Congenital Hemiplegia and the Neglected Upper Limb

A Thesis for the Degree of Doctor of Philosophy in Medicine

Dr Remo Nunzio Russo

2011

Flinders University School of Medicine
DEDICATION

This thesis is dedicated to the memory of my father, Eduardo Domenico Russo, who died after a brave battle with lymphoma in 1991. He recognized the value of pursuing your dreams and goals, and working hard to bring them into reality. He instilled in me a real passion for working towards a goal, and for knowing the truth about how things in life really work – two vital skills for anyone wanting to complete a PhD. His motto was “Find your passion, aim to be the best, and never give up!”

My wish is that he could know how helpful he was to me during this difficult and challenging pursuit, and how grateful I am for his influence in my life.

Eduardo Domenico Russo
# Table of Contents

DEDICATION ....................................................................................................................... ii
DECLARATION STATEMENT .......................................................................................... 6
ACKNOWLEDGEMENTS ................................................................................................. 7
CO-AUTHORS’ CONTRIBUTION TO PUBLISHED WORKS .......................................... 9
SUMMARY OF ABBREVIATIONS ................................................................................. 10
THESIS SUMMARY .......................................................................................................... 12
CHAPTER 1: INTRODUCTION ....................................................................................... 14
  1.1 Aims and Hypotheses .......................................................................................... 16
    1.1a Hypothesis 1 – Functioning ........................................................................ 16
    1.1b Hypothesis 2 – Outcomes Associated with Functioning ............................ 17
    1.1c Hypothesis 3 – Interventions to Improve Function ................................. 17
CHAPTER 2: METHODS ................................................................................................. 18
  2.1 Ethics ................................................................................................................ 18
  2.2 Part 1 - Descriptive Study ................................................................................ 18
    2.2a Participants ................................................................................................. 18
    2.2b Recruitment, Part 1 ................................................................ ................. 18
    2.2c Data Collection and Instruments ................................................................ 19
    2.2d Self-esteem, Self-concept and Quality of Life Matched Pairs Study .......... 28
  2.3 Part 2 - Intervention Trial ................................................................................. 30
    2.3a Participants ................................................................................................. 30
    2.3b Randomization ............................................................................................ 30
    2.3c Statistical Analyses ..................................................................................... 33
  2.4 Data Collection - Instrument Choice for the Studies ........................................ 37
CHAPTER 3: IMPAIRMENT LEVEL CORRELATES OF UPPER LIMB FUNCTION .......... 42
  3.1 Upper Limb Functioning in Children with Hemiplegic Cerebral Palsy ........... 42
  3.2 Determinants of Upper Limb Functioning ....................................................... 43
  3.3 Results .............................................................................................................. 49
    3.3a Functional Measures ................................................................................... 52
    3.3b Impairment Level Measures ....................................................................... 53
    3.3c Analysis of Function in Relation to Muscle Tone, Power and Sensation . 59
    3.3d Model of Functional Outcome for Children with HCP .............................. 60
    3.3e The Latent Variables .................................................................................. 60
  3.4 Discussion ........................................................................................................ 69
CHAPTER 4: THE IMPACT OF PAIN ON FUNCTION – FREQUENCY, DISTRIBUTION AND SEVERITY ........................................................................................................ 76
  4.1 Pain Results ...................................................................................................... 78
  4.2 Pain Discussion ................................................................................................ 84
CHAPTER 5: SELF ESTEEM, SELF CONCEPT AND QUALITY OF LIFE – HOW CHILDREN WITH HCP COMPARE WITH TYPICALLY DEVELOPING PEERS .......... 93
  5.1 Results – Self Concept and Quality of Life .................................................... 95
  5.2 Discussion – Self Concept and Quality of Life .............................................. 100
CHAPTER 6: SELF-CONCEPT AND QUALITY OF LIFE – IS THERE A RELATIONSHIP TO FUNCTION? ........................................................................................................ 107
  6.1 Results ............................................................................................................ 107
    6.1a Correlations .............................................................................................. 107
    6.1b Regression Analyses ................................................................................. 109
