<td>Perinatal hypoxic injury</td>
<td>Generalized dystonia and choreoathetosis</td>
</tr>
<tr>
<td>5</td>
<td>11</td>
<td>M</td>
<td>16</td>
<td>9</td>
<td>11.5</td>
<td>11</td>
<td>4</td>
<td>4</td>
<td>Perinatal hypoxic injury</td>
<td>Generalized dystonia and choreoathetosis</td>
</tr>
<tr>
<td>6</td>
<td>13</td>
<td>M</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>Perinatal hypoxic injury</td>
<td>Mild generalized dystonia and writer’s cramp</td>
</tr>
<tr>
<td>7</td>
<td>13</td>
<td>F</td>
<td>9</td>
<td>9</td>
<td>13</td>
<td>12</td>
<td>4</td>
<td>3</td>
<td>Perinatal hypoxic injury</td>
<td>Generalized dystonia and choreoathetosis</td>
</tr>
</tbody>
</table>

BFM = Burke-Fahn-Marsden Dystonia Rating Scale; BAD = Barry-Albright Dystonia Scale; UDRS = Unified Dystonia Rating Scale.
there is a speed-accuracy trade-off, so that speed of movement varies significantly with target size.\textsuperscript{48} The magnitude of this effect is different for different children. Therefore, to reduce the effect of target size on variability, we chose to examine the quality of outward reaching movements without requiring subjects to contact the target and without specifying a required accuracy. We use the “finger-to-nose” reaching task commonly performed during routine neurologic evaluation because this task can be performed by all subjects and results in reliable attempts at outward reaching. This task is also a common and functionally relevant movement involved with reaching to grasp an object, self-feeding, and use of communication devices or other electronic controls. However, owing to the child’s own head movements and possible motion of the target, some additional variability could be introduced. We attempt to compensate for such variability in the analysis (see below).

Children were asked to use a single finger to alternately touch their nose and a target placed directly in front of the child at the level of the nose and at full arms-length distance. (The target was usually the examiner’s fingertip, but an equivalent-sized target on a small toy was used for the youngest subject, 1.) No measure of success or failure was given, although children were asked to perform the task “as fast as possible without missing.” Each child performed 40 complete back-and-forth cycles with each hand (subject 5 was able to complete the task only on the left side owing to severe dystonia in the right arm; the left hand of subject 2 was unaffected and was not analyzed). Only the data from outward reaches (starting at the nose and finishing at the target) were used in the analysis.

Following data acquisition, a three-dimensional graphic reconstruction of the kinematic data mapped onto an appropriately sized upper body skeleton model was displayed simultaneously with the time-synchronized video images and a plot of the radial component of the hand velocity (custom software). Outward reaches were identified on the video, and data between successive zeros of the radial hand velocity were saved for further analysis.

Numeric analysis was performed using Matlab, version 6.5, and the Matlab statistics toolbox (Mathworks Inc., Natick MA). Children at different ages are expected to have different maximal distances and velocities of reaching,\textsuperscript{43,44} so all trajectories were scaled to the same distance and average speed. For each subject, data from the left and right hands were grouped separately, and the velocity trace of each reach was spline-interpolated and resampled to exactly 120 time points (interp1() function in Matlab). The magnitude of each point in the resampled velocity data was multiplied by the ratio of total movement time (seconds) to total movement distance (centimeters).

Movement of the start position (the subject’s nose) or the end position (the examiner’s finger or target) could potentially introduce additional variation into the trajectories owing to a change in the straight-line path between start and end points. As long as the target remains in front of the child, a change in target direction will require only a constant offset in the shoulder angle, but it will not result in a change in shoulder angular velocity and therefore will not affect subsequent calculations. A change in target distance will require a decrease in magnitude of elbow extension, but this is unlikely because full arm extension was required on every reach. Movement of the target during the reach will introduce a constant offset into the velocity profile that could be different between successive reaches. To eliminate this effect, the mean of the joint angular velocity for each reach was subtracted from each joint angle prior to further calculations. We are not able to eliminate other possible effects, such as changes in trajectory shape as a function of target position or different effects of gravity for different movement directions. However, these effects are expected to be small, and they were not seen in the normal subjects. From visual review of videotapes of the testing, the target position did not move more than a few centimeters in any direction.

Acceleration and jerk were calculated by numeric differentiation.

