Congenital Hemiplegia and the Neglected Upper Limb

A Thesis for the Degree of Doctor of Philosophy in Medicine

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2011

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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

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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

Russo RN, Crotty M, Miller MD, Murchland S, Flett P, Haan E. Upper-limb botulinum toxin A injection and occupational therapy in children with hemiplegic cerebral palsy identified from a population register: a single-blind, randomized, controlled trial. *Pediatrics* 2007; 119:e1149-58. 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.
Russo RN, Goodwin EJ, Miller MD, Haan EA, Connell TM, Crotty M. Self-esteem, self-concept, and quality of life in children with hemiplegic cerebral palsy. *J Pediatr* 2008; 153:473-7. 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.
Russo RN, Miller MD, Haan E, Cameron ID, Crotty M. Pain characteristics and their association with quality of life and self-concept in children with hemiplegic cerebral palsy identified from a population register. *Clin J Pain* 2008; 24:335-342. 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.
Russo RN, Atkins R, Haan E, Crotty M. Upper limb orthoses and assistive technology utilisation in children with hemiplegic cerebral palsy recruited from a population register. *Dev Neurorehabil.* 2009; 12: 92-99 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

23. PEDI – Pediatric Evaluation of Disability Inventory

24. PedsQL – Pediatric Quality of Life Inventory

25. PRP – Paediatric Rehabilitation Physician

26. QUEST – Quality of Upper Extremity Skills Test

27. R1 – Range of motion at “first catch”

28. R2 – Full passive range of motion

29. RMSEA – Root Mean Square Error of Approximation

30. SACPR – South Australian Cerebral Palsy Register

31. SAE – Serious Adverse Event

32. SPSS – Statistical Package for the Social Sciences

33. UPLIFn – SACPR Upper Limb Functional Assessment Scale

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.

CHAPTER 1: INTRODUCTION

Cerebral palsy (CP) is the most common pediatric physical disability, with an incidence of 2.0–2.5 cases per 1,000 births (Reddihough and Collins 2003). Children with HCP are born at a rate of 0.66-1.0/1,000 population (Uvebrant 1988; Cioni et al 1999; Sakzewski et al 2009). Children with CP deal with many complex health, physical, cognitive, and family issues. They have significant disability (Rice et al 2008) despite being in the subgroup of children with CP more likely to function alongside typically developing peers (Michelsen et al 2005). There is a wide range of severity in this population of children, with many children relatively minimally affected and others who are more severely affected (Uvebrant 1988). Treatment is multidisciplinary and includes therapy, special education, oral medications, surgery and assistive devices (Flett 2003; Wake et al 2003). Despite this, children with HCP are in the sub-group of individuals with CP most likely to complete mainstream schooling and attain gainful employment (Michelsen et al 2005). They are expected to function at peer levels and any negative impact that upper limb dysfunction may have will disadvantage this subgroup of children. However the physical and cognitive difficulties can potentially place children with HCP at a disadvantage in a mainstream environment.

Children with HCP have significant physical and cognitive limitations (Khaw et al 1994; Odding et al 2006) that require support with the use of orthoses and assistive technologies (AT), and other intervention modalities including therapy, Botulinum toxin injection and surgery. In approximately 80 - 90% of children with CP, the motor deficit is spasticity (Graham 2000; Surman et al 2006). In hemiplegic CP,

almost all children achieve independent walking (Uvebrant 1988), but many have significant difficulty in every day functional activities due to involvement of the upper limb (Boyd et al 2001) with more severe limitation in bimanual fine motor activity (Beckung and Hagberg 2002; Rice et al 2008). The upper limb functional impairments can also impact on participation, although this aspect of limitation has not been studied systematically (Sakzewski et al 2009). Reduced self-esteem and self-worth may be an issue amongst all children with CP, however the magnitude of the deficit, the impact on functional level and the influence on the effectiveness of treatment programs are unknown.

The World Health Organisation (WHO) has suggested that, when assessing function in children/adolescents/adults with disability, a framework is used known as the International Classification of Functioning (ICF) (WHO 2001). This framework attempts to define the experience of disability in biological and social frameworks (Beckung and Hagberg 2002) at three different levels; body, person and society (Boyd and Hays 2001b). In this model body structures and function relate to functioning at an organ level, for example, at the level of muscle power across a joint. Activities and participation refer to tasks that are necessary to complete at the level of personal functioning (eg. dressing) and to the degree of involvement a person undertakes in society (such as interactions with peers and school attendance). Environmental factors that impact on personal experiences of disability are also included in the model, and are inclusive of such factors as attitudes toward disability and the actual physical environment. These domains of functioning ensure that most facets of the disabling condition are included in any study, report or account of the disability. In this way, the limitations experienced by groups of people with disabling

conditions can be expressed in more relevant terms for the purposes of comparison and assessment of impact. This model has been adopted for the outcomes presented in this thesis.

1.1 Aims and Hypotheses

The aim of this work was to assess a population based cohort of children with HCP recruited from a population register and to:

1. define the children's level of impairment
2. describe the association between impairment and function
3. describe the relationship between self-esteem, self-concept, pain, quality of life and function
4. investigate common clinical interventions (such as the pattern of utilisation of therapy, orthotics and assistive devices) and investigate the impact of botulinum toxin use with therapy compared to therapy alone in a single blind controlled trial.

To more completely assess function, and the factors that may influence function, a broad approach to the experience that the child has with their disabling condition, under an ICF framework, was undertaken.

1.1 a Hypothesis 1 – Functioning

1.1 The negative attributes of the upper motor neurone syndrome in HCP (such as muscle weakness) have an effect of similar magnitude to positive attributes (such as spasticity) on function and motor control.

1.1b Hypothesis 2 – Outcomes Associated with Functioning

2.1 Children with HCP and pain experience lower functional levels, quality of life and self-concept.

2.2 There are no significant differences when comparing children with HCP to peers with typical development on measure of self-esteem.

2.3 Quality of life and some self-concept domains differ to typically developing peers, favoring the peer group.

1.1c Hypothesis 3 – Interventions to Improve Function

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.

3.2 The prescription of orthotics and assistive devices will be utilised with a high rate of adherence.

3.3 Children with HCP undergoing upper limb treatment with botulinum toxin A (BoNT-A) and therapy have significantly better outcomes than children having therapy alone for all measures of body structure and activities/participation.

Four studies were undertaken to address these aims and hypotheses in a framework that consisted of 2 main parts. Part 1 was a cross-sectional evaluation of the participants which yielded results reported in chapters 3 (determinants of upper limb functioning; hypothesis 1.1), 4 (pain and functioning; hypothesis 2.1), 5 (self-esteem, self-concept and quality of life; hypotheses 2.2 & 2.3) and 7 (orthotics, therapy and AT; hypotheses 3.1 & 3.2). Part 2 was a single blind randomized control trial evaluating upper limb treatment with botulinum toxin A and therapy versus therapy alone (Chapter 9, hypothesis 3.3).

CHAPTER 2: METHODS

2.1 Ethics

The study (Part 1 and Part 2) was approved by the Research and Ethics Committees of the Flinders Medical Centre and the Women's and Children's Hospital, South Australia (Approval number: 1553/3/2010).

2.2 Part 1 - Descriptive Study

2.2a Participants

Children were recruited (June 2004 - September 2005) from the South Australian Cerebral Palsy Register (SACPR) (Register 2005) which contains details of all children with CP (confirmed after physical examination) living in metropolitan, rural and remote areas of South Australia. It is estimated that approximately 85% of all children with CP are entered onto the CP Register, and that the database is representative of all children with CP living within the community (Register 2005).

2.2b Recruitment, Part 1

All children diagnosed with of HCP, aged 3-16 years, on the CP Register were invited to participate. The reported ascertainment rate of 2.1 per 1000 births (Register 2005) is similar to other published data (Reddihough and Collins 2003). The register accepts the notifying clinician's clinical diagnosis of hemiplegia and this is confirmed at a clinical review when the child is 5 years of age according to the register's protocol (Register 2005). There were 128 children with hemiplegia identified on the register and 108 families (84%) agreed to participate. One child, on review, did not have HCP but another topographical form of CP, and was excluded

from the study. Twenty one families either could not be contacted or did not agree to participate. The children and their families were initially contacted by telephone, and written informed consent was obtained from the parent. If the children had hemiplegic CP and wanted to participate in the study there were no exclusion criteria imposed. The children underwent review in person by a Pediatric Rehabilitation Physician (PRP) and an Occupational Therapist (OT).

2.2c Data Collection and Instruments

Data was extracted from the SACPR for gestation, birthweight, intelligence quotient (IQ), Gross Motor Functional Classification System (GMFCS) (Palisano et al 1997) level and current education. Age, gender and affected side were collected at the time of review, as were some further details about educational level and estimated IQ completed by the PRP (12 subjects given current education classification; 16 subjects estimated IQ based on SACPR criteria).

Measures undertaken by the PRP for the body structures/function domain of the ICF (WHO 2001) included a neurological assessment (deep tendon reflexes, power rating scale, coordination, visual examination, and sensory testing [stereognosis, 2 point discrimination, graphesthesia, joint position sense, vibration sense, and sensory and visual inattention – to a total of 30 items]). There were also measures of affected upper limb spans using a non-stretch tape measure and bony landmarks, and the modified Ashworth scale (MAS) (Bohannon and Smith 1987) and Tardieu scales (Gracies et al 2000) taken at the affected elbow and wrist. The use of upper limb orthoses (with duration of wear and utility) and the use and utilization of AT and therapy were recorded in a standardized fashion using a printed proforma.

Upper Limb Growth

This was measured clinically using a non-stretch tape measure (in centimetres) over 3 segments; the humeral length (tip of acromion to lateral epicondyle of the humerus) (Tachdjian and Minear 1958) forearm length (from the lateral epicondyle of the humerus to the tip of the styloid process of the ulna) and hand span. Hand span was the maximal active stretch of the hand possible for the child, who then placed their hand on a sheet of paper. The little finger and thumb were outlined with a pencil, then a horizontal line drawn at the tip of each outline. The perpendicular to that line was drawn so as to intersect it at the tip of the finger outline and the distance between the middle of the crosses of the little finger and thumb was measured by metric ruler in centimetres. By convention, unaffected then affected sides were recorded at each level.

Tone

Tone was measured at the elbow, wrist, forearm and thumb using the MAS. For testing at the wrist, the fingers were flexed to remove the influence of tight finger flexors. The joint was moved through its range of motion and the scale figure recorded. These results are reported as percentage of children displaying at least a catch (1+ or greater) on the scale. The modified Tardieu was also used and the angle between initial catch and full range of motion was recorded for the elbow and wrist. Reported are the percentage of children who had a measurable angle across the joint.

Range of Joint Motion

Range of motion was measured in degrees of passive motion across the elbow,

forearm, wrist and thumb and was measured with a goniometer. Elbow range was taken as 0˚ (full flexion) to 180˚ (full extension); fore arm 0˚ (neutral position) and 90˚ for pronation, 90˚ for supination; wrist 0˚ (neutral position) 90˚ each for flexion and extension; thumb at 0˚ fully adducted against the border of the hand to 90˚ fully abducted. The results were summarised as either full range of motion, or restriction of full range of motion and reported as a percentage of children with restricted motion.

Muscle Power

Manual muscle testing was conducted for both affected and unaffected sides and the power rating scale (out of 5) was used (Brown et al 1987; Dubowitz 1995). The side contralateral to the hemiplegia was taken as "normal power" in all of the comparison's and scored 5/5. Power rating included the shoulder (abduction, adduction, flexion and extension), the elbow (flexion and extension), the forearm (supination and pronation), the thumb (flexion, extension, abduction and adduction), and the fingers (flexion, extension, abduction and adduction). Grip strength using a rolled blood pressure cuff (Helewa et al 1981) was also recorded for the affected side.

Coordination and Reflexes

Coordination and reflexes included finger nose testing (the child touching their nose and then the finger-tip of the examiner's hand placed at maximal reach and repeated 3 times). Deep tendon reflexes (DTRs) were tested across the biceps, triceps, supinators, knees and ankles. DTRs that were classified as 3+ and 4+ were taken to be hyper-reflexive. Plantar responses were recorded as definitely up-going (extensor)

or normal (down-going, equivocal or “absent”).

Sensation

For all tests of sensation, vision was occluded by a standardised barrier placed in front of the eyes. By convention, and to ensure best responses were obtained, first the unaffected side, then the affected side was tested sequentially for each test (Tachdjian and Minear 1958; Tizard et al 1954), starting with stereognosis, followed by finger identification, 2 point discrimination, and graphaesthesia. Stereognosis – objects were placed in the hand and the child had to identify what the objects were. For young children and children with communication problems, a copy of all of the objects present (placed to the side within their visual field) was used so they could point to the object they thought they were feeling (House et al 1981). This included 10 items (in standard order presented to all participants – toy car, pencil, flannel, ball, key, safety pin, coin, marble, button and toothbrush). Finger identification – with the hand being tested occluded from view, the dorsal aspect of the thumb and each finger was touched with a cotton bud and the child had to identify which finger was being touched, aided by a picture of a hand with labelled fingers which was placed in their visual field. 2 point discrimination – with vision occluded all 5 fingers (palmar aspect of the finger tips) were tested using a standard distance of 8mm (House et al 1981; Tizard et al 1954). The child was asked if they could feel 1 point or 2 points, results scored according to if the response was correct. Graphaesthesia – the palmar aspect of each hand was drawn upon, with the smooth back end of a pen, the following figures, presented in this order and in a standard fashion for each child – I, O, V, 8, X, and 3. The child was aided by a picture of each form to assist in identification and vision was occluded as for the other sensory tests.

Motor Control

Children were tested for motor control using the Dynamic Interference of Abnormal Tone Upper Limb (DIAT) measure, Manipulative hand skills (ManHandS) measure and the Cerebral Palsy Register Hand Function for Children with HCP (CPRHand) measure (Register 2005).

The DIAT was adapted from a measure of selective (voluntary) motor control used to assess brain injured patients (Evans 1976). There are six levels of control, from 0 (No voluntary movements) to 5 (Normal movements) grading voluntary movement patterns sequentially from the shoulder through the elbow, wrist, hand and fingers. The ManHands is a measure of hand function adapted from McCue 1970 (McCue et al 1970). It is a categorical scale with 6 categories, from 0 (no voluntary hand function) to 5 (Complex in-hand manipulations) with grasping activity the main determinants of classification of hand function. The CPRHand tool has 5 categories ranging from “no apparent problem” (1) to “Non-functional upper limb” (5) with descriptive grades of spontaneous upper limb use in manual functioning. This was adapted from Lindon 1963 (Lindon 1963) and categorises hand function for hemiplegic patients.

Children’s upper limb function was also described by a categorical scale assessing the ability of the child to self feed and dress, derived from the SACPR and checked at the assessments of the children. This was the Upper Limb Functional Assessment scale (UPLIFn), a categorical scale assessing if the child has no problem with bimanual tasks, some difficulty with bimanual tasks but can feed themselves, unable to put on shirt but able to self-feed, and unable to put on shirt and unable to self-feed

(Rice et al 2008).

Pain

Pain was reported using the Wong-Baker FACES Pain Rating Scale. This scale is a valid and reliable pain rating scale (Luffy and Grove 2003; Soetenga et al 1999) that can be used for children from 3 years of age. Assessment of the location of the pain experienced, severity of the pain, quality of the pain, the effects of the pain on activities, what exacerbated the pain, what relieved the pain, and what the family and child thought was the cause of the pain was recorded in a standardised fashion. For cause of pain this was divided into "disease related", "treatment related", "ageing and growth", "Not sure/uncertain" and "Other". There were also two pictures of a body outline (front and back in the coronal plane) so the child could mark where on the body they experienced the pain. Children were asked if they experienced regular pain. Any pain experienced at the time of data collection was excluded if it was inconsistent with the nature of the regular pain described by the child. In all cases where developmentally appropriate, the child self-reported the pain. In some children < 5 years and in a small number over 5 years with cognitive difficulties, a family member confirmed the pain experience if this was reported by the child. For tabulation of pain severity in the children who experienced pain, items on the Wong-Baker FACES Pain Rating Scale were grouped as "Mild" and "Moderate" pain indicating the mild to moderate group respectively, and "Severe", "Very Severe" and "Overwhelming" indicating the severe group.

Assessment of Motor and Process Skills

The activities-participation measure (WHO 2001) was the Assessment of Motor and Process Skills (AMPS). The AMPS is a reliable and valid tool used to measure instrumental (complex or domestic) activities of daily living (ADL) (Fisher 2003; Kottorp et al 2003), where key skills and actions that facilitate or hinder performance in ADL at the level of expected achievement are identified (Fisher 2003). Two activities routine for the child were chosen for assessment, which is undertaken in the person's usual environment (Park et al 1994). The ADL activity was rated on what the individual was observed "to do" at the assessment (Van Zelst et al 2006), giving a measure of real life performance. A trained OT undertook the assessment in the child's home. Examples of tasks undertaken included making a sandwich, brushing teeth, and upper body dressing. The motor skill component evaluated actions used to complete the task, and the process skill component evaluated the child's ability to organise the activity and overcome problems encountered in completing the task (Van Zelst et al 2006). Higher logit scores on the test indicate greater motor and process abilities, with scores ranging from -3 to +3 for both motor and process scales.

Self-Perception

The Self-Perception Profile for Children (Harter 1985) and The Pictorial Scale of Perceived Competence and Social Acceptance for Young Children (Harter and Pike 1984) (also referred to collectively as the Harter scales) are valid and reliable (Granleese and Joseph 1994; Harter and Pike 1984) (Pereda and Forns 2004) measures used to evaluate children's self perception. In both measures, a scenario is presented to the child and they have to decide which they are most like. For example,

in the Social Acceptance domain, children are presented with the statement “some kids find it hard to make friends, but other kids find it pretty easy to make friends”. The children have to decide which they are most like, and decide if this is sort of true for them or really true for them. The items are scored from 1 (minimum score) to 4 (maximum score) depending on their responses. Higher scores for the domains indicate a higher self-concept for that domain of functioning.

The Self-Perception Profile for Children is a 36 item scale for children ≥8 years of age and was designed to evaluate domain specific judgements of children’s perceived competence in the domains of scholastic competence, social acceptance, athletic competence, physical appearance, behavioral competence, and global self worth. This measure explores such areas as the child’s perception about how they look, (the Physical Appearance domain), their perception of how well they make friends, the number of friends they have and their popularity (the Social Acceptance domain), the degree to which they perform at physical activities including athletics (the Athletic Competence domain) how competent the child feels with respect to school work, asking whether children feel they are smart, and how well they retain information (the Scholastic Competence domain), and whether they feel they behave in the “right” way (the Behavioural Competence domain). Global self-worth is a measure of self-esteem and is included in this profile. Therefore, measures of self-esteem are reported only for the children ≥8 years of age.

The Scale of Perceived Competence and Social Acceptance for Young Children was designed for young children up to age seven years. Twenty four items evaluating self perception are shown in picture form representing two ends of a continuum and the

child decides which they are most like. The scoring allows evaluation in the domains of cognitive competence, physical competence, peer acceptance, and maternal acceptance (Harter and Pike 1984). The Cognitive Competence domain reflects how well the child feels they are with maths and literacy, and generally how much they know. The Physical Competence domain measures the degree to which children feel they are competent at activities such as skipping, hopping, running, swinging and tying shoes. The Peer Acceptance subscale rates the child's perception of their peer relationships. The Maternal Acceptance subscale rates the child's perception of how much time they spend with their mother and whether they undertake activities specifically chosen by the child.

Quality of Life

Quality of life was measured using the Pediatric Quality of Life Inventory [PedsQL^{TM} Version 4.0] (Varni et al 2001) which was administered to all parents, and children >4 years of age. An overall score for quality of life can be determined for the child (child total scale score) and parent (parent total scale score). This instrument is valid (Berrin et al 2007) and reliable (Varni et al 2001; Varni et al 2006b; Varni et al 2007a). It consists of 23 items and has a child self-report (for children > 4 years of age) as well as a parent proxy-report (Varni et al 2001). The child and parent are asked how much of a problem each item has been for them in the past month, with responses on a 5 point scale ranging from "never a problem" to "always a problem". Four subscales can be determined; Physical Functioning, Emotional Functioning, Social Functioning and School Functioning. The Physical Health Summary Score and the Psychosocial Health Summary Score can be derived from the four subscales. The Physical Health Summary Score is equivalent to the

Physical Functioning Sub-scale (Varni et al 2007c), and the Psychosocial Health Summary score is derived by the sum of the items divided by the number of items answered in the Emotional, Social and School Functioning subscales (Varni et al 2005). The items are transformed to a 0-100 scale such that a higher score indicates a greater quality of life (Varni et al 2005).

Burden of Care

The Pediatric Evaluation of Disability Inventory (PEDI) (Haley et al 1992) is a valid and reliable tool (McCarthy et al 2002). The self-care domain was used in this study. This scale represents what the child is capable of completing without the assistance of a care-giver (Bourke-Taylor 2003), and covers such items as feeding, dressing and toileting. The subscales begin with basic tasks (for example, toothbrushing – "opens mouth for teeth to be brushed") and progresses through levels of independence (in this example, to "prepares toothbrush with toothpaste"). Each item is scored as capable (1 mark) or unable (0 marks). The items the child is capable of completing are added. The self-care domain consists of 73 capability items in 15 skill areas (Haley et al 1992), with 73 the maximal score.

2.2d Self-esteem, Self-concept and Quality of Life Matched Pairs Study

This study was a cross sectional evaluation of children with HCP registered with the South Australian Cerebral Palsy Register (SACPR) compared to age and gender matched peers.

Children with HCP

Of the 107 children with HCP recruited, there were n= 86 with a complete data set for the self-concept measures. Children who did not have a complete data set on the self-concept measure were excluded. The 86 children with a complete data set were included for comparison to age and gender matched peers with typical development.

Peers with Typical Development

Children were recruited as part of a larger study of healthy eating practices. Limited exclusion criteria were imposed. Recruitment occurred during October and November 2006. Participants were recruited through advertisement across an email distribution list of the Flinders Medical Centre, and a newsletter at a local independent Catholic School. Inclusion criteria were children aged 3-16 years attending a mainstream school not requiring special support and parent/care-giver able to speak and write English. Once written informed consent was obtained the child was enrolled into the study and matched to a child with HCP. Children were matched on gender and to within 1 year of the date of birth of a child with HCP. Children were then asked to complete the relevant Self-concept measure and PedsQL by a research student.

The data was collected on 2 separate occasions (once with the PRP and once with the OT). All protocols for the test items were followed strictly.

2.3 Part 2 - Intervention Trial

2.3a Participants

Children reviewed in Part 1 of the study, who had passive joint range of motion within defined limits (elbow extension to neutral, wrist extension to 30 degrees past neutral with fingers extended, supination of the forearm of 30 degrees past neutral, and thumb extension to neutral), ability to initiate movement of the fingers, and a MAS spasticity score of greater than or equal to 2/4 at the elbow or wrist were invited to participate in the study. Children were ineligible if they had received an injection of botulinum toxin in the upper limb up to one year prior to the study and in the lower limb up to six months prior to the study (Lowe et al 2006). Informed written consent was obtained from parents and from children cognitively able to consent (otherwise only the parental consent was obtained).

2.3b Randomization

Randomization occurred in blocks of 10. The randomization schedule and envelopes (concealed, opaque, and foil lined) were prepared by an independent statistician using a computer-generated table of random numbers. The Pharmacy Department at the Repatriation General Hospital maintained the envelopes. The research assistant telephoned the Pharmacy Department to obtain the assignment group, organize the referral for occupational therapy and, if applicable, referred to the PRP for scheduling of injection. Allocation was recorded in a logbook locked in a filing cabinet and was not revealed to the research OT at any time.

Intervention Group

Children allocated to the intervention group received individually prescribed and localized injections of botulinum toxin A (BoNT-A) into the affected upper limb and weekly occupational therapy for four weeks. Children were admitted to the day patient ward at the Women's and Children's Hospital or the Flinders Medical Centre for injection of the BoNT-A under general anesthesia. A muscle stimulator (Gorman 2002) assisted with localization of the muscles injected.

The maximal dose of BoNT-A per muscle according to Russman (Russman et al 1997) was followed, however all muscles across the upper limb were injected if tone was affected (tone [MAS] = 0 the muscle was not injected; if MAS = 1 to 1+/4 half the maximal dose was injected; if MAS = 2 to 3/4 the maximal dose was injected). Total injected dose did not exceed 12 units per kilogram of body weight, to a maximum dose of 300 units of Botox® (Allergan Australia Pty Ltd). The dilution of botulinum toxin used was 100 units of Botox® per 1 ml of normal saline. Post-injection the children were allowed to leave hospital once they were medically stable. Weekly one hour standardized occupational therapy sessions under the supervision of an OT were performed over four weeks. The focus of each therapy session was on upper extremity weight bearing, ball skills, fine motor strengthening and bilateral functional activities. Prior to outcome assessment, participants were instructed to avoid revealing treatment allocation to the research staff.

Control Group

The control group received the standardized occupational therapy program. No placebo injections were performed in the control group as this was not allowed ethically due to the requirement for general anesthesia for injection.

Data Collection and Instruments; Intervention Trial

Measures of body function included a neurological assessment, the MAS and the Tardieu scale. All measures were performed at baseline, three months and six months by a PRP. Participants also reported if they felt they were the same, worse or better since the intervention with respect to function and cosmesis. All assessments performed by the PRP were unblinded.

The primary outcome measures of activity-participation were the Assessment of Motor and Process Skills (AMPS) and the Goal Attainment Scale (GAS) (Kiresuk et al 1982). The AMPS was carried out as per Part 1 of the study, but evaluations took place at baseline, three and six months.

The GAS is a sensitive measure used to assess individualised goals after treatment (McLaren and Rodger 2003) and is recommended for children undergoing BoNT-A injection (Russman et al 1997). Desired outcomes are ranked from -2 (much less than expected outcome) to +2 (much greater than expected outcome). The scores are converted to a T-score with 50 (SD 10) the expected or average outcome score (Daley 1987). Each child and family nominated 3 areas of functioning they wanted to see improve as their goals. Examples of levels of functioning as measured by the

GAS included picking up an object (impairment level), tying shoe laces (activity level), and playing cards (to assist in games with other children – participation level). Each goal was evaluated at three and six months. Both measures were undertaken by a trained assessor blind to treatment allocation.

The AMPS was used as well as other measures including the Self-care Domain of the PEDI, and the PedsQL Version 4.0. Assessments were under taken at baseline, three months and six months by a blind assessor. Pain was reported at baseline and at the three and six month follow-up using the Wong-Baker FACES Pain rating scale. Self-concept was undertaken at baseline, 3 and 6 months using the Harter scales according to the child's age.

Serious adverse events (SAE - an event that was life threatening, fatal, or resulted in hospitalization or permanent disability) were reported by participants and their families at all follow up assessments. They also reported any other event or complication they felt was related to the procedure or with their involvement in the trial.

