HIV encephalopathy: definition of the natural history, physical characteristics and imaging findings in group of children with gait abnormalities

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University of Cape Town, South Africa
PILOT STUDY

Spastic diplegia in children with HIV encephalopathy: first description of gait and physical status

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Langerak et al. DMCN. 2014;56(7):686-94

Three-dimensional gait analysis
RESEARCH QUESTIONS

- Why did some of the children with HIVE and spastic diplegia walk with a pathological CP gait pattern, while others walked more ‘normal’?

- Is there a relation between the observed gait patterns and central nervous system (CNS) abnormalities?

- Is the gait pattern in HIVE static (non-progressive) as seen in CP?

- Are the physical impairments and CNS lesions related to the age of ART initiation?
ORIGINAL CIPHER PROJECT

Stellenbosch University

2013 / 2014
Base line

HIVE
ART < 1yr
n = 20
3D Gait analysis
Physical exam

ART ≥ 1yr
n = 20

2014 / 2015
1 year follow-up

HIVE
ART < 1yr
n = 20
3D Gait analysis
Physical exam

ART ≥ 1yr
n = 20

University of Cape Town

Brain + spine MRI

Brain + spine MRI
Negotiated about costs for brain and spine MRI-scans

✦ Include CP study-cohort
✦ Focus on more holistic approach
HOLISTIC APPROACH

International Classification of Function (ICF) model
published by the World Health Organization.
Children with spastic diplegia

HIVE
ART < 1yr
n = 20

HIVE
ART ≥ 1yr
n = 20

Body Function & Structure
- 3DGA
- PE
- Brain + spine MRI

Activity

Participation

Personal factors

Environmental factors

3DGA: Three-dimensional gait analysis; PE: Physical exam
Children with spastic diplegia

HIVE ART < 1yr n = 20
HIVE ART ≥ 1yr n = 20
CP n = 20

Body Function & Structure
- 3DGA
- PE
- Brain + spine MRI
- Neurocognitive tests

Activity
- PEDI - CAT
- GMFM

Participation
- PEDI - CAT

Personal factors

Environmental factors

3DGA: Three-dimensional gait analysis; PE: Physical exam; GMFM: Gross Motor Function Measure; PEDI – CAT: Pediatric Evaluation of Disability Inventory Computer Adaptive Test
## AMENDMENT CIPHER PROJECT

### 2013 / 2014

**Base line**

<table>
<thead>
<tr>
<th>HIVE</th>
<th>CP</th>
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</thead>
<tbody>
<tr>
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<td>Gross Motor Function Measure</td>
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<td>PEDI-CAT</td>
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### 2014 / 2015

**1 year follow-up**

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CURRENT STATUS

Delay in data collection

- Brain and spine MRI-scans:
  
  Renovations at Red Cross War Memorial Children’s Hospital Radiology Department

  Bookings September, October, November, December 2014……..
CURRENT STATUS

Delay in data collection

- Recruitment challenges
  - Moved from Cape Town
  - Comorbidities
  - Not ambulant
  - Lost contact
- Change in clinical presentation
Observation of resolved lower limb tone abnormalities in children with HIV encephalopathy on antiretroviral treatment

Nelleke G. Langerak, Theresa N. Mann, Kathleen G Walker, Kirsten A Donald
## Preliminary Data

### Study-Cohort

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
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<tbody>
<tr>
<td><strong>Diagnosis:</strong></td>
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</tr>
<tr>
<td>- Diagnosis of HIVE according to CDC Criteria</td>
<td>- History of prematurity (&lt;32 weeks) or other neonatal encephalopathy</td>
</tr>
<tr>
<td>- Infected perinatally</td>
<td>- Other neuromuscular or CNS disorders</td>
</tr>
<tr>
<td>- Significant gait abnormalities</td>
<td><strong>Symptoms:</strong></td>
</tr>
<tr>
<td><strong>Symptoms:</strong></td>
<td>- Dystonic, athetotic, ataxia, and hypotonic</td>
</tr>
<tr>
<td>- Classified as spastic diplegia</td>
<td><strong>Treatment:</strong></td>
</tr>
<tr>
<td>- Ambulant</td>
<td>- Any orthopaedic- and neurosurgical interventions on the lower extremities in the last year</td>
</tr>
<tr>
<td><strong>Personal factors:</strong></td>
<td>- Botulinum toxin injections in lower extremities in last 6 months</td>
</tr>
<tr>
<td>- 5 – 12 years of age</td>
<td><strong>Other:</strong></td>
</tr>
<tr>
<td>- Currently living in Cape Town</td>
<td>- Any fibromagnetic metallic implant, pacemaker, aneurysm clip or cochlear implant</td>
</tr>
<tr>
<td>- Cognitive level sufficient to co-operate with the gait analysis</td>
<td></td>
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Methods

Database (n=45)
HIV clinic at Red Cross War Memorial Children’s Hospital between 2008 and 2013

Selection (n=32)
Diagnosis of HIVE and spastic diplegia or increased muscle tone with brisk reflexes in the lower limbs

Screening (n=16)
- Assessment of muscle tone in the lower limbs
- Visual inspection of the child’s gait pattern
PRELIMINARY DATA

16 children (6 girls)
mean age: 8.5 ± 1.8 years
mean follow-up time: 2.4 ± 1.6 years

Group A (n=5)
Increased muscle tone and a typical spastic diplegic gait pattern

Group B (n=11)
No abnormalities
PRELIMINARY DATA

Group A (n=5)
Increased muscle tone and a typical spastic diplegic gait pattern

Group B (n=11)
No abnormalities

No significant differences in
* Age at the initial assessment
* Follow-up time

Group A:
Children specifically described with spastic diplegia at initial assessment
Conclusions

- Our observations suggest that increased muscle tone in the lower limbs in children with HIVE may resolve over time on standard ART regimens.

- However, children presenting with spastic diplegia do not seem to show the same improvement over time.

- Current observations may be of immediate relevance to healthcare professionals who may wish to consider the current findings when assessing the prognosis and treatment options for children with HIVE who present with increased tone in the lower limbs.

- Further investigation of the natural history of HIVE and spastic diplegia is required to confirm these findings.
OUTCOMES CIPHER PROJECT

Provides insight into the description and course of gait abnormalities with physical impairments, CNS lesions, psychological status, and level of activities and participation in daily live in children with HIVE and spastic diplegia, which might be related to age of ART initiation.
Clinical Research Topic of the CIPHER Grant program:
‘Studies evaluating optimal antiretroviral therapy (ART) initiation, Long-term management and complications in children (especially Children over two years of age) and adolescents.’

⇒ Recommendation for treatment of secondary abnormalities in children with HIVE and spastic diplegia.

Leading to societal and economic benefits.
Publications
2014

• Neurosurgery Division, University of Cape Town (www.neurosurgery.uct.ac.za)

Planned for 2014/2015

• Opinion piece (see abstract HIV Pediatrics workshop)
• Gait, physical exam and MRI outcomes (study I)
• Functional measures (GMFM and PEDI-CAT) (study II)
• Neurocognitive results (study III)

Planned for 2015/2016:

• 1 year follow-up studies of I–III
OUTPUTS

Presentations

2013
• School of Child & Adolescent Health (SCAH) Annual research days
• Western Cape South African Neurodevelopmental Therapy Association
• Course: Gait analysis & other outcome measures related to the ICF-Model

2014
• 6th HIV Pediatrics Workshop (Virology Education)
• 10th South African Neurodevelopmental Therapy Association Congress

Planned 2015
• 69th annual American Academy for Cerebral Palsy and Developmental Medicine (AACPDM) meeting
• International AIDS meeting 2015
Grant applications

2013

- National Research Foundation (NRF) Research Career Advancement Fellowship Award
- NRF researcher rating
- Faculty of Health Sciences, Postdoctoral Fellowship Grant for Dr T. Mann

2014

- University Research Committee (URC) Travel grant
- Career award Medical Research Council (MRC)
- MRC Self-Initiated-Grant

Planned 2015…
COLLABORATIONS

University of Cape Town

Prof AG Fieggen
HoD Neurosurgery
Mentor

Dr K Donald
HoD Developmental Paediatrics

Dr T Kilborn
Head of Clinical Unit Radiology

Stellenbosch University

Dr B Laughton
Children’s Infectious Diseases Clinical Research Unit

Dr J du Toit
HoD Orthopaedic surgery
NEW COLLABORATORS

University of Cape Town

Dr L Schrieff
Applied Cognitive Science and Experimental Neuro-Psychology (ASCENT) Lab

Ms D Gamxamus
Master student Psychology

Stellenbosch University

Dr RP Lamberts
Head of Orthopaedic Research, Exercise physiologist, Pysiotherapist

Dr T Mann
Postdoctoral fellow Exercise scientist
New collaborations?...... Future projects?.........

Human Movement Sciences

- Neuroscience
- Biomedical engineering
- Radiology
- Anatomy
- Physiology
- Psychology

- Orthopaedic surgery
- Allied health sciences

- Neurosurgery

- Neuro-development
- Gait and posture
- Brain function
- Fitness and lifestyle
- Physiology and anatomy

HMS
ACKNOWLEDGEMENTS

- ViiV, IAS and CIPHER
- Children, parents and guardians
- Specialized schools
- Collaborators
- Assistants

Thank you!

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