For each subject, after trajectory data had been scaled to a fixed distance and average speed, the reaches for each hand were aligned in time on the position of the peak of the radial (outward) component of hand velocity. For each movement, a single vector containing the time series of all seven joint angles was constructed. For each subject, the covariance matrix of the joint angle vectors was calculated (cov() function in Matlab) and principal components were extracted (eig() function in Matlab). By its definition, the first principal component is the single time series of joint angles that is the best linear approximation to the complete set of joint-angle time series. The remaining principal components describe the dimensions of variability deviating from the best approximation. The percentage of the total movement variance that could be accounted for by the first principal component was calculated as the ratio of the first eigenvalue to the sum of the remaining eigenvalues. Since this ratio reflects the ratio of the power in the best-fit trajectory to the power owing to variability in the trajectory, we label it the signal-to-noise ratio. If a trajectory is reliably repeated, no matter how complicated, it will have a very high signal-to-noise ratio. Conversely, if movements are generated entirely by random noise, then all principal components will have the same variance (equivalently, the eigenvalues will all be equal) and the signal-to-noise ratio will be equal to one divided by the number of components.

For each subject, the ratio of the total hand path length (in three cartesian dimensions of hand position) to the straight-line distance from the initial point to the end point was calculated for each trajectory and the mean over all trajectories was taken as the index of curvature.\textsuperscript{51,52} Index of curvature and jerk are measures of the complexity of the trajectory, but they do not measure variability.

Statistical tests include linear regression of signal-to-noise ratio, jerk, and index of curvature on subject age for control subjects, and one-way analysis of variance (ANOVA) comparison between subjects with dyskinetic cerebral palsy and controls for signal-to-noise ratio, jerk, and index of curvature corrected for regression on age. Pairwise comparison of the signal-to-noise ratio was also performed by a one-way t-test between subjects with dyskinetic cerebral palsy and an age-matched subset of the controls (age-matching performed using the nearest best match). Linear regression of the upper extremity subscores of the Burke-Fahn-Marsden Dystonia Rating Scale,\textsuperscript{45} the Barry-Albright Dystonia Scale,\textsuperscript{46} and the Unified Dystonia Rating Scale\textsuperscript{47} were performed with age and either signal-to-noise ratio, jerk, or index of curvature as independent variables.

In preliminary analyses of the control subjects, no significant group or pairwise difference was found between left and right hands; therefore, statistics were also calculated from left- and right-hand movements...
combined. The level of significance for all statistical tests was set at $P < .05$, corrected for multiple comparisons (Bonferroni method).

RESULTS

Figure 1 shows example hand trajectories in the sagittal plane for three control subjects and three children with dyskinetic cerebral palsy. Increased variability and a lack of straight-line trajectories are evident for the children with cerebral palsy.

Regression of signal-to-noise ratio, jerk, and index of curvature on age for the control subjects is significant, although it accounts for only a small amount of the total variance (signal-to-noise ratio: $r = .41$, $P = .008$, 95% confidence interval for the slope = 0.10 to 0.64; jerk: $r = .57$, $P = .0001$, 95% confidence interval = $-0.01$ to $-0.05$; index of curvature: $r = .56$, $P = .0001$, 95% confidence interval = $-0.006$ to $-0.002$). Therefore, one-way ANOVA comparing signal-to-noise ratio, jerk, and index of curvature between controls and children with cerebral palsy was performed after linear correction for age.

Figure 2 shows plots of the first 10 principal components for each individual subject. The signal-to-noise ratio is calculated as the ratio of the first component to the sum of the remaining components. The mean signal-to-noise ratio for controls is 6.4 (SD 2.8) and for subjects with cerebral palsy is 2.7 (SD 2.5). ANOVA comparison of the signal-to-noise ratio following age correction between children with cerebral palsy and the full set of controls is significant for both hands combined ($F = 17.3$, $P = .0001$) and for right ($F = 4.3$, $P = .049$) and left ($F = 14.1$, $P = .001$) hands individually. Pairwise one-way $t$-test comparison of the signal to noise ratio (without age correction) between children with cerebral palsy and an age-matched subset of controls is significant for both hands combined ($P < .0002$) and right ($P < .03$) and left ($P < .0006$) hands individually.

Mean jerk is 0.22 (SD 0.05) for controls and 0.59 (SD 0.63) for children with cerebral palsy. ANOVA comparison of jerk after correction for age is significant ($F = 13.22$, $P < .0007$). Mean index of curvature is 1.46 (SD 0.02) for controls and 1.73 (SD 0.52) for children with cerebral palsy. ANOVA comparison of index of curvature after correction for age is significant ($F = 11.63$, $P < .002$). All three comparisons remain significant after Bonferroni correction.

Linear regression of the Burke-Fahn-Marsden and Barry-Albright dystonia rating scales on signal-to-noise ratio was not significant after correction for age and multiple comparisons. Regression of the Unified Dystonia Rating Scale on the signal-to-noise ratio was significant (slope = $-1.24$, 95% confidence...