2.3c Statistical Analyses

Analyses for all Studies

Final analyses of the data were completed using Statistical Package for the Social Sciences (SPSS) 17.0 (SPSS Inc. Chicago Ill. USA). Means (95% CI) and medians (95% CI) [and SD where indicated] are reported depending on distribution of data. Comparisons between groups for categorical variables were made using Pearson's χ^2. For group comparisons of continuous variables the Student t-test or Mann-

Whitney U test was used depending on data distribution. A significance level of 0.05 was used unless otherwise stated.

Assessment of the determinants of function

Confirmatory factor analyses (CFAs) were used to explore the respective contributions of each category of factors examined (muscle power, muscle tone, sensation, growth, age and IQ) to the variance in function in three separate models. The first with motor control, and the second with function. A third model was tested combining the two models showing how the latent variables related to functional outcome. The analyses utilised analysis of a moment structure (AMOS) in SPSS version 17.0 (SPSS Inc. Chicago Ill. USA). The analyses were performed from the covariance matrix, and various indices of goodness of fit were calculated for all models and analysed. The indices reported are the Comparative Fit Index (CFI) and Root Mean Square Error of Approximation (RMSEA). Reported general parameters for acceptable fit of data for continuous variables are a CFI ≥ 0.95 and RMSEA < 0.06 (Schreiber et al 2006). The theoretical models constructed required a level of complexity that meant between 30-33 parameters had to be estimated by the model. This means that the sample size of 107 is below that required to be confident of the stability of the parameter estimates (Schreiber et al 2006) for repeated samples. However, a minimum number that is acceptable for this type of analysis is 100 subjects (Watson and Thompson 2006) and it was considered feasible to proceed with the analyses. Missing data was handled using maximum likelihood estimations acceptable for this type of analyses with normally distributed data (Schreiber et al 2006).

Sample Size for the Intervention Trial

Published AMPS data for children 3-12 years old were used to calculate the sample size required to observe an improvement of 0.5 on the AMPS logit scale (Fisher 2003). The AMPS data report a mean of 1.63 and a standard deviation of 0.58. It was estimated that the number of children required to detect a significant difference between the two groups was 36 (18 per group; assuming power 80%, alpha 0.05 and a one sided test). The sample size was increased by 20% to n = 44 (22 per group) to ensure the study would not become underpowered if participants were lost to follow-up.

For the intervention trial analyses were on an intention-to-treat basis. Comparisons between groups for categorical variables were made using the χ^2 or Fisher's exact test. For group comparisons of continuous variables the Independent sample *t*-test or the Mann-Whitney U test was used. As repeated measures were undertaken, a General Linear Model (GLM) analysis was employed using repeated measures to assess for treatment, time and interaction effects for Global Self-Worth, Athletic Competence and Physical Appearance.

GLM analysis was also undertaken for the impairment level measures of sensation, muscle power, tone, limb span and motor control. This was used to assess treatment, time and interaction effects for these variables comparing the two treatment modalities.

Pain Trial

For the pain analyses an adjusted significance level of 0.05 was divided by the

number of comparisons within each domain of functioning (body structure/function, activities participation, quality of life and self perception) and this adjusted significance level was then used in order to control for multiple comparisons. Also, logistic regression was performed to assess the impact of the independent variables (Parent PedsQL; Child PedsQL; Scholastic Competence and Behavioural Competence) on the likelihood that children with HCP reported the experience of pain.

Matched Pairs Trial

Analyses for children matched to typically developing peers included group comparisons for matched data (the paired sample t-test (PedsQL) or the Wilcoxon signed rank test (Self-concept)). Pearson's correlation was used to examine the relationship between quality of life and Global Self-Worth. Multiple linear regression analysis was used to assess the association between self-esteem (Global Self-Worth) and quality of life while controlling for age, gender, GMFCS level and intelligence. This was also used to assess two independent variables in relation to function. The first was Cognitive Competence (controlling for age, gender and burden of care) and then for Physical Competence (controlling for age, motor skills and burden of care). Power calculations were not undertaken for this study as there was an attempt to include all children able to participate with a complete data set, but based on participant numbers from a previous study the matched pairs trial was sufficiently powered to detect significant differences on the self-concept scales (Shields et al 2007).

Orthotics, Assistive Devices and Therapy Trial

For the orthotics trial and due to multiple comparisons, effect size was calculated for all significant findings. The significant findings with a large effect size (Phi > 0.5; r > 0.3; Eta squared > .06 (Cohen 1988)) were used in regression models for the three highest scoring variables. This was performed for the prescription (and abandonment of) orthoses and AT, but as only three independent variables were significantly associated with therapy provision, these three variables were used in that model without calculation of effect size. Direct logistic regression was performed to assess the impact of these independent variables on the likelihood that children with HCP would be prescribed an upper limb orthosis, AT and therapy, and the odds ratio of characteristics associated with abandonment of prescribed orthoses.

2.4 Data Collection - Instrument Choice for the Studies

There are a significant number of instruments available for the evaluation of function, self-esteem and self-concept, quality of life and pain for children reviewed in this study. A rationale for choosing the instruments used as opposed to others that may have been available is presented in the following discussion.

The aim of choosing the instruments for Part 1 and Part 2 of the study was to have an assessment of real world functioning, and not a measure that was undertaken under instruction with standardised assessments, meaning that the measure was likely to be out of the realm of real world functioning for most children. In this sense, the primary outcome measures using the AMPS and GAS for the intervention trial was the best choice. Other investigators have relied on measures that assess the maximal ability of performance in the upper limb using the Melbourne Assessment of Upper

Limb Function (Bourke-Taylor 2003; Randall et al 2001) and/or the Quality of Upper Extremity Skills Test (QUEST) (DeMatteo et al 1992). However typical use of the upper limbs in this group was felt to best reflect real world or participation level functioning and so the AMPS was selected over these other measures. For goal attainment, the Canadian Occupational Performance Measure (Law et al 1990) has the added benefit over the GAS of indicating the child/family's satisfaction with the goal, however the Canadian Occupational Performance Measure is more time consuming than the GAS. Due to the multiple outcome measures used in this study to gain an appreciation of the impact of the disability on the child and family, it was felt using the valid and reliable measure of the GAS was most appropriate. The GAS has been shown to be a very effective tool and to have adequate responsiveness to detect clinically significant changes and is felt to be superior to other activity/participation level outcome measures in this respect (Sakzewski et al 2007).

At the impairment level of function, the aim was to measure the independent variables with tools that were clinically relevant and readily available, rather than more sophisticated measures that would have less relevance in the clinical setting. This was especially significant when assessing the impairment level independent variables (such as muscle tone) in the predictive models. For example, the use of wrist resonant frequency (Corry et al 1997) is an objective measure of wrist "stiffness" in CP and is arguably more objective than the MAS. However, the predictive model presented in this thesis relating MAS score tone to need for orthotic prescription is more meaningful and relevant clinically, due to the accessibility of this measure over resonant frequency. This was also the rationale used in the choice of all of the measures of impairment level functioning.

There are many measures used to assess quality of life in the literature (Garratt et al 2002) but the most important factors in choosing an appropriate measures are reliability, validity and responsiveness (Schneider et al 2001). This is somewhat easier for disease specific outcome measures (Garratt et al 2002), and due to the disease specific nature of the Pediatric Quality of Life Inventory Version 4.0 (Varni et al 2001), as well as reliability, validity and utility data of this measure (Varni et al 2006b; Varni et al 2006a), it was chosen for use in this study.

Self-esteem and self-concept measures are not as numerous in the paediatric literature, and a rationale for selection of the Harter scales was used primarily for the ability to test children less than 8 years of age. The requirements for this scale were that the measure required appropriate validity and reliability for children down to 4 years of age, required the use of child generated items (for relevance) in pictorial form (for ease of administration), and was required to be more globally relevant and not restrictive to one population or culture. Using these criteria, it was felt that only the Harter scales were the most appropriate (Cremeens et al 2006). The major criticism of this scale being that it lacks sufficient published evidence for test-retest reliability, although evidence for its internal consistency and validity are very strong (Cremeens et al 2006).

Pain was measured using the valid and reliable Wong-Baker FACES pain rating scale. Because of the discrepancy between child and parental reports of pain (Chambers et al 1999; Chambers et al 1998) it was felt that a reliable and valid tool was required to allow for self-reporting of pain down to 3 years of age. Parental

"proxy reports" were used only for a very small number of children with cognitive or communication impairments. The Wong-Baker FACES pain rating scale was also found to be the preferred method of reporting when compared to a visual analogue scale and had much higher reliability in children (Luffy and Grove 2003). However, this scale has a smiling face to indicate "no pain", a factor which has been associated with reporting of higher levels of pain in comparison to neutral faces reporting "no pain" (Chambers and Craig 1998). This factor was taken into consideration when analysing the results in the pain section of this thesis.

It would have been useful to include the Manual Ability Classification System (MACS) (Eliasson et al 2006b) as a classification system for upper limb function in this population of children. This would not be for detecting change, but as a classification similar to the GMFCS to allow for an overall global description of the population. This valid and reliable tool is gaining clinical acceptance and should be utilised in future studies of upper limb functioning in children with CP.

Finally, since the completion of Part 1 and Part 2 of this study, there has been the development of the Assisting Hand Assessment (AHA) (Krumlinde-Sundholm et al 2007), a reliable and valid instrument to measure how effectively the hemiplegic hand is used for functional activities, and can be used to document upper limb functional change in children with HCP. It is a measure which captures the typical use of the upper limb in the child with HCP, in keeping with the theme of detecting change at participation level of function. The AHA measure was not developed when the preliminary planning work for this thesis and studies were undertaken, but is a useful measure to include for this patient group and could be used for future work

evaluating functional outcome in children with HCP.

CHAPTER 3: IMPAIRMENT LEVEL CORRELATES OF UPPER LIMB FUNCTION

3.1 Upper Limb Functioning in Children with Hemiplegic Cerebral Palsy

Children with CP experience a number of both negative symptoms (such as muscle weakness and loss of sensation) and positive symptoms (such as muscle spasticity) due to the upper motor neurone syndrome, which is common in HCP (Uvebrant 1988). These factors can adversely impact on upper limb functioning for the child with HCP. Upper limb dysfunction in this population is common (Arner et al 2008; Rice et al 2008), and in children with HCP is a relatively understudied area of research, with few randomized controlled trials evaluating functional outcomes and interventions with respect to real world functioning (Boyd et al 2001). Moreover, the relative contributions of the deficits in muscle power, sensation, tone, motor control and other factors that reduced upper limb function have not yet been evaluated systematically. There are several publications indicating which impairments are the most critical, but these are based on opinion rather than on evaluation of well conducted studies following recruitment of a representative sample of children with CP (Bourke-Taylor 2003; Pagliano et al 2001; Arner et al 2008; Van Heest et al 1993; Tachdjian and Minear 1958; Tizard et al 1954). Therefore the relative contribution of these impairments to functional outcome is not known.

This is important as currently there is great emphasis on the management of some of the positive symptoms of the upper motor neurone syndrome, such as spasticity management, which may be misguided if these factors are treated in isolation and are not the most significant determinants of function. An appreciation of the most

significant determinants of function would allow for multifaceted interventions more likely to be successful in the treatment of upper limb dysfunction in this population of children and adolescents. Some facets of impairment may be more influential than others, and thus may emerge, if known, as a focus for intervention. It is likely that any ability to significantly and favourable affect upper limb function in children with HCP will require a focus on several facets of the upper motor neurone syndrome, however knowing which are more strongly correlated to functional outcome would assist in determining how to prioritise interventions.

3.2 Determinants of Upper Limb Functioning

Weakness is a common problem experienced by children with HCP. Patients with upper motor neurone lesions suffer difficulties with muscle power impacting on grip strength (Blank and Hermsdorfer 2009), reach, elevation of the limb and other gross and fine motor motion about the wrist and elbow (Colebatch and Gandevia 1989). Brown (Brown et al 1987), in a review of 25 children with HCP, found a significant reduction in distal muscle power and speed of movement on the hemiplegic side, with proximal power relatively well preserved. Fatigue of use on the hemiplegic side was also a factor. Hand function was found to correlate well with the loss of distal power and loss of speed of movement. Pagliano (Pagliano et al 2001) noted functional improvements over time in 20 children with HCP, coincident with improvements in grip strength. However, the study population was not representative of children with HCP as there were only a small number of children studied, and the outcome measures were not validated. Despite these limitations, there were interesting results of their intervention trial reported in the same manuscript, indicating that the children who changed function the most were those less functional

at the start (Pagliano et al 2001) and this was related to improvements in grip strength.

Grip strength was one of two statistically significant predictors of good outcome in one study reviewing the effects of botulinum toxin injection (Fehlings et al 2001), and indirectly supports muscle power as a significant factor in contributing to functional outcome. Another study (Eliasson et al 1998) evaluated 20 children after upper limb surgery. The investigators found that by promoting wrist extension and forearm supination, grip strength increased, which correlated with an improvement in functional grip, lending further support to the idea that power is central to functional outcome. However, even in children with CP with good functional use of the upper limb [MACS level 1 (Eliasson et al 2006a)], weakness was common (Blank and Hermsdorfer 2009). Thus while weakness is associated with reduced functional capacity in CP generally, and in HCP specifically, the relative contribution of muscle power to function is not known in relation to other impairments and requires clarification to assess to what degree it needs to be a target of intervention to promote functional improvement.

Sensory dysfunction in children with HCP is common, is significantly different when compared to control children, and can sometimes involve the contralateral upper limb (Cooper et al 1995). The predominant sensory deficit in CP is one of cortical discriminatory sensation, affecting stereognosis, 2 point discrimination, graphaesthesia, and joint position sense (Tachdjian and Minear 1958; Uvebrant 1988). Loss of sensation in the upper limb is also common in children with HCP (Van Heest et al 1993; Tachdjian and Minear 1958; Tizard et al 1954). van Heest

(Van Heest et al 1993) found that 97% of 63 children with HCP had sensory deficits. This rate is high but the objects needing identification for stereognosis were small (in size) and there were similar objects used (such as a button and a coin) and so likely had a high sensitivity when compared to other studies reporting a lower rate of sensory deficits (Tizard et al 1954; Tachdjian and Minear 1958). Stereognosis was the most common deficit found in CP in the literature cited, which indicates that sensation involves in-hand manipulation and may also be reliant on motor function. Also, 2 point discrimination was found to be deficient in one study (Gordon and Duff 1999b) and was associated with grip force adaptation, relating to functional use of the upper extremity.

The importance of sensibility in the affected upper limb is well recognised in upper limb surgery in children with CP, with voluntary muscle control and sensibility determined to be the best predictive factors in one study of 56 consecutive patients with CP (House et al 1981) undergoing a total of 156 upper limb surgical procedures. However, not all case series have concluded that sensation is important in relation to functional abilities. In a selected group of 25 (out of 120) children with HCP, Brown (Brown et al 1987) found that sensory testing did not discriminate between the two hands, but was more related to age. However, this select subgroup was high functioning (based on their selection criteria) and this may have introduced type 2 error (with such a small number of children they may have been underpowered to find any differences in this subgroup). Despite the significant deficiencies of these studies (small numbers, non-representative samples and non-standardised measures) there is compelling clinical evidence that sensory deficits contribute to the reduction in functional outcome in children with HCP, again

without any real ability to discern the relative contribution of sensory deficit to upper limb function.

Spasticity and alterations of muscle tone impacting on upper limb function in children with HCP is common, with 80% of children with CP presenting with the spastic forms (Uvebrant 1988). Alteration in muscle tone in children with HCP can produce specific upper limb postures (typically varying combinations of internal rotation at the shoulder, flexion at the elbow, forearm pronation, wrist and finger flexion, and thumb flexion and adduction), and these postures can interfere with function (Mayer et al 1997). Spasticity and muscle stiffness associated with CP has been linked to difficulties with functional deficits in grip force adaptation (Gordon and Duff 1999a), manual function (on the Jebsen-Taylor Hand Function Test) (Taylor et al 1973; Vaz et al 2006), and in activities of daily living (Law et al 2008). Brown (Brown et al 1987) reported that muscle tone was significantly increased on the affected side as measured by a significant rise in measured resonant frequency, but found a great deal of variation between muscle tone and functioning and so did not report any correlation between spasticity and function. Decreasing spasticity is felt to improve movement patterns, elongate shortened muscles and strengthen antagonist muscles, leading to improvements in functioning (Fehlings et al 2000). However, the literature evaluating tone reduction by use of botulinum toxin A injection has shown some (but not dramatic) improvements in function (Boyd and Hays 2001a; Lannin et al 2006; Sakzewski et al 2009). The contribution of spasticity to functional outcome may be present but may not be significant, otherwise greater improvements in function may have been expected.

Motor control is how the central nervous system controls movement (Eliasson 2006), denoting the ability of the child to effect a motion in the upper limb voluntarily or in response to a verbal command. It is an important aspect in the completion of functional tasks. Motor control is a parameter of functioning found to be worse in HCP when compared to the other topographic types of CP such as diplegia and quadriplegia (Law et al 2008). Motor control in relation to precision grip has been systematically studied, with evidence that it is impaired in children with HCP (Gordon et al 1999), and (as well as sensory functioning) is related to the successful outcome for upper limb operative intervention (House et al 1981). However, precise motor ability is dependent upon sensory input (Cooper et al 1995), and the degree to which motor control can truly be measured as an independent variable is questionable. Simple motor control task completion proximally has not been studied systematically (such as isolation of shoulder movement) in children with CP. Investigators have studied more complex distal activities such as grip-lift synergies (Forssberg et al 1999) and other grip functions using instruments to examine grip (Eliasson and Gordon 2000). These tasks are functions reliant on sensation and motor skills combined. These can be considered in themselves functional outcomes, and so motor control is considered an outcome that is reliant on impairments such as spasticity, muscle weakness and sensory deficit, and can be adapted to a model of functioning which is above impairment level function (such as spasticity) but below more complex function tasks at the activity level of function (such as task completion on an AMPS measure).

There are other factors related to function that can be measured and should be considered in any model assessing functional outcome in a cohort of children with

HCP. Cognition is critical to upper limb functioning and can impact on real world functioning significantly, with the quality of movement in the upper extremity being influenced by cognition, as well as sensation and motor function (Bourke-Taylor 2003). Age is an important determinant of hand function and is said to significantly increase to 14 years of age in children with CP and HCP (Law et al 2008; Pagliano et al 2001). Eliasson (Eliasson 2006) noted efficiency in grasping function had developed over a 13 year period in 12 children with CP, with improved time for task completion, suggesting that improvements in hand function occur during a longer time frame than might otherwise be expected. Pagliano et. al. (Pagliano et al 2001) demonstrated that there was an age related global improvement in upper limb functioning over time, with grip strength improving greater than spontaneous hand use in the first five years of life in children with HCP. Another factor to consider is limb growth. Reduced growth of the upper limb in children with HCP is common (Uvebrant 1988). Although children with reduced growth may have good function, there is evidence of a positive correlation between sensory dysfunction and limb growth (Van Heest et al 1993) and any consideration of functional outcome should also include upper limb growth discrepancy as a factor.

In summary, our understanding of the contributions of impairments in the upper limb to upper limb function in CP is limited, with studies featuring small numbers of children using non-validated measures and a non-representative sample of children, with a heterogeneous cohort of children with multiple topographical forms of CP. They also included mainly children recruited from a hospital setting, with children far more likely to be more severely involved and not representative of community populations.

To overcome these deficiencies an evaluation of 107 children with HCP recruited from a population register was undertaken to examine the relationship between level of impairment and function. Unlike previous studies, the aim was to evaluate the relative contributions of measurable impairments and construct a theoretical and statistical model to describe the relative contributions of power, sensation, spasticity and other parameters on motor control and participation level functioning. However, these previous studies allowed a theoretical framework to be established to postulate the likely relationships of the independent (exogenous) latent variables to the dependent (endogenous) variables of function. Based on previous studies it was postulated that function would relate to muscle power most strongly. This evaluation was felt to be important because it could help inform the focus for therapeutic interventions for this population of children. This cross sectional study assessed the relative and simultaneous impact of the measured impairments of muscle power, muscle tone, sensation of the affected upper limb, growth of the hemiplegic upper limb, age and IQ on function as defined by the AMPS and PEDI, and separately with motor control. The objective was to quantify the relative contributions of these independent variables in explaining variations in the functional level of children with HCP.

Methods – see 2.2a, b & c, and 2.3c.

3.3 Results

Age, gender, affected side, gestation, birth weight, IQ, GMFCS level and current educational arrangement are reported in Table 3.1. For all measures, the majority of

children lie in the normal to near normal range, and in particular for gait (the GMFCS levels) are very functional. The study population primarily functioned in regular classes (either with or without support) with most assessed as having average IQ. Four children were functioning at GMFCS level 4 and 5. Three of these children had epilepsy. Two children were under 3 years of age at the time of assessment and had been making slow progress in ambulation but also had cognitive impairment that was felt to impact on acquisition of mobility skills. Two children had hydrocephalus including the child at GMFCS level 5 who also had severe intellectual impairment which was felt to have impacted on poor mobility. However, for all of these children the predominant pattern of motor disturbance involved one side of the body only and so they were not excluded from the analysis.

Table 3.1: Demographic Characteristics of 107 Children with Hemiplegic CP Recruited From a Population Register

Demographic	N of Children*
Age (Mean [95%CI])	8.9 (8.2, 9.7)
Gender (Male : Female)	61:46 (1.3:1)
Affected Side (Right : Left)	58:49 (1.2:1)
Gestation	
≥37 weeks	61
33-36 weeks	11
<33 weeks	20
missing	15
Birth Weight	
>2,500 grams	62
≤2,500 grams	29
missing	16
Intelligence Quotient	
≥110	18
90-109	41
70-89	27
≤69	17
missing	4
GMFCS Level	
I	85
II	15
III - V	7
Current Education (Class)	
Regular; no support	41
Regular; supported	37
Special Class	22
Missing	7

* unless otherwise stated

3.3a Functional Measures

Total results for the AMPS and PEDI with means, SD, minimum and maximum values can be seen in Table 3.2.

Table 3.2: Results on the AMPS and PEDI for 107 Children with HCP Recruited From a Population Register

	ADL motor score	ADL process score	PEDI SCORE
Mean	.45	.14	56.51
Std. Deviation	.84	1.05	15.31
Minimum	-2.93	-3.00	10.00
Maximum	2.44	2.04	73.00

The functional outcome measures noted in Table 3.3 include results for the AMPS (ADL motor and ADL process skills), compared with normative data for children under and over 8 years of age. Children with HCP function below the normative means for both motor and process skill abilities.

Table 3.3: AMPS data for 107 Children with HCP Recruited From a Population Register Compared with Normative Data

	3-8 yo (n=42)		≥9 (n=62)	
	Motor	Process	Motor	Process
AMPS				
Mean	.17 (1.8)	-.45 (0.8)	.68 (2.6)	.97 (1.5)
SD	.90 (0.8)	.56 (0.7)	.78 (0.7)	.12 (0.7)

Note: Values in parentheses indicate normative data (3-8 yo n=496; >9 yo n=620) (Fisher 2003) . Missing data for 3 children.

Similarly for the PEDI, results for 106 of the 107 children revealed significantly lower functioning in the study participants compared to a normative population of children [Study population of children with HCP revealed a mean (SD) of 56.51 (15.3), with a range of (10.0-73.0). Normative data (Group October 1992) for the PEDI reveals a mean (SD) of 85.9 (11.7) with a range of (37.4-61.9)].

3.3b Impairment Level Measures

When comparing the two sides (where possible), the affected upper limb was significantly different than the “unaffected” upper limb (Table 3.4). Results show significant differences for limb spans, total sensation (number correct as measured), finger/nose test of coordination, and reflexes (at all levels) and repetitive movements. DTRs of 3+ and 4+ were taken as hyper-reflexive for reporting of the data. However, when comparing both sides in the individual child/adolescent, the involved side was more reflexive than the uninvolved side for 76.2% of children for the biceps jerk, 86.7% of children for the knee jerk, and 73.5% of children for the ankle jerk.

Table 3.4: Impairment Characteristics Comparing Affected versus Unaffected Side for 107 Children with Hemiplegic CP Recruited From a Population Register

Clinical Characteristic	Affected side	Unaffected side	P
Limb spans* in cm			
Hand	13.0 (12.3,13.8)	15.3 (14.6,15.9)	<.001
Forearm	19.2 (18.5,19.9)	20.1 (19.4,20.9)	<.001
Upper arm	24.5 (23.6,25.4)	25.5 (24.5,26.4)	<.001
Total Sensory† [n correct out of 26 (95% CI)]	12.4 (10.6,14.2)	17.1 (15.3,19.0)	<.001
Finger/nose test of coordination‡			
Tremor	64	4	<.001
Normal	32	92	
Reflexes‡ (n)			
Biceps			
Normal	52	105	<.001
Hyper-reflexia	53	0	
Triceps			
Normal	75	105	<.001
Hyper-reflexia	30	0	
Supinator			
Normal	78	105	<.001
Hyper-reflexia	27	0	
Knee			
Normal	21	103	<.001
Hyper-reflexia	84	2	
Ankle			
Normal	85	105	<.001
Hyper-reflexia	17	0	
Plantar			
Normal	6	104	<.001
Extensor	99	1	
Repetitive movements			
Normal	22	90	<.001
Slow	68	3	

*Paired samples t-test; † Wilcoxon signed ranks test; ‡ Pearson $\chi 2$.

Tone, Power and Range of Motion

For tone, power, range of motion and motor control, the affected side was compared relative to the unaffected side (with the unaffected side being considered as "normal"). Therefore there are no comparison figures. When assessing the affected side (Table 3.5), power was worse affected distally, impacting primarily on forearm supination, wrist extension, and finger/thumb extension, adduction and abduction, with flexion at this level relatively preserved. However, most children in the cohort had some signs of weakness when compared to the unaffected side.

Approximately half the children had a "catch" or a measurable angle (on the modified Tardieu) across the elbow and wrist, indicating significant levels of spasticity. Also, when assessing MAS tone across all the levels, only 32.7% of children did not have a catch, indicating less significant tone only in this subgroup. However, 71.4% of this subgroup had an increase in tone of 1/4 on a MAS, indicating 91.6% of children had signs of spasticity overall. There were relatively few children with reduction in range of motion across the elbow, forearm and wrist in this community based population.

Table 3.5: Power, Range of Motion and Tone for the Affected Side in 107 Children with Hemiplegic CP

	Power *	**Tone**		**Range of motion**
	(%with weakness [≤ 3 on PRS])	**MAS** (%with a catch on MAS)	**Tardieu** (%with a measurable angle on the Tardieu)	(%with reduction in full range)
Shoulder				
Abduction	17.9			
Adduction	1.3			
Flexion	5.1			
Extension	19.2			
Elbow				
Flexion	5.2			
Extension	18.2	53.8	47.7	17.1
Fore arm				
Supination	43.6			18.1
Pronation	20.8	56.2		
Wrist				
Flexion	15.4			
Extension	33.3	44.3	56.3	15.1
Thumb				
Abduction	47.4			
Adduction	27.3	27.4		
Flexion	18.4			
Extension	46.8			
Finger				
Abduction	52.7			
Adduction	50.7			
Flexion	21.3			
Extension	46.7			

* Grip strength using a rolled sphygmomanometer (mmHg); Mean 48.2 ± 40.4 (range 0-200 mmHg). PRS – Power Rating Scale;

Sensation

Total sensation scores for the affected upper limb can be seen in Table 3.6. Children seemed to be affected most for stereognosis and less so for finger identification. Specifically, the percentage of children not achieving expected results (full identification) were 84.1% for stereognosis, 82.2% for graphaesthesia, 72.0% for 2 point discrimination, 56.1% for finger identification, and 93.5% overall. Vibration sense was intact at the wrist for all but 4.7% of children, and joint position sense (using the affected thumb) was reported incorrectly for 18.1% of the children.

