Dystonia: A “Missed” Diagnosis in Cerebral Palsy

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Bloorview Children’s Hospital Foundation Chair in Developmental Paediatrics
Objectives: Flow= 5 parts

- Understand the definition of dystonia (Part 1)
- Understand how Dystonia helps in the classification of the CP sub-type (Part 2)
- Gain knowledge in diagnosing and measuring dystonia using the HAT (Hypertonia Assessment Tool) –(Part 3)
- Gain knowledge in measuring dystonia –(Part 4)
- Understand “medical” treatment options for Dystonic CP (Part 5)
Part 1: Definition of Dystonia
Definition and Classification of Disorders Causing Hypertonia in Childhood
Terence D. Sanger, Mauricio R. Delgado, Deborah Gaebler-Spira, Mark Hallett and Jonathan W. Mink
*Pediatrics* 2003;111:e89-e97

Definition and Classification of Negative Motor Signs in Childhood
Terence D. Sanger, Daofen Chen, Mauricio R. Delgado, Deborah Gaebler-Spira, Mark Hallett, Jonathan W. Mink and the Taskforce on Childhood Motor Disorders
*Pediatrics* 2006;118:2159-2167
DOI: 10.1542/peds.2005-3016

Definition and Classification of Hyperkinetic Movement Disorders in Childhood
Terence Sanger, Daofen Chen, Darcy Fehlings, Mark Hallett, Anthony Lang; Jon Mink and Taskforce on Childhood Motor Disorders

**Movement Disorders**

*Movement Disorders*
Vol. 25, No. 11, 2010, pp. 1538–1549
© 2010 Movement Disorder Society
• Hypertonia: defined as ‘abnormally increased resistance to passive stretch’

• Three types of neurologically mediated hypertonia: spasticity, dystonia, and rigidity

• Dystonia is ‘a movement disorder in which involuntary sustained or intermittent muscle contractions cause twisting and repetitive movements, abnormal postures or both’
• Hypertonia: defined as ‘abnormally increased resistance to passive stretch’

• Three types of neurologically mediated hypertonia: spasticity, dystonia, and rigidity

• Dystonia is ‘a movement disorder in which involuntary sustained or intermittent muscle contractions cause twisting and repetitive movements, abnormal postures or both’
• Spasticity is hypertonia in which ‘resistance to externally imposed movement increases with increasing speed of stretch and/or resistance to externally imposed movement rises rapidly above a threshold speed or angle’

• Rigidity is ‘velocity-independent bidirectional resistance which may involve simultaneous co-contraction of agonists and antagonists’

• **Mixed tone**: occurs when more than one subtype of hypertonia co-exist
Dystonia is ‘a movement disorder in which involuntary sustained or intermittent muscle contractions cause twisting and repetitive movements, abnormal postures or both’
“Is an ongoing random-appearing sequence of one or more discrete involuntary movements or movement fragments”
Athetosis: Definition

“Is a slow continuous, involuntary writhing movement that prevents the maintenance of a stable posture”
Hallmark Features of Dystonia

• Dystonia is both an involuntary movement disorder and a cause of hypertonia

• Tone is variable

• Stiff movement

• Sustained postures (often twisting)

• Involuntary movements/postures/tone are triggered by voluntary movement, excitement, tactile stimuli
Part 2: Dystonia and Cerebral Palsy
“A group of *permanent* disorders of the development of *movement or posture* causing *activity limitation* that are attributed to *nonprogressive* disturbances that occurred in the developing fetal or infant brain.

