

**BOTOX® TO REDUCE DROOLING IN SOUTH AFRICAN
NEUROLOGICALLY IMPAIRED CHILDREN:
A RETROSPECTIVE STUDY**

Nicola Michelle Hay

A dissertation submitted in fulfillment of the requirements for the degree of
Master of Arts in Speech Pathology in the Faculty of Humanities,
University of the Witwatersrand, Johannesburg,

Johannesburg, May 2008

ABSTRACT

Drooling management in the neurologically impaired pediatric population is a challenge. Surgery is considered an invasive procedure, while behaviour modification techniques, correction of situational factors and oral-motor therapy do not always produce sustained improvement. In recent years Botox® has been investigated. This study comprised analyses of clinical data obtained from a Drooling Treatment Project (DTP) conducted at a school for special needs children in South Africa. The aims of the DTP were to establish the response of drooling in a number of different contexts, following bilateral submandibular salivary gland injections of Botox®. Two groups of children were involved, 7 children with cerebral palsy and 2 children with operculum syndrome. Drooling was assessed in 5 different situations and at different time points pre- and post Botox® injection up to 6 months. Parents/primary caregivers' perceptions of drooling and treatment with Botox® were also measured using an interview form and a quality of life questionnaire. Results showed that drooling was reduced in all situations, with significant reductions in the general and communicating situations. These results indicate that the context in which drooling occurs is an important factor and suggest the value of considering the situational context when making drooling judgements. Further, there was a difference in the pattern of response between the 2 groups. This finding has implications, not only for future research, but also for models of explanation of the effects of Botox®. Most parents/primary caregivers felt their children's lives and their own had improved following the Botox® injection and would repeat the treatment. Clinical and research implications are discussed, with reference to the South African context.

KEY WORDS: Cerebral palsy, operculum syndrome, drooling, salivary glands, Botulinum toxin type A, Botox®, quality of life, drooling measures, severity and frequency rating scales.

DECLARATION

I declare that this dissertation is my own unaided work. It is submitted for the degree of Master of Arts in Speech Pathology in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any other degree or examination in any other university.

Nicola Michelle Hay

_____ day of _____, 2008

Signed _____

ACKNOWLEDGEMENTS

I would like to express my sincere thanks to the following people and agencies:

Professor Claire Penn, my supervisor, for her guidance, support, encouragement and belief that I could be a researcher as well as a clinician. Dr Jean Bowker, co-supervisor at the beginning of this process, for her support and encouragement.

The children and their parents/primary caregivers who were involved in the Drooling Treatment Project. I am exceedingly grateful that you allowed me to use the data from the Drooling Treatment Project.

Mr Peter Fridjhon for his advice on statistical procedures.

The speech, language and hearing therapists who were involved in the Drooling Treatment Project: Jenny Green, Dena Rachbuch, Vicky Macrides and Kashnee Jeebodh for their help with the assessments. You are all amazing therapists.

The speech, language and hearing therapist who acted as the blind independent rater. Your time and expertise, given so willingly, was greatly appreciated.

Professor Chris Joseph, who donated his services to administer the Botox®; Mr David Hadley, who donated the use of the Morningside Clinic, Rosebank; and Dr A. Milner, who donated her services for the anesthetic.

Genop South Africa, distributors of Botox® for Allergan Ltd. who donated all of the Botox® used in the Drooling Treatment Project.

My family, who allowed me the space and time to complete this dissertation.

Finally, to my daughter, whose courage during 2007 inspired and motivated me to continue working on this dissertation. My love to you, always.