Table 3.6: Total sensory correct for the affected side for tests of stereognosis, finger identification, graphaesthesia, and 2 point discrimination for 107 children with HCP recruited from a population register

	Tot_ster_a	Tot_FID_a	Tot_graph_a	Tot_2Pt_a
Mean	6.3	4.2	3.7	2.9
Std. Deviation	3.4	1.4	2.0	2.2
Minimum	0	0	0	0
Maximum	10	5	6	5

Tot – total; Ster – stereognosis; FID – finger identification; graph – graphaesthesia; 2Pt – 2 point discrimination; a – affected side; SD – standard deviation.

Growth

Mean span differences (unaffected – affected spans [cm]), SD and minimum and maximum values can be seen for the 107 children in Table 3.7. The negative values indicates the affected limb was larger/longer than the unaffected limb. The growth discrepancy is largest for hand spans, and less so for upper arm and forearm length. Overall the mean difference in growth for the affected upper limb was 4.09 cm.

Table 3.7: Growth differences for hand span, forearm span and upper arm span in 107 children with HCP recruited from a population register

	hand span difference	forearm difference	upper arm difference
Mean	2.21	.94	.94
Std. Deviation	2.63	.98	1.03
Minimum	-2.00	-1.00	-1.00
Maximum	10.80	3.50	4.50

Motor Control

Distal motor control for very simple functions (in particular, response to "wiggle your index/pointer finger") revealed that 93% of children were able to do so. However, more complex measures of motor control revealed reduced function in 78.1%, 63.2% and 64.8% of children for the CPRegisterUL, ManHandS and the DIAT respectively, with most children having some degree of motor control about the hand, wrist and elbow see Table 3.8.

Table 3.8: DIAT results for 107 children with HCP recruited from a population register

	Frequency	Percent
No voluntary movement	1	.9
Some shoulder movement	1	.9
Shoulder; some elbow movement	4	3.7
Shoulder; elbow; some wrist movement	33	30.9
Shoulder; elbow; wrist; some finger movement	29	27.2
Normal movement	37	34.6
Missing	2	1.8
Total	107	100

Correlation of Impairment Level Measures with Function

To assist in establishing a model of function for children with HCP, a series of correlations with functional outcome was undertaken to show the relationship of the relevant independent variables to the dependent variables of AMPS motor function and the PEDI (see Table 3.9).

Table 3.9:* Correlation between impairment level measures and function in 107 children with HCP recruited from a population register

	AMPSmot	PEDI	DIAT	Wr/Flexion	Stereog.	TardieuE
AMPSmot	1	.58	.35	.35	.49	.28
PEDI	<.001	1	.23	.11	.48	.01
DIAT	<.001	<.05	1	.59	.57	.34
Wr/Flexion	<.01	ns	<.001	1	.53	.27
Stereog.	<.001	<.001	<.001	<.001	1	.18
TardieuE	<.01	ns	<.001	<.05	ns	1

* Pearson correlation (unshaded), significance (2-tailed) shaded. AMPSmot – AMPS motor score; Wr/Flexion – power of wrist flexion; Stereog. – total correct affected upper limb for stereognosis; TardieuE – Tardieu at elbow affected upper limb.

3.3c Analysis of Function in Relation to Muscle Tone, Power and Sensation

To assess what the differences were for children with respect to sensation, tone, and power, these variables were tested against the AMPS and PEDI to see which groups were functionally superior. Based on the findings presented, two groups of children were evaluated based on the following criteria; sensation (children ≤ 12/26 correct vs. those > 12 correct), muscle tone (i.e. spasticity - children with “no catch” on a MAS at the elbow vs. children with a “catch”), and power (children at or below the median value for grip vs. those above this value). Results can be seen in Table 3.10. Only the PEDI result for sensory function reached significance, with more functional children more likely to score better on tests of sensation [median (95%CI) 67.5 (62.7,67.2) vs. 52.5 (44.0,53.1); p < .001].

Table 3.10: Functional performance in relation to sensation, muscle tone and muscle power for 107 children with HCP recruited from a population register

		FUNCTION		
		ADL mot*	**ADL proc***	**PEDI†**
Sensory	≤12/26	.35 (.12, .59)	.02 (-.27, .30)	52.5 (44.0,53.1)
	>12/26	.54 (.31, .78)	.25 (-.05, .55)	67.5 (62.7,67.2)
Tone	No	.51 (.26, .77)	.02 (-.30, .30)	55.0 (50.0,60.0)
(catch)	Yes	.39 (.17, .62)	.26 (-.03, .54)	57.1 (53.2, 61.0)
Power	≤ 40 mmHg	.28 (.03, .54)	-.01 (-.34, .33)	55.9 (52.0, 60.0)
(Grip)	> 40 mmHg	.56 (.34, .78)	.25 (-.02, .51)	56.4 (51.8, 61.0)

* denotes means (95% CI) and student t-test. † denotes medians (95% CI) and Mann-Whitney-U test. Significant differences were found only for the PEDI ($p<.001$) for sensory – otherwise differences were not significant.

3.3d Model of Functional Outcome for Children with HCP

As there exists significant correlations and relationship between the impairment level measures and the activity/participation level measures, a theoretical framework for factor analysis was established to assess the relative impact of the measured independent variables in 107 children with HCP (in relation to muscle power, muscle tone, sensation, growth, age of the child and IQ values) on the dependent variables of motor control and function.

This theoretical framework is also based on clinical modelling with reference to the previous literature presented, as well as statistical modelling to show the relationship between the variables. This model is presented diagrammatically to show the relationship of the independent impairment level variables to the dependent activity/participation level variables of function.

3.3e The Latent Variables

Age of the child (in months) and IQ were taken as measured. To enable the factor analysis to be undertaken the measured variables were combined within the model to

establish the latent variables of Growth Discrepancy, Power, Muscle Tone, Sensation, Motor Control and Function. Each latent variable was made up of several independent variables used to measure that construct. Growth Discrepancy was established using the three measured growth differences of the upper arm, forearm and hand span; Power was established from the four independent variables of grip strength, elbow flexion, wrist flexion and finger flexion. Muscle Tone was established using the four measured independent variables of the MAS and Tardieu scores at the wrist and elbow, and Sensation was established from the three measured variables of stereognosis, graphaesthesia and 2 point discrimination. Motor Control was established using the measured variables of the DIAT, the ManHands and the CPRHand. Function was established using the independent variables of the AMPS (motor and process skills) and the PEDI, and the UPLIFn. See Figures 3.1-3.3.

Principle Component Analysis

Principle component analysis revealed the factor loadings for each of the measured variables making up the latent variable (Table 3.11). The loading of the measured variable on the latent variable represents the correlation of that measured variable with the latent variable, values of > 0.4 being acceptable (Watson and Thompson 2006).

Table 3.11: Factor loadings for the measured variables on the latent variables in a model of functioning for 107 children with HCP recruited from a population register

LATENT VARIABLES	MEASURED VARIABLES	FACTOR LOADINGS
Function	PEDI	.841
	AMPS mot	.865
	AMPS proc	.891
	UPLIFn	.667
Motor Control	DIAT	.921
	ManHands	.974
	CPRHand	.925
Sensation	Stereognosis	.865
	Graphaesthesia	.872
	2 Pt Discrimination	.898
Power	Elbow flexion	.694
	Wrist flexion	.846
	Finger flexion	.892
	Grip Strength	.718
Muscle Tone	MAS Elbow	.878
	MAS Wrist	.869
	Tardieu Elbow	.811
	Tardieu Wrist	.869
Limb Spans Differences	Hand Span	.799
	Forearm Span	.806
	Upper Arm Span	.560

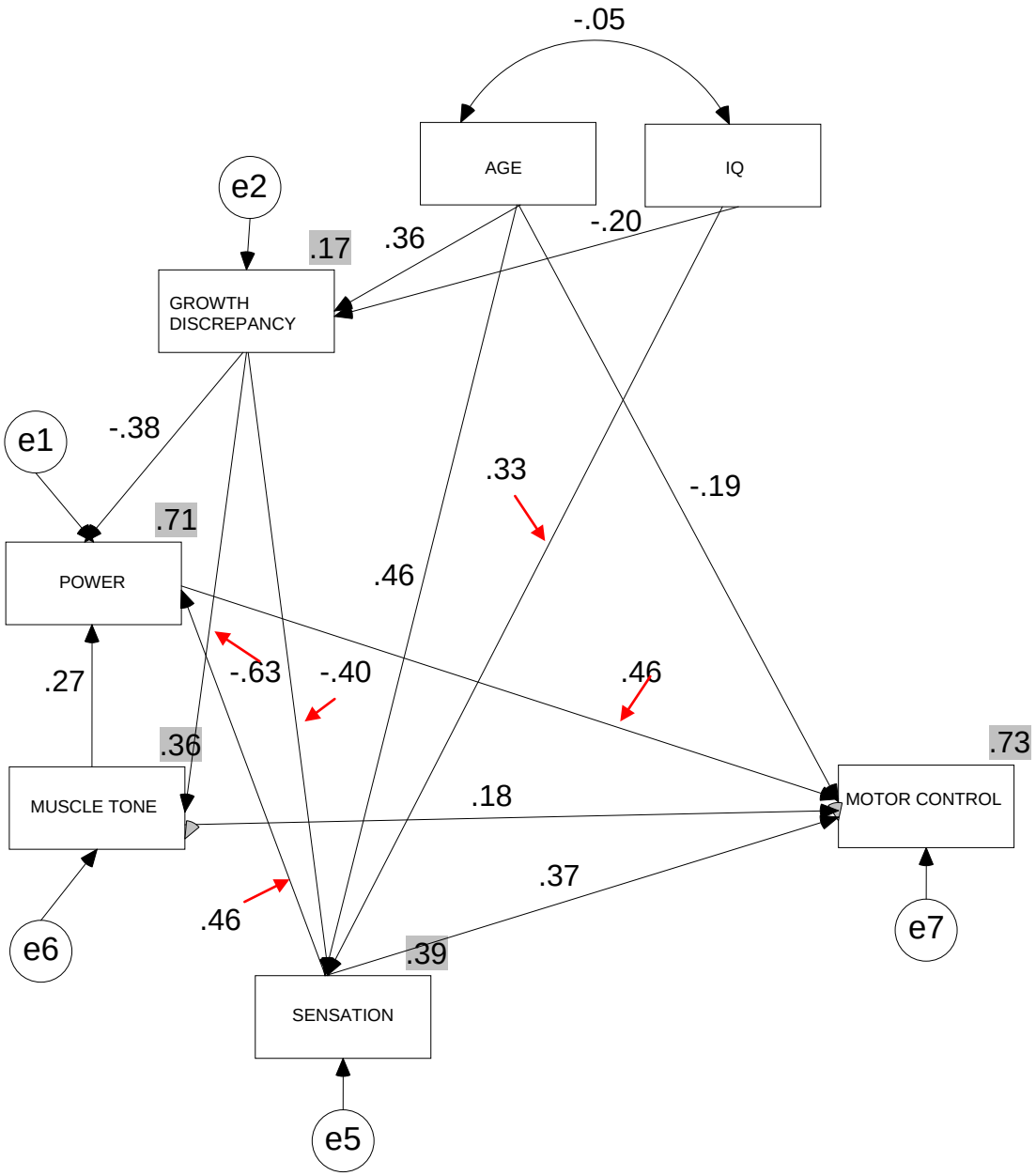
mot – motor; proc – process; 2 pt – two point.

Analysis for Motor Control (Figure 3.1)

The model was associated with a χ^2 value of 3.84 (Degrees of freedom = 5; p = 0.573). This indicates that there is no significant departure of the data from the hypothetical model. The hypothetical model is associated with a CFI = 1.00 and an RMSEA = .000 indicating a good fit with the data. As shown in Figure 3.1, the model explains 73% of the variance in motor control. The largest direct link between the latent variables and motor control is muscle power (0.46). Sensation has the next largest impact on the variance in Motor Control (0.37), followed by age (-0.19) and muscle tone (0.18).

Within the model, growth discrepancy correlates negatively with power, muscle tone and sensation, indicating as the growth discrepancy increases (worsening involvement) the other factors reduce. Also, the impact of muscle tone on motor control acts directly, but it also acts through it's influence on muscle power. IQ is positively correlated with sensory function, but negatively correlated with severity (in growth).

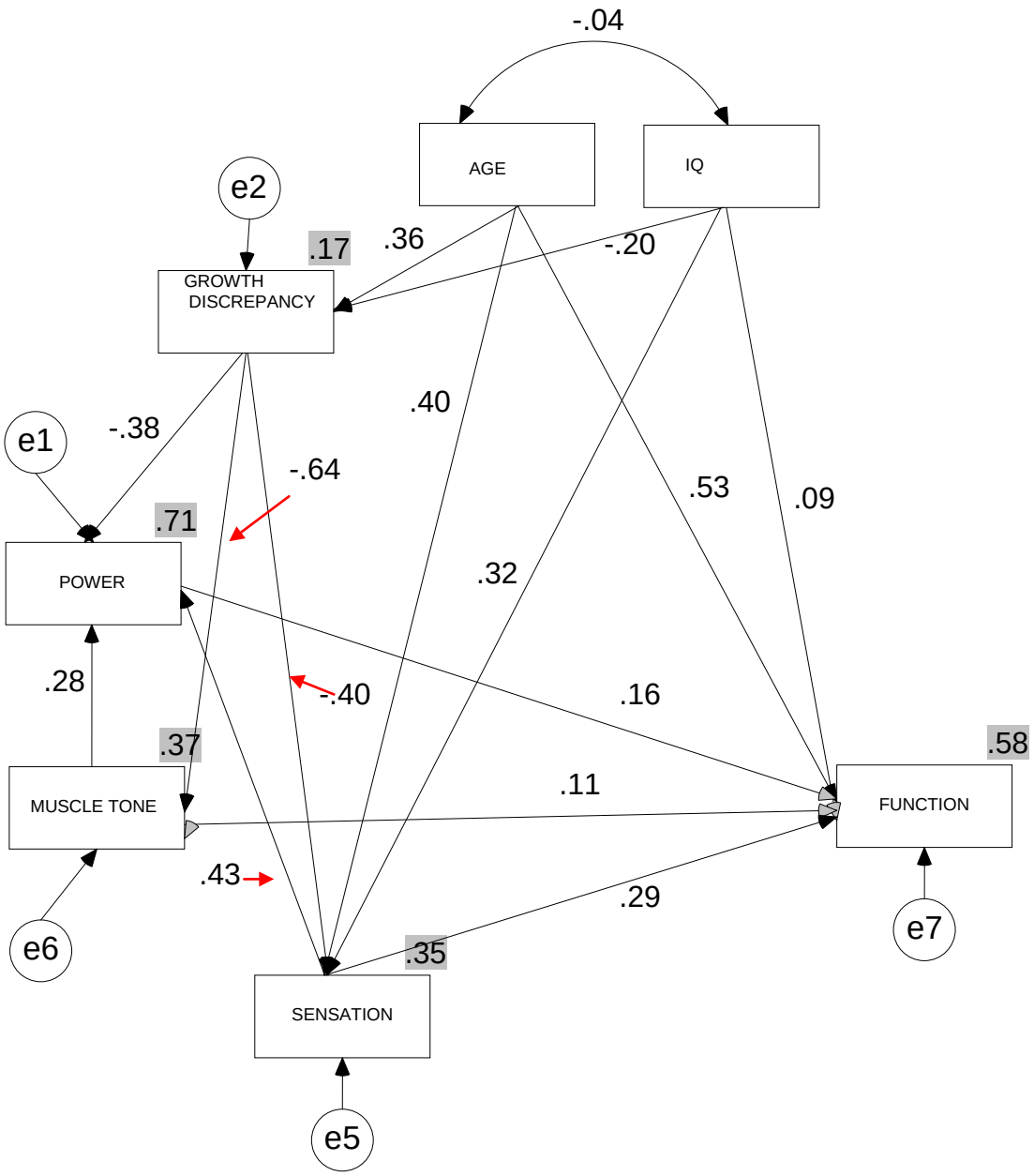
Figure 3.1: Motor Control



Analysis for Function (Figure 3.2)

The model was associated with a χ^2 value of 3.90 (Degrees of freedom = 5; p = 0.560). This indicates that there is no significant departure of the data from the hypothetical model. The hypothetical model is associated with a CFI = 1.00 and an RMSEA = .000, and therefore has a good fit with the data. This model explains 58% of the variance in function. Figure 3.2 shows the strongest direct link is with age (0.53), followed by sensation (0.29), power (0.16), tone (0.11) and IQ (0.09). The negative correlations with growth discrepancy is noted, with muscle tone again shown to act directly but also through power.

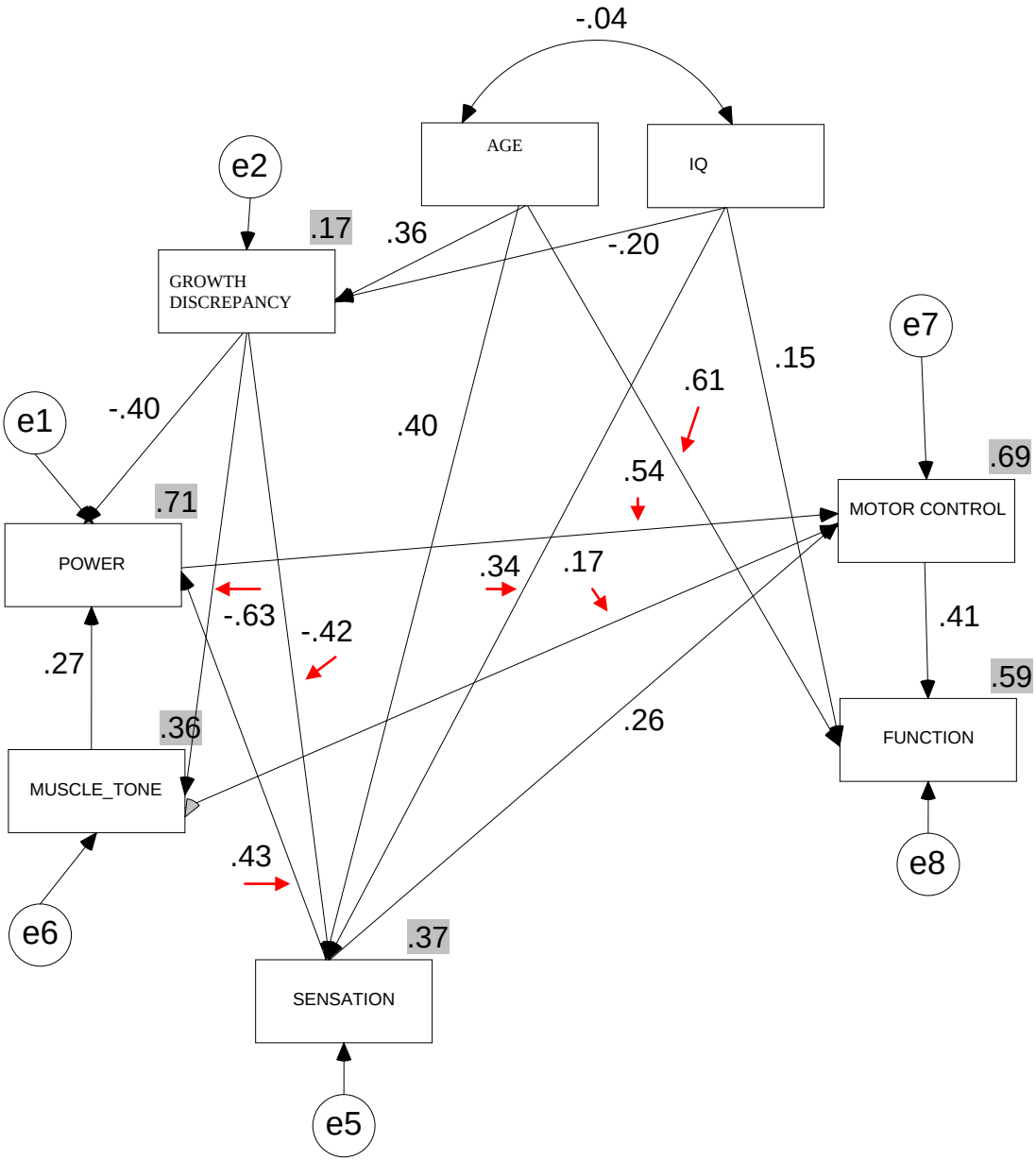
Figure 3.2: Function



Analysis for the Combined Model (Figure 3.3)

The model explains 69% of the variance in motor control, and 59% of the variance in function. The model was associated with a χ^2 value of 14.4 (Degrees of freedom = 11; p = 0.231). This indicates that there is no significant departure of the data from the hypothetical model. The hypothetical model has a good fit with the data, as it is associated with a CFI = 0.990 and an RMSEA = .054. As indicated in Figure 3.3, the largest direct link between the latent variables and function (as evaluated by the AMPS and PEDI) is age (0.61). Motor Control has the next largest impact on the variance in function (0.41), followed by IQ (0.15). Power, muscle tone and sensation act on function through their influence on motor control.

Figure 3.3: Function



3.4 Discussion

This descriptive study evaluated a population of 107 children with HCP recruited from a population register and describes models for motor control and functional activity which have been established through factor analysis. The main findings are that children with HCP function close to their peer level with respect to mainstream schooling, IQ level, gestation, birth weight and ambulatory ability, however they have significant impairment level deficits that impact significantly on functional outcome.

With respect to the outcomes as measured by the AMPS and PEDI, children function well below population norms, and so influencing impairment level functioning can greatly assist this group of children. Older children scored better on these outcome measures, and so age has emerged as a factor related to functional outcome that is supported by some recent studies (Pagliano et al 2001; Eliasson 2006; Law et al 2008), as well as the factor analysis presented, and argues for continuing support beyond early intervention for children with HCP.

The results of this study parallel closely the findings of previous studies and aide in the assessment of their findings. For example, Pagliano (Pagliano et al 2001) showed (in 20 children with hemiplegia) that hand function improved over a mean of 13 years (children were enrolled at 4 years of age and followed prospectively). This was in the form of power rather than spontaneous hand use. Sensory function (through their test of spontaneous hand use) did not change over time. This is in keeping with the models shown in this analysis as the link between muscle power and motor

control and function is strong. This also highlights another important issue, in that muscle power can be influenced over time (Damiano and Abel 1998). It may be more difficult or not possible at all to influence sensory function. This is suggested by the study by Pagliano (Pagliano et al 2001) because spontaneous use may rely more-so on sensory function (sensation and motor control) than power – power improving over time but not sensory function. However the study raises questions as to whether sensory function can be successfully altered, as over the time of the cited trial the children's grip changed from grasp to pincer – a more refined level of function that involves sensation as well as power. This was not able to be determined in the study because the investigators did not test sensory level in the study population, so this question remains to be addressed in future studies.

As in the findings by Blank (Blank and Hermsdorfer 2009), weakness was common. Muscle power was reduced at all levels, but was more commonly distal with proximal power relatively spared. According to the results of the DIAT, most children had some shoulder and elbow control, but nearly all had difficulties distally with only 34.6% reporting normal movement of the hand and fingers, reflecting weakness at this level. These results parallel closely those of muscle weakness and motor control in stroke patients with the upper motor neurone syndrome (Colebatch and Gandevia 1989).

Traditionally there has been a greater emphasis on the treatment of the positive features of the upper motor neurone syndrome, such as spasticity, rather than on the negative features, such as muscle weakness (Graham 2001). Muscle weakness was considered one result of the spasticity (Damiano et al 2001), so that when spasticity

was appropriately managed, muscle weakness was also felt to be influenced. Clinically it was felt that managing muscle tone would assist with muscle power. Other findings suggest that spasticity is associated with reduced muscle power (Damiano et al 2001) as well as histological changes within the muscle fibres in CP (Dietz 1995). However, there is evidence that the primary deficit producing muscle weakness is in the agonist muscle, and not as a result of the spasticity (Leonard et al 1990). The findings of this thesis indicate that muscle power is a key element to influence if there is a need to improve functional outcome in the child with HCP, with spasticity a lesser contributor such that the focus of intervention should lean more strongly to trying to influence muscle power rather than spasticity alone.

Muscle power can be influenced with therapy and should be a focus for any intervention attempting to influence upper limb functional activity. Damiano (Damiano and Abel 1998) demonstrated that muscle power in the lower limbs of children with CP could be influenced with therapy, and this had positive effects on functional outcome. It has been demonstrated that in the lower limb of children with CP, agonist muscle strength can be increased at a similar rate to people without central nervous system disorder (Damiano et al 1995). As well as the associated findings of muscle power improving over time (Pagliano et al 2001; Eliasson 2006), Burtner (Burtner et al 2008) demonstrated that dynamic splinting in children with CP can influence muscle force production leading to improved function, but did not investigate muscle strengthening directly. However, studies of muscle power and how power can be influenced in the upper limb of children with HCP has been lacking, and direct evidence of the efficacy of strengthening is required.

Sensory modalities can reliably be tested in children with HCP from 5 years of age (Tizard et al 1954), and missing data in the cross sectional study in this thesis represents the youngest of the HCP population. The outcomes related to sensory function are similar to the findings of other investigators. Twitchell (Twitchell 1966) reported that of 19 children with HCP, 9 (47%) had defects of 2 point discrimination, 12 (63%) had affected stereognosis, 10 (53%) had graphaesthesia and 8 (42%) had disturbed joint position sense. Participants sensation results were similar to levels of impairment in the literature, however not for vibration sense which was well preserved in the study cohort of children. Overall deficit in children with HCP is similar to that reported by vanHeest (Van Heest et al 1993). Similar to other studies, stereognosis was the sensory modality most commonly deficient in this population of children. Tachdjian (Tachdjian and Minear 1958) reported on a total of 96 out of a potential 800 patients who presented with CP (64 of whom had HCP) and correlated sensory deficit with degree of impairment of motor function. However "function" was not defined and this sub-population cannot be seen as being representative and thus introduces potential bias. The findings presented in this thesis show a strong correlation between sensory abilities and functional outcome, and this is significant in relation to correlation and factor analysis for the PEDI, the AMPS and for Motor Control. A greater emphasis needs to be developed in clinical practice to document the level of sensation in children with HCP. Studies investigating the potential to influence sensory function are required.