The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems”
Figure 2: Hierarchical classification tree of cerebral palsy sub-types.
Cerebral Palsy

- Spastic
  - Bilateral
    - Diplegic
  - Unilateral
    - Hemiplegic
- Dyskinetic
  - Hypokinetic
  - Hyperkinetic
- Ataxic
  - Dystonic
  - Choreoathetosis

Dyskinetic: involuntary movement disorder with varying tone
Mixed CP: combination of subtypes
Dystonic CP: Key Features

- Hypokinesia (reduced activity, stiff movement)
- Variable hypertonia

- Versus Choreo-athetotic CP
  - Hyperkinesia (increased activity)
  - Hypotonia
Dystonia and CP: Some Issues

- Many children diagnosed with Spastic Quadriplegic CP have a significant dystonic component that is “hidden” and are better thought of as MIXED CP.
- Some children diagnosed with Spastic Quadriplegic CP don’t have spasticity and instead have a pre-dominant dystonic component that is missed.
- Chorea, Athetosis, and Dystonia frequently exist together.
- Dystonia is in both hyperkinetic and hypokinetic frameworks.
- Hypotonic CP often evolves into Dystonic CP.
- Two different ways of dealing with mixed neurologic patterns—Mixed versus “Pre-dominant”.
- Makes registry work “messy”.

Holland Bloorview
Kids Rehabilitation Hospital

UNIVERSITY OF TORONTO
Part 3: Diagnosing Dystonia with the HAT
• Numerous scales exist to “quantify” the severity of hypertonia (e.g. Tardieu, MAS, ASA, BAD)

• A standardized clinical tool to differentiate the different forms of hypertonia does not exist

• Current standard is the neurological examination (lacks standardization and is experience dependent)

• Potential **Uses** of the HAT:
  
  1) Clinical: to guide treatment (e.g. medication type and dose may depend on the type of hypertonia)
  
  2) Research: to “describe” subjects

  3) **Prevents “missing” dystonia!!!**
Methods

• Guyatt framework for measure development (Item Generation, Item Reduction, Pre-testing, Reliability and Validity)

• Item Generation: items generated through Childhood Motor Taskgroup, literature review and interviews with experts

• Item Reduction: Kuder-Richardson Formula 20 (KR-20) determined the internal consistency of items within the spasticity, rigidity and dystonia subsets
<table>
<thead>
<tr>
<th>Item description</th>
<th>Type of hypertonia identified by item</th>
<th>KR-20z&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Agreement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Caregiver history of variability in tone with sleep compared with awake time</td>
<td>Dystonia</td>
<td>0.77</td>
<td>NA</td>
</tr>
<tr>
<td>(2) Caregiver history of an increase in tone with activity/movement</td>
<td>Dystonia</td>
<td>0.75</td>
<td>NA</td>
</tr>
<tr>
<td>(3) Involuntary twisting movements</td>
<td>Dystonia</td>
<td>0.74</td>
<td>43</td>
</tr>
<tr>
<td>(4) Variable abnormal postures</td>
<td>Dystonia</td>
<td>0.73</td>
<td>43</td>
</tr>
<tr>
<td>(5) Increased involuntary movements/postures with purposeful movement of a distant body part</td>
<td>Dystonia</td>
<td>0.72</td>
<td>78</td>
</tr>
<tr>
<td>(6) Increased involuntary movements/postures with tactile stimulus of a distant body part</td>
<td>Dystonia</td>
<td>0.78</td>
<td>60</td>
</tr>
<tr>
<td>(7) Fluctuation of tone with multiple passive stretches</td>
<td>Dystonia</td>
<td>0.76</td>
<td>26</td>
</tr>
<tr>
<td>(8) Intermittent low tone during a passive stretch of the muscle</td>
<td>Dystonia</td>
<td>0.72</td>
<td>47</td>
</tr>
<tr>
<td>(9) Increased tone with purposeful movement of a distant body part</td>
<td>Dystonia</td>
<td>0.82</td>
<td>78</td>
</tr>
<tr>
<td>(10) Velocity-dependent resistance to passive stretch</td>
<td>Spasticity</td>
<td>0.38</td>
<td>65</td>
</tr>
<tr>
<td>(11) Presence of a spastic catch</td>
<td>Spasticity</td>
<td>0.38</td>
<td>78</td>
</tr>
<tr>
<td>(12) Hyperreflexia</td>
<td>Spasticity</td>
<td>1.0</td>
<td>NA</td>
</tr>
<tr>
<td>(13) Equal resistance to passive stretch in bidirectional passive movement of a joint</td>
<td>R rigidity</td>
<td>NA</td>
<td>96</td>
</tr>
<tr>
<td>(14) Maintenance of limb position after passive movement</td>
<td>Rigidity</td>
<td>NA</td>
<td>100</td>
</tr>
</tbody>
</table>

