Evaluation and insights in secondary dystonia and choreoathetosis in dyskinetic CP

Monbaliu E, Feys H
AACPDM 68th Annual Meeting, 2014-09-11, San Diego

Overview
• Introduction
• Evaluation
• Clinical cases

Definition and classification

- Describes a group of disorders of the development of movement and posture
- Causing activity limitation
- The motor disorders of CP are often accompanied by disturbances of sensation, cognition, communication, perception, and/or a seizure disorder

Disclosure Information
AACPDM 68th Annual Meeting September October 10-13, 2014

Speakers Name: MONBALIU Elegast, FEYS Hilde

Disclosure of Relevant Financial Relationships:
No financial relationships to disclose.

Disclosure of Off-Label and/or investigative uses:
We will not discuss off label use and/or investigational use in my presentation

CEREBRAL PALSY
3/1000 °
Spasticity
79.1%
Dyskinesia
14.4%  (0.3/1000°)
Ataxia
3.9%
Choreo-athetosis
Dystonia
Chorea
Athetosis

SCPE 2000,2007 Dev Med Child Neurol
SCPE 2005, R&TM of the SCPE
Bax e.a. 2006
JAMA
Rosenbaum e.a. 2006, 2007 Dev Med Child Neurol
Sanger e.a. 2010
Mov Disord

Definition and classification

CEREBRAL PALSY

Spasticity
Dyskinesia
Ataxia
Choreo-athetosis
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Overview
• Introduction
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• Clinical cases
**Definition and classification**

CEREBRAL PALSY

- Spasticity
- Dyskinesia
- Ataxia
- Chorea-athetosis
- Dystonia
- Athetosis

**Dyskinetic CP**
- Involuntary, uncontrolled, recurring, occasionally stereotyped movements
- Primitive reflex patterns predominate
- Muscle tone is varying

**Prevalence**

<table>
<thead>
<tr>
<th>Study #</th>
<th>Participants</th>
<th>Spastic CP</th>
<th>Dyskinetic CP</th>
<th>Ataxic CP</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bax e.a. 2006</td>
<td>Cross sectional</td>
<td>558</td>
<td>79.1%</td>
<td>14.4%</td>
<td>2.6%</td>
</tr>
</tbody>
</table>

**Prevalence Tendency**

- 6.4% Turkey - Serdaroglu 2006
- 3% N. Ireland - Parks 2005
- 15% Sweden - Himmelmann 2007
- 6% Norway - Anderson 2008
- 1.8% Australia - Robinson 2008

**Clinical picture**

**Motor Severity**

Gross Motor Function Classification System Scale (GMFCS)

- Dyskinetic Population study (N=48)
  - Level I & II → 8.3% (n=4)
  - Level III → 12.5% (n=6)
  - Level IV → 20.8% (n=10)
  - Level V → 58.3% (n=28) **79.1%**
Clinical picture

Accompanying impairments

Definition and classification

CEREBRAL PALSY

Spasticity

Dyskinesia

Alaxia

Choreo-athetosis

Dystonia

- Spasticity
  - involuntary movements, distorted voluntary movements and abnormal postures due to sustained muscle contractions (slow rotation, extension, flexion of body parts)

- Dyskinesia
  - a movement disorder with involuntary sustained or intermittent muscle contractions

- Athetosis
  - a movement disorder with involuntary sustained or intermittent muscle contractions

- Chorea
  - rapid, involuntary, jerky, often fragmented movements

- Ataxia
  - slower, constantly changing, writhing or contorting movements

- Dystonia
  - a slow continuous, involuntary writhing movement that prevents maintenance of stable postures

Definition and classification

Dystonia versus Choreoathetosis
Pathogenesis

- Hyperbilirubinemia
- Neonatal asphyxia & brain damage in the thalamus and basal ganglia during the 3rd trimester of pregnancy are strongly associated with dyskinetic CP.