Abnormal muscle tone affected approximately half the children across the elbow and wrist, but when assessing the total cohort almost all (90.6%) had signs of increased tone on a MAS. However when assessing significant tone (at least a catch on a MAS)

there were 67.3% of children affected. This compares to 80% in the cohort of children from Uvebrant's (Uvebrant 1988) series. This does not exclude other forms of tone (such as dystonia) which was not assessed in this study but now known to be a significant factor in this group of children (Rice et al 2008).

Tachdjian (Tachdjian and Minear 1958) reports on the total growth discrepancy of the affected vs. unaffected/less affected upper limb [mean (range) = 3.5 cm (1.3-7.6)] which compares to a mean of 4.09 cm in this study. Tachdjian's cohort of children were on average 10 years of age, and so growth discrepancy may have been postulated to be greater, as the average age of this study's cohort was older than that presented in this thesis. Only 67% of Tachdjian's cohort had HCP, and so this could also contribute to the differences. Tizard (Tizard et al 1954) stated that there existed a definite relationship between growth discrepancy and sensory function, but no supportive data was published. The results of this thesis have shown that there does exist a relationship through correlations with power, sensation and muscle tone and so growth should be evaluated as part of any study assessing functional outcome in this group of children. Also, given the degree of growth discrepancy noted, span measures (especially hand span) should be documented as part of the clinical evaluation of all children with HCP.

The demographic results of this thesis are comparable to those of previous studies in HCP. The male to female ratio compares with ratios from other studies which range from 1.4:1 to 1.6:1 (Uvebrant 1988; Brown et al 1987; Khaw et al 1994). Similarly, the findings of 54% right sided hemiplegia compares to 53% (Uvebrant 1988) and 56% (Khaw et al 1994) in previous studies. Ninety four percent of children were

walking without the use of aides, which compares favourably to the work by Uvebrant (Uvebrant 1988) who showed that only 2% of that study cohort of children with HCP did not achieve independent walking.

Strengths of this study include recruitment form a population cohort of children with HCP with inclusion of children experiencing a wide range of severity. This is the first factor analysis of functional determinants in children with HCP, and the first to suggest the relative contributions of the impairment level independent variables on functional outcome. Study weaknesses include a cross sectional design, with no ability to suggest reasons for the correlations stated. The factor analysis was undertaken on a population number that are considered to be only just adequate for this type of analysis (Schreiber et al 2006; Watson and Thompson 2006) and so repeating this in a much larger cohort of children is required. Another major weakness is that the measures for motor control have not been extensively validated, and there exists no data reporting the reliability of the measures, and this remains an area for further evaluation in future studies.

In summary, the results of this analysis show that children with HCP, while expected to perform at peer levels, have significant deficits in impairment level functioning that impact on activity and participation level functioning. Attempts to improve function must consider the modalities of muscle power and sensory function, as well as muscle tone, to assist children with HCP achieve a higher functional status.

Other factors that could potentially affect activity and participation level functioning were explored. These include the potential impact of pain, self-concept/self-esteem,

and the use of therapeutic modalities. Relationships that existed between functional outcome and these factors are presented, starting with the relationship of the experience of pain in this cohort of children with HCP.

CHAPTER 4: THE IMPACT OF PAIN ON FUNCTION– FREQUENCY, DISTRIBUTION AND SEVERITY

Pain is common in people with CP (Hadden and von Baeyer 2002; Tervo et al 2006; Andersson and Mattsson 2001; Houlihan et al 2004) and represents a significant problem for this population in childhood (Hadden and von Baeyer 2002; Berrin et al 2007; Houlihan et al 2004). Children with CP experience more pain when compared to population norms (Liptak et al 2001; Wake et al 2003; Vargus-Adams 2005) and the presence of pain appears to persist into adulthood (Andersson and Mattsson 2001; Engel et al 2003; Odding et al 2006).

In hemiplegic CP the factors related to the experience of pain are uncertain. In a community based sample of children with all forms of CP, pain was found to affect 13.5% of children studied (Kennes et al 2002). Children with more severe CP have been reported to have a higher pain frequency than children with less severe CP (Houlihan et al 2004; Wake et al 2003). Other associations for pain in CP include pain being more frequently reported in girls (Houlihan et al 2004; Tervo et al 2006), accidental pain being more frequent in children with greater mobility (Breau et al 2003), and adults with CP experiencing pain more frequently in the lower back, hip and leg (Engel et al 2003). Despite finding some associations with the experience of pain, currently there is a lack of information regarding pain characteristics in children with CP (Tervo et al 2006).

The lack of recognition of pain and failure to appropriately manage pain in children with CP is likely to adversely impact on the child and family's quality of life. Tervo (Tervo et al 2006) in a cross sectional study of a convenience sample of 77

ambulatory children with different types of spastic CP found that pain correlated with reduced ambulation and interference with normal activities, indicating pain can impact on function. Social and attentional problems were also associated with the pain, with the possibility that the experience of pain could impact on developmental opportunities for children experiencing the pain, leading to further reduction in functioning. Similarly Houlihan (Houlihan et al 2004) showed that pain in a more severely affected population of children with different types of CP correlated with missed school days, days spent in bed and less participation in the child's usual activities.

The association of pain not only relates to missed opportunity for the child at the time they experience pain, but also on missed opportunity to maximise social integration and academic progress, further adversely influencing development in this vulnerable population of children. Berrin (Berrin et al 2007), in a study assessing the impact of pain and fatigue in a cohort of children with different forms of spastic CP, found that children with greater pain had lower school functioning. This is concerning as there is the potential that the pain experience could adversely impact on the child's level of participation in their daily life.

Self-concept and its relation to pain has not been studied in children with CP. However, studies in self-concept have revealed differences for children with CP in some domains of self-concept, but no differences in self-esteem when compared to a peer group (King et al 1993; Magill and Hurlbut 1986; Schuengel et al 2006; Teplin et al 1981). Whether the same holds true for children with CP experiencing pain is not known. However, children with CP are known to function lower for some self-

concept domains, and the pain experience could impact on these domains in many ways. For example, children with lower limb pain may miss opportunities for physical interaction and play, with consequent reductions in self-concept domains of physical and athletic competencies. Again the issue of pain relates not only to the time point of the pain experience, but can have further effects if there is an association with the self-concept domains. The interactions, if found, are likely to be complex and in the context of a cross sectional analysis, is likely to reveal associations only, with no ability to detect causal pathways.

Children with HCP have a unique pattern of neurological disorder which is different to children with other forms of CP. The topography of their disorder may produce pain experiences and pain behaviours that may be different to children with other forms of CP. This is currently not known, and due to the significant potential for pain to impact on functioning in this group of children, it is important to characterise their experience of pain.

Methods – see 2.2a, b & c, and 2.3c.

4.1 Pain Results

All but one child completed the pain measure, all completed the body structure measures and all parents completed the quality of life measure. Seventeen children did not complete the self-perception measure, and 30 did not complete the quality of life measure, and nearly all of these children were under 5 years of age.

Prevalence of Pain and its Associations

Table 4.1 shows the demographic data for children with and without pain. Fifty one children (48%) reported pain. There was no relationship between the presence of pain and age, gender, side of hemiplegia, gestation, birthweight, IQ, GMFCS level and current educational level.

Table 4.1: Demographic characteristics of 107 children with HCP who did and did not experience pain

	Presence of pain		**P**
	No Pain (n=56[52%])	**Pain (n=51[48%])**	
Demographic			
Age* Mean (95%CI)	8.42(7.44,9.40)	9.52(8.47,10.57)	ns
Gender† (Male : Female)	34:22	27:24	ns
Affected Side† (Right : Left)	28:28	30:21	ns
Gestation†			
≥37 weeks	34	27	ns
33-36 weeks	8	3	
<33 weeks	8	12	
Birth Weight†			
>2,500 grams	35	27	ns
≤2,500 grams	15	14	
Intelligence Quotient†			
≥110	12	6	ns
90-109	15	18	
70-89	11	9	
≤69	8	9	
GMFCS Level †			
I	39	33	ns
II	2	8	
III	1	1	
IV	2	0	
V	1	0	
Current Education(Class) †			
Regular; no support	23	18	ns
Regular; supported	11	19	
Special Class	12	5	

Fifty one children (48%) reported pain; * student t-test; † Pearson Chi squared; ns indicates not significant

Characteristics of Pain

The characteristics of the pain experienced can be seen in Table 4.2. The pain was predominantly on the same side as the hemiplegia and affected either the leg alone or both the arm and leg. Pain was more likely minimal to moderate in severity, of an aching quality and impacted on movement and activity. Movement and fatigue was more likely to intensify the pain, and the most common methods of pain relief were rest/sleep and massage. The most common explanation offered for the pain was "disease related" in 40% of children who experienced pain, with 16% "uncertain" as to a cause, 6% as "treatment related" and 4% due to "ageing and growth". Thirty four percent felt it was due to some other cause but did not provide any further details.

Table 4.2: Characteristics of pain in 51 children with HCP

Characteristic	N
Side of pain	
Ipsilateral	28
Contralateral	2
Bilateral	13
Central	7
Site of Pain	
Leg Only	19
Arm & Leg	10
Multiple	9
Arm Only	6
Head & Neck	4
Chest & Back	2
Severity of pain	
Mild	33
Moderate to Severe	18
Quality of pain	
Aching	29
Dull, tingling, numb	9
Sharp, burning, stabbing	5
Combination	8
Impact of pain on…	
Movement and activity	35
Sleep and rest	5
Emotions and concentration	9
Other	2
Intensifiers of pain	
Movement	20
Immobility	8
Fatigue	7
Heat	1
Combination of above	1
Other	9
Methods of pain relief	
Analgesia	8
Massage or change in position	15
Rest and sleep	10
Combination	6
Other	5
None	7

Pain and its Associations with ICF Domains, Quality of Life and Self Concept

Table 4.3 shows the comparison of the presence of pain and the ICF domains as well as quality of life and self-concept. To allow for multiple comparisons, the significance value ($p<.05$) was divided by the number of measures in that construct. There were no differences for participation level functioning, or for children with and without pain for any of the body structures/function measures. Differences when comparing the two groups reached significance for quality of life as measured by the PedsQL with higher scores for children not experiencing pain. For measures of self-concept for children ≥ 8 years (N=54; [51%]), the domains of Scholastic Competence, and Behavioral Competence reached significance favoring those who did not report pain. For the younger age group there were no differences in any of the self-perception domains.

Table 4.3: Comparisons of presence of pain and ICF domains, quality of life and self-concept in 107 children with HCP

	Presence of pain		P
	No Pain	**Pain**	
Body structure/function			
Length*			
Hand span	12.61(11.68,13.55)	13.54(12.43,14.65)	ns
Forearm span	18.81(17.82,19.81)	19.65(18.35,20.79)	ns
Upper arm span	23.80(22.61,25.00	23.38(24.00,26.76)	ns
Sensation†			
No. Correct [30 items]	11.2 (8.9,13.6)	13.8(11.1,16.4)	ns
Modified Ashworth Scale ‡ (median; IQR)			
Elbow	1+(1-2)	1+(1-2)	ns
Wrist	1(1-2)	1(1-2)	ns
Tardieu*			
Elbow	42.59(30.27,53.13)	39.51(26.27,51.13)	ns
Wrist	25.85(16.73,35.00)	28.18(18.55,37.81)	ns
Activities/Participation			
PEDI† (median; 95% CI)	61.0 (51.9,60.7)	60.0 (53.3,61.0)	ns
AMPS*			
Motor	.47(.25,.70)	.47(.22,.73)	ns
Process	.10(-.18,.37)	.21(-.10,.53)	ns
Quality of Life			
PedsQL*			
Parent	60.10(55.10,65.11)	50.21(45.94,54.47)	<.01
Child	75.76(68.37,83.15)	60.49(55.39,65.60)	<.01
Self-perception *§			
Younger child [<7 y.o.]			
Cognitive	3.19(2.84,3.55)	3.02(2.58,3.47)	ns
Competence	2.82(2.50,3.15)	2.95(2.54,3.36)	ns
Peer Acceptance	3.00(2.71,3.29)	2.58(2.16,3.01)	ns
Physical Comp.	3.27(3.01,3.53)	2.95(2.56,3.35)	ns
Maternal Comp.			
Older child [>/=8 y.o.]			
Scholastic Comp.	3.02(2.78,3.26)	2.55(2.31,2.79)	<.01
Social Acceptance	3.16(2.91,3.41)	3.00(2.74,3.26)	ns
Athletic Comp.	2.85(2.59,3.12)	2.58(2.29,2.88)	ns
Physical Appearance	3.26(3.04,3.48)	2.90(2.63,3.17)	ns
Behavioral Comp.	3.33(3.07,3.60)	2.88(2.70,3.06)	<.01
Global Self-worth	3.74(3.14,4.34)	3.17(2.92,3.43)	ns

All data presented as mean (95% CI) unless stated otherwise; *Student t-test; † Mann-Whitney U test; ‡ Pearson Chi squared test; § n= 87 for Younger Child; n= 54 for Older Child; ns indicates not significant; Comp. - Competence.

Direct logistic regression was performed to assess the impact of the independent variables which showed significant differences in the direct comparisons (Child and Parent PedsQL, Scholastic Competence and Behavioural Competence) on the dependent variable “do you have pain?”. The regression model was able to distinguish children reporting a pain experience, with a full model χ^2 (4, N=56) = 15.2 (p = 0.004). The percentage of variance explained by the model (Cox&Snell R^2 and Nagelkerke R^2) was 23.7 – 31.7% and the model was able to correctly classify 73.2% of cases. The independent variable that made a unique, statistically significant contribution to the model was Behavioural Competence, recording an odds ratio of 0.32 (95% CI 0.13,0.99) indicating that as Behavioural Competence scores decreased children were more likely to report pain.

4.2 Pain Discussion

Nearly half the children with HCP experienced pain that was primarily minimal to moderate in severity on the side of the hemiplegia and impacting on movement and activity. There was a significant relationship between the presence of pain, quality of life and self-concept when comparing children with pain to children reporting no pain. Importantly, there were no significant differences found for impairment level functioning, nor for participation. Children who reported pain were also more likely to report a lower perception of their own behavioural competence.

Fifty one children experienced pain, and over half of these experienced ipsilateral pain of an aching quality. Quality of pain and responses to it can help to suggest an aetiology, with aching qualities to the pain, pain impacting on movement and

activity, and methods of pain relief including massage and rest all indicating a nociceptive cause (Ross 2004). In children with HCP, nociceptor stimulation could relate to muscle spasm and hypertonicity, which are commonly experienced. There could also be involvement of the affected side in traumatic accidental injury, contributing to chronic pain states if repeated injury occurs. This could be felt by the child and family as related to the condition of HCP, with 40% indicating the cause of pain was disease related. Overuse of the uninvolved side may be a factor to account for bilateral and contralateral pain, with overuse being a recognised phenomenon in children with HCP (Murphy et al 1995). Gait pattern analysis also indicates that children with HCP spend a significantly greater period of time in stance on the uninvolved limb during gait when compared to the affected limb and to limbs of children who do not have impairment (Cimolin et al 2007) such that contralateral overuse may result in degenerative conditions and produce pain.

A neuropathic mechanism may also explain the experience of pain, as 22 children (43%) described pain as tingling, numb, sharp, burning or one of these qualities in combination with an aching quality (Ross 2004). Neuropathic pain is due to direct or indirect damage to the central or peripheral nervous system and pain is experienced by the facilitation of sensory input or the loss of central inhibitory influences. As hemiplegic CP is due to a non-progressive lesion of the immature brain (Taft 1995) neuropathic pain could be one possible result. Also, it is known that stimulation of nociceptors can result in changes in the nervous system leading to chronic pain states (Loeser 1994) and untreated or under-treated nociceptive pain in this population could result in neuropathic pain.

It was interesting that analgesia was a relatively unused method of pain relief (16% of those experiencing pain). Perquin (Perquin et al 2000b) found that 39% of typically developing children experiencing pain used medication, and the authors also noted that medication use was predicted by limb pain, intensity and age, but there were no such trends noted in these children with HCP in this study. Analgesic use was low despite most children indicating limb pain. However, Perquin (Perquin et al 2000b) reported on a population of typically developing Dutch children and the influence of culture and race could have been other factors. The pain relief methods more commonly used in this thesis of children with HCP were massage, rest and sleep.

The limited use of analgesic medication in this population is of concern and questions arise as to why analgesic medication is not used. Children and their families may perceive pain as being a part of the underlying condition, and may not seek medical attention for the treatment of pain. Clinicians may share this view and may be less likely to offer analgesic medication when consulted. Further studies could investigate the low prevalence of analgesic use as well as effectiveness of pain relief methods in this population, as the prevalence of pain is high with significant impact on self-concept and quality of life.

Reduced quality of life in children with CP experiencing pain has been noted in previous work (Houlihan et al 2004; Tervo et al 2006). However this included a more heterogeneous group of slightly older children and not one specific subgroup of children with CP, as in this thesis. This was felt to be important given that patterns of injury and involvement of spasticity may relate to the topography of the disorder. For

example, Tervo (Tervo et al 2006) found an association with walking ability and experience of pain. However, in the cohort of children with HCP in this thesis, almost all were independently ambulant (GMFCS levels I and II). Therefore in the study population factors other than mobility can impact on the experience of pain and evaluating these factors for children with a specific topographic involvement is important.

In this thesis hemiplegic children reporting no pain (but not hemiplegic children reporting pain) had similar results on the PedsQL when compared to previous work in children with HCP (Varni et al 2005) and this was true for both the child self-report and the parent proxy report. This is important as it validates the findings of this thesis and allows for comparisons with published data. However children experiencing pain had similar or lower scores (both for child and parent reports) when compared to reported scores for children undergoing treatment for cancer and those with more severe subtypes of CP (Varni et al 2005). This indicated that children experiencing pain had added burden that contributed to a perception of a lower quality of life. This is important as treatment of pain and methods used to improve on the pain experience can have significant effects on the child and family's perception of their quality of life.

Gender differences have been noted in previous work (Breau et al 2004; Tervo et al 2006; Perquin et al 2000a). However the presence of pain in this thesis was not different when comparing males to females and this is different to published data in children which show a trend towards significantly more pain experiences in females (Perquin et al 2000a; Tervo et al 2006). Also, pain behaviours have been noted to be

different, with females more likely to use medication in response to pain when compared to males (Roth-Isigkeit et al 2005; Perquin et al 2000b). However, in the group of children with HCP in this thesis there were no differences between males and females for methods of pain relief. Other gender differences are well described for children experiencing pain with females reporting more chronic, multiple and severe pain (Perquin et al 2000b). There are also gender differences apparent across a number of painful childhood conditions (Goodman and McGrath 1991), and future studies are required to further evaluate these gender differences in children with CP.

There was no relationship between the presence of pain and severity of CP as measured by the GMFCS levels as was shown by Houlihan (Houlihan et al 2004). However, as expected in children with HCP, the numbers in the more severe categories (levels 3-5) are small. Wake (Wake et al 2003) in a study of 80 children with CP of mild to more severe involvement showed children more severely affected experienced more pain. However when other measures of severity were used (tone, limb growth, sensory impairment, intelligence) there was no relationship between those children experiencing pain with those reporting no pain in this thesis, and so severity of involvement does not appear to be a factor in the experience of pain in this population of children. This is consistent with the findings of Kennes et. al. (Kennes et al 2002) who found that in a population of 408 community based school aged children with CP there was no correlation of presence of pain with severity of functional limitations.

Children with HCP over eight years of age reporting pain perceived themselves as less competent scholastically and behaviorally when compared to children not

reporting pain. Comparison with previous studies (King et al 1993; Saigal et al 2002; Sherrill et al 1990) suggest that children with HCP reporting no pain scored closer to populations norms for these domains but children with HCP who experience pain scored similar to, or lower than, children of extremely low birthweight (Saigal et al 2002), disabled young athletes (a study cohort of children with CP, blindness, short stature, spinal cord injury and other disabilities) (Sherrill et al 1990), and adolescents with disabilities (a population of adolescents with spastic CP, spina bifida and cleft lip/palate) (King et al 1993). While the overall level of disability is difficult to determine in these studies reviewed, HCP is the sub-type of CP where children are more likely to function in schools alongside their non-affected peers (Michelsen et al 2005), and so the potential effect for this group of children of any significant differences can impact a great deal on functioning.

Developmental influences may explain these differences. Younger children with pain may focus less on self-perceived competencies in the behavioural and cognitive domains, these areas of functioning becoming more important as they grow and develop. Alternatively, older children who view themselves as less competent in the cognitive and behavioral domains may also report higher levels of pain, thereby providing an explanation for their decreased abilities. The result of the logistic regression are of interest, showing that children with perceived higher levels of behavioural competence are less likely to report the experience of pain. Behavioural competence indicates whether children perceive they behave in the right way or do the right things. Possibilities for this finding include children who perceive they behave in the correct way do not report pain, or that children who perceived they undertake less acceptable behaviour report more pain to account for their behaviour.

Alternatively children who experience pain may behave in ways they feel are less acceptable. The impact of reduced scores in this domain may reflect that their behaviour during times of pain experiences is not desirable, and they recognise this to be true. This is concerning as children who experience pain may behave in ways they recognise as maladaptive and this has the potential to promote negative feelings.

The low levels of perceived competence in the areas described can impact adversely on a child's sense of self worth, which in turn risks feelings of depression (Harter 1990), an affective state which could impact on pain perception (Margetic et al 2005) (Bruusgaard et al 2000). Breaking this cycle may be assisted by adequately treating the child's pain. It is possible that Global Self-Worth (a measure of self-esteem) may be independent of the pain experience and may relate to other factors, although this was not determined in this thesis.

The treatment of pain for children with hemiplegic CP is important, given the potential for adverse schooling, social and family consequences. Treatment options include therapies involving the physical modalities (stretching, range of motion exercises, heat and other techniques), oral medications (Vargus-Adams et al 2004) as well as more specialized techniques such as Botulinum toxin injection which has been reported to improve pain in adults after stroke (Bhakta et al 1996) and in children with CP (Awaad et al 1999). However, treatment modalities alone are unlikely to assist as the pain experience in hemiplegic children is under-recognised. Strategies such as educating allied health and medical clinicians to ask about and manage pain are important. Also, providing education to children and their families

that pain is common and can be treated may influence them to seek attention and treatment.

The data set was complete for almost all measures, the missing data attributed to the youngest children. Cause of pain was not noted systematically, and this should be explored in future as it will help to inform appropriate management options. Children were asked about whether they experienced regular pain, but not the duration of the pain. No assessment of sample size was undertaken because this study included all available children from a statewide population register.

Pain was a significant factor affecting the lives of children with HCP. A description of many of the characteristics of the pain these children experience has been provided. Pain was associated with a reduced quality of life in all age groups, and lower self-concept for some of the self-concept domains in older children. However, children with HCP and pain are resilient, with levels of participation equal to their peers who do not experience pain. Despite pain, children complete functional tasks relevant to their daily functioning, but have significant issues in relation to quality of life and self-concept. Clinicians managing children with HCP should assess and actively treat their pain. Managing pain is important as the potential for improving these areas of functioning are great for this population of children.

These findings are relevant within the group of children with HCP, indicating that the self-concept and quality of life for children with HCP experiencing pain are affected. However, how the domains of self-concept and quality of life compare to a group of typically developing peers is of great interest for this group of children, as

one of the most relevant themes significant to children with HCP is that they are the subgroup of children with CP most likely to function alongside peers of typical development, both in childhood/adolescence and in adult life (Michelsen et al 2005). The next chapter will explore these issues and relate differences found in comparison to peers of typical development to the experience of children with HCP.

CHAPTER 5: SELF ESTEEM, SELF CONCEPT AND QUALITY OF LIFE – HOW CHILDREN WITH HCP COMPARE WITH TYPICALLY DEVELOPING PEERS

Self-concept refers to how children view themselves, but self-esteem defines how children value themselves (King et al 1993). These are separate but related constructs (Harter 1990). One of the determinants of self-esteem is self-concept (Willoughby et al 1996). Self-esteem is based not only on how children view themselves, but also on the importance a child places on the different self-concept domains of functioning, as well as the support received by the child within their emotional environment (Harter 1990). There may be important differences for children with a diagnosis of HCP when compared to the development in these domains in typically developing peers. This could impact on functional development and performance, so that differences between the groups should be considered in any analysis of functional outcomes.

Self-esteem has a profound significance on personal development (Brooks 1992) and problems in self-esteem for an individual can be pervasive. Adolescents with low self-esteem are significantly more likely to develop mental illness, suffer poor physical health, risk more criminal convictions and have fewer economic prospects in adult life when compared to adolescents with high self-esteem (Trzesniewski et al 2006). Children with HCP have a set of impairments that can impact on self-esteem, as well as have functional deficits that can impair their self-perception. There may also be factors that can modify their perceptions, and comparisons to their typically developing peer group can give insights that can be used to assist functioning.

There is an assumption that children with CP experience a low self-esteem (Fox 2002; Shields et al 2006). However, previous investigations have not shown this to

be valid (King et al 1993; Magill and Hurlbut 1986; Schuengel et al 2006; Buran et al 2004; Manuel et al 2003b; Mrug and Wallander 2002; Magill-Evans and Restall 1991; Shields et al 2007). In a systematic review of the literature Shields (Shields et al 2006) showed that reduced self-concept (but not reduced self-esteem) was found only for adolescent females with CP. The findings that self-esteem in children with CP is no different than that of their unaffected peer group brings into question why children with CP experience lower quality of life scores (Wake et al 2003; Varni et al 2005; Liptak et al 2001; Vargus-Adams 2005). Children with CP self-report the most impaired health related quality of life when compared to other chronic conditions in childhood (Varni et al 2007b), and knowing this makes it seem likely that children with HCP will experience lower self-esteem. However this assumption requires further evaluation. For children with HCP who usually experience mild to moderate impairment, expectations on them to perform at peer levels in all aspects of functioning may leave them vulnerable to adverse consequences of a low self-concept and self-esteem.

Quality of life has been reported for children with CP (Varni et al 2005; Wake et al 2003; Liptak et al 2001; Vargus-Adams 2005). The relationship of quality of life to the degree of impairment is not clear, with many children of mild impairment reporting reduced psychosocial quality of life that seems out of proportion to their disability (Pirpiris et al 2006; Wake et al 2003). However, these studies found a positive correlation of the physical domains of quality of life to actual physical functioning. How this relates to children with HCP is not clear, given that no studies have assessed children with this topographical form of CP, in which most children

are ambulant and may have low levels of physical impairment when compared to other topographical groups of children with CP.

Methods – see 2.2 c & d, and 2.3c.

5.1 Results – Self Concept and Quality of Life

Characteristics of study population

Typically developing peers had a mean age of 9.5 years with n=54 (63%) male. Children with HCP had a mean age of 9.4 years with hemiplegia affecting the right side in 51 children (59%) and were predominantly of male gender (n=54; 63%). Of the 107 children recruited, 21 did not have a complete data set for the self-concept measures and were excluded. The reason for the incomplete data set was lack of understanding and/or communication difficulties (12/21) or some of the test items incomplete on the score sheet (4/21). For 5 children, the test was not completed but the reason for this was not recorded on the outcomes sheet.