<sup>a</sup>The number reflects the Kuder–Richardson 20 (KR-20) index when the item is eliminated. NA, not applicable.
<table>
<thead>
<tr>
<th></th>
<th>Positive agreement</th>
<th>Negative agreement</th>
<th>PABAK</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spasticity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test-retest</td>
<td>1.00</td>
<td>0.10</td>
<td>1.00</td>
</tr>
<tr>
<td>Interrater</td>
<td>0.90</td>
<td>0.33</td>
<td>0.65</td>
</tr>
<tr>
<td>Validity (physician 1)</td>
<td>0.93</td>
<td>0.40</td>
<td>0.74</td>
</tr>
<tr>
<td>Validity (physician 2)</td>
<td>0.87</td>
<td>0.40</td>
<td>0.57</td>
</tr>
<tr>
<td><strong>Dystonia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test-retest</td>
<td>0.80</td>
<td>0.50</td>
<td>0.43</td>
</tr>
<tr>
<td>Interrater</td>
<td>0.75</td>
<td>0.43</td>
<td>0.30</td>
</tr>
<tr>
<td>Validity (physician 1)</td>
<td>0.75</td>
<td>0.43</td>
<td>0.30</td>
</tr>
<tr>
<td>Validity (physician 2)</td>
<td>0.89</td>
<td>0.60</td>
<td>0.65</td>
</tr>
<tr>
<td><strong>Rigidity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test-retest</td>
<td>0</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Interrater</td>
<td>0</td>
<td>0.98</td>
<td>0.91</td>
</tr>
<tr>
<td>Validity (physician 1)</td>
<td>0</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Validity (physician 2)</td>
<td>0</td>
<td>0.98</td>
<td>0.91</td>
</tr>
</tbody>
</table>
HAT “Discussion”

- The majority of children had mixed tone
- Rigidity was absent in the children with CP in this study group
- Items that describe the classic presentation of dystonia (twisting postures at rest) were eliminated in the item reduction stage as they were only present in children with severe dystonia
- Is the neurologic examination the gold standard?
- Video did not enhance the reliability of dystonia scores but enhanced standardization of HAT administration improved dystonia reliability (moderate)
<table>
<thead>
<tr>
<th>HAT ITEM</th>
<th>SCORING GUIDELINES (0=negative or 1=positive)</th>
<th>SCORE (0=negative or 1=positive)</th>
<th>TYPE OF HYPERTONIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Increased involuntary movements/postures of the designated limb with</td>
<td>0= No involuntary movements or postures observed</td>
<td>0</td>
<td>DYSTONIA</td>
</tr>
<tr>
<td>tactile stimulus of another body part</td>
<td>1= Involuntary movements or postures observed</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2. Increased involuntary movements/postures with purposeful movements</td>
<td>0= No involuntary movements or postures observed</td>
<td>0</td>
<td>DYSTONIA</td>
</tr>
<tr>
<td>of another body part</td>
<td>1= Involuntary movements or postures observed</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>3. Velocity dependent resistance to stretch</td>
<td>0= No increased resistance noticed during fast stretch compared to slow stretch</td>
<td>0</td>
<td>SPASTICITY</td>
</tr>
<tr>
<td></td>
<td>1= Increased resistance noticed during fast stretch compared to slow stretch</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>4. Presence of a spastic catch</td>
<td>0= No spastic catch noted</td>
<td>0</td>
<td>SPASTICITY</td>
</tr>
<tr>
<td></td>
<td>1= Spastic catch noted</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>5. Equal resistance to passive stretch during bi-directional movement</td>
<td>0= Equal resistance not noted with bi-directional movement</td>
<td>0</td>
<td>RIGIDITY</td>
</tr>
<tr>
<td></td>
<td>1= Equal resistance noted with bi-directional movement</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>6. Increased tone with movement of another body part</td>
<td>0= No increased tone noted with purposeful movement</td>
<td>0</td>
<td>DYSTONIA</td>
</tr>
<tr>
<td></td>
<td>1= Greater tone noted with purposeful movement</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>7. Maintenance of limb position after passive movement</td>
<td>0= Limb returns (partially or fully) to original position</td>
<td>0</td>
<td>RIGIDITY</td>
</tr>
<tr>
<td></td>
<td>1= Limb remains in final position of stretch</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
Part 4: Measuring Dystonia
Interaction between Components of the ICF - WHO 2001