Kyllermann, 1982 Acta Paediatr Scand
Himmelmann, 2009 Dev. Med. Child Neurol

IMPACT Brain Lesions in Basal Ganglia & Thalamus

Therapy

Medical interventions
- Oral medication
- Intrathecal baclofen
- Deep Brain stimulation (DBS)
- Botulinum Toxin

International Classification of Functioning, Disability & Health (World Health Organisation)

Therapy

Rehabilitation
- Physical therapy
- Occupational therapy
- Speech therapy
- Mobility aids
- Orthotics

↓ pathological movements &
↑ function, activity, participation and quality of life

Problem
1. Little is known about the clinical presentation of dystonia and choreoathetosis in dyskinetic CP => difficult for targeted therapy
2. Dystonia and choreoathetosis are complex movement disorders => measurement of therapy effects?
Overview

• Introduction
• Evaluation
• Clinical cases

Evaluation

Clinical Rating Scales

<table>
<thead>
<tr>
<th>Scale</th>
<th>Description</th>
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<tbody>
<tr>
<td>No scales available</td>
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<tr>
<td>Primary Dystonia Scales</td>
<td>– Burke Fahn Marsden Scale (BFMS), Burke e.a. 1985 Neurology</td>
</tr>
<tr>
<td>– Unified Dystonia Rating Scale, UDRS, Comella e.a. 2003 Movement Disorders</td>
<td></td>
</tr>
<tr>
<td>Secondary Dystonia Scales</td>
<td>– Barry Albright Dystonia Scale (BADS), Barry e.a. 1999 Dev. Med. Child Neurol</td>
</tr>
</tbody>
</table>

Evaluation studies

**Study 1:**
Rating scales for Dystonia in Cerebral Palsy: Reliability and Validity
published Dev. Med. Child Neurol 2010

**Study 2:**
The Dyskinesia Impairment Scale: a new instrument to measure dystonia and choreoathetosis in Cerebral Palsy

**Study 3:**
Can the Dyskinesia Impairment Scale be used by inexperienced raters? A reliability study.
published European Journal of Paediatric Neurology 2013

Evaluation

Clinical Rating Scales

1. How reliable, valid and sensitive are the existing dystonia scales?

2. There is a need for a new evaluation scale to measure dystonia and choreoathetosis in a similar scoring construct.

Objectives study 1

1. To investigate the reliability of the three dystonia scales in dyskinetic CP

2. To assess the validity of the three scales in dyskinetic CP
Methods

Dystonia Scales

Primary Dystonia Scale

- Burke Fahn Marsden Movement Scale, BFMS, Burke e.a. 1985 Neurology
- Unified Dystonia Rating Scale, UDRS, Comella e.a. 2003 Movement Disorders

Secondary Dystonia Scale

- Barry Albright Dystonia Scale, BADS, Barry e.a. 1999 Dev Med Child Neurol

BFMS

Ordinal scale

Movement Scale

Disability Scale

Provoking Factor

Severity Factor

8 body regions range 0-8

9 body regions range 0-8

BADS

Ordinal scale

Global Dystonia Score

8 body regions range 0-4

UDRS

Ordinal scale

Duration Factor

Motor Severity Factor

14 body regions range 0-4

Interval=0.5

14 body regions range 0-4

Interval=1
Methods

Procedures

Videotaping protocol
- Extended version of the proposed Video Protocol for Dystonia (Comella et al., 1997)
- Standard montage
  - 12 body regions
  - Rest/activity

Raters
- N=3
  - 2 child neurologists
  - 1 physical therapist

Results

- Intraclass Correlation Coefficients
  - Moderate to high intrarater reliability for the total scores
  - Low to moderate interrater reliability for the itemscores
- Cronbach’s α: good internal consistency
- Correlation: good relationship between BFMMDRS, UDRDS, BADS

Results

- Standard Error of Measurement (SEM) and Minimal Detectable Difference
  - High MDD % make the scales insufficiently useful for intervention studies and longitudinal follow-up
- Content analysis:
  - No differentiation between action/rest
  - No differentiation between duration and amplitude
  - No differentiation between proximal and distal limbs

Conclusion

- Need for a new scale
  - Evaluation of dystonia and choreo-athetosis in a similar scoring construct

Evaluation studies

Study 1:
Rating scales for Dystonia in Cerebral Palsy: Reliability and Validity
published Dev Med Child Neurol 2010

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The Dyskinesia Impairment Scale: a new instrument to measure dystonia and choreoathetosis in Cerebral Palsy
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Scale Development

Rating Scales for Dyskinesia

Evaluation Scale Development

Rating Scales for Dystonia in CP: Reliability and Validity
published Dev Med Child Neurol 2010

Primary Dystonia Scales
- Burke Fahn Marsden Scale, BFMMS (Burke et al., 1985), Neurology
- Unified Dystonia Rating Scale, UDRDS (Comella et al., 2003), Movement Disorders

Secondary Dystonia Scales
- Barry Albright Dystonia Scale, BADS (Barry et al., 1999), Dev Med Child Neurol
Objectives study 2

To assess the **reliability** and **validity** of the DIS in **dyskinetic CP**

Methods

**Procedures**

- **Videotaping protocol**
  - Extended version of the proposed Video Protocol for Dystonia
    - Dystonia Study Group, 1997
    - Comella et al., 2002
  - Standard montage
    - 12 body regions
    - action/rest

- **Raters**
  - N=2 PTs

Results

1. **Intraclass Correlation Coefficients**
   - dystonia subscale: very good interrater reliability
   - choreoathetosis subscale: excellent interrater reliability

2. **SEM-MDD**: low measurement errors

3. **Cronbach’s α**: very good internal Consistency

4. **Pearson's correlation coefficient (r)**: good concurrent validity between Dystonia subscale and BADS

Evaluation studies

- **Study 1**: Rating scales for Dystonia in Cerebral Palsy: Reliability and Validity
  - published Dev Med Child Neurol 2010

- **Study 2**: The Dyskinesia Impairment Scale: a new instrument to measure dystonia and choreoathetosis in Cerebral Palsy
  - published Dev Med Child Neurol 2012

- **Study 3**: Can the Dyskinesia Impairment Scale be used by inexperienced raters? A reliability study
  - published European Journal of Paediatric Neurology 2013

Objectives study 3

1. To assess the **reliability** of the DIS in hands of **inexperienced raters**, new to discriminating between dystonia and choreoathetosis

2. To determine the effects of **clinical experience** on reliability
Methods

Procedures

Raters
- N=5 PT
  - 3 senior PTs
  - 2 junior PTs

Results

- Interrater reliability
  - Choreoathetosis total scores: good to excellent reliability for all inexperienced raters
  - Dystonia: total scores: moderate to good reliability for all inexperienced raters
  - No difference in reliability between senior/junior PT

- Internal consistency
  - Similar Cronbach's alpha between experienced and inexperienced raters

Results

- Interrater reliability inexperienced raters
  - Region scores generally ranged from poor to good
  - For dystonia subscale lower reliability during rest than during activity

- SEM & MDD
  - Higher measurement errors than experienced raters

Conclusion study 2 & 3

- Experienced raters > inexperienced raters
- Choreo-athetosis scale is more reliable than the dystonia scale for inexperienced raters
- No effect of clinical expertise

- Good acquaintance of operational definitions is crucial to enhance the reliability
- A manual of the DIS and (online) training is necessary

Conclusion study 2 & 3

Dyskinesia Impairment Scale

Useful tool to increase further understanding of dystonia and choreoathetosis

Clinical pattern analysis of secondary dystonia and choreoathetosis in dyskinetic CP

E. Mostali, E. Ottobrun, P. Prinzen, P. De Cocker, K. Klinghoffer, L. Heymans, H. Feyts

<table>
<thead>
<tr>
<th>Max Keith Press Poster Prize</th>
<th>EACD, 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mac Keith Press Promising Career Award</td>
<td>AACPDM, 2013</td>
</tr>
</tbody>
</table>
**Objectives**

1. To map the clinical patterns of dystonia and choreoathetosis in dyskinetic CP
2. To assess the relationship with functional classification scales
3. To determine the relation with lesions in the basal ganglia and thalamus

**Methods**

**Participants**

- Characteristics
  - N=55 (30 male; 25 female)
  - age 5-22 yrs
  - Mean age=14y6mo ; SD=4y1mo
- Inclusion criteria
  - predominant dyskinetic CP
  - able to understand test instructions
- Exclusion criteria
  - orthopaedic or neurosurgical interventions < 12 months
  - spine fusion

**Measurement & Classification**

- **Measurement**
  - Dyskinesia Impairment Scale (DIS) Montaliu et al 2012, Dev Med Child Neurol
- **Functional Classification Scales**
  - Gross Motor Function Classification Scale (GMFCS)
  - Manual Ability Classification Scale (MACS)
  - Communication Function Classification Scale (CFCS)