  6.2 Discussion ...................................................................................................... 110
CHAPTER 7: THE NEED FOR ASSISTANCE – ORTHOTICS, THERAPY AND ASSISTIVE TECHNOLOGIES .......................................................... 114
  7.1 Results - Orthotics, Therapy and Adaptive Technologies ......................... 115
    7.1a Characteristics of Study Population ...................................................... 115
    7.1b Use of Orthoses ...................................................................................... 117
    7.1c Assistive Technologies ........................................................................... 118
    7.1d Abandonment of Orthosis ..................................................................... 120
    7.1e Orthotic Prescription ............................................................................. 121
    7.1f Prescription of Assistive Technology ..................................................... 121
    7.1g Therapy ................................................................................................. 121
    7.1h Use / Abandonment of the Orthotic ...................................................... 122
  7.2 Discussion, Orthotics, Therapy and Adaptive Devices ................................ 124
CHAPTER 8: SUMMARY OF THE MAJOR FINDINGS IN PART 1 – HEMIPLEGIA AND THE NEGLECTED UPPER LIMB ................................................. 129
CHAPTER 9: INTERVENTION TRIAL – THE USE OF BOTULINUM TOXIN INJECTION TO IMPROVE FUNCTIONAL OUTCOME ........................................ 132
  9.1 Results - Intervention trial ......................................................................... 134
    9.1a Study population .................................................................................... 134
    9.1b Dose of BoNT-A and Occupational Therapy .......................................... 137
    9.1c Activity-Participation Measures (Table 9.4) ............................................ 139
    9.1d Body Function Measures (Table 9.4) ...................................................... 140
    9.1e Safety ..................................................................................................... 146
    9.1f Analysis of Impairment Level Measures – Power, Sensation, Tone, Growth and Motor Control .............................................................. 147
    9.1g Power .................................................................................................... 149
    9.1h Sensation ............................................................................................... 150
    9.1i Muscle tone ............................................................................................ 151
    9.1j Hand Span ............................................................................................. 152
    9.1k Motor Control – DIAT ......................................................................... 153
  9.2 Discussion - Intervention trial .................................................................... 154
CHAPTER 10: CONCLUSION ............................................................................. 161
  10.1 Hypothesis 1 - Functioning ..................................................................... 161
    2.1 Children with HCP and pain experience lower functional levels, quality of life and self-concept ................................................................. 161
    2.2 There are no significant differences when comparing children with HCP to peers with typical development on measure of self-esteem ...................... 162
    2.3 Quality of life and some self-concept domains differ to typically developing peers, favoring the peer group ................................................. 162
  10.3 Hypothesis 3 – Interventions to improve function .................................... 163
    3.1 Children with HCP who have more severe involvement neurologically (with greater impairment) are least functional and more dependent for care, with a greater reliance on upper limb orthotics, therapy and assistive devices ......... 163
    3.2 The prescription of orthotics and assistive devices will be utilised with a high rate of adherence ................................................................. 163
    3.3 Children with HCP undergoing upper limb treatment with BoNT- A and therapy have significantly better outcomes than children having therapy alone for all measures of body structure and activities/participation .......... 163
  10.4 Conclusion ............................................................................................... 164
  10.5 Future Directions .................................................................................... 166
DECLARATION STATEMENT

I certify that this thesis does not incorporate, without acknowledgement, any material previously submitted for a degree or diploma in any university and to the best of my knowledge and belief it does not contain any material previously published or written by another person except where due reference is made in the text.

Signature____________________________  Date______/______/_______

Dr Remo Nunzio Russo
ACKNOWLEDGEMENTS

I would like to thank the following people for their valuable contribution to this thesis:

My wife, Teresa, and son Edward, for their unwavering and strong support and understanding which enabled me to complete this thesis. I thank you sincerely for helping me – it would not have been possible without your support.

My supervisors – Prof. Maria Crotty for her invaluable guidance, Assoc. Prof. Peter Flett and Prof. Ian Cameron for their ongoing support and advice.