Figure 1. Example hand trajectories in the x-z (sagittal) plane of movement. Left column: control subjects (ages from top to bottom: 7, 10, 16 years); right column: subjects with dyskinetic cerebral palsy (numbers 4, 5, and 7).
interval = −2.1 to −0.39, r = 0.82, P < .004), and a plot of the data is shown in Figure 3.

**DISCUSSION**

These results confirm the prediction of increased variability in the arm trajectories of children with dyskinetic cerebral palsy. This finding is consistent with the hypothesis that an inability to remove unwanted and variable components of movement might underlie the movement disorder. It is not consistent with the alternate hypotheses that the movement disorder is due to inappropriate selection or planning of an incorrect trajectory or that it is due to fixed dystonic postures. The results do not exclude the possibility that the increased variability might be at least partly due to compensatory movements, although it would remain difficult to explain the lack of repeatability unless the compensatory movements were themselves random.

These results show that measures of signal-to-noise ratio, jerk, and index of curvature can distinguish between unaffected children and children with dyskinetic cerebral palsy. Further, the signal-to-noise ratio is inversely correlated with the Unified Dystonia Rating Scale. Although distinction of dyskinetic cerebral palsy from normal movement is not difficult, the results do suggest the possibility of a quantitative measure of severity. Validation of such a measure will require a significantly larger sample of affected children.

We cannot determine the origin of the variability in the arm trajectories. One possibility is that there is an inability to remove unwanted noise components, as illustrated in Figure 4. The noise might reflect unrelated neural activity, perhaps owing to irrelevant sensory input. The unwanted components could also be due to a “noise generator” that is injecting a new or increased source of noise. We cannot determine whether the variability is due to basal ganglia injury or perhaps to injury to other motor structures, including the cerebellum or brain stem.

Three different clinical rating scales were tested, but only the Unified Dystonia Rating Scale showed a significant regression on the signal-to-noise ratio. One possible explanation for this is that the Unified Dystonia Rating Scale is particularly sensitive to hyperkinetic movements, whereas the Burke-Fahn-Marsden and Barry-Albright dystonia scales are more likely to be sensitive to hypertonic symptoms. Since the study population included several children with hyperkinetic symptoms, this is reflected by the greater variance in the Unified Dystonia Rating Scale scores, and this greater variance likely contributed to the significance of the regression. Although dyskinetic cerebral palsy traditionally includes both hyperkinetic and dystonic symptoms, it is not known whether these two types of symptoms are, in fact, distinguishable or whether they represent different variations of a single underlying movement disorder.

The design of this experiment suffers from several weaknesses that are imposed by the necessity to study children at a variety of ages, cognitive abilities, and motor abilities. The younger children would not tolerate being strapped to the examining chair, and any attempt at restraint could worsen dystonia. Nevertheless, the lack of trunk support for some of the children might have modified the reaching movements. In addition, there is an increased use of trunk movement during reaching in younger children, and this could artificially decrease the maximum distance, joint excursion, and velocity at the elbow and shoulder joints. It would have been preferable to have fixed start and end targets rather than using the child’s nose and the examiner’s finger, but several of the subjects had great difficulty contacting button targets. Thus, we opted to use a task that encourages outward reaching without requiring accuracy. It would have been preferable to have children move at a fixed average velocity by timing movements to a metronome, but most of the children would be unable to perform a timed movement task with regularity. It would have been preferable to have confined movements to a single plane or perhaps rotation about only one or two joint axes, but dystonia often makes any form of arm restraint impossible. It would be helpful to test arm movements with the eyes closed to eliminate the effect of visual feedback, but potential variation in proprioceptive sensitivity...
would then be likely to influence the results. Despite these weaknesses, the experimental design captures many of the features of unconstrained reaching movements in the child’s natural environment, and the results will therefore be an accurate representation of the effect of dyskinetic cerebral palsy on reaching movements during routine activities of daily living.

Further assessment of the value of these measurement techniques will require a larger sample of subjects. It will be important to measure the variability and predictability of movement over a period of several years as children develop and attempt to learn new skills. It will also be important to measure changes in response to medication or other therapy. It will be important to compare the results with those of children with other movement disorders, such as tremor or ataxia. The results reported here show that movements in dyskinetic cerebral palsy have increased variability, which is consistent with the hypothesis of decreased filtering and removal of unwanted signals. It is hoped that these results will provide a foundation for the quantitative analysis of dyskinetic reaching movements.

Acknowledgments
I wish to acknowledge the invaluable assistance of Abe Ishihara, Jason Kaiser, Brian Placek, Kimberly Murphy, and Sara Sherman-Levine.

References