The study population differed significantly from the exclusion group as they were more likely to be male and older, have right hemiplegia, better motor ability on the GMFCS, a greater IQ and score better on tests of participation level functioning as based on the AMPS testing. However on the quality of life measure there were no differences (see Table 5.1)

Table 5.1: Baseline characteristics of the study participants with HCP compared with the excluded group of children

Characteristic	Participants (n=86)	Exclusion group (n=21)	Mean difference (95% CI)	P
Age[*] mean (95% CI)	9.4 (8.6,10.2)	7.2 (5.6,8.7)	2.2 (0.56,3.84)	.014
Gender[†] (Male/Female)	54/32	7/14		.009
Side of hemiplegia [†] (Right/Left)	51/35	7/14		.021
GMFCS Level[†]				
I	70	15		.002
II	13	2		
III	3	0		
IV	0	3		
V	0	1		
Intellectual Status[†,‡]				
Above Avg. (> 110)	16	2		.001
Avg. (90 – 109)	31	2		
Below Avg.(70 – 89)	17	3		
Cog. Impairment (<70)	8	9		
Quality of Life (PedsQL) *				
Parent Proxy Report total score	54.5 (51.1,58.0)	60.2 (39.4,81.0)	5.7 (-1.6,13.0)	.667
Child Self Report total score	67.6 (62.7,72.6)	70.3 (51.3,89.4)	2.7 (-12.6,18.0)	.761
AMPS *[,§]				
Motor, mean(95% CI)	0.63 (0.48,0.78)	-0.23 (-0.77,0.32)	0.86 (0.31,1.41)	<.001
Process, mean(95% CI)	0.40 (0.22,0.58)	-0.94 (-1.54,-0.34)	1.3 (0.77,1.89)	<.001

[*] Independent student t-test; [†] Pearson χ^2; [‡] Complete data for n=72 study group and n=17 exclusion group; [§]Assessment of Motor and Process Skills; Avg. – average; Cog. – cognitive.

Self-concept, Younger Age-group

Table 5.2 shows results for the self-concept domains for 31 matched participants aged 3-7 years. The Physical Competence subscale revealed significant differences favoring the peers with typical development, but for Maternal Acceptance significant differences favoured the children with HCP. There was no difference between the groups for Cognitive Competence and Peer Acceptance.

Self-esteem and Self-concept, Older Age-group

Table 5.2 shows results for the self-esteem (Global self-worth) and self-concept domains for 55 matched children aged 8-16 years. Results indicated significant differences favoring the peers with typical development for Athletic Competence and Scholastic Competence. Global Self-worth revealed no significant differences, nor did Physical Appearance, Social Acceptance, or Behavioral Competence.

Quality of Life

Table 5.2 shows results for the PedsQL total score and subscales. Results indicate significant differences favoring the peers with typical development for both parent and child reports. The parent reports are very similar to the child reports for peers with typical development but lower for the parent reports when compared to the child reports in the group of children with HCP. The PedsQL subscale analysis revealed significantly lower scores favoring peers with typical development for all but the Emotional Functioning subscale for the child self-report.

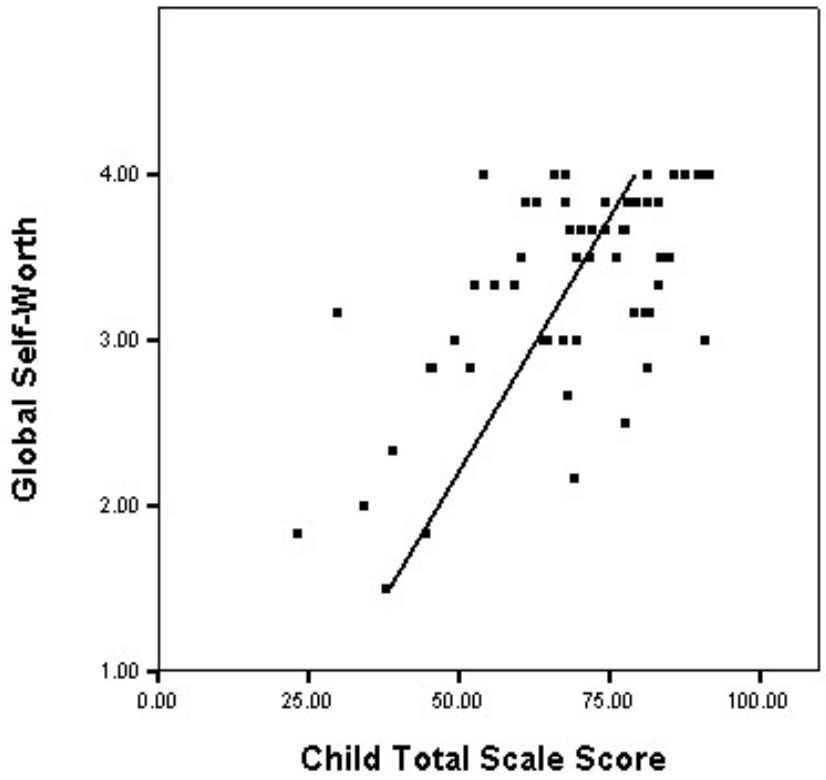
Table 5.2: Self-esteem, self-concept and quality of life measures for children with HCP and matched peers with typical development

Characteristic	Hemiplegia	Peer	Mean Difference (95%CI)	P
Self-concept* -Young child (n=31) – median (95% CI)				
Cognitive Competence	3.1 (2.8,3.4)	3.4 (3.2,3.6)	.33 (.01,.65)	.062
Physical Competence	2.8 (2.5,3.0)	3.2 (3.1,3.3)	.44 (.18,.69)	.002
Peer Acceptance	2.8 (2.6,3.1)	3.0 (2.8,3.2)	.14 (-.13,.41)	.231
Maternal Acceptance	3.1 (2.9,3.3)	2.7 (2.5,3.0)	.43 (.17,.68)	.004
Self-concept* - Older Child (n=55)– median (95% CI)				
Global Self-worth	3.3 (3.1,3.5)	3.3 (3.2,3.4)	.04 (-.24,.15)	.233
Physical Appearance	3.0 (2.9,3.2)	3.0 (2.9,3.2)	.01 (-.21,.23)	.828
Social Acceptance	3.1 (2.9,3.2)	3.2 (3.0,3.3)	.13 (-.07,.33)	.241
Athletic Competence	2.7 (2.5,2.9)	3.1 (3.0,3.3)	.43 (.18,.68)	.002
Scholastic Competence	2.8 (2.6,3.0)	3.1 (3.0,3.3)	.34 (.08,.59)	.013
Behavioral Competence	3.1 (2.9,3.2)	3.0 (2.8,3.1)	.10 (-.28,.07)	.169
PedsQL† - mean (95% CI)				
Parent Proxy Report				
Total Score	54.5 (51.1,58.0)	80.6 (78.3,82.9)	24.2 (20.3,28.2)	<.001
Physical Health	56.5 (51.9,61.2)	86.5 (84.0,89.1)	28.7 (23.7,33.8)	<.001
Psychosocial Health	53.9 (50.5,57.2)	78.6 (76.1,81.0)	22.7 (18.6,26.8)	<.001
Emotional Functioning	62.0 (57.6,66.5)	74.1 (70.7,77.5)	10.5 (5.5,15.5)	<.001
Social Functioning	51.1 (46.3,55.8)	83.4 (79.7,87.0)	30.5 (24.6,36.4)	<.001
School Functioning	48.5 (45.1,51.8)	78.3 (75.4,81.1)	27.2 (22.6,31.9)	<.001
Child Self-Report				
Total Score	67.6 (62.9,72.6)	80.6 (78.1,83.1)	13.0 (7.4,18.6)	<.001
Physical Health	71.4 (66.4,76.3)	85.1 (82.4,87.9)	14.5 (9.2,19.8)	<.001
Psychosocial Health	66.4 (61.0,71.7)	77.3 (74.0,80.7)	12.5 (6.3,18.6)	<.001
Emotional Functioning	73.8 (61.6,86.0)	73.3 (69.0,77.7)	1.4 (-11.6,14.4)	.829
Social Functioning	67.1 (60.9,73.3)	81.0 (76.6,85.3)	16.0 (9.4,22.6)	<.001
School Functioning	58.2 (54.6,61.8)	77.7 (74.3,81.0)	20.0 (14.7,25.2)	<.001

* Wilcoxon Signed Ranks test; †Paired samples t-test

There was a high positive correlation ($r=0.625$, $p<0.001$) between PedsQL Child total scale scores and scores for Global Self-Worth for children with hemiplegic CP≥8 years old (Figure 5.1). The regression model explained 42% of the variance in Self-esteem (Global Self-worth) [$F(6, 37) = 6.019$; $p<0.001$] with PedsQL Child Psychosocial Health Summary Score as the variable that made the strongest unique contribution ($\beta = 0.524$; $p = 0.003$).

Figure 5.1: Relationship between self-esteem (GSW) and PedsQL child (child total scale score) for 55 children with HCP aged 8-16 years



5.2 Discussion – Self Concept and Quality of Life

Children with HCP have lower scores on measures of quality of life and self-concept, in particular Physical Competence in the younger age-group, and Athletic Competence and Scholastic Competence in the older age-group than age and gender matched peers. However on the measure of self-esteem there are no differences, and in the younger age-group children with HCP scored higher for Maternal Acceptance.

Resilience in self-esteem has been demonstrated in other studies of children with CP (King et al 1993; Schuengel et al 2006; Manuel et al 2003b; Shields et al 2007). Self-

esteem has been shown to correlate with the domains of Physical Appearance (Harter 1986; Appleton et al 1994), followed by Social Acceptance and Scholastic Competence (Granleese and Joseph 1994). The Physical Appearance and Social Acceptance domains in this thesis did not show any significant differences with the peer group. The Scholastic Competence subscale revealed significantly lower scores for children with HCP, but the differences were either not severe enough to impact on self-esteem overall, or there was some other modifying factor to account for the result. Also, the children tended to score higher than their peer group for the two domains of Behavioural Competence and Physical Appearance, although no significant differences existed. It may be that these domains could be weighted differently in their influence on the development of self-esteem, and so have modified the impact of any potential differences in self-esteem.

Other factors may impact on this resilience, for example the protective features employed by a stigmatized group (Crocker and Major 1989). In this conceptual model members of the stigmatized group are protected by attributing negative feedback to prejudice, compare outcomes only with affected peers, selectively devalue domains that are inherently more difficult for them, and value dimensions in which their group may excel. Especially if children and adolescents with HCP meet with similarly affected peers, they may develop attitudes and views that can assist in protecting them from factors that may alter self-esteem, although this was not evaluated in this thesis. Another protective feature may include parents of children with disability admitting to consciously trying to foster a positive self-image in their children through their own attitudes and behaviors (Teplin et al 1981). This may

relate to the findings of significantly greater Maternal Acceptance for children with HCP.

Considering the added time parents of children with disabilities need to spend with their children in care activities (Crowe and Florez 2006) it is perhaps not surprising that this subscale is rated higher in the children with HCP. In children with CP, perceived parental over-protectiveness has been shown to correlate negatively with level of self-esteem (Manuel et al 2003a), but the Maternal Acceptance subscale measures parent involvement with the child as perceived by the child and not over-protectiveness. This may have a more profound effect than initially anticipated because of the positive impact that parental support has on fostering self-esteem (Brooks 1992), more so in younger children (Harter 1995). This is less influential to the older child (Harter 1990), when peer support is equivalent to parental support in its influence on self-esteem. The results of the Maternal Acceptance subscale have important implications for pediatric practice, where clinicians can support the additional time families spend with their children with special needs, reassuring them that time spent with the child in child-directed activities may assist self-esteem in the longer term.

Young children with HCP find physical activities more challenging. This is paralleled in the older age-group in the Athletic Competence domain, where children with HCP scored significantly lower than peers with typical development. Children with HCP realise their physical limitations from a young age, and timing physical programs to begin early in the development of children with HCP is supported from a psychological perspective. These data follow closely the results of other studies in

self-concept in children with physical disabilities where athletic and physical competencies are lower than peers with typical development (King et al 1993; Magill and Hurlbut 1986; Buran et al 2004; Schuengel et al 2006; Shields et al 2007; Appleton et al 1994; Armstrong et al 1992). Clinicians treating children with HCP need to be aware of these results and support intervention strategies. For example, undertaking physical programs has been found to impact positively on athletic competence (Verschuren et al 2007) and physical appearance (Darrah 1999) in children with CP, and clinicians can prescribe and advocate for these types of interventions for this group of children.

Scholastic Competence for older children was significantly lower in the children with HCP than peers with typical development. Children with HCP can have cognitive problems (Odding et al 2006) and difficulties with processing skills (Van Zelst et al 2006), and they perceive themselves as less able in this area of competence. Shields (Shields et al 2007) also noted differences in Scholastic Competence when comparing children with CP to an unaffected peer group. Whether this reduced self-concept domain relates to cognitive difficulties, impairments in sensory function (such as vision and hearing) or associated medical conditions (such as epilepsy) should be assessed by clinicians to assist the child in maximizing their learning abilities.

There was a reduced quality of life for children with HCP which was not unexpected. The pattern of similar scores for parent and child reports for peers with typical development, and lower scores for parent reports than child reports for the HCP population are similar to other published work (Varni et al 2005; Berrin et al 2007).

In the HCP group, both children and parents reported that the child was worse off physically, scoring significantly lower than the peer group. Both also reported that social functioning and school functioning were worse. However the emotional subscale (indicating if the child felt angry, sad, scared, worried or had trouble sleeping) was different for parent and child, indicating a reported emotional stability by the child similar to that of their peers, but not perceived as such by their parents. Whether the difference in this domain has any impact on children with HCP is not known.

The hypothesis that physical functioning domains of quality of life correlate more closely with physical disability and that psychosocial aspects of quality of life are out of proportion with the degree of physical disability (Pirpiris et al 2006; Wake et al 2003) was not supported in this thesis. The significantly reduced scores in the physical functioning domains (for both parent and child) when compared to their peers is relevant, given that most of the population of children were functioning at the highest levels of motor function (GMFCS Level 1 = 70/86 = 82%). It is not appropriate to assume quality of life domains for physical functioning may be acceptable for children with even the mildest impairments, as these data demonstrate that children and parents report a negative impact of the physical domains. This is supported in the findings in self-concept, where children at all ages studied perceived lower levels of physical competencies.

There was a significant positive correlation for self-esteem and quality of life for the child report. Regression analysis revealed that the children's psychosocial health predicted higher self-esteem. This has important implications for clinicians wanting

to assist children with HCP. For example, supporting a parenting style of acceptance and autonomy has been found to correlate positively with quality of life (Rapin 2007), and the findings of this thesis suggest that supporting this type of intervention could assist in improving self-esteem in children with HCP.

Strengths of this study are that children were recruited from a relatively large representative sample of children within a homogeneous subgroup of CP from a population register. The exclusion group was well defined such that more accurate inferences for children with HCP can be drawn from the data. Self-concept was also tested from a younger age than most other studies, indicating that the self-concept domains are affected at a young age and helps guide intervention timing and strategies. A limitation of this study is the cross sectional design such that causal links cannot be determined.

In conclusion children with HCP experience a reduced quality of life and self-concept when compared to peers with typical development. This research demonstrates that children with HCP recognize that they are not as competent in the domains of physical and scholastic functioning but despite this demonstrate a resilience in self-esteem. Given the significant adverse effects negative self-concept and self-esteem can have on children's development, health and functioning, clinicians need to consider appropriate intervention strategies when treating children with HCP. This study is unique given the homogeneous nature of the study population, recruitment of participants from a population register and comparison to peers with typical development. This is the first study to show a positive correlation between self-esteem and quality of life in children with HCP. Further prospective

studies exploring self-esteem and quality of life in this patient population could help suggest the basis for this relationship and factors that may explain the correlation.

With the current data set, it is now possible to explore how self-concept and quality of life for this group of children relates to functional outcome. For these analyses, the complete data set will be tested to find any relationships with the AMPS motor, AMPS process and the PEDI as the dependent variables.

CHAPTER 6: SELF-CONCEPT AND QUALITY OF LIFE – IS THERE A RELATIONSHIP TO FUNCTION?

Self-concept, self-esteem and quality of life have been measured in the cohort of 107 children with HCP. Correlation analyses were undertaken to explore whether there were any associations with self-concept, self-esteem, quality of life and function as defined by the AMPS and PEDI.

This analysis was felt to be relevant because of the complex nature of feeling about the self (Robert et al 1999; Rosenberg 1986) and particularly as it relates to level of functioning. Self-concept domains could be influenced if there was a know relationship between these variables, and efforts to assist children with HCP could potentially improve these areas of functioning. These analyses were undertaken for 60 children ≥ 8 years of age (Harter's adolescent profile) and 39 children < 8 years (Harter's child profile) with 8 children with missing data overall (3 children missing data for the child profile, and 5 children with missing data for the adolescent profile).

Methods – see 2.2a, b & c.

6.1 Results

6.1a Correlations

Correlations between function (the AMPS [motor and process scores] and the PEDI) with self-concept and self-esteem can be seen in Table 6.1. For self-concept there were significant positive correlations between Cognitive Competence and Physical Competence and AMPS ADL processing skills in the younger (<8) age groups only.

For the PEDI there was a significant correlation with Physical Competence in the younger (<8) age groups only. There were no significant correlations for the adolescent (≥8 years) group. For quality of life there were significant positive correlations with the PEDI alone, but not AMPS functioning. There were no other significant correlations noted.

Table 6.1: Pearson correlations between quality of life, self-concept and self-esteem with function for 107 children with HCP recruited from a population register

	ALL CHILDREN		Children ≥ 8 years of age						Children < 8 years of age			
	PedsQL Parent	PedsQL Child	SCH COM	SOC ACC	ATH COM	PHYS APP	BEH COM	GSW	COG COMP	PEER ACC	PHYS COM	MAT ACC
ADL mot	.062	.003	-.032	.056	-.174	-.154	-.053	.011	.304	.060	.265	.071
ADL proc	-.007	.159	-.080	.110	-.254	-.245	-.088	-.075	.524**	.325	.630**	-.071
PEDI	.260**	.426**	.189	.003	.098	.110	.170	.198	.274	.243	.535**	.173

** p < .01 – no other correlations reached significance at p<.05; mot = motor; proc = process; SCH COM = scholastic competence; SOC ACC = social acceptance; ATH COM = athletic competence; PHYS APP = physical appearance; BEH COM = behavioural competence; GSW = global self-worth (self-esteem); COG COMP = cognitive competence; PEER ACC = peer acceptance; PHYS COM = physical competence; MAT ACC = maternal acceptance.

Table 6.2 shows results for cognitive competence and physical competence for the younger age-group in relation to functioning on the AMPS and PEDI. Comparisons were undertaken about the median value for Cognitive Competence and Physical Competence, as there are no published values for assessing better vs. worse functioning on these domains (a similar process was followed for the PedsQL Parent and Child). There were no significant differences for quality of life (results not shown). However, there were significant differences in functional level favoring the children with higher scores for Physical Competence for all areas of functioning on the AMPS and PEDI, and for ADL processing skills for children with higher scores

for Cognitive Competence.

Table 6.2: Functional comparisons for 107 children with HCP above and below the median values for cognitive and physical competencies

	Cognitive Competence		P	Physical Competence		P
	≤ median	> median		≤ median	> median	
ADL mot*	.23(-.26, .46)	.46(.21, .72)	ns	.06 (-.29,.40)	.68 (.41,.95)	.005
ADL pro*	-.42(-.71,-.13)	-.01(-.26,.25)	.032	-.57 (-.77,-.36)	.21 (.02,.42)	<.001
PEDI†	52.5(42.9,59.4)	57.0(48.4,60.3)	ns	48.5(39.7,53.4)	61.0(55.9,64.2)	.002

mot = motor; pro = process; ***** denotes normally distributed data and the student t-test.
†denotes non-normally distributed data and the Mann-Whitney-U test.

6.1b Regression Analyses

Using the results of the above analyses two models were tested. The first was the relationship between function and Cognitive Competence, and the second between function and Physical Competence.

Multiple regression analysis was undertaken to assess the ability of function to predict the level of Cognitive Competence in children with HCP while controlling for age, gender and burden of care. The regression model was able to explain 30.3% of the variance in Cognitive Competence [$F(4,26) = 2.83$; $p = .045$] with AMPS ADL process score as the variable that made the strongest unique contribution ($\beta = 0.621$; $p = .022$).

Similarly, regression analysis was used to explore the relationship between function and Physical Competence controlling for age, motor skills and burden of care. This model explained 56.4% of the variance in Physical Competence [$F(4, 26) = 8.40$; $p = .001$] with ADL process score as the variable that made the strongest unique contribution to the model ($\beta = 0.977$; $p = .001$).

6.2 Discussion

There exists a relationship between function and self-concept for younger children (<8 years) which does not exist for older children. While there was a correlation with function and quality of life, there were no significant relationships found on further statistical analysis.

The findings that better processing skill ability (as measured on the AMPS) predicts higher cognitive and physical competencies broadens the perspective that must be taken to understand functioning in children with HCP. A high proportion of children with HCP are known to have bilateral lesions on brain imaging (Mercuri et al 1999), with pathology that affects functioning on the "unaffected" side (Cooper et al 1995). Involvement of brain lesions that are more widespread than the motor area is known to occur in CP (Steinlin et al 1993; Cioni et al 1999). It is therefore not surprising that children with HCP can have significantly reduced processing skill abilities that impact on motor function (Van Zelst et al 2006). These reduced process skill abilities are associated with feelings of reduced competency in the cognitive and physical domains, reflecting their reduces level of functioning.

Quality of life is not related to mobility (Rosenbaum et al 2007), however in one study (Rosenbaum et al 2007) of 203 adolescents with CP, there was a reduction in "dexterity" in one measure in relation to mobility. However, although this study also examined quality of life, there was no comparison of dexterity with quality of life. The relationship of gross motor function in the lower limb with that of the upper limb has also been found by other investigators in children with CP (Kennes et al 2002) (Rice et al 2008). Even when function is considered with respect to mobility alone,

there does not appear to exist any relationship to emotion and pain (which themselves could impact on quality of life (King et al 2000; King et al 2006; Kennes et al 2002)) and so no clear relationship exists between function and quality of life for children with CP. The results of this thesis show a correlation between the PEDI and quality of life and so some relationship has been shown between functional level and quality of life. There is also an association between quality of life and the prescription of adaptive aides which will be presented and explored in chapter 7 of this thesis.

The relationship between function and self-concept may be different to that between function and quality of life. In one randomized control trial (Verschuren et al 2007), children with CP undergoing a training program (compared to controls) had a significant increase in their level of perceived athletic competence, supporting the link between level of functioning and self-concept domains. The construct of self-esteem, however, did not alter. Other investigators have also shown a shift in self-concept with physical programs in CP (Dodd et al 2004; Darrah 1999) further supporting this association. In one study of a small number of participants with CP undertaking a strengthening program (Dodd et al 2004), self-concept was worse for the intervention group for cognitive competence and social acceptance. However, in a larger trial (Verschuren et al 2007) and another of similar patient numbers (Darrah 1999) there was a positive shift for the intervention group within the physical domains.

These studies provide some insight into the effects of an exercise program on perceived competencies. Other aspects of the exercise program which may not have

been measured and may have influenced self-concept could also have been a factor. Expectations of the investigators that changes to self-concept may arise during times of intervention are reasonable, given that children are re-focusing their attention and efforts on trying to improve their impairments, with consequences that are likely to expand beyond the intervention itself.

Although causality cannot be determined due to the cross-sectional nature of this data, it may follow that improvements in functioning may assist with improvements in cognitive and physical self-concept. This seems to hold true only for younger children and not older children. Younger children may form self-concept more strictly related to their immediate environment and functional level, with older children linking feelings of competency with other, perhaps more abstract concepts that are different to the younger child. There are known differences in what influences how younger and older children value themselves (level of self-esteem). Parental support is a critical factor in shaping feelings of self-worth (Brooks 1992) and this is more important in the young child (Harter 1995). In the older child, peer acceptance is equivalent to parental support in influencing self-esteem (Harter 1990) and so differences are evident between younger and older children in relation to self-concept domains.

In conclusion, the self-concept of young children is associated with their level of functioning, and any intervention assessing change in functioning in children with HCP should include self-concept as an important aspect of the evaluation. Children with HCP require significant input to assist them in maximizing their functional capacities. This comes in many forms, but some of the more traditional methods

relate to the provision of therapy and assistive devices (such as orthoses and equipment). For children with HCP it is not known how the provision of these technologies assists the children and adolescents. Therefore a cross sectional analysis to evaluate the provision of this type of assistance on function in this group of children was undertaken to explore these issues.

CHAPTER 7: THE NEED FOR ASSISTANCE – ORTHOTICS, THERAPY AND ASSISTIVE TECHNOLOGIES

Children with HCP are known to have significant physical and cognitive limitations (Khaw et al 1994) that require support with the use of orthoses, AT and therapy. Upper limb orthoses are defined as any device applied to an external surface of an extremity used to provide better positioning, maintain correction of posture and improve function (Schutt 1992). Upper limb orthoses may improve grip strength (Farrell et al 2007), however there is little evidence that they can improve function or play for children (Teplicky et al 2002). AT can include portable aides and environmental modifications used to increase, maintain or improve a person's functional capabilities (Freedman et al 2006). Orthoses, AT and therapy are felt to be necessary for children with the set of impairments common in HCP, but little is known about prescribing practices and child characteristics associated with prescription of these devices and for therapy. The efficacy of therapy is also unproven (Sakzewski et al 2009), with little guidance for the dose and type of therapy that could be effective in influencing upper limb function. The prescription of orthoses, AT and therapy is expensive and little is known about adherence to the prescribed devices and therapy programs, or who is more likely to benefit from this assistance. This would be helpful to clinicians managing children prescribed this support as there is currently a paucity of literature evaluating these issues (Teplicky et al 2002) .

As part of this cross sectional study, the reported prescription and use of orthotics and AT, and provision of therapy, was examined. Defining the study participants with respect to functioning, self-concept and self-esteem, quality of life and burden

of care was felt to be important as these areas of functioning could be impacted upon by these treatment modalities, and functioning in these domains could influence the prescription of therapy and assistive devices.

Methods – see 2.2a, b & c, and 2.3c.

7.1 Results - Orthotics, Therapy and Adaptive Technologies

7.1a Characteristics of Study Population

Demographic data for gestation, birth weight, intelligence, motor ability (GMFCS) and current educational level have been reported in Chapter 3, Table 3.1. Fifty-six percent had been prescribed an upper limb orthosis (Table 7.1), most commonly a thumb/hand orthosis. Only 48% of children prescribed a wrist/hand orthotic were currently using it, and only 29/60 (48%) of those prescribed an orthosis wore it for > 4 hours per day. The reported reasons for abandonment was the orthosis was outgrown (26%), was no longer needed (23%), had no effect (13%) , was refused outright (35%) or offered no response (one child). In contrast, of the 49 children prescribed AT, 98% were currently using them. More commonly this was a mobility (18%), feeding (23%), self-care (20%) or bathroom (22%) aide. Eighty five percent of children were currently involved in a therapy program, primarily a non-intensive (< once per week) provision of occupational therapy. However, nearly 1 in 5 children were receiving intensive therapy (defined as ≥ 1 time per week). All of the therapy was community based with none undergoing hospital based therapy for the upper limb.

Table 7.1: Summary of prescription and use of orthoses, adaptive equipment and therapy for 107 children with HCP recruited from a population register

	Orthoses* n (%)		Adaptive Equipment n (%)		Therapy n (%)	
Current prescription?						
YES	60 (56)		49 (46)		91 (85)	
NO	47 (44)		58 (54)		16 (15)	
Type	Arm/elbow	9	Mobility	19	OT	57 (63)
	Thumb/hand	28	Communication	6	PT	32 (35)
	Wrist support	23	Feeding	24	SP	26 (29)
			Self-care	21	Ps	4 (5)
			Bathroom Aids	23		
Current use/dose of therapy?						
YES	29 (48)		48 (98)		Intensive	20 (19)
NO	31 (52)		1 (2)		N/I	68 (64)
					Missing	3 (3)

* Only upper limb orthoses are reported. OT – occupational therapy; PT – physiotherapy; SP – speech pathology; Ps – psychology; Intensive = >1 time per week; N/I – non intensive meaning ≤1 time per week.

7.1b Use of Orthoses

Table 7.2 shows comparisons for functional outcomes for children prescribed an upper limb orthosis. There were significant differences for MAS, hand span, grip strength, modified Tardieu, AMPS and self-esteem favoring the children who were not prescribed an orthosis. Large effect size was detected for MAS at the wrist, grip strength and hand span.

Table 7.2: Functional outcomes for children who were or were not prescribed an upper limb orthosis in 107 children with HCP

Measure	Prescription of Orthoses		P	Effect Size
	Yes (n=60)	No (n=47)		
MAS (n)* Elbow				
0-1+	28	38	**<0.001**	0.37 [a]
2-3	32	8		
MAS (n)* Wrist				
0-1+	25	42	**<0.001**	0.51 [a]
2-3	35	4		
Hand span† (cm)	12.1 (11.3,12.9)	14.3 (13.1,15.4)	**0.002**	0.08 [b]
Grip strength† (mmHg)	36.4 (26.1,46.6)	63.9 (49.7,78.0)	**0.002**	0.12 [b]
Tardieu elbow (Y) *				
Absent	18	33	**<0.001**	0.40 [a]
Present	42	14		
Tardieu wrist (Y) *				
Absent	21	37	**<0.001**	0.41 [a]
Present	35	10		
AMPS†				
Motor score	0.28 (.07,.48)	0.72 (.45,.99)	**0.010**	0.06 [b]
Global self-worth‡	3.3 (3.0,3.4)	3.8 (3.1,3.8)	**0.031**	0.28 [c]

* Pearson χ^2 ; † Student t-test and reports mean (95%CI); ‡ Mann-Whitney U test and reports median (95%CI); no significant results for comparisons for age, gender, affected side, sensory function, intellectual status, provision of therapy, AMPS process score, PedsQL and PEDI. [a] Phi; [b] Eta squared; [c] r.

7.1c Assistive Technologies

Table 7.3 shows comparisons for functional outcomes for children prescribed AT. There were significant differences for MAS, hand span, grip strength, AMPS, quality of life (PedsQL Parent), self-esteem and caregiver burden (PEDI) favoring the children who were not prescribed AT. Large effect size was detected for PedsQL Parent, the PEDI and hand span.

Table 7.3: Functional outcomes for children who were or were not prescribed assistive technologies (AT) in 107 children with HCP

Measure	Prescription of AT		P	Effect Size
	Yes (n=49)	No (n=58)		
MAS* (n) Elbow				
0-1+	25	41	0.03	0.22 [a]
2-3	24	16		
MAS* (n) Wrist				
0-1+	24	43	<0.01	0.27 [a]
2-3	25	14		
Hand span† (cm)	12.1 (11.1,13.1)	13.9 (12.9,14.9)	0.010	0.06 [b]
Grip strength† (mmHg)	37.2 (26.7,47.8)	57.2 (44.1,70.4)	0.023	0.06 [b]
AMPS† -				
Motor score	0.28 (.02,.54)	0.63 (.41,.85)	0.04	0.04 [b]
Peds QL Parent†	50.5 (46.2,54.9)	60.4 (56.9,64.0)	0.001	0.11 [b]
Global Self-worth‡	3.1 (2.9,3.4)	3.7 (3.2,3.6)	0.029	0.29 [c]
PEDI ‡	57.0 (46.7,56.3)	65.0 (57.8,64.5)	<0.001	0.34 [c]

* Pearson χ^2 ; † Student t-test, and reports mean (95%CI); ‡ Mann-Whitney U test and reports median (95%CI) no significant results for comparisons for age, gender, affected side, intellectual status, provision of therapy, modified Ashworth score at the elbow, AMPS process score, PedsQL child. [a] Phi; [b] Eta squared; [c] r

Therapy

Table 7.4 shows the results for children who were prescribed therapy vs. children who were not prescribed therapy. There were significant differences for the AMPS motor score, Cognitive Competence and Physical Competence, with no significant differences for the other measures. Children who were less functional were prescribed therapy. Effect size was not calculated as regression analysis used only the three variables that showed significant differences. However, the table is included for completeness of the analysis of assistance to children with HCP.

Table 7.4: Functional outcomes for children who were and were not prescribed therapy in 107 children with HCP

Domain	Therapy	No therapy	P
AMPS*			
AMPS Motor	.39 (.21,.56)	.98 (.50,1.46)	**.013**
AMPS Process	.08 (-.14,.31)	.56 (.01,1.11)	.106
Age of child*	8.7 (8.0,9.5)	10.5 (8.4,12.6)	.060
Self-concept†			
Cognitive Competence	3.0 (2.7,3.3)	3.9 (3.8,4.0)	**.024**
Physical Competence	2.5 (2.5,3.0)	3.6 (3.0,4.0)	**.024**

*Student t-test and reports mean (95%CI); † Mann-Whitney U test and reports median (95%CI); no significant results for comparisons for PedsQL Parent and Child; gender; sensory function; MAS tone at the elbow and wrist; Gestation; GMFCS level; affected side; intellectual status; hand spans; Tardieu; grip strength or PEDI. For the self-concept domains, only those reported were significantly different.

7.1d Abandonment of Orthosis

Table 7.5 shows results for children who abandoned the use of their orthosis. These children were significantly older and had greater scores for limb spans, AMPS motor and process scores, self-concept and self-care. However they were perceived to have a lower quality of life by their parents than children who adhered to orthotic use. A large effect size was noted for AMPS Process score, forearm length and age.

Table 7.5: Functional outcome for 60 children who used and did not use a prescribed upper limb orthosis

Measure		Use of Orthoses		P	Effect Size
		Yes (n=29)	No (n=31)		
Age (years) †		7.8 (6.6,9.1)	10.8 (9.4,12.2)	**0.002**	0.15[b]
Spans (cm) †	Hand	10.9 (9.9,12.0)	13.2 (11.9,14.5)	**0.006**	0.12 [b]
	Forearm	17.9 (16.6,19.2)	20.7 (19.3,22.1)	**0.002**	0.15 [b]
	Humeral	23.4 (21.6,25.1)	26.4 (24.5,28.0)	**0.013**	0.10 [b]
AMPS†					
	Motor score	0.01 (-0.27,0.30)	0.53 (0.25,0.81)	**0.011**	0.11 [b]
	Process score	-0.38 (-0.73,-0.26)	0.55 (0.19,0.90)	**<0.001**	0.21 [b]
Peds QL†	Parent	58.3 (52.5,64.1)	49.3 (44.3,54.2)	**0.018**	0.09 [b]
Schol. Comp. ‡		2.3 (1.9,2.8)	2.9 (2.6,3.1)	**0.030**	0.37[c]
PEDI ‡		51.3 (45.2,57.4)	58.8 (53.8,63.7)	**0.038**	0.27 [c]

† Student t-test and reports mean (95%CI); ‡ Mann-Whitney U test and reports median (95%CI); no significant results for comparisons for, gender, affected side, sensory function, intellectual status, Tardieu, MAS and grip strength. Schol. Comp. – scholastic competence. [b] Eta squared; [c] r

As there is a paucity of literature assessing the associations of prescription of orthoses AT and therapy, and abandonment of orthoses in children with HCP, each was tested in a separate logistic regression model using 3 independent variables that had the strongest association (largest effect size) for each intervention and for

abandonment of orthoses. The results are presented in Table 7.6. All models were statistically significant ($M\chi^2$ value) and the percentage of variance explained by the model for each analysis is given in the table (Cox and Snell R squared and Nagelkerke R squared), as is the percentage of cases correctly classified by the model.

7.1e Orthotic Prescription

The model was able to distinguish between children prescribed orthotics. Only MAS wrist made a unique, statistically significant contribution to the model, recording an odds ratio of 39.6, indicating that children with a MAS score across the wrist of ≥2 were nearly 40 times more likely to be prescribed an upper limb orthotic device than a child with less tone across the wrist.

7.1f Prescription of Assistive Technology

When the three predictor variables are considered together, they significantly predict whether or not a child with HCP was prescribed AT. Only PedsQL Parent was a statistically significant predictor, indicating that a higher parental perception of quality of life predicted the child was less likely to have been prescribed AT.

7.1g Therapy

The model was valid but the independent variables were not statistically significant predictors. The model cannot be used as a predictor model on the basis of these findings.

7.1h Use / Abandonment of the Orthotic

The model was able to distinguish between children using their orthotics. Only AMPS process score made a unique, statistically significant contribution to the model, recording an odds ratio of 2.5. This indicates that the odds of abandoning the upper limb orthosis is increasingly greater as process skill ability scores increase, controlling for other factors in the model.

Table 7.6: Logistic regression predicting the likelihood of being prescribed an Orthotic, AT and therapy, and the likelihood of orthotic abandonment in 107 children with HCP

	B	*S.E.*	*W*	*P*	*OR*	*95% CI for O R* *Lower*	*Upper*	*CS R^2 (%)*	*N R^2 (%)*	*M χ^2 [d,n]*	*M P*	*% C/C*
Orthotic												
MAS Wrist	3.7	1.1	11.8	**.001**	**39.6**	4.8	323	37.7	50.6	38.8	**.001**	78.0
Avg. Grip	-.01	.01	.34	.562	1.0	.98	1.0			[3,n=82]		
Hand Span	-.14	.10	2.1	.149	.86	.72	1.1					
AT												
PedsQL(P)	-.05	.02	8.2	**.004**	**.95**	.92	0.98	18.0	24.1	20.5	**.001**	52.4
PEDI	-.02	.02	1.3	.255	.97	.94	1.02			[3,n=103]		
Hand Span	-.10	.08	1.6	.207	.91	.77	1.06					
Therapy												
AMPS mot	-5.81	3.8	2.3	.126	.003	0.0	5.2	36.0	68.0	14.3	**.003**	93.8
Cog Comp	-9.19	6.5	2.0	.155	.000	0.0	32.1			[3,n=32]		
Phys Comp	-3.64	3.6	0.99	.319	.026	0.0	33.5					
Abandonment												
Age	.70	.20	.13	.722	1.07	0.73	1.57	21.2	28.2	13.8	**.003**	67.2
Forearm Length	.01	.21	.001	.907	1.01	.067	1.53			[3, n=58]		
AMPS proc	.91	-.80	3.91	**.048**	**2.48**	1.01	6.12					

MAS – modified Ashworth scale; Elb. – elbow; Avg. Grip – average grip strength; PedsQL(P) – Pediatric Quality of Life (Parent); PEDI – Pediatric Evaluation of Disability Inventory (self-care subscale); AMPS – Assessment of Motor (Mot) and Process (Proc) Skills. Cog Comp – Cognitive Competence; Phys Comp – Physical Competence; B – beta coefficient; SE – standard error; W – Wald test; P – predictor variable p value; OR – Odds Ratio; CS R^2 – Cox & Snell R^2; N R^2 – Nagelkerke R^2; Mχ^2 - Chi squared value for regression model; M P – model p value; % C/C – percentage correctly classified by the regression model.

7.2 Discussion, Orthotics, Therapy and Adaptive Devices

A significant proportion of children with HCP living in the community are prescribed upper limb orthoses, AT and therapy. Nearly half of the population studied were prescribed these devices and had therapy, indicating an active approach to management. As expected, children with more severe involvement with lower scores on the functional outcome measures were targeted for intervention, the comparisons demonstrating they were a more vulnerable sub-group with higher levels of impairment and lower levels of functioning.

In the prescription of orthoses and AT, clinicians focus on technical issues of the device, but families focus more on functional outcomes and day-to-day management (McDonald et al 2003). This may be one reason why AT had such a high utility in this group. AT are prescribed for functional tasks that assist necessary activities the child and family need to complete on a daily basis. If the equipment offers the child and family a true functional advantage it should have a higher utility, supporting compliance.

In contrast the difference in the prescription of upper limb orthoses and utilization of these devices on history was clinically significant, indicating poor adherence. Reasons for poor adherence were given by the children and their families and in 74% of individuals were not related to improper fit. Younger children were more likely to adhere, which may reflect parental supervision and support for use. Children more capable in functional tasks were found to be over twice as likely to abandon the orthosis than children who were less functional. Greater process skill ability was

most strongly associated with the disuse of the orthosis, suggesting the orthosis interfered with daily functioning. Process skill ability indicates the child's ability to overcome problems encountered in completing functional tasks. Children with increased process skill abilities may simply be more likely to abandon the orthosis if that orthosis interferes with completion of functional tasks, a child with less process skill ability choosing to persevere with the orthosis. Alternatively, the child may have felt that the functional benefits of the device failed to offset the stigma they may have perceived associated with its use.

AT and orthoses represent two different modalities of intervention and direct comparisons may not be valid. In considering AT such as bathroom aides, these are unlikely to be needed on any one occasion for any extended length of time, compared to orthotic use which usually requires several hours of wear. Another consideration is that abandonment of the orthotic and utilisation of the AT devices may be the result of expectations. In one study (Burtner et al 2003) the prescription of different upper limb orthoses had both positive and negative effects on different upper limb functions including grip strength, pinch and dexterity, which were either enhanced or diminished related to orthotic design. AT is often designed for and utilised within a lower standard of expectations, and so direct comparisons may not be valid.

Taking time to educate the child and family about the benefits of the orthosis may assist with compliance, as well as considering individual circumstances in the counseling of when the orthotic should be worn so as to maximize function and reduce abandonment. Using the orthosis at times other than when the child needs to complete activities of daily living tasks (for maintaining posture), or designing the

orthosis specifically to assist in completing the activity of daily living task is required, taking care in evaluating the impact of the orthosis on the child's level of functioning. These data support the need for a more comprehensive evaluation prior to orthotic prescription so as not to waste resources.

Quality of life was lower on the parent scale for children prescribed AT, and this was the independent variable most strongly associated with this outcome in the regression model. Parents may perceive a lower quality of life for their child because the disability experienced may be very evident when using the equipment, reinforcing the negative impact of the lack of function. It may also require more time from the parent, as shown by the significantly lower score on the PEDI, indicating the child was not capable of completing self-care tasks and needed assistance.

The regression model on upper limb orthotic prescription indicated that increased tone as measured by the MAS is associated with the likelihood of prescription of upper limb orthoses. In this model, children with tone on the MAS across the wrist of ≥2 were nearly 40 times more likely to be prescribed an orthotic than children with lesser tone. This can help in counseling families of young children with a new diagnosis of HCP. Clinicians can use the MAS at the wrist, which can be measured in early childhood, as an indicator of the need for future intervention. As therapy services are evolving into a more proactive model of care for children with CP (Cooley 2004), knowing the likely level of support a young child with HCP will need could assist in service planning and provision. The benefits of such intervention, however, require evaluation with prospective randomized trials.

The data presented in this thesis represents the prescribing practices of a large cohort of physicians and therapists, each of whom may have had their own criteria and clinical biases for the prescription of upper limb orthoses and AT. Data on individual prescribers was not collected systematically, thus there were no strict criteria for the prescription of these devices and to the extent that these criteria existed, they were likely to vary from referral source to referral source.

In relation to functioning, there was a significantly greater prescription of orthotic/adaptive devices and therapy for children who were less functional. This was seen in all three areas of assistance for reduced motor scores on the AMPS, and for AT for the PEDI. The association of prescription of orthotic devices for children with increased wrist tone indicates provision of this technology at the impairment level of functioning, but consistently children who functioned less well than their peers at the participation level of functioning were targeted for therapy. As well, it was the most functional group that abandoned their orthoses, again indicating the link between provision of assistance and level of functioning.

Strengths of this study include recruitment of children from a population based register so that more accurate inferences can be made from the data. Limitations of this study include the paucity of specific details of the orthotic and AT design and manufacture (such as materials used, device flexibility, device encumbrances and trim lines) and any correlation between acceptance/abandonment of the orthosis and its type and biomechanical application is not possible. Also, an important factor affecting the prescription of orthoses and AT is the attitudes and beliefs of the prescribing clinicians, and given the study design these could not be explored. The

duration of use of the orthotic was based on parental/child histories, and may thus be inaccurate, introducing bias in the analyses.

In summary children with more severe HCP receive more assistance with assistive devices and therapy, and this is clinically appropriate. Compliance with AT is high, but compliance with upper limb orthotic prescription is low. Reasons for this should be explored in future studies. Children with higher tone across the upper limb are statistically more likely to require orthotic prescription and this can assist in counseling and planning for future service provision.

CHAPTER 8: SUMMARY OF THE MAJOR FINDINGS IN PART 1 – HEMIPLEGIA AND THE NEGLECTED UPPER LIMB

The results of the Part 1 studies are representative of children with HCP, as there was a high rate of participation (85% of available subjects participated). Children in this study have HCP with varying degrees of severity, however they are a highly functional group when considering broad parameters of functioning and participation such as IQ and schooling. They are a group of children who are functioning alongside their typically developing peers, with functional differences in narrower domains likely to impact on their daily lives. Consistent with the ICF model of disability, a broad range of factors that can be impacted upon by the disability were explored.

In relation to function, children with HCP performed well below population norms as defined by the AMPS and PEDI. Children with HCP have significant impairment level deficiencies which can all impact on participation. The most strongly correlated impairment level independent variable impacting on participation level functioning was upper limb sensory function, followed by upper limb muscle power. Therefore, any attempt to alter functional outcome in children with HCP needs to focus on interventions that can influence these modalities to be effective.

The pain these children experienced was mostly mild in severity, more commonly ipsilateral involving the leg or arm and leg together. Children reported qualities to the pain that can be interpreted as nociceptive in origin. The pain impacted mostly on movement and was most commonly relieved by rest and massage. The experience of pain was significant in this group of children, and this left them vulnerable to

problems associated with lower quality of life and self-concept. Through these parameters, pain can have a negative influence on participation and needs to be evaluated and treated in children with this form of CP. However, the experience of pain per se has not been shown to be associated with level of functioning, with both groups of children with HCP (experiencing pain compared to those not experiencing pain) having equivalent levels of functioning as measured by the AMPS and PEDI. It may be feasible to address pain in any intervention trial, but whether the experience of pain alters throughout the trial is unlikely to impact on functional outcome according to these findings. Older children with pain reported significantly lower scores for scholastic and behavioural competencies. Regression analysis has shown that children who report pain perceive a lower behavioural competence; a factor that could increase negative feelings and reduce function and participation.

In comparison to their peer group, a relatively higher functioning subgroup of children with HCP were more vulnerable to functional deficit, with lower reported levels of quality of life (across both physical and psychosocial domains) and lower levels of perceived physical and scholastic competencies. These differences leave the child more prone to problems in relation to participation level functioning. Young children with HCP with reduced levels of functioning as defined by the AMPS ADL process scores have reduced levels of cognitive and physical competencies. This means that in relation to their peers, these children feel less able in the physical and cognitive areas, and this insight is occurring at a young age. Intervention strategies need to be focused on functional improvements from a young age. Despite these differences, self-esteem was equivalent, with children with HCP reporting a degree of emotional functioning similar to their peer group. This is important given the

findings of the relationship between the child's psychosocial health and self-esteem.

Efforts to assist children with HCP, who are functioning alongside their non-affected peers within typical schooling environments, are great, with more severely affected children with HCP receiving assistance in the form of orthotics, AT and therapy. Logistic regression analysis has given insights into how the independent variables relate to these modes of assistance, with more vulnerable children on impairment level functioning having related deficits in the areas of quality of life and participation level functioning.

In an effort to assist participation level functioning, there has been the development of therapies and specific interventional technologies. One of these, BoNT-A, was postulated to assist children in the domains of participation level functioning, and the results of this intervention trial are reported in the next chapter. Using the results of the series of studies in Part 1, a focus on the factors that influence function was included to help maximise the results of the trial, as factors associated with good functional outcomes were now more fully understood.

CHAPTER 9: INTERVENTION TRIAL – THE USE OF BOTULINUM TOXIN INJECTION TO IMPROVE FUNCTIONAL OUTCOME

BoNT-A injection into the upper limb of children with CP has been studied in several non-randomized trials (Autti-Ramo et al 2001; Friedman et al 2000; Hurwitz et al 2000; Wallen et al 2004; Wong et al 2002; Yang et al 2003) with varying degrees of improvement in spasticity, cosmesis, and non-validated participation level outcome measures. In randomized trials involving children with HCP, BoNT-A injection into the upper limb has been shown to reduce muscle tone (Boyd et al 2003; Corry et al 1997; Lowe et al 2006), improve joint range of motion (Corry et al 1997; Lowe et al 2006; Speth et al 2005) and improve some aspects of function (Boyd et al 2003; Lowe et al 2006; Fehlings et al 2000). Both Fehlings (Fehlings et al 2000) and Lowe (Lowe et al 2006) demonstrated an improvement on the QUEST. However this measure, which is tested under verbal instruction, illustrates what the child can do, not what they actually do in real life situations. Lowe (Lowe et al 2006) also used the GAS to demonstrate that function could improve, indicating a benefit favoring the intervention group. In both of these trials, therapy for the control group was undertaken and the control groups improved on the outcome measures from baseline, but there was no evaluation of the amount or type of therapy given.

In two other studies investigating the effects of BoNT-A injection in the upper limb, a modest dose of therapy [weekly therapy for six weeks (Boyd et al 2003)] and intensive therapy [30 minutes of therapy three times per week for six months (Speth et al 2005)] resulted in similar changes in both control and intervention groups so the effect of therapy remains unclear (Boyd et al 2003). Moreover, what therapy to

deliver, and in what dose, has not been determined, although a recent meta-analysis has indicated that BoNT-A can supplement a variety of upper limb treatment approaches with positive outcomes for treated children (Sakzewski et al 2009).

Sufficient evidence to support routine treatment with BoNT-A has been lacking (Wasiak et al 2004; Reeuwijk et al 2006), with BoNT-A shown to provide only a supplementary benefit to other treatment modalities (Sakzewski et al 2009). There is a need to include reliable and valid outcomes that measure children's abilities to carry out necessary activities of daily living and meet specified goals (Wasiak et al 2004) at different levels of functioning to evaluate the impact of treatment (Reeuwijk et al 2006). For this reason, the outcome measures of the GAS and the AMPS were chosen as the principle outcome measures for this randomized control trial.

Because there was no consensus as to the most appropriate therapy intervention for children with HCP undergoing BoNT-A injection (Hoare and Imms 2004; Lannin et al 2006; Sakzewski et al 2009), nor enough evidence about intensity of therapy (Huang et al 2009), a therapy program was established that focused on muscle strengthening and bimanual tasks to assist the children entering the trial. The end result was an eclectic mix of therapies including weight bearing (on the upper limb), ball skills, fine motor strengthening, and bilateral functional tasks. All therapy methods had the effect of strengthening the upper limb which, based on the analyses in Part 1 of the study, were most likely to influence functional outcome.

The purpose of this trial was to assess the effect of an individually prescribed and localised injection of BoNT-A and occupational therapy compared to occupational

therapy alone on body structure, activities/participation, and self-perception in a community based sample of children with HCP.

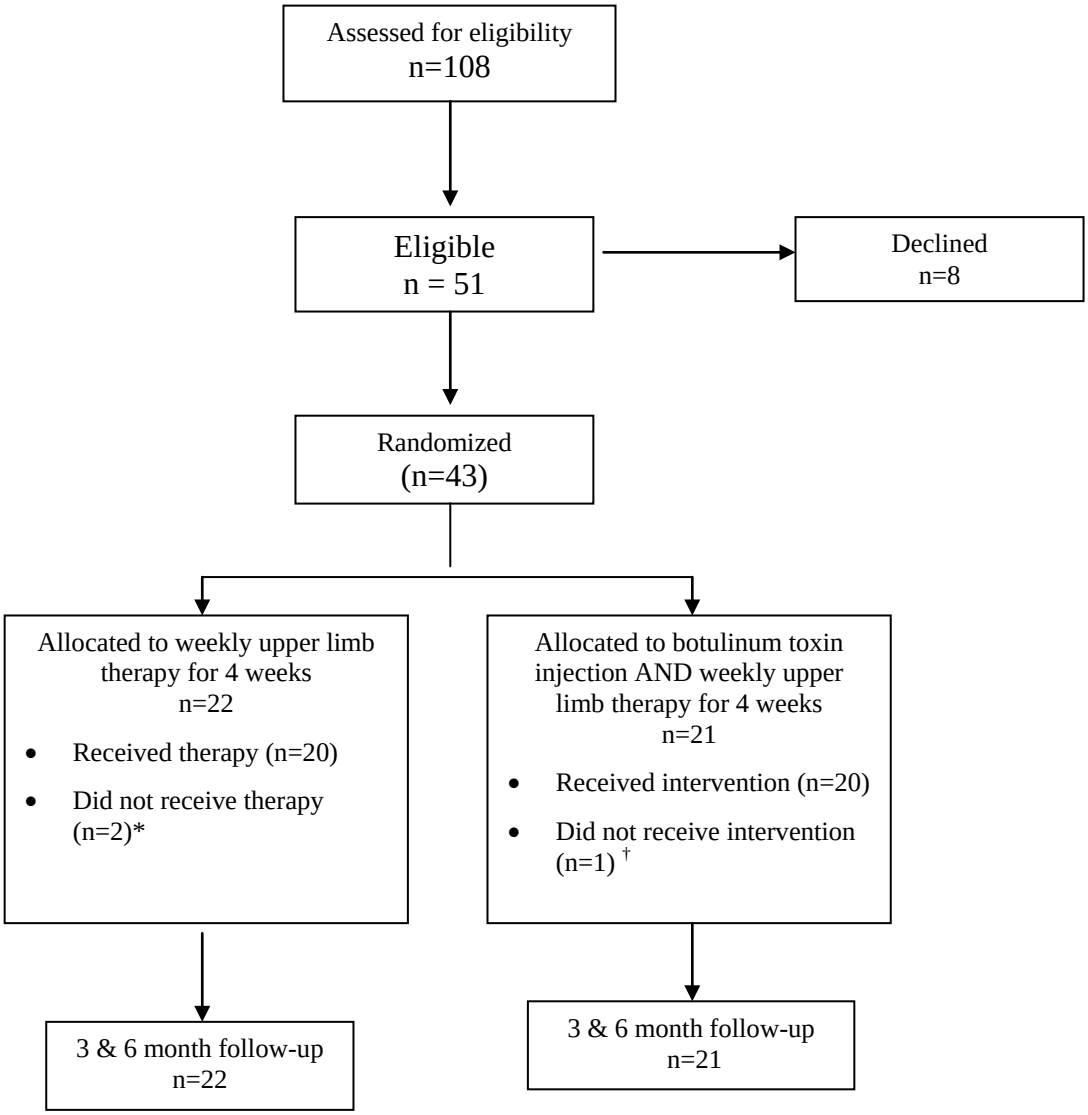
Methods – see 2.3a, b & c.

9.1 Results - Intervention trial

9.1a Study population

Of the 143 children with hemiplegic CP (aged 3-16 years) identified from the South Australian Cerebral Palsy Register, 108 (76%) were assessed and 51 (47%) were eligible to participate. Forty three (84% of eligible children) consented and were randomized, with eight children refusing participation (Figure 9.1). Twenty-two were randomized to the control group and 21 to the intervention group. Follow-up data were obtained for all participants at three and six months. After allocation to the control group, two participants did not undertake the prescribed therapy. Also, one participant refused injection of botulinum toxin after random allocation to the intervention group, but undertook the prescribed therapy. All children presented for their review (outcome) appointments and results were analysed under an intention to treat model.

Figure 9.1: Flow of participants through each stage of the randomized controlled trial



* After enrolment two children did not undertake therapy but intention to treat follow-up completed. † After enrolment family refused intervention but intention to treat follow-up completed

Baseline comparisons

The demographic, functional and quality of life characteristics of the study groups were similar at baseline (Table 9.1). The mean (95% CI) age was 8.6 (7.4, 9.8) years. The majority of participants were male (n=23; M:F ratio = 1.2:1), had hemiplegia affecting the right side (n=25; R:L ratio = 1.4:1), and were not receiving occupational therapy at the time of the study (n=27; 63%). Both groups had

significant levels of tone across the wrist and elbow (MAS and Tardieu values) but there were no differences between the groups. Twenty-one participants (49%) reported pain, 13 mild-moderate and 8 severe. The self-concept domain of Athletic Competence was significantly different at baseline favoring the control group. The self-concept domain of Physical Appearance was significantly different at baseline favoring the intervention group. There were no other significant differences in the measured variables at baseline.

Table 9.1: Baseline characteristics of the study participants

Characteristic	Control (n=22)	Intervention (n=21)	P
Demographic			
Age*, mean (95% CI)	8.7 (7.0,10.4)	8.4 (6.5,10.2)	.772
Gender† (Male/Female)	12/10	11/10	.887
Side of hemiplegia† (Right/Left)	11/11	14/7	.268
Body Function/Structure			
Tardieu R2-R1(degrees ± SD) *			
Elbow	69.4 (52.1,86.8)	74.3 (59.8,88.7)	.503
Wrist	120.6 (91.7,149.4)	93.5 (56.3,130.7)	.256
MAS ‡			
Elbow median (IQR)	2 (1^+ – 2)	2 (1^+ – 2)	.725
Wrist median (IQR)	2 (1^+ – 2)	2 (1 – 2)	.201
Activity-Participation			
PEDI, mean (95% CI) *	55.2 (49.5,61.0)	54.1 (46.8,61.4)	.801
PEDsQL (mean ± SD) *			
Parent	54.7 (48.1,61.4)	55.6 (47.1,64.1)	.982
Child	66.5 (59.3,73.7)	71.9 (62.2,81.7)	.334
AMPS *			
Motor, mean (95% CI)	.18 (-0.12,0.49)	.08 (-0.36,0.52)	.684
Process, mean (95% CI)	.16 (0.22,0.53)	-.20 (-0.75,-0.36)	.276
Self-concept, Median (95% CI)§,‡			
Athletic competence	3.2 (2.7,3.5)	2.6 (1.0,3.2)	**.050**
Physical appearance	2.8 (2.7,3.2)	3.4 (3.1,3.7)	**.042**
Global Self Worth	3.3 (3.0,3.7)	3.5 (2.8,4.0)	.616

* Independent student t-test; † Pearson χ^2; ‡ Mann-Whitney U Test; § only older children ≥ 8 years, n= 22

9.1b Dose of BoNT-A and Occupational Therapy

The total dose of BoNT-A (Botox®) injected per kilogram of bodyweight and amount of toxin injected per muscle, can be seen in Table 9.2. Overall the total dose did not exceed 12 units per kilogram of bodyweight per child, with a mean dose per child of

8 units per kilogram of body weight and a range of 5-11.6 units of Botox® per kilogram of body weight.

Table 9.2: Mean, minimum and maximum number of units Botox® injected per kilogram (U/kg) of bodyweight and per muscle injected (n=20)

	MEAN (SD)	Minimum	Maximum
U/kg bodyweight	8.0 (2.2)	5.0	11.6
Units per muscle			
BR	23.2 (9.7)	10	40
Biceps	44.7 (16.6)	20	80
PQ	27.4 (12.4)	10	50
PT	27.4 (12.4)	10	50
FCR	39.4 (17.8)	5	60
FCU	39.4 (17.8)	5	60
AP	15.3 (4.9)	10	25
Opponens	15.3 (4.9)	10	25
FPB	12.5 (3.5)	10	15
FDP	16.7 (12.5)	10	25
FDB	16.7 (15.0)	10	25

BR – brachioradialis; PQ – pronator quadratus; PT – pronator teres; FCR – flexor carpi radialis; FCU – flexor carpi ulnaris; AP – adductor pollicis; FPB – flexor pollicis brevis; FDP – flexor digitorum profundus; FDB – flexor digitorum brevis

The dose of occupational therapy received by each participant was equivalent with no significant differences between the two groups (Table 9.3). In both groups the number of sessions averaged below the maximal number available (4), however the number of minutes spent in therapy was felt to be maximal for the time available. There was essentially equal time spent with weight bearing activities, ball skills and fine motor strengthening, with (approximately) 40-45% of the time spent on bilateral functional activities.

Table 9.3: Dose and type of occupational therapy per child – mean (95% CI) number of sessions, time spent in therapy and time per activity

	Control		Intervention		P*
Sessions	3.4 (3.4-3.4)		3.8 (3.8-3.8)		0.24
Time (minutes) in therapy per session	50.2 (50.0-50.5)		51.4 (51.3-51.5)		0.81
Time (minutes) in activity per session	WB	9.0 (8.9-9.1)	WB	7.9 (7.8-7.9)	0.41
	BS	11.0 (10.9-11.1)	BS	8.6 (8.6-8.6)	0.10
	FS	11.7 (11.6-11.8)	FS	13.7 (13.7-13.8)	0.37
	BF	21.0 (20.8-21.0)	BF	22.7 (22.6-22.8)	0.59

*Independent student t-test; WB – weight bearing; BS – ball skills; FS – fine motor strengthening; BF – bilateral functional

9.1c Activity-Participation Measures (Table 9.4)

At three months children receiving the botulinum toxin injection achieved greater improvements in the GAS and Global Self Worth than children receiving occupational therapy alone, but were worse off for Athletic Competence. At six months none of these differences persisted. Both groups improved their motor and process skill ability on the AMPS measure from baseline (Figure 9.2) however the differences between the groups were not significant at any one time point. Similarly there were no significant differences between the groups for the PEDI or PedsQL. However there were changes from baseline for Global Self-Worth (see Figure 9.3), Athletic Competence (see Figure 9.4) and Physical Appearance (see Figure 9.5).

A breakdown of the GAS goals revealed that in the intervention group, for a total of 63 goals stated by all the intervention participants, 8% were impairment level, 60.3% were activity level, and 31.7% were participation level goals. For the control group (for a total of 66 goals stated) the breakdown was 10% impairment level, 69.7%

activity level and 21.2% participation level. For each goal set (goal 1; goal 2; goal 3) there were no statistically significant differences between intervention and control group with respect to the categories of functioning (impairment, activity and participation) within each goal. χ^2 vales were, for goal 1 = .092 (p=.784), for goal 2 = 1.77 (p=.412) and for goal 3 = .529 (p=.768)

9.1d Body Function Measures (Table 9.4)

At three and six months elbow and wrist tone were significantly improved in the intervention group compared with the control group. Similarly, elbow and wrist spasticity improved significantly in the children who received the intervention at three and six months compared with the control group.

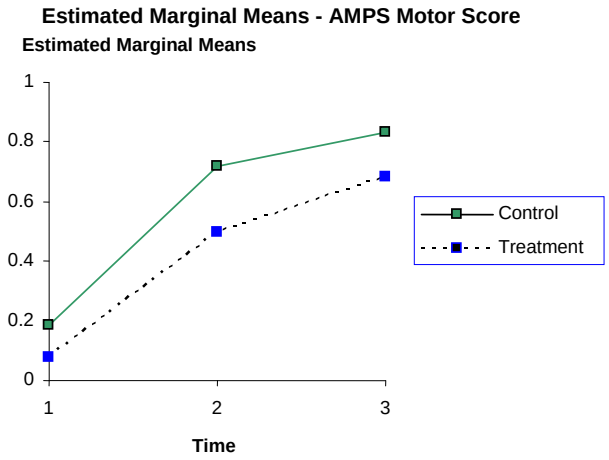
At three months fewer children reported pain (n=2 intervention group; n=2 control group) than at baseline. Both groups had one participant with mild-moderate pain. The severe to overwhelming pain at three months reported by two participants was resolved by 6 months. At six months two children reported mild-moderate pain, one in each of the study groups. At each time point, there were no significant differences (Pearson χ^2) in the two groups with respect to children's reports of pain (baseline p=.169; 3 month p= .679 and 6 month p= .744). Subjective evaluation of the effects of treatment on function and cosmesis (aesthetics) at three and six months revealed significant differences at both times for function, favoring the intervention participants. χ^2 analysis revealed that, for cosmetic appearance, significantly more children in the intervention group improved at three months compared to the control group (14/21 vs. 1/22, P<0.001), but this significant difference did not persist at 6 months (4/21 intervention vs. 1/22 control; P=0.185)

Table 9.4: Outcome of the study participants at 3 and 6 months

Characteristic			*Control (n=22)*	*Intervention (n=21)*	*P*
AMPS*					
Motor, mean (95% CI)	3 month		.72 (0.44, 0.99)	.50 (0.14, 0.86)	.326
	6 month		.83 (0.62, 1.03)	.68 (0.25, 1.12)	.518
Process, mean (95% CI)	3 month		.51 (0.18, 0.84)	.37 (0.00, 0.74)	.563
	6 month		.70 (0.41, 0.99)	.52 (0.11, 0.93)	.465
GAS, mean (95% CI)*	3 month		31.6 (27.1, 36.0)	44.6 (38.2, 50.9)	**.001**
	6 month		39.2 (32.5, 46.0)	43.1 (34.9, 51.2)	.453
Self-concept †, ‡					
Global self worth	3 months		3.0 (3.0,3.5)	3.7 (3.3,4.0)	**.030**
	6 months		3.3 (3.0,3.8)	3.8 (3.0,4.0)	.149
Athletic competence	3 months		3.0 (2.7,3.7)	2.5 (2.2,2.8)	**.016**
	6 months		3.2 (2.7,3.5)	3.2 (2.2,3.7)	.474
Physical appearance	3 months		3.2 (2.9,3.5)	3.5 (3.1,3.8)	.053
	6 months		3.0 (2.5,3.3)	3.6 (3.2,3.9)	.164
PEDI, mean (95% CI)*	3 month		59.7 (54.4, 65.0)	54.8 (48.6, 61.0)	.214
	6 month		59.6 (54.5, 64.7)	58.8 (52.5, 65.1)	.842
PEDsQL, mean (95% CI)*					
3 month	Total score	Parent	60.3 (52.9, 67.6)	56.4 (45.7, 67.0)	.976
		Child	67.8 (59.0, 76.6)	64.8 (56.7, 73.0)	.800
6 month	Total score	Parent	60.0 (52.6, 67.4)	60.6 (52.1, 69.1)	.998
		Child	72.2 (64.0, 80.4)	73.5 (62.5, 84.6)	.535
Tardieu degrees mean (95% CI)*					
3 Month	R2-R1	Elbow	99.7 (61.7, 137.7)	9.0 (-9.83, 27.8)	**.000**
		Wrist	122.6 (95.6, 149.7)	15.0 (-6.8, 36.8)	**.000**
6 Month	R2-R1	Elbow	66.4 (58.0, 74.8)	39.5 (22.6, 56.4)	**.006**
		Wrist	142.8 (115.3, 170.3)	31.0 (1.4, 60.6)	**.000**
MAS scores median (95%CI)‡					
3 Month		Elbow	2 (1, 2)	1 (1, 1)	**.000**
		Wrist	2 (1+, 2)	1 (0, 1)	**.000**
6 Month		Elbow	2 (1+, 2)	1+ (1, 1+)	**.001**
		Wrist	2 (1+, 2)	1 (1, 1+)	**.000**
Reported Functional Effects§					
3 month	Worse/No Change		17	2	**.000**
		Better	3	19	
6 month	Worse/No Change		15	3	
		Better	6	18	**.001**

*Independent student t-test; † all other domains showed no significant differences; ‡ Mann-Whitney U Test; § Pearson χ^2

Figure 9.2: Estimated marginal means for ADL motor score (top) and ADL process score (bottom) for treatment vs. control groups at baseline, 3 and 6 months are shown (see 9.1c "Activity-Participation Measures").



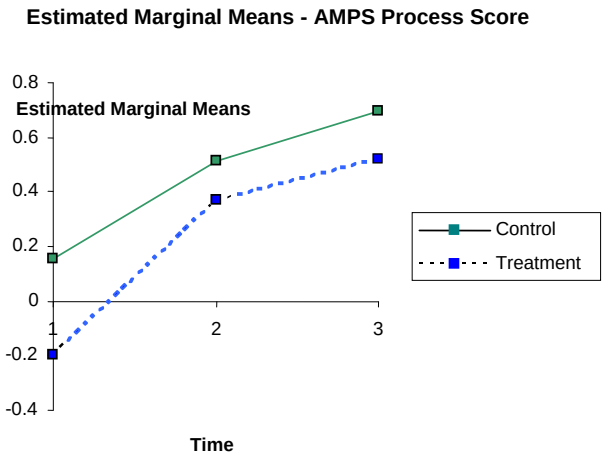


Figure 9.3: Estimated marginal means for Global Self Worth for treatment vs. control groups at baseline, 3 and 6 months are shown (see 9.1c "Activity-Participation Measures").

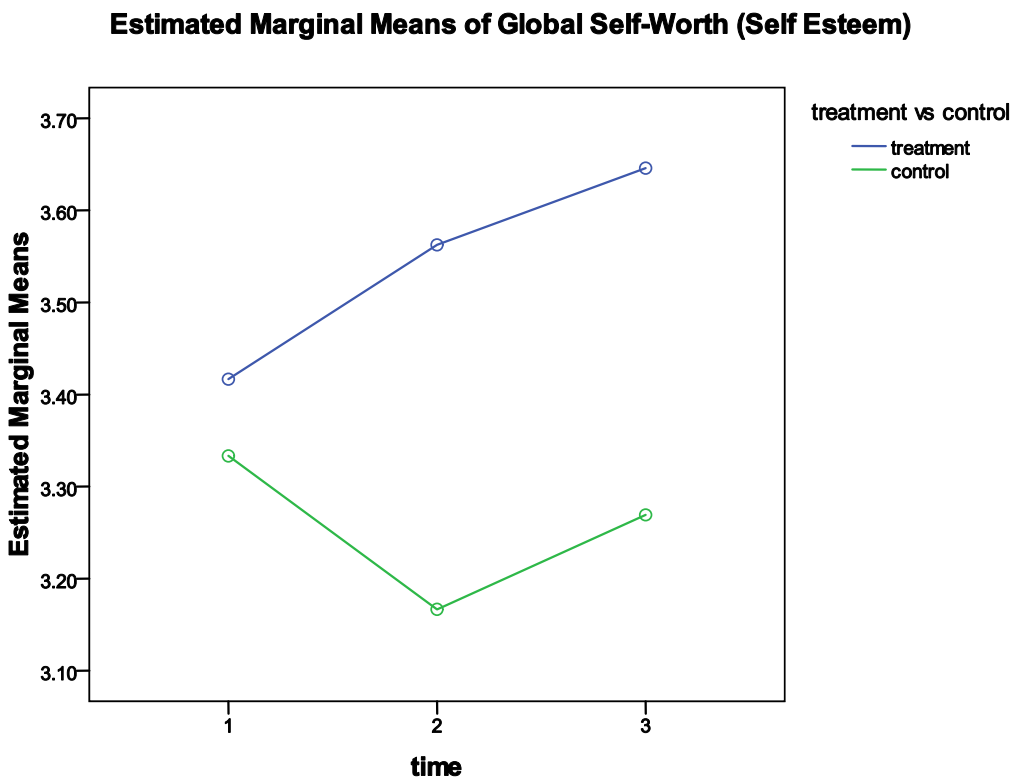


Figure 9.4: Estimated marginal means for Athletic Competence for treatment vs. control groups at baseline, 3 and 6 months are shown (see 9.1c "Activity-Participation Measures").

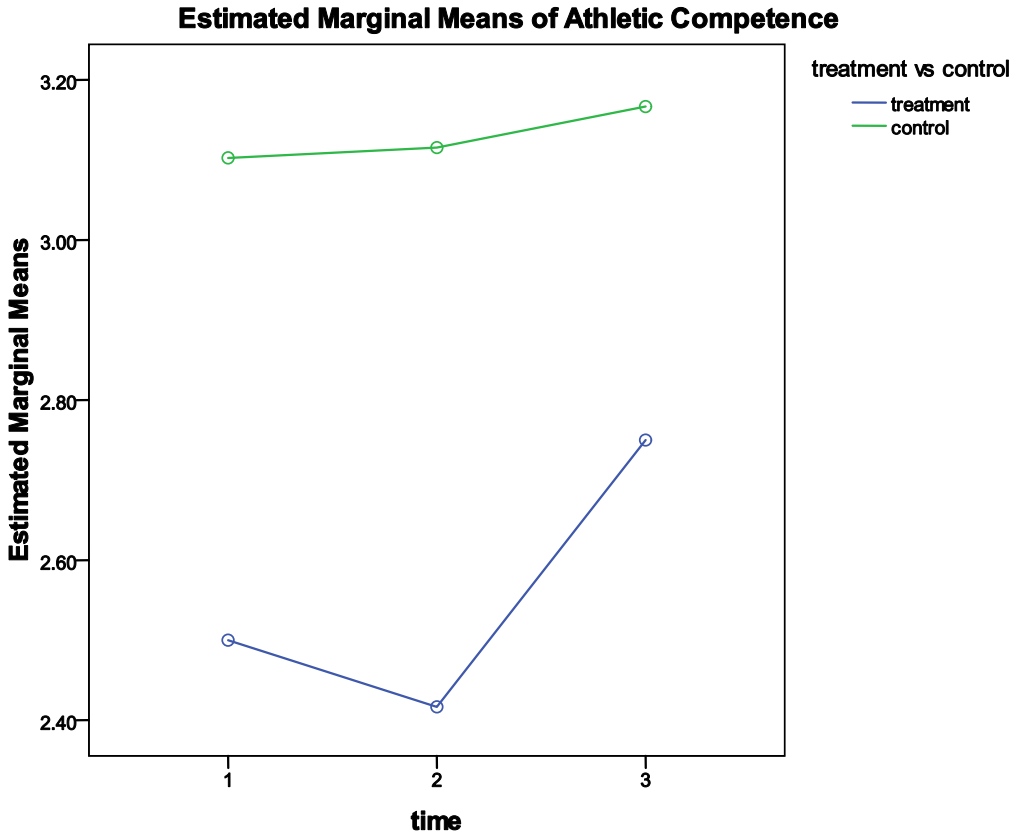
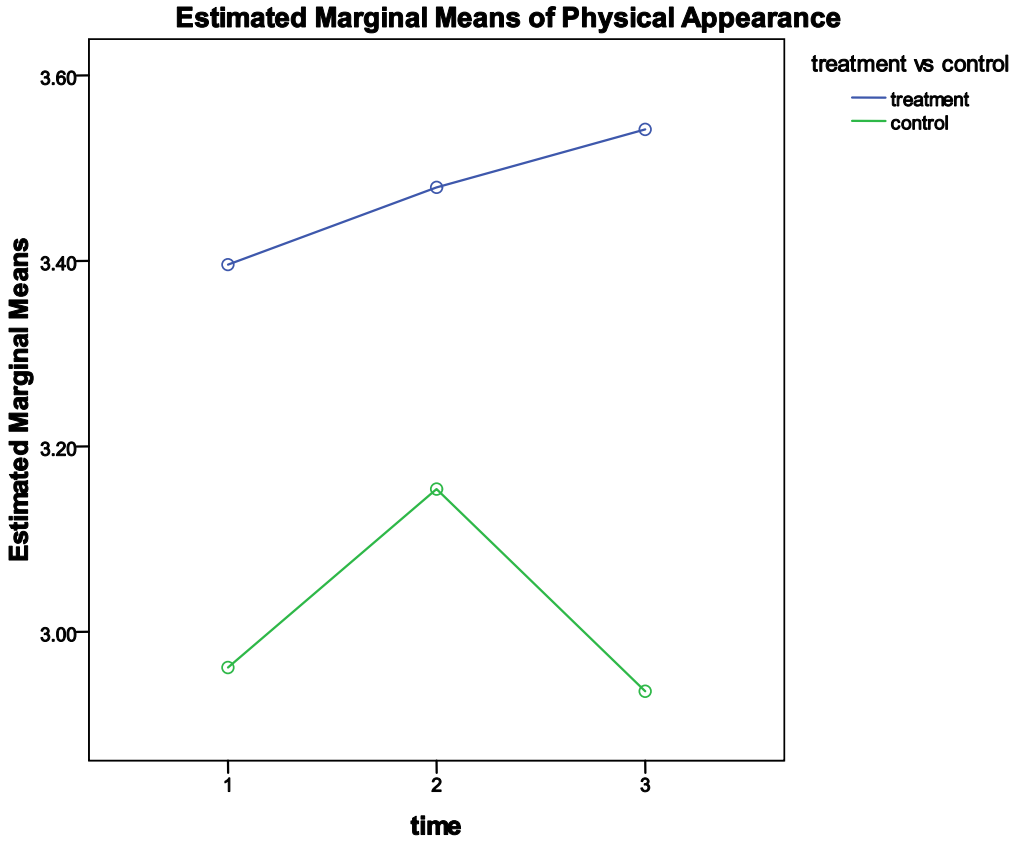


Figure 9.5: Estimated marginal means for Physical Appearance for treatment vs. control groups at baseline, 3 and 6 months are shown (see 9.1c "Activity-Participation Measures").



A between subject analysis of variance was conducted to assess the impact of the two different interventions (BoNT-A & occupational therapy vs. occupational therapy alone) on participants scores for Global Self-Worth, Athletic Competence and Physical Appearance over the course of the study. The results of this analysis are summarised in Table 9.5. The interaction effect (program type/time) is not statistically significant, indicating the change in scores over time are not the same for the two groups. The main effect for time was not significant for any comparisons, indicating that there was no significant change in scores over time. The between-subject effect comparing the two types of interventions was significant for Athletic Competence and Physical Appearance but not Global Self-Worth, with a recorded

partial eta squared value > .14 indicating a large effect size (Cohen 1988). This indicates that there was a statistically significant difference in Athletic Competence and Physical Appearance between the two interventions. The graphs indicate that for Athletic competence, there was an initial reduction and then recovery in the treatment group, with no real changes in the control groups of participants. For Physical Appearance there was an initial increase in the control group, which then fell back, but a sustained increase in the intervention group.

Table 9.5: Between subject analysis of variance for treatment and control groups over the course of the study for Global Self Worth, Athletic Competence and Physical Appearance

	Program type/time			**Time**			**Between Subject Effect**		
	WL	F [1,19]	P	WL	F [1,19]	P	F [1,19]	P	p/eta^2
GSW	.89	1.14	.343	.97	.28	.763	4.04	.059	.175
AC	.93	.97	.397	.83	1.91	.178	6.92	.016	.267
PA	.95	.46	.641	.88	1.28	.304	8.62	.008	.312

WL – Wilks Lambda; p/eta^2 - partial eta squared; GSW – Global Self-Worth; AC – Athletic Competence PA – Physical Appearance.

9.1e Safety

There were 29 adverse events reported by 20 participants over six months. Five serious adverse events (SAE) were reported by control participants (2 hospital admissions for seizures in one child with epilepsy, 3 hospital admissions for medical reasons in another). There were no minor adverse events reported by the control group. There were 23 adverse events which occurred in the intervention group, one of which was a SAE in a child with epilepsy (admission to hospital after a seizure). None of the SAE were felt to be related to the BoNT-A effect. The most frequently reported adverse events during the study were feeling unwell after the anesthetic (vomiting, cough) in four children, and excessive weakness in the injected limb in

five children. Headache was reported by two participants. Flu-like symptoms were experienced by one child for one day. A fainting episode experienced by one child occurred on a hot day and he recovered with rest and fluids. He had experienced these episodes in the past. One adolescent participant experienced anxiety and one depression, but each had similar episodes in the past, and both recovered without specific intervention. One child experience alopecia and had skin scrapings which confirmed fungal infection and this was treated appropriately. The family of one child with fatigue felt this was related to activities at the end of the school term.

9.1f Analysis of Impairment Level Measures – Power, Sensation, Tone, Growth and Motor Control

Due to the findings of the factor analysis in Part 1 of the study indicating that the independent latent variables of power, sensation, muscle tone, difference in limb spans and motor control were all factors that influenced function, a series of analyses were carried out for each independent variable. This was undertaken to gain further insight into the relative changes in the independent variables, given that overall there was improvement for both groups in functional outcome according to the AMPS.

Data was compared at each time point for total power, stereognosis, Tardieu at the elbow, hand span and the DIAT. On direct comparison, there were no significant differences for any of the measured independent variables except for muscle tone at 3 and 6 months for the Tardieu (see Table 9.4).

To analyse the data further, mixed between-within subjects analysis of variance was used. This was undertaken to assess how the independent variables change between

subjects (control vs. intervention group) and also within subjects over the 3 time points (baseline, 3 and 6 months). The results can be seen in Table 9.6.

Table 9.6: Between subject analysis of variance for treatment and control groups over the course of the study for power, stereognosis, muscle tone, limb growth and motor control

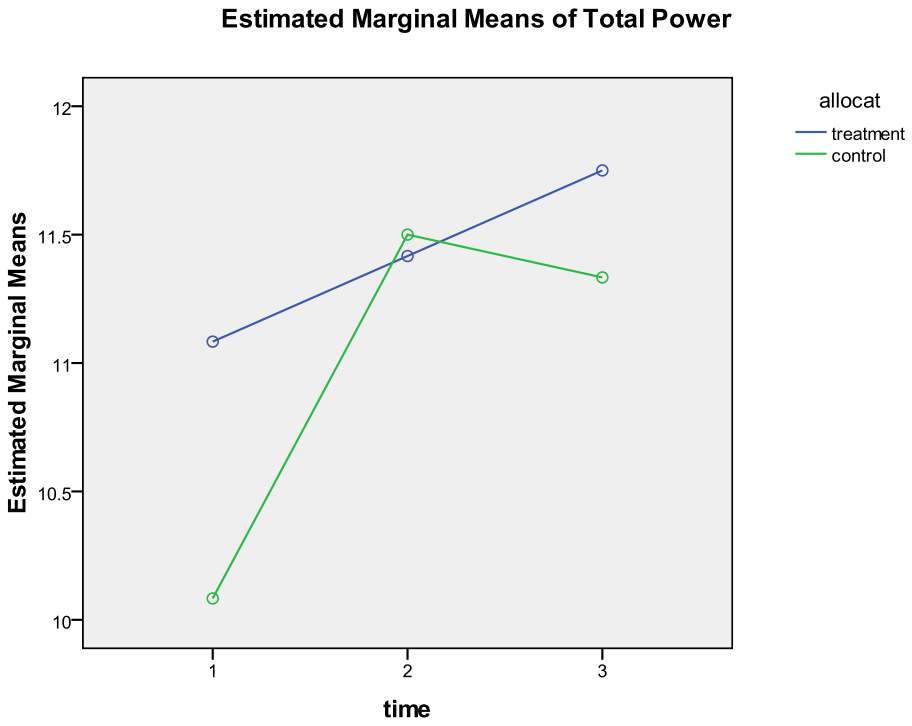
	Program type/time				**Time**				**Between Subject Effect**		
	WL	F	P	pe^2	WL	F	P	pe^2	F	P	pe^2
Power	.871	1.55	.236	.129	.776	3.18	.062	.232	1.53	.229	.065
Ster.	.901	1.64	.211	.099	.800	3.75	**.035**	**.200**	.074	.787	.002
Tone	.596	11.87	**.000**	**.404**	.780	4.93	**.013**	**.220**	15.77	**.000**	**.305**
Growth	1.00	0.01	.995	.000	.919	1.54	.228	.081	.728	.399	.020
M/Control*	.974	.489	.617	.026	.567	13.75	**.000**	**.433**	.256	.616	.007

* motor control was treated as a continuous variable. WL – Wilks Lambda; pe^2 - partial eta squared; Ster – stereognosis. M/Control – motor control.

9.1g Power

Muscle power was measured using manual muscle testing and graded out of 5 (see methods, chapter 2). To establish total muscle power the values of elbow flexion, wrist flexion and finger flexion were added at each time point and the results of "total power" are compared. A mixed between-within subject analysis of variance was conducted to assess the impact of allocation in the trial on total power. There was no significant interaction effect nor any effect over time or attributable to group allocation. There was a non-significant improvement in power over time, with both groups improving overall (see Figure 9.6).

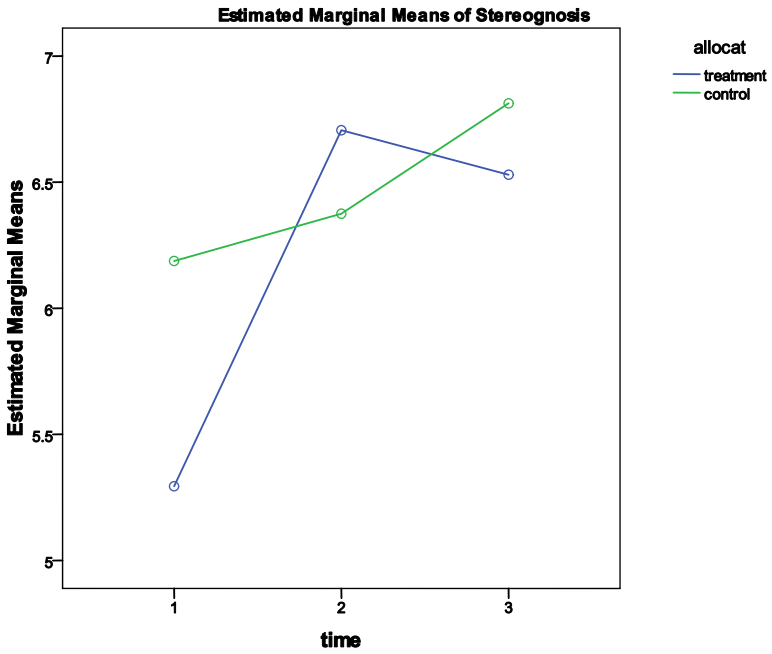
Figure 9.6: Estimated marginal means for total power for treatment and control groups at baseline, 3 and 6 months are shown



9.1h Sensation

Sensation was taken as stereognosis for the purpose of the analysis. This is the variable most strongly associated with functional outcomes in previous studies. It was also the sensory variable in the data set with the least missing data. The variable indicates the total number correct (out of 10) that the child scored at each time point. A mixed between-within subject analysis of variance revealed a significant main effect for time [associated with a large effect size (Cohen 1988)], with both groups showing significant improvement in stereognosis as the trial progressed (see Figure 9.7).

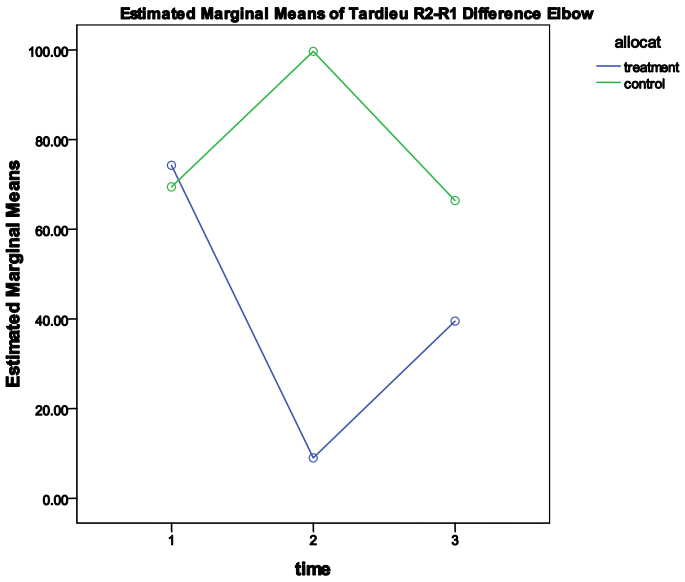
Figure 9.7: Estimated marginal means for stereognosis for treatment and control groups at baseline, 3 and 6 months are shown



9.1i Muscle tone

Muscle tone measures were the R2 minus R1 values at each time point for the Tardieu at the elbow. Mixed between-within analysis of variance did show a significant interaction effect, but this may have occurred given that at 3 months tone actually increased for the control group and decreased for the intervention group. There was a significant main effect for time and a significant between subject effect showing significant reduction in tone for the intervention group. This would suggest the effectiveness of the intervention in influencing muscle tone (see Figure 9.8).

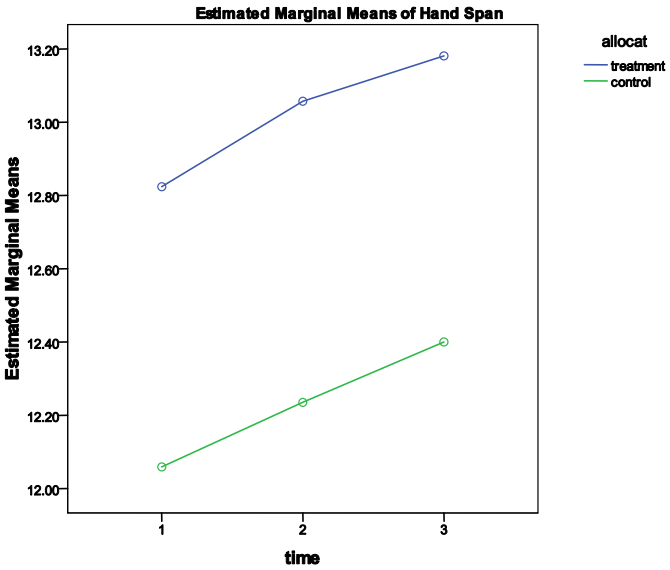
Figure 9.8: Estimated marginal means for Tardieu Elbow for treatment and control groups at baseline, 3 and 6 months are shown



9.1j Hand Span

Hand span was chosen as the growth parameter for analysis as it was felt that this would likely influence function the most in relation to growth. Hand span increase for both groups over time (see Figure 9.9) but there were no significant differences between groups over time for this variable. Over time both groups showed an increase in spans over the 6 months of the trial, and probably reflected normal growth in this group of children.

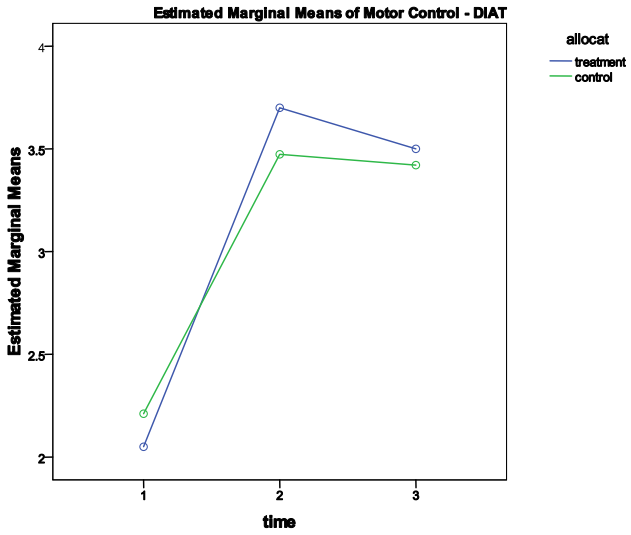
Figure 9.9: Estimated marginal means for hand span for treatment and control groups at baseline, 3 and 6 months are shown



9.1k Motor Control – DIAT

The DIAT was chosen for motor control. As there are 6 categories this variable was treated as continuous for the purpose of the analysis. There was no significant interaction between allocation and time. There was a substantial main effect for time, with both groups showing an increase in motor control across the three time periods. The main effect comparing the two interventions was not significant, indicating no difference in the effectiveness of the two approaches for influencing motor control (see Figure 9.10).

Figure 9.10: Estimated marginal means for motor control for treatment and control groups at baseline, 3 and 6 months are shown



9.2 Discussion - Intervention trial

This single blind randomized controlled clinical trial supports the use of upper limb BoNT-A injection and therapy in children with hemiplegic CP. When compared to the control group there was a statistically significant improvement in body structure/function at three and six months, as well as statistically significant improvements in activity-participation level function on the GAS and Global Self Worth at three months.

These improvement in self worth are important given the critical role that self-esteem has in development (Brooks 1992). Children with HCP are more likely to function in mainstream school environments alongside their typically developing peers when compared to other CP types (Michelsen et al 2005), and improvements in self worth are likely to influence their socialisation, peer relations and other areas of functioning. The use of BoNT-A has been noted to enhance self-esteem by diminishing inappropriate motor responses (Koman et al 2003), however inappropriate motor responses were not evaluated in this study, and so the impact of this cannot be explored. This thesis has demonstrated that self-esteem can be positively influenced and should be measured in future studies evaluating interventions in children with CP. In light of the findings in improved self-worth, it is interesting that there were no reported changes in quality of life. According to the analysis in chapter 5 showing the linear relationship between quality of life (as reported by the child) and self-esteem, an expectation that quality of life could improve (as a result of BoNT-A injection and therapy) may seem valid. However quality of life may be dependent on multiple factors not influenced by the

intervention, or may reflect response shift with children's internal standards and values changing over time (Schwartz et al 1999; De Civita et al 2005).

While there was a significant difference in Athletic Competence at three months, favoring the control group, this did not persist to six months when both groups improved. Athletic Competence in the control group was significantly better at baseline, which may explain the significant difference at three months and is possibly a result of type one error. Alternatively, the tone reducing effects of the BoNT-A may have altered the child's perceived ability to perform at their usual level of athletic skill. This potential effect requires further investigation to clarify the pre-injection counseling of children and their families. For example, in the context of competitive sporting activities, children and their families may elect to alter the timing of injections to minimize the impact of these changes.

Similarly there were significant differences at baseline for Physical Appearance favoring the intervention group. This difference reduced as the trial progressed to three months, despite the intervention group reporting more significant changes in cosmetic appearance at 3 months when compared to controls. However, this reporting related to the affected limb (whereas the Physical Appearance measure relates to broader concepts related to how the adolescent feels that they are good looking and are pleased with their overall appearance). Involvement in the trial altered these perceptions for the children and requires consideration for any intervention involving children with HCP. For example, one study noted positive changes in physical appearance with physical interventions alone (Darrah 1999) despite no associated improvements in athletic and physical competencies, which

might have been expected from such interventions, strengthening the concept that establishment of these competencies is complex.

The mixed between/within subject analysis of variance did not reveal any significant interaction between allocation and time, nor were there any significant main effects for time. However there were significant differences for the main effect comparing the two types of treatment. For Athletic Competence, there was an initial reduction and then recovery in the treatment group, with no real changes in the control groups of participants. For Physical Appearance there was an initial increase in the control group which then fell back, but a sustained increase in the intervention group. This would suggest that the intervention of BoNT-A and occupational therapy was responsible for the reduced level of perceived competence in athletic ability, and that being in the occupational therapy group alone was the reason for the differences in perceived physical appearance, supporting the findings of better cosmetic outcome in the intervention group.

The improvement in the GAS outcome measure for the intervention group at three months was statistically significant, but not at six months due to the control group improving between three and six months. Children in the intervention group reached their desired goals sooner than the control group, and then stabilized, a finding which is consistent with previous work (Lowe et al 2006). The ability for the intervention to allow the child to realize their stated goals more quickly may have widespread positive effects in relation to their sense of achievement and self-perception, and is supported by the finding that global self worth was also significantly better for the intervention group at this time point.

These results support the findings of previous studies on the effect of BoNT-A on tone and spasticity (Wallen et al 2004; Corry et al 1997; Lowe et al 2006). The duration of the effect was well beyond the published therapeutic effect of the botulinum toxin, being 12-16 weeks of clinically useful relaxation (Graham 2000). The prolonged duration of effect may relate to the assessment for tone and spasticity being unblinded at three and six months, or that muscles were injected that may not routinely be injected (tone <2 on a MAS), although this method was not adopted by previous investigators who also reported a prolonged effect (Lowe et al 2006; Wallen et al 2004). There may also have been an augmenting effect provided by the occupational therapy, with tone reductions being prolonged in the injected children. While there is general agreement that the physical modalities must continue after injection of BoNT-A to maximize the treatment episode (Boyd and Hays 2001a) (Flett 2003), the combined effects of BoNT-A injection and therapy remain unclear and warrant further investigation (Lannin et al 2006; Sakzewski et al 2009). The amount of therapy received by all of the participants was quantified within this thesis, but comparison to a true control group (i.e. who received no therapy) was not undertaken. This may not be ethically feasible in future studies given the growing efficacy of therapy for upper limb function (Sakzewski et al 2009) in children with CP. However, it is likely that the amount of therapy had a significant effect on the outcome of the study, with a recent meta-analysis indicating a total intervention dose of therapy between 4 and 12 hours was associated with significant changes in function (Sakzewski et al 2009). This review also concluded that the use of BoNT-A in the upper limb provided a supplementary benefit to a variety of upper limb

training approaches, with further research needed to assess which type of upper limb therapy is best in this clinical situation.

The analysis of the latent variables that predicted function in the factor analysis in Part 1 of the study (power, sensation, muscle tone, difference in limb spans and motor control) are interesting. There were significant main effects for time for stereognosis, muscle tone and motor control (with power increasing but just outside the limit of significance). This is consistent with the factor analysis model and supports the outcome in improved function as measured by the AMPS motor and process scores. Hand span also increased in the trial, but this may have been measurement error or secondary to natural growth of young children. Also, each independent variable was measured by a non blinded assessor in the trial, leading to possible bias in the results. For stereognosis, there could have been a practice effect with an upward trend in the results, which is true for the findings in muscle power. However, this preliminary data raises the exciting possibility that sensation may be able to be favorably altered. This hypothesis warrants further exploration in future studies. Motor control may have been misclassified systematically as the trial progressed, again introducing possible bias. As well, the numbers of children measured within the individual groups are small, also introducing errors of power.

However, it is interesting to note that one of the only differences in “direction” for the independent variables between the control and intervention participants was in “muscle tone”, which showed an interaction effect as well as significant time and treatment main effects favoring the intervention group. This may help explain why functional improvement was delayed in the control group, with muscle tone

increasing for the control group (and reducing the benefits of intervention through therapy according to the factor analysis model) that was not experienced by the intervention group due to the effects of the BoNT-A.

In general, the injection procedure was well tolerated. The hospital admissions for prolonged seizures for the two participants (one intervention and one control) were known epilepsy sufferers prior to inclusion in the study. One subject in the control group had three admissions to hospital for unrelated medical reasons but this child recovered fully on each occasion. The children experiencing the fainting, fatigue, anxiety and depression had these problems in the past. The child with the alopecia recovered fully. The remaining adverse events were relatively minor and self limited, and are consistent with the known adverse events occurring with general anesthetic (Cunningham et al 2005) and BoNT-A injection (Davis and Barnes 2000; Russman et al 1997). Weakness experienced by two participants was prolonged. Excessive weakness has been previously reported (Wallen et al 2004; Corry et al 1997). Prolonged atrophy experienced in masseteric hypertrophy after injection of BoNT-A up to 12 months is known to occur (To et al 2001), but how this relates to the duration of effect of injection in other muscles is unclear. The individualized injection plans used in this clinical trial resulted in treatment of muscles affected by a lesser degree of spasticity (MAS 1-1+) which may also be a factor.

A high incidence of pain was reported at the initial assessment. Previous studies have reported a similar incidence of pain in children with CP (Hadden and von Baeyer 2002; Houlihan et al 2004; Tervo et al 2006). Regardless of where the pain

originated, it improved over time for both the treatment and control groups, and there were no significant differences for this outcome at any time-point.

Limitations of this study include the inability to give placebo, the single blinded nature of follow-up, the relatively short time-frame of follow-up and the lack of true controls who received no therapy. Children and their families knew their assignment group. This may have led to unintentional disclosure which may have influenced the results. These methodological problems in pediatric research are difficult to overcome (Caldwell et al 2004). Moreover, it is argued that drug trials should test medication against standard therapy and not placebo alone (Sutcliffe and Wong 2006).

In conclusion, botulinum toxin injected into the affected upper limb of children with hemiplegic CP and a moderate intensity program of occupational therapy achieves significant improvements in body function, activity-participation and self perception. This study adds to previous studies investigating the effects of injection of botulinum toxin in the upper limb of children with CP but is unique given the findings related to improvement in self-concept and self worth.

CHAPTER 10: CONCLUSION

The studies undertaken in Parts 1 and 2 have addressed the hypotheses stated in chapter 1.

10.1 Hypothesis 1 - Functioning

1.1 The negative attributes of the upper motor neurone syndrome in HCP (such as muscle weakness) have an effect of similar magnitude to positive attributes (such as spasticity) on function and motor control.

The null hypothesis (that there are no differences between the positive and negative attributes of the upper motor neurone effects) has been shown to be false in the initial analyses (showing a strong association with sensory function) and also in the confirmatory factor analyses diagrams. These data show strong positive correlations between function and motor control, sensation, and muscle power, with the least contribution from muscle tone (the factor that seems to be the focus for a significant number of interventions).

10.2 Hypothesis 2 – Outcomes associated with functioning

2.1 Children with HCP and pain experience lower functional levels, quality of life and self-concept

This hypothesis was not supported fully, in that while quality of life, Behavioural Competence and Scholastic Competence scores were significantly lower in children experiencing pain, there were no differences in function on direct comparisons as

measured by the PEDI and AMPS. This is surprising given the lower functional level of children experiencing pain in the literature reviewed. However, the data in the published studies were from a group of children that were more heterogeneous (in topography and ambulatory ability) and thus may not represent the subgroup of children with HCP accurately. Overall children with HCP experience a high rate of pain which impacts on self-concept and quality of life and this needs to be addressed.

2.2 There are no significant differences when comparing children with HCP to peers with typical development on measure of self-esteem

The self-esteem data shows that children with HCP are equivalent to their peers for this measure, and so this hypothesis is supported. These findings are similar to other published work and support the resilience of this group of children. Further studies addressing the resilience in self-esteem would be helpful to understand the basis for this clinical phenomenon.

2.3 Quality of life and some self-concept domains differ to typically developing peers, favoring the peer group

Athletic/Physical competencies in all age groups, and in scholastic competence for the older (≥8 year old) age group, are significantly lower in children with HCP. For the younger age group children with HCP scored significantly higher for Maternal Acceptance than their peers. Social Acceptance was no different between the two groups, which was found to be significantly lower in the literature in relation to children with other topographical forms of CP which may account for the differences. Quality of life was also shown to be significantly different from the peer group, with scores for the parental scale significantly lower than the child scale for the children with HCP.

10.3 Hypothesis 3 – Interventions to improve function

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

This hypothesis is supported by the data presented in Part 1 of the thesis. Children with more severe involvement were targeted for these interventions.

3.2 The prescription of orthotics and assistive devices will be utilised with a high rate of adherence

This was only true for children prescribed AT, and not upper limb orthoses. The older and more functional children (as defined by scores on their processing abilities) were more likely to abandon their orthoses.

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

Children with HCP who were in the intervention group reached their stated goals (and improved functionally) more quickly than children who were not injected, however both groups improved equally by 6 months. Thus the hypothesis is not supported. However, several important issues arise from the findings. Children who more quickly reached their goals also have a significant increase in self-esteem, a factor that could assist children's quality of life (as these two variables were shown to be positively correlated in Part 1 of the thesis). Although there were no changes in quality of life outcomes during the trial, the improvements may require a longer time frame, or even repeated treatments, to be detected. Also, the changes noted in the impairment level measures over the course on the trial lend strong support to the factor analysis models of functioning and support the use of therapy in assisting with

functional improvements in this group of children.

10.4 Conclusion

Children with HCP are active amongst their typically developing peers, however, they suffer from disabilities in the areas of self-concept as well as experiencing a lower quality of life, lower levels of real world functioning, and more difficulties at impairment level functioning than their typically developing peer group.

The novel findings in this thesis are multiple, and include several important clinical points.

The path analysis has shown the relationships of the impairment level measures to participation level functioning, with the relative contributions of these independent variables, which has not previously been described in HCP in the literature. In clinical practice there is a strong focus on the reduction of spasticity in this group of children, with the development of several treatment modalities such as injection of BoNT-A to assist. However, the data presented in this thesis leads to understanding the importance of treatments that address the other modalities of impairment level functioning to assist in maximising functional gain. This argues for a much stronger influence of the other impairment level measures (such as muscle strengthening) that are more strongly associated with functional outcome when compared with muscle tone. Impairment level modalities such as muscle power can be influenced by therapy and should be a strong focus for intervention when attempting to improve functional outcome in children with HCP.

The prevalence of pain, with a description of its distribution and link to self-concept and quality of life has not before been demonstrated for a population based subgroup of children with HCP. Children with HCP experiencing pain need to be recognised and assisted. This means that clinicians need to actively ask about the experience of pain in these children, educating the family that the pain should be adequately managed.

Children with CP are known to have a lower quality of life than their non-affected peer group, but the self-concept data in this thesis is unique given the findings that children recognise their impairments from a young age, and that Maternal Acceptance is higher in the HCP group, providing some evidence of one factor that may assist in the well described resilience in self-esteem found in these children. There was a strong positive association between children's quality of life and self-esteem. There was also an association between cognitive and physical competencies in younger children with HCP and function, an association which has not previously been described in the literature, and defines a unique contribution for this group of children. These findings allow for a greater understanding in how self-concept impacts or is impacted upon by function.

Children with more severe involvement are targeted for intervention, however the findings from Part 1 of the study assist clinicians in managing children with HCP. For example, children who present from a young age with significant tone across the wrist are far more likely to require intervention, and the data presented in this thesis assist clinicians in deciding how to counsel families with children with a new diagnosis of HCP. This is clinically very relevant and not previously described for

this group of children.

The intervention trial has shown that there is a boost in self-esteem in children treated with BoNT-A which has not previously been described in the literature. Also, the analysis of the changes in impairment level functioning in the intervention trial is unique and further studies evaluating improvements in function need to consider these changes at the impairment level. Most exciting is the possibility that sensory function may be favourably influenced and sensory function should be a focus for future studies evaluating these children.

Children with HCP deserve assistance with their level of functioning. The results of this thesis have helped in bringing to light important associations with functional level, and has described further how function is impacted, providing small but important advances in our understanding of these concepts. However, further challenges remain.

10.5 Future Directions

One important area for further exploration is whether sensory function can be altered. This may seem impossible, as there is no literature in the paediatric CP field that has investigated this concept. However, because of its strong association with functional outcome, sensation should be explored further. The accurate documentation of sensory function in children with impairment due to CP would allow for further understanding of the level of deficit, classified under the Manual Ability Classification System. This could then lead to trials attempting to alter function and re-assess level of sensation to see if there are any alterations. Built up from a

theoretical framework, the potential areas that could be influenced could be studied further. For example, altering hand opening through spasticity reduction could assist in stereognosis (the hand is now more “available” to grasp and manipulate objects more efficiently) and determining the associations stereognosis has with hand functioning could assist in building on this framework.

Another important aspect is in quality of life. For all of the interventions undertaken to assist this group of children, no changes in quality of life have been noted in this thesis and few published in the literature. Efforts to improve this aspect of care are critical because quality of life is linked with self-esteem and can impact on family functioning and other areas of care. A further understanding of the determinants of quality of life are important to expand the way that this concept is handled in research, so that key factors that influence quality of life are detected.

The issue of pain in this group of children should be explored further. The prevalence of pain in the subgroup of children with HCP was surprising, with little focus on the impact of pain on this group in the literature. Future studies require exploration of the factors that can assist clinicians managing children with HCP about pain and how to deal with the pain experience.

Further studies to assist in our understanding of the management of functional outcome in this group of children needs to continue so that further improvements in the comprehensive management of this condition can occur. Whether this continues to focus on spasticity management or includes a wider view of other impairment level domains such as sensation and muscle power remains to be seen. However

more recently there has been a return to focusing on therapy in association with spasticity management for upper limb dysfunction (Hoare et al 2010) which fits with the models explored in this thesis.

The study of the upper limb in HCP, until recently, has been a relatively neglected area of research. Fortunately there are far more publications of high quality studies evaluating upper limb interventions to assist function in children with HCP. The work from this thesis has assisted in allowing for potential improvements in this subgroup of children with CP.

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APPENDIX 1: PUBLICATION TRANSCRIPTS

APPENDIX 2: LIST OF TABLES