Ms Michelle Miller for her invaluable guidance in the process of completing my PhD. As well as her contributions to study design, data collection and input, analysis and manuscript preparation, she is a mentor and friend and I greatly appreciated her advice and assistance.

Ms Cherie Archer for data collection and entry (Intervention trial; Pain trial; Matched pairs trial – hemiplegia group; Orthotics and adaptive equipment trial)

Ms Lynne Giles for assistance with data analysis (Intervention trial; Pain trial)

Ms Kylie Lange for assistance with data analysis (Intervention trial; Pain trial; Matched pairs trial)

Ms Jacqueline Stepien-Hulleman for assistance with data entry (Intervention trial; Pain trial) and assistance with Intervention trial organization (randomisation process)

Mr. Pawel Piotr Skuza for assistance with data analysis (factor analysis and orthotics and adaptive equipment trial)

Occupational Therapists at Novita Children Services under the supervision of Ms Sonya Murchland for the provision of the occupational therapy program (Intervention trial)

Ms Belinda Henning for assistance with data collection and entry, Part 1

Dr Phil Egan for comments on the manuscript (Matched pairs trial)
The Intervention trial research protocol was investigator led with funding for study personnel conducted with support from the following sources: Financial Markets Foundation for Children and Allergan Australia Pty Ltd.

This trial has been registered with the Australian Clinical Trials Registry, ACTR #12605000127606.
CO-AUTHORS’ CONTRIBUTION TO PUBLISHED WORKS


Remo Russo undertook all facets of study design, data collection, entry and analysis, and wrote the manuscript; Maria Crotty assisted in study design, data analysis and writing of the manuscript. Michelle Miller assisted in study design, data entry and analysis, and writing of the manuscript. Sonya Murchland assisted in data collection and analysis, and writing of the manuscript. Peter Flett assisted in study design, data analysis and review of the manuscript. Eric Haan assisted in study design and review of the manuscript.


Remo Russo undertook all facets of study design, data collection, entry and analysis, and wrote the manuscript. Emma Goodwin undertook data collection and entry for the peer group, and assisted in writing the manuscript. Michelle Miller undertook data entry and analysis, and assisted in writing of the manuscript. Eric Haan assisted in study design and in the writing of the manuscript. Tim Connell assisted in theoretical construct, data analysis and in writing the manuscript. Maria Crotty assisted in study design, data analysis and review of the manuscript.


Remo Russo undertook all facets of study design, data collection, analysis and wrote the manuscript. Michelle Miller assisted in study design and undertook data entry and analysis, and assisted in writing of the manuscript. Eric Haan undertook data analysis, and assisted in writing of the manuscript. Ian Cameron assisted in data analysis, theoretical framework, and writing of the manuscript. Maria Crotty assisted in study design, data analysis and writing of the manuscript.


Remo Russo undertook all facets of study design, data collection, analysis and wrote the manuscript. Renae Atkins undertook data analysis and interpretation of clinical meaning, and assisted in writing the manuscript. Eric Haan undertook data analysis, and assisted in writing of the manuscript. Maria Crotty assisted in study design, data analysis and writing of the manuscript.
**SUMMARY OF ABBREVIATIONS**

1. ACTR – Australian Clinical Trials Registry
2. ADL – Activities of daily living
3. AMOS – Analysis of a moment structure
4. AMPS – Assessment of motor and process skills test
5. AT – Assistive technologies
6. BoNT-A – Botulinum toxin A
7. CFA – Confirmatory Factor Analysis
8. CFI – Comparative fit index
9. CP – Cerebral Palsy
10. CPRHand – Cerebral Palsy Register measure of Hand Function
11. DIAT – Dynamic Interference of Tone - Upper Limb
12. DTRs – Deep tendon reflexes
13. GAS – Goal Attainment Scale
14. GLM – General Linear Modelling
15. GMFCS – Gross Motor Function Classification System
16. HCP – Hemiplegic Cerebral Palsy
17. ICF – International Classification of Functioning
18. IQ – Intelligence Quotient
19. MACS – Manual Ability Classification System
20. ManHands – Manipulative Hand Skills
21. MAS – Modified Ashworth Scale
22. OT – Occupational Therapist
<table>
<thead>
<tr>
<th></th>
<th>Acronym</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>23.</td>
<td>PEDI</td>
<td>Pediatric Evaluation of Disability Inventory</td>
</tr>
<tr>
<td>24.</td>
<td>PedsQL</td>
<td>Pediatric Quality of Life Inventory</td>
</tr>
<tr>
<td>25.</td>
<td>PRP</td>
<td>Paediatric Rehabilitation Physician</td>
</tr>
<tr>
<td>26.</td>
<td>QUEST</td>
<td>Quality of Upper Extremity Skills Test</td>
</tr>
<tr>
<td>27.</td>
<td>R1</td>
<td>Range of motion at “first catch”</td>
</tr>
<tr>
<td>28.</td>
<td>R2</td>
<td>Full passive range of motion</td>
</tr>
<tr>
<td>29.</td>
<td>RMSEA</td>
<td>Root Mean Square Error of Approximation</td>
</tr>
<tr>
<td>30.</td>
<td>SACPR</td>
<td>South Australian Cerebral Palsy Register</td>
</tr>
<tr>
<td>31.</td>
<td>SAE</td>
<td>Serious Adverse Event</td>
</tr>
<tr>
<td>32.</td>
<td>SPSS</td>
<td>Statistical Package for the Social Sciences</td>
</tr>
<tr>
<td>33.</td>
<td>UPLIFn</td>
<td>SACPR Upper Limb Functional Assessment Scale</td>
</tr>
</tbody>
</table>
THESIS SUMMARY

Hemiplegic cerebral palsy (HCP) is a static neurological condition that primarily affects one side of the body. There are associated cognitive and functional problems impacting on the life of affected children. Lower limb effects have been extensively studied with clinical/laboratory based tools, to the point of being very reliable to assist families in decision making to achieve better functional outcomes. However, there is a paucity of evidence for the effects on upper limb dysfunction. Some reasons for this lack of evidence is that upper limb function, not being reliant on repetitive, stereotypic motor and sensory function like the lower limb, is impacted upon by many related factors including cognition, environment (including adaptive devices), self-concept, pain, quality of life and other factors interacting in a complex manner.

The primary focus of this work is on functioning and independence, with an exploration of the clinically relevant factors that could be measured that impact on these functional outcomes. Associations in the areas of self-esteem and self-concept, quality of life and the experience of pain are explored. The secondary aim is to explore the effects of botulinum toxin injection to improve functioning.

These aims are achieved through conducting two related studies. The first (Part 1) was a cross sectional analysis of children with HCP recruited from a population based cerebral palsy register, with an analysis of the children’s functional level as defined by the Assessment of Motor and Process Skills, clinical neurological examination, as well as measures of quality of life, self-esteem/self-concept, pain,
caregiver burden, and use of orthoses and assistive devices. The second (Part 2) was a single blind randomized control trial recruiting children from Part 1, with a focus on functional improvement and the attainment of individualised predefined goals. All participants undertook regular occupational therapy and the intervention group had upper limb botulinum toxin injection.

Children with hemiplegic cerebral palsy are resilient, with levels of self-esteem equivalent to sex and age matched typically developing peers. They report significantly lower levels in some self-concept domains (such as physical and scholastic competencies), and children recognise their limitations from a young age. They self-report lower levels of quality of life, and higher levels of pain. The impairments most strongly associated with functional level and independence are muscle power and sensation, indicating prediction of and improvement in functional independence requires a focus on sensory testing and strengthening. Tone is less strongly associated, however the degree of upper limb tone is related to the need for intervention. Knowing the degree of upper limb muscle tone from a young age is helpful in assisting families with children with a new diagnosis of HCP. Children who had an acute reduction in tone with the use of botulinum toxin injection, however, achieved their stated functional goals more quickly, with an associated boost in self-esteem, unlike the control group, who had lower levels of self-esteem during the study period possibly related to a focus on functional gain with a slower rate of improvement with therapy alone.