**Methods**

- MRI

**Results**

1. Clinical patterns of dystonia and choreoathetosis in dyskinetic CP
2. Relationship with functional classification scales
3. Relation with basal ganglia and thalamus lesions

**Results**

**Dystonia versus Choreoathetosis**

<table>
<thead>
<tr>
<th></th>
<th>DISYTONIA Median (IQ)</th>
<th>CHOREOATHETOSIS Median (IQ)</th>
<th>Wilcoxon Signed-rank test (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total body</td>
<td>70.2 (52.1-90.9)</td>
<td>26.7 (14.5-41.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arms</td>
<td>82.2 (62.5-94.4)</td>
<td>26.1 (13.5-53.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arms-proximal</td>
<td>83.3 (70.8-95.4)</td>
<td>31.3 (9.3-58.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arms-distal</td>
<td>93.8 (74.6-97.3)</td>
<td>26.1 (14.6-50.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Legs</td>
<td>78.8 (50.6-87.5)</td>
<td>16.7 (7.3-43.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Legs-proximal</td>
<td>86.8 (52.3-91.3)</td>
<td>18.6 (4.3-37.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Legs-distal</td>
<td>82.3 (72.9-90.3)</td>
<td>20.8 (0.0-43.8)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Scores of dystonia higher than choreoathetosis scores

Significant difference
Results

Activity versus Rest

<table>
<thead>
<tr>
<th></th>
<th>Activity Median (IQR)</th>
<th>Rest Median (IQR)</th>
<th>Wilcoxon signed-rank test (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dystonia</td>
<td>60.0 (44.1-67.5)</td>
<td>57.3 (26.0-75.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Choreoathetosis</td>
<td>38.1 (17.2-51.2)</td>
<td>18.8 (11.5-32.2)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Higher scores during action than in rest

Significant difference

DIS Regions Arms/Legs

<table>
<thead>
<tr>
<th></th>
<th>Arms Median (IQR)</th>
<th>Legs Median (IQR)</th>
<th>Wilcoxon signed-rank test (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dystonia</td>
<td>83.3 (65.9-94.8)</td>
<td>78.1 (49.0-87.5)</td>
<td>0.019</td>
</tr>
<tr>
<td>Choreoathetosis</td>
<td>31.3 (13.5-53.1)</td>
<td>18.8 (7.3-44.2)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Arm scores higher than leg scores

Significant difference

Results

1. Clinical patterns of dystonia and choreoathetosis in dyskinetic CP

2. Relationship with functional classification scales

3. Relation with basal ganglia and thalamus lesions

Results

DIS Regions Arms prox/dist

<table>
<thead>
<tr>
<th></th>
<th>Arms proximal Median (IQR)</th>
<th>Arms distal Median (IQR)</th>
<th>Wilcoxon signed-rank test (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dystonia</td>
<td>83.3 (47.9-94.8)</td>
<td>93.8 (66.7-97.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Choreoathetosis</td>
<td>31.3 (9.3-54.3)</td>
<td>38.1 (14.6-56.1)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Dystonia: distal arm scores higher than proximal arm scores

Significant difference

Results

DIS Regions Legs prox/dist

<table>
<thead>
<tr>
<th></th>
<th>Legs proximal Median (IQR)</th>
<th>Legs distal Median (IQR)</th>
<th>Wilcoxon signed-rank test (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dystonia</td>
<td>68.0 (31.3-91.3)</td>
<td>83.3 (72.9-93.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Choreoathetosis</td>
<td>18.8 (4.2-37.5)</td>
<td>26.6 (12.6-58.8)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Dystonia: distal leg scores higher than proximal leg scores

Significant difference

Results

Gross motor classification: GMFCS

Dystonia

Choreoathetosis

Good relationship: $r_s=0.70$

No relationship: $r_s=0.17$
### Results

**Manual ability classification: MACS**

<table>
<thead>
<tr>
<th>Dystonia</th>
<th>Choreoathetosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good relationship: $r_s = 0.68$</td>
<td>No relationship: $r_s = 0.21$</td>
</tr>
</tbody>
</table>

**Communication classification: CFCS**

<table>
<thead>
<tr>
<th>Dystonia</th>
<th>Choreoathetosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fair relationship: $r_s = 0.36$</td>
<td>No relationship: $r_s = -0.24$</td>
</tr>
</tbody>
</table>

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### Discussion

1. **Clinical patterns**
   - Dystonia > choreoathetosis  
     - New finding
   - Activity > rest  
     - Corresponds with descriptions Sanger et al (2010)
   - Arms > legs  
     - Corresponds with descriptions Sanger et al (2010)
   - Dystonia: distal arms/legs > proximal arms/legs  
     - New finding
2. Relation with motor classifications

- Higher correlation between dystonia and motor classification scales
- Suggests that dystonia has a larger impact on functionality
- Higher correlation between dystonia and motor classification scales $\Rightarrow$ future research activity scales

3. Relation with Th & BG lesion

- 70% of the participants showed lesions in Th & BG
- No relation with dystonia and pure Th & BG lesions
- Pure thalamus and basal ganglia lesions seem to be particularly associated with choreoathetosis

Critical reflections

1. Age range 5-22 years is large
2. No distinction between different age groups
3. Brain lesions
   - Based on existing MRIs
   - Low number of participants
   - Many participants mixed brain lesions

Conclusion

1. Simultaneous presence of dystonia and choreoathetosis with predominance of dystonia
2. Higher presence of dystonia and choreoathetosis during activities
3. Dystonia $\Rightarrow$ larger impact on functional abilities
4. Choreoathetosis is associated with lesions in the Th & BG

Overview

- Introduction
- Evaluation
- Clinical cases

Neck

<table>
<thead>
<tr>
<th>Duration Factor</th>
<th>Amplitude Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = D/CA is absent</td>
<td></td>
</tr>
<tr>
<td>1 = D/CA is occasionally present $&lt;10%$</td>
<td></td>
</tr>
<tr>
<td>2 = D/CA is frequently present $&gt;10 &lt;50%$</td>
<td></td>
</tr>
<tr>
<td>3 = D/CA is mostly present $&gt;50 &lt;90%$</td>
<td></td>
</tr>
<tr>
<td>4 = D/CA is always present $&gt;90%$</td>
<td></td>
</tr>
<tr>
<td>0 = D/CA is absent</td>
<td></td>
</tr>
<tr>
<td>1 = D/CA is small range of motion $&lt;10%$</td>
<td></td>
</tr>
<tr>
<td>2 = D/CA is moderate range of motion $&gt;10 &lt;50%$</td>
<td></td>
</tr>
<tr>
<td>3 = D/CA is substantial range of motion $&gt;50 &lt;90%$</td>
<td></td>
</tr>
<tr>
<td>4 = D/CA is maximal range of motion $&gt;90%$</td>
<td></td>
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</tbody>
</table>
### Upper Limb Distal

<table>
<thead>
<tr>
<th>Duration Factor</th>
<th>Amplitude Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = D/CA is absent</td>
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<tr>
<td>1 = D/CA is occasionally present ≤10%</td>
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</tr>
<tr>
<td>2 = D/CA is frequently present &gt;10% ≤30%</td>
<td>2 = D/CA is moderately present &gt;10% ≤30%</td>
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<td>3 = D/CA is mostly present &gt;30% ≤60%</td>
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<td>4 = D/CA is always present &gt;60%</td>
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### Upper Limb Proximal

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<td>4 = D/CA is always present &gt;60%</td>
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### Lower Limb Distal

<table>
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<tr>
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<td>4 = D/CA is always present &gt;60%</td>
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### Mouth

<table>
<thead>
<tr>
<th>Duration Factor</th>
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</tr>
</thead>
<tbody>
<tr>
<td>0 = D/CA is absent</td>
<td>0 = D/CA is absent</td>
</tr>
<tr>
<td>1 = D/CA is occasionally present ≤10%</td>
<td>1 = D/CA is occasionally present ≤10%</td>
</tr>
<tr>
<td>2 = D/CA is frequently present &gt;10% ≤30%</td>
<td>2 = D/CA is moderately present &gt;10% ≤30%</td>
</tr>
<tr>
<td>3 = D/CA is mostly present &gt;30% ≤60%</td>
<td>3 = D/CA is mostly present &gt;30% ≤60%</td>
</tr>
<tr>
<td>4 = D/CA is always present &gt;60%</td>
<td>4 = D/CA is always present &gt;60%</td>
</tr>
</tbody>
</table>
Thank you for your attention

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