Health Condition
(disorder/disease)

Impairment
(function/structure)

Activities
(task/action)

Participation
(involvement in life situation)

ENVIRONMENTAL FACTORS

PERSONAL FACTORS
Measuring Dystonia: Your Options

- Barry Albright Dystonia Scale – BAD
- Kinematic Dystonia Measure – KDM
- Dyskinesia Impairment Scale
- Individualized Goal Setting (COPM) in response to treatment
Overview of the Scale

- **Description of the Scale**
  - 8 body regions:
    - *Eyes, mouth, neck, trunk and 4 extremities*
  - Dystonia is rated as:
    - *None (0), slight (1), mild (2), moderate (3), and severe (4)*

- **Administration (video)**
  - Patients are asked to remain still
  - Then to perform functional tasks depending on ability and age
Test condition:
rest one arm, tap contralateral fingers.

Device: Optotrak kinematic and EMG recordings.

Tests one aspect of dystonia: involuntary movement triggered by voluntary movement
Design: Case-Control Study with prospective repeated measures

11 children (mean age 9 years) with CP and UE dystonia and 6 controls (mean age 8 years 3 months)

KDM measured at baseline and at 30 minutes

QUEST and BAD measured at baseline

Results: Subjects with CP showed significantly greater KDM scores (168 degrees SD 100) compared to controls (51 degrees SD 32)

Test-retest reliability ICC = 0.95
Concurrent Validity

Correlation: 176bpm Tapping vs. Total BAD Score

KDM Score (Deg) vs. BAD Score

$r=0.792$
The Dyskinesia Impairment Scale: a new instrument to measure dystonia and choreoathetosis in dyskinetic cerebral palsy

- Consists of two subscales (dystonia and choreoathetosis)
- Evaluation of duration and amplitude in 12 body regions
- Looks at both action and rest
- Maximum score is 288
- (scored with a video)

DOI: 10.1111/j.1469-8749.2011.04209.x
Part 4: Treating Dystonia
Why Treat Dystonia?

- Improve motor function
- More commonly we aim to relieve pain associated with dystonia or decrease tone to facilitate care-giving
Characteristics of Pain in Children and Youth With Cerebral Palsy
Melanie Penner, Wen Yan Xie, Navneet Binepal, Lauren Switzer and Darcy Fehlings
*Pediatrics* 2013;132:e407; originally published online July 15, 2013;
DOI: 10.1542/peds.2013-0224

- **1 - No Pain**: 45.2%
- **2 - Mild/moderate pain that does not affect activity**: 30.4%
- **3 - Moderate pain that prevents a few activities**: 13.2%
- **4 - Moderate/severe pain that prevents some activities**: 7.6%
- **5 - Severe pain that prevents most activities**: 3.6%
Treatments for Dystonia

- Oral Medications
- Botulinum Toxin A
- Intrathecal Baclofen
- Deep Brain Stimulation
Slide Organization:
Drug/Main Category of Usage

• Mechanism of Action
• Dosage
• Side Effects
• Efficacy/Effectiveness
• Evidence
Oral Pharmacotherapy for Dystonia

- Antiparkinsonian drugs:
  - anticholinergic
  - dopaminergic
Oral Pharmacotherapy for Dystonia: Trihexyphenidyl (Artane)

- **Mechanism of Action:** anticholinergic (suppresses an excess of cholinergic activity present in dystonia)
- **Dosage:**
  - **Starting Dosage:** 0.5 mg bid (<15 kg) and 1.0 mg bid (>15 kg) [available in a 2 mg tablet] – can work up to 0.5 to 0.75 mg/kg/day
  - **Usual dosage range:** 1 to 10 mg bid to qid
- **Side effects:** dry mouth, nausea, blurred vision, urinary retention, drug rash, chorea
- **Efficacy:** mixed results, can help with drooling!
- **Evidence:** U

Holland Bloorview Kids Rehabilitation Hospital
Prospective Open-label Clinical Trial of Trihexyphenidyl in Children with Secondary Dystonia due to CP:

*Sanger et al J of Child Neurol: 2007 22(5)*

- 23 children ages 4 to 15 years completed the study
- Dosage of 0.75 mg/kg/day
- Improvement of arm function at 15 weeks
- Subgroup of 10 with “hyperkinetic” dystonia worsened at 9 weeks
- Also great study by Dr. James Rice – RCT crossover – no improvement with high dose artane!
Oral Pharmacotherapy: Baclofen

- Binds GABA$_B$ receptors of spinal interneurons presynaptically

- Dosage: 2mg/kg/day (80 mg max) po divided tid to qid

- Side Effects: drowsiness (can be minimized by increasing the dosage slowly)

- Efficacy: some reduction in dystonia initially but tolerance can develop

- Evidence: U
Animal F GABA$_b$ specific binding
Oral Pharmacotherapy for Dystonia: Carbidopa/L-Dopa

- **Mechanism of Action:** Dopaminergic

- **Dosage:** Available as Sinemet e.g. 100/25 (one tablet contains 100 mg levodopa and 25 mg carbidopa); 1-2 tablets bid to tid

- **Side effect:** nausea (most common), other side effects include a decrease in blood pressure, depression, tremor, chorea, psychosis

- **Efficacy:** Treatment of Choice in Dopamine Responsive Dystonia (can be misdiagnosed with CP)
Oral Medications for Dystonia: General Comments

- Potential role in generalized dystonia (versus focal dystonia)
- Significant variability amongst health care providers in the use of oral meds
- Minimal information on the long-term cognitive effects of the oral medications
- "My Practice": reserve for children with severe generalized dystonia (start with artane for child with predominant dystonia and baclofen for mixed tone)
Oral Medications for Dystonia: General Comments

- Gabapentin (pain relief)
- Diazepam (for dystonic storms)
Botulinum Toxin A

dePaiva *et al.* 1999
Intrathecal Baclofen (ITB™) Therapy
Bilateral pallidal deep brain stimulation for the treatment of patients with dystonia-choreoathetosis cerebral palsy: a prospective pilot study

Marie Vidailhet, Jerome Yelnik, Christelle Lagrange, Valerie Fraix, David Grabli, Stephane Thobois, Pierre Burbaud, Marie-Laure Welter,
• N=13
• Age at implant 20 to 44 years
• Pre-op Burke-Fahn Marsden Scores (BFMS) 44 ± 21
• Post-op at one year BFMS 35 ± 22 (p < 0.009)


Effects of deep brain stimulation in dyskinetic cerebral palsy: a meta-analysis.
Koy A¹, Hellmich M, Pauls KA, Marks W, Lin JP, Fricke O, Timmermann L.
Conclusion

- Dystonia is a frequent cause of hypertonia and involuntary movements in children with CP
- Dystonia is characterized by “stiff postures”
- Dystonia is a frequent cause of pain in children with CP
- Dystonia can be diagnosed using the HAT
- We require more evidence for medical treatments for dystonia! (Oral Meds, BTA, ITB, DBS)
- We require **better treatments** for Dystonia!
Thank-you