CONTENTS

	Page
Abstract	. ii
Declaration	iii
Acknowledgements	iv
List of Tables	. x
List of Figures	xii
 CHAPTER 1	 1
INTRODUCTION	.. 1
 CHAPTER 2	 6
TWO CHILDHOOD NEUROLOGICAL IMPAIRMENTS AND THE EFFECT ON QUALITY OF LIFE	.. 6
2.1: Cerebral Palsy	... 6
Definitions of Cerebral palsy	6
Classification of Cerebral palsy	8
Types of Cerebral Palsy	9
Neurophysiology of Cerebral Palsy	.. 11
Severity of Cerebral Palsy	11
Causes of Cerebral Palsy	.. 12
Prevalence of Cerebral Palsy in South Africa	.. 12
2.2: Operculum Syndrome	13
Neurophysiology of the Operculum	.. 13
Symptoms of Operculum Syndrome	. 15
Causes of Operculum Syndrome	... 16
Prevalence of Operculum Syndrome in South Africa	... 16
2.3: Speech Characteristics of Cerebral Palsied and Operculum Syndrome Children	17
2.4: Feeding Problems in Cerebral Palsied and Operculum Syndrome Children	.. 18

2.5: The Role of the Speech, Language and Hearing Therapist	18
2.6: The South African Perspective on Childhood Disability	19
2.7: Quality of Life	21
Definitions of Quality of life	21
Measures of Quality of Life/Health-Related Quality of Life	24
2.8: Quality of Life in South Africa	27
2.9: Quality of Life for Neurologically Impaired Children	28
2.10: The "Disability Paradox"	31
2.11: The Relationship between Drooling and Quality of Life	32

CHAPTER 3

35

SALIVA, DROOLING AND BOTOX®	35
3.1: Saliva	35
Neurophysiology of Salivation	36
Functions of Saliva	41
Factors Affecting the Production of Saliva	41
3.2: Drooling	42
Definition of Drooling	42
Development of Drooling	43
Etiology of Drooling	44
3.3: Factors that Exacerbate Drooling	46
Complications of Drooling	47
3.4: Prevalence of Drooling	48
3.5: Techniques to Measure Drooling	49
3.6: Management Options	53
3.7: Treatment Strategies	54
3.8: Botulinum Toxin Type A: Botox®	60
Historical Perspective	60
Pharmacology of Botulinum Toxin	61
3.9: Clinical Use of Botox® with Specific Reference to the Fields of Speech Pathology and Audiology	64
3.10: Botox® to Control Drooling	67

CHAPTER 4	76
METHODOLOGY	76
4.1: Aims of the Study	76
4.2: The Drooling Treatment Project (DTP)	77
Context of the DTP and the Present Study	77
The DTP of 2006	78
4.3: Research Design	81
Phase One	81
Phase Two	82
4.4: Participants	82
Demographic Information	82
Sampling Strategy	85
4.5: Ethical Considerations	85
4.6: Data Collection	85
Case History Information	86
Saliva Control Assessment	86
Drooling Rating Scales	86
Procedures for Rating Severity and Frequency of Drooling	89
Interview Form	89
Questionnaire	89
Digital Photographs	90
Pilot Study	92
Data Collection in Phases One and Two of the Study	93
Phase One	93
Phase Two	94
4.7: Data Analyses	94
Case History Information and Therapy Notes	95
Saliva Control Assessment Information	95
Results from the Severity and Frequency Rating Scales	95
Reliability Measures	95
Statistical Analyses	96
Descriptive Analyses	97

CHAPTER 5	99
RESULTS AND DISCUSSION	99
5.1: Phase One	99
Case History Information and Therapy Notes	99
The Saliva Control Assessment Form	99
5.2: Reliability Measures in Phase One	104
5.3: Quantitative Results	105
Reduction of Drooling in Neurologically Impaired Participants	105
Reduction of Drooling in Different Situations	109
5.4: Descriptive Analysis	114
Reductions in Drooling in the Cerebral Palsied Participants	114
versus the Operculum Syndrome Participants	
Response of Different Types of Cerebral Palsy to Botox®	120
Influence of Baseline Severity of Drooling	123
Duration of Effect	123
Parental/primary Caregivers' Perceptions	125
5.5: Phase Two	134
Reliability Measures in Phase Two	134
5.6: An Additional Consequence from the Use of Botox®?	135
CHAPTER 6	139
CONCLUSIONS	139
6.1: Clinical Implications	139
6.2: Quality of Life Revisited	146
6.3: Research Implications	148
6.4: Limitations of the Study	150
6.5: Concluding Remarks	151
APPENDICES	
Appendix A - Clearance Certificate from the Human Research Ethics Committee. Protocol Number M070540	152
Appendix B - GDE Approval to Conduct Academic Research	153

Appendix C ĩ Permission from the ENT Specialist toé é é é é é é é é . 154
Use All Data from the DTP

Appendix D ĩ Principal Consent Formé é é é é é é é é é é é é é é . 155

Appendix E ĩ Parents/Primary Caregiver Consent Formé é é é é é é é é . 156

Appendix F ĩ Child Assent Formé é é é é é é é é é é é é é é é . 157

Appendix G ĩ Saliva Control Assessment Formé é é é é é é é é é é .. 158

Appendix H ĩ TherapistsôAssessment Form for Droolingé é é é é é é .. 160
Severity and Frequency at Baseline, 8 Weeks
and 24-26 Weeks Post Injection

Appendix I ĩ ParentsôAssessment Form for Droolingé é é é é é é é é é . 164
Severity and Frequency at Baseline, 8 Weeks
and 24-26 Weeks Post Injection

Appendix J ĩ Interview Questions for Parentsé é é é é é é é é é é é . 165

Appendix K ĩ Questionnaire to Parentsé é é é é é é é é é é é é ... 167

Appendix L ĩ Independent Raterôs Assessment Form foré é é é é é é é 168
Severity of Drooling

REFERENCESé 169

LIST OF TABLES

	Page
2.1.1: Components of Cerebral Palsy Classification	9
2.1.2: Characteristics of the Types of Cerebral Palsy	10
2.1.3: Overview of the Gross Motor Functional Classification System	11
2.7.1: Quality of Life Themes Important to Parents and Cerebral Palsied Children	26
2.11.1: The Effects of Drooling on Quality of Life	33
3.1.1: Factors that Influence the Production of Saliva	42
3.2.1: Developmental Stages of Drooling	43
3.2.2: The Etiology of Drooling	45
3.7.1: Surgical Options for Drooling	59
3.9.1: Clinical Applications of Botulinum Toxin	65
3.10.1: Studies that have Used Botulinum Toxin Type A to Treat Drooling in Children	70
4.4.1: Participant Demographics	84
4.6.1: Rating Scores for Severity and Frequency of Drooling	87
4.6.2: Records of Data Analyzed	94
5.1.1: Number of Participants Rated by the Parents/Primary Caregivers on Different Components of the Saliva Control Assessment Form	100
5.2.1: Cohen's Kappa Coefficients for Parents and Therapists	104
5.3.1: Overall Mean Scores and Standard Deviations for Severity and Frequency Ratings of Drooling	107
5.3.2: Significant Values and Effect Sizes for Severity and Frequency Ratings of Drooling	108
5.3.3: Effect Sizes and Significant Reductions in Drooling Severity for Each Situation	112
5.3.4: Effect Sizes and Significant Reductions in Drooling Frequency for Each Situation	113
5.4.1: Percentage Values of Drooling Reduction According to Diagnosis	117
5.4.2: Participant Demographics, Baseline and 8 Weeks's Severity Ratings	121

for Each Participant, Across All Situations	
5.4.3: Parental/Primary Caregiver Severity Ratings of Drooling during Activities/Feelings from the Quality of Life Questionnaire	127
5.4.4: Parental/Primary Caregivers' Perceptions of Drooling Improvement in Activities/Feelings following Botox® Treatment	128
5.4.5: Parental/Primary Caregivers' Perceptions of their Children's Social Interaction	131
5.5.1: Cohen's Kappa Coefficients for Therapists and 'Blind' Independent Rater	134

LIST OF FIGURES

	Page
2.1.1: The ICF Model of Human Functioning and Disability	8
2.2.1: The Operculum Insulae of the Left Hemisphere with Areas 44 and 45	14
3.1.1: The Positions of the Salivary Glands	36
3.1.2: Fibers of the Sympathetic Nervous System	38
3.1.3: Fibers of the Parasympathetic Nervous System	39
3.5.1: The Teacher Drooling Score	51
3.5.2: Drooling Frequency and Severity Scales	52
4.6.1: Edited Photographs of Participants During Different Activities Before and 8 Weeks After the Botox® Injection	91
5.3.1: Severity Rating Totals of Drooling for All Children across All Five Situations in the Study	106
5.3.2: Frequency Rating Totals of Drooling for All Children across All Five Situations in the Study	106
5.3.3: Severity Drooling Rates of All Children in Different Situations	110
5.3.4: Frequency Drooling Rates of All Children in Different Situations	111
5.4.1: Comparison of Drooling Reduction for Severity between the CP and the Operculum Syndrome Participants	115
5.4.2: Comparison of Drooling Reduction for Frequency between the CP and the Operculum Syndrome Participants	116
5.4.3: Total Individual Severity Drooling Responses to Botox® Organized by Diagnosis	118
5.4.4: Total Individual Frequency Drooling Responses to Botox® Organized by Diagnosis	119
5.4.5: Parental/primary caregivers' Perceptions of the Time of Day Drooling Peaked, Before and After Botox® Treatment	126
6.1.1: Proposed Assessment Model to Determine Eligibility for the Use of Botox® to Reduce Drooling in Neurologically Impaired Children	143
6.1.2: Possible Benefits from the Use of Botox® to Decrease Drooling	145

CHAPTER 1

INTRODUCTION

The management of drooling in the neurologically impaired population is a challenge to all who work and live within this field. Ear, nose and throat surgeons (ENTs), speech, language and hearing therapists, plastic surgeons, neurologists, radiologists, medical doctors, dentists, physiotherapists, occupational therapists, nurses and last but by no means least, parents and neurologically impaired individuals, are just some of the people involved in the challenge. Correction of situational factors, behaviour modification techniques, oral-motor therapy, pharmacologic treatment, and surgery have been advocated to improve drooling.

While correction of situational factors, behaviour modification techniques and oral-motor therapy should be the first line of attack, not all individuals respond favourably. In a study by Thomas-Stonell and Greenberg (1988) only 66% of patients treated conservatively had improved drooling. Anti-cholinergic medications can produce a decrease in drooling, but often have debilitating side effects, resulting in patients discontinuing their use. Surgical options in the treatment of drooling include removal of salivary glands, rerouting of salivary ducts and denervation of the salivary glands. Reid, Johnstone, Westbury, Rawicki and Reddihough (2008) report an 80% success rate with surgery at their institution. This can be considered an excellent outcome. However, surgery is an invasive procedure, not without risk and side effects can be unpleasant. Depending on the procedure there may also be a return to previous levels of drooling.

As a practising speech, language and hearing therapist in daily contact with children who drool and in frequent contact with their parents/primary caregivers, I have had the opportunity to discover their perceptions towards drooling treatments. It seems nowadays that parents/primary caregivers and the children themselves are looking for less drastic/invasive means to improve drooling, when conservative methods have not produced the desired results.

Since 1999 Botulinum toxin type A (Botox®, Allergan Inc. Irvine, California, USA) has been used by a variety of researchers in an attempt to find a minimally invasive method to reduce drooling in the neurologically impaired population.

Initial studies used adults with diseases such as Parkinson's disease (Pal, Calne, Calne and Tsui, 2000). Research then moved onto the use of neurologically impaired children with severe drooling. These children were usually diagnosed with mental retardation, cerebral palsy and/or operculum syndrome (Bothwell, Clarke, Dooley, Gordon, Anderson, Wood, Camfield and Camfield, 2002; Jongerius, van den Hoogen, van Limbeek, Gabreëls, van Hulst and Rotteveel, 2004; Savarese, Diamond, Elovic and Millis, 2004; Suskind and Tilton, 2002). Results from these studies proved to be favourable.

In 2006 I was involved in a Drooling Treatment Project (DTP) that was conducted at a school for learners with special education needs (LSEN) in Gauteng, South Africa. Nine neurologically impaired children, seven diagnosed with different types of cerebral palsy and two diagnosed with operculum syndrome, were included in the project. The aims of the DTP were to investigate the response of drooling to bilateral submandibular salivary gland injections of Botox® under a number of different situations and over a period of six months. The present study is a record review and an analysis of the clinical data obtained from the DTP.

At that time, Botox® had been used in South Africa in the neurologically impaired population, but not to treat drooling in children. As far as I know, this report on the DTP is a first for South Africa. Previous published studies have looked at parental perceptions of a reduction in drooling. Van der Burg, Jongerius, van Limbeek, van Hulst and Rotteveel (2006a) investigated parental perceptions of decreased drooling in different situations, as part of their study on the impact of drooling on daily life, social interaction and self-esteem. However, the opinions of speech, language and hearing therapists on a reduction of drooling, following Botox® injections in different daily situations, have not been considered.

The consequences of drooling for children and their families are numerous. There can be clinical, social, educational and emotional issues (Lal & Hotaling, 2006). With the emphasis on the biopsychosocial model of disability (WHO, 2001), it is important to consider these issues and the possible effects of drooling on the quality of life (QoL) of the drooling child and his/her family. South Africa has a unique socio-demographic people and at this stage very little is known about the QoL of South African neurologically impaired children and their parents/primary caregivers.

In South Africa there are frequent challenges of poverty, disease and often basic health, welfare and educational needs are not catered for. We do not know whether South African parents/primary caregivers consider drooling to be a contributing factor to a negative quality of life. The relevance of international published studies that do consider drooling to have a negative influence has yet to be assessed in the South African context. The viability of using Botox® injections to reduce drooling in children in South Africa is also unknown. The essential question is: can the use of Botox® injections to reduce drooling be relevant in our society, where the majority of families with a disabled child do not receive sufficient fundamental support?

Recently some authors have encouraged South African speech, language and hearing therapists to make our research socially relevant (Barratt, 2007; Kathard, Naude, Pillay & Ross, 2007). The Malamulele Onward-Ongoing support for Africa's Children project and the training of caregivers at the LSEN School where I work, a project funded by The Nelson Mandela Children's Fund, are excellent examples of socially relevant work that is being carried out by therapists in this country. I believe the review of the clinical data from the DTP is socially relevant as it has provided the following:

- some insight into South African parents' primary caregivers' perceptions of drooling;
- insight into the impact drooling has on their child's life as well as their own;

- information regarding the effect on drooling of Botox® injections to the salivary glands, in a number of daily situations encountered by all South African neurologically impaired children;
- how long the effect of Botox® can be expected to last;
- information that paves the way for speech, language and hearing therapists in South Africa to be able to make informed decisions with regards to the possible treatment of drooling with the use of Botox®.

The National Health Plan for South Africa (African National Congress, 1994, p.7) states "every person has the right to optimal health care." If for some drooling individuals Botox® is the optimal treatment, then those individuals have the right to access that treatment, irrespective of their age, gender, race, or socio-economic status. It is our job, as socially responsible professionals working in the field of neurologically impaired individuals, to facilitate that access. This facilitation may mean: approaching pharmaceutical companies for sponsorship or even continued research to find an easier, cheaper mode of drug administration; or lobbying education and health departments at a national level to include Botox® on the list of available items that are on government tender at hospitals.

If the use of Botox® to control drooling is the way forward, we as practicing clinicians are bound to ensure that our conclusions and ultimately our petitions are based on sound scientific research. Perhaps clinicians, in order to stay relevant, especially in a context such as South Africa, should become clinician-researchers and take on board scientific methods for measuring effectiveness (Penn, 2007; Swanepoel, 2007). I propose to do this. As Penn (2007, p.16) clearly states "we cannot afford to be lukewarm about scientific endeavour." If we are, we will only have ourselves to blame if we are viewed in this negative light; it is the therapist's personality and approach to her patients rather than what she does which is to their advantage (Leary, 1997 in Penn, 2007, p.14). More importantly we will have committed a grave disservice to those we swore an oath to help.

The following outline is a guide to what is included in each chapter.

Chapter 2 provides a literature review on cerebral palsy and operculum syndrome, with reference to the unique South African context. Quality of life, measures thereof and the impact drooling has on quality of life, once again considering the South African situation are also discussed. Chapter 3 examines the functions of saliva and factors that affect saliva production. Drooling, techniques to measure drooling and treatment strategies are also considered. Botulinum toxin type A (Botox®) is described and the use of Botox® in a variety of neurological problems, but specifically its use to reduce drooling is critically discussed. The research methodology is explained in chapter 4 and chapter 5 deals with the results and discussion. Chapter 6 presents the clinical implications, areas for future research, limitations of the study and concluding remarks.

CHAPTER 2

TWO CHILDHOOD NEUROLOGICAL IMPAIRMENTS AND THE EFFECT ON QUALITY OF LIFE

The focus of this study is on two childhood neurological impairments, which are discussed in this chapter with reference to their definitions, causes, site of lesions, prevalence within South Africa, speech characteristics and feeding problems. The role of the speech, language and hearing therapist and the South African perspective on childhood disability is considered. Thereafter I discuss quality of life (QoL), the various definitions and measures of QoL, QoL in South Africa, with reference to neurologically impaired children, the 'disability paradox' and the relationship between drooling and QoL.

2.1. Cerebral Palsy

Definitions of Cerebral Palsy

There have been many definitions of cerebral palsy and much discussion by eminent authorities on the subject of a definition of cerebral palsy and its classification. In 1964 Bax (p. 295) defined it as 'a disorder of movement and posture due to a defect or lesion of the immature brain.' Karel Bobath's definition was as follows: 'The brain lesion is nonprogressive and causes variable impairment of the coordinated muscles of action, with resulting inability of the child to maintain normal postures and perform normal movements. This central motor handicap is frequently associated with affected speech, vision and hearing, with various types of perceptual disturbances, some degree of mental retardation and/or epilepsy' (1980, p. 1). Mutch and his colleagues modified the definition of cerebral palsy in 1992 to include the concepts of an 'umbrella term,' and a 'group of non-progressive, but often changing motor impairments' (Mutch, Alberman, Hagberg, Kodama & Velickovic, 1992, p. 549).

An international workshop on the definition and classification of cerebral palsy was held in the United States of America in July 2004. From this workshop The Definition and Classification of Cerebral Palsy April 2006 arose, compiled by Peter Rosenbaum and colleagues. It states the following: "cerebral palsy (CP) describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication and behaviour; by epilepsy and by secondary musculoskeletal problems" (Rosenbaum, Paneth, Leviton, Goldstein & Bax, 2007, p. 9). This definition is relevant for the speech, language and hearing therapist working with a cerebral palsied child who drools, as drooling is often caused by impaired oral neuromuscular control, and can be exacerbated by poor body positioning, inadequate head control and diminished oral tactile sensitivity.

Rosenbaum et al's (2007) definition follows concepts introduced by the World Health Organization's International Classification of Functioning, Disability and Health, ICF (WHO, 2001). The ICF puts the notion of "health" and "disability" in a new light and acknowledges that every person can experience a decrease in health, resulting in some degree of disability. By shifting the focus from cause to impact and function, all health conditions are considered equal and disability is brought into the mainstream and recognized as a universal human experience. As can be seen from Figure 2.1.1 on the following page, the ICF takes into account the social aspects of disability and does not see disability only as a "medical" or "biological" dysfunction. It acknowledges the importance of both the individual and the environment in which the individual lives (Schneider & Saloojee, 2007).

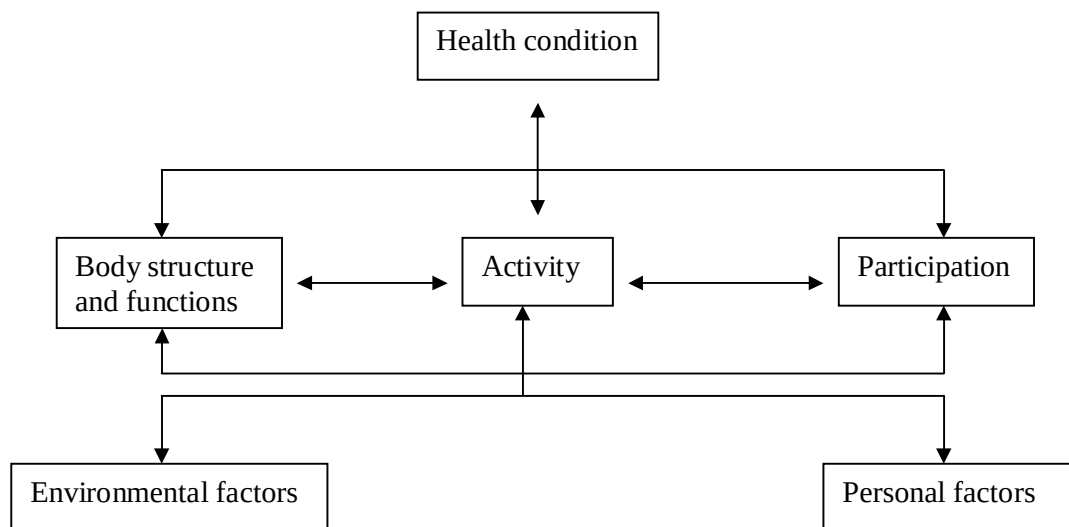


Figure 2.1.1: The ICF Model of Human Functioning and Disability (WHO, 2001)

Classification of Cerebral Palsy

Rosenbaum et al (2007) components of CP classification are shown in Table 2.1.1. Of particular importance to the speech, language and hearing therapist is section 1B – Functional Motor Abilities, which includes the oral-motor and speech functions and section 2 – Accompanying Impairments, which includes communicative deficits. Difficulties in these areas can produce important activity limitations, including activity limitations imposed by excessive drooling. As yet, there is no activity limitation scale for such functions. Rosenbaum et al (2007) feel there is a high research priority to develop a scale for speech and pharyngeal activity limitation in cerebral palsy.

Table 2.1.1: Components of CP Classification (Rosenbaum et al, 2007)

1.	MOTOR ABNORMALITIES A. NATURE AND TYPOLOGY OF THE MOTOR DISORDER: The observed tonal abnormalities assessed on examination (eg. Hyper or hypotonia) as well as the diagnosed movement disorder present, such as spasticity, ataxia, dystonia, athetosis. B. FUNCTIONAL MOTOR ABILITIES: The extent to which the individual is limited in his/her motor function, including oral-motor and speech function.
2.	ACCOMPANYING IMPAIRMENTS The presence or absence of later-developing musculoskeletal problems and/or accompanying non-motor neurodevelopmental or sensory problems, such as seizures, hearing or vision impairments, or attentional, behavioural, communicative and/or cognitive deficits, and the extent to which impairments interact in individuals with cerebral palsy.
3.	ANATOMICAL AND NEURO-IMAGING FINDINGS A. ANATOMIC DISTRIBUTION: The parts of the body affected by motor impairments or limitations. B. NEURO-IMAGING FINDINGS: The neuroanatomic findings on CT or MRI imaging, such as ventricular enlargement, white matter loss or brain anomaly.
4.	CAUSATION AND TIMING Whether there is a clearly identified cause, as is usually the case with post-natal CP (eg. Meningitis, head injury) or when brain malformations are present and the presumed time frame during which the injury occurred, if known.

Types of Cerebral Palsy

According to Howle (2002) cerebral palsy can be classified into five types, related to the associated muscle tone and movement characteristics of the individual. As can be seen from Table 2.1.2 there are four main types of CP, with the fifth type being a mixed type where symptoms of more than one type of involvement are present.

Table 2.1.2: Characteristics of the Types of Cerebral Palsy (Howle, 2002)

TYPE	CHARACTERISTICS
Spastic	Stiff muscles. Muscle tone increased with velocity-dependent resistance to passive movement. Selective motor control reduced. Abnormal and limited movement patterns. Excessive co-activation of muscular activity. Limited range of motion. Slow muscle activation and postural responses.
Dyskinetic	Movements appear uncontrolled and involuntary. Includes athetosis, rigidity and tremor. Resistance seen through range of movement in rigidity. Movements are abnormal in timing, direction and spatial characteristics. Reversal of movement and/or latency of movement. Impaired postural stability. Fluctuating muscle tone.
Hypotonic	Diminished resting muscle tension. Decreased ability to generate voluntary muscle force. Excessive joint flexibility. Postural instability. Flaccid, low toned muscles. Often transient with evolution to spasticity or athetosis.
Ataxic	Impaired postural control. Disordered balance. Imprecise control in timing of coordinated movement. Frequently associated with hypotonia. Decreased force during active movement. Tremor may be present.

In addition to classifying CP into types, the degree or distribution of limb involvement can also be categorized: monoplegia meaning one extremity; hemiplegia meaning the arm and leg on the same side of the body; diplegia meaning all extremities, but the legs more involved than the arms; quadriplegia meaning all extremities, arms and legs equally involved, or the arms and upper body more involved than the legs; triplegia meaning three limbs involved; and paraplegia meaning only the legs involved (Workinger, 2005). Rosenbaum et al (2007) suggest the discontinuation of the terms diplegia and quadriplegia, as the imprecision of these terms in clinical practice has been documented. Rather the terms bilateral or unilateral should be used. However, in South Africa the terms diplegia and quadriplegia are still used.

Neurophysiology of Cerebral Palsy

According to Bax, Flodmark and Tydeman (2007) spastic diplegia can be caused by white matter damage of immaturity (WMDI) including periventricular leukomalacia and periventricular haemorrhage. Spastic quadriplegia can be caused by more extensive WMDI and cortical-subcortical lesions. Hemiplegia is caused by stroke, periventricular leukomalacia and asymmetrical WMDI, as a result of damage to one side of the brain. With athetoid CP the lesion is in the basal ganglia and thalami. Ataxic CP, the least common type, is usually associated with genetic syndromes rather than discrete anatomic lesions.

Severity of Cerebral Palsy

The severity of CP can be classified using the Gross Motor Functional Classification System (GMFCS) (Palisano, Rosenbaum, Walter, Russell, Wood, & Galuppi, 1997). Table 2.1.3 illustrates the five levels of classification with the associated abilities. From this table it can be seen that the system is useful to determine the functional mobility irrespective of the type or distribution of the motor disorder. However, it has limited value for the speech, language and hearing therapist in determining oral-motor functioning and drooling severity and frequency.

Table 2.1.3: Overview of the Gross Motor Functional Classification System
(Palisano et al, 1997)

LEVEL	ABILITY
I	Walks without assistance
II	Walks without assistive devices, limitations outdoors and in the community
III	Walks with assistive devices, limitations outdoors and in the community, requiring wheelchair use in these settings
IV	Self-mobility in wheelchair with limitations, transported or uses power mobility in a community
V	Very limited self-mobility, even with assistive technology

Although Thomas-Stonell and Greenberg (1988) found a strong association between mobility and a positive treatment outcome for drooling, this does not imply that because a child can walk, he/she does not drool. The relationship and possible correlation between gross motor functional level and the ability to control saliva has not been investigated in depth. One might assume that a child classified on level V would exhibit severe deficits in saliva control and subsequent drooling problems. However, this is not always the case.

Causes of Cerebral Palsy

CP does not have a single cause. The many causes can be classified into two groups i acquired and congenital.

a). Acquired Cerebral Palsy

Children who sustain brain damage during the first two years of life before anatomical or physiological maturation of the brain is complete are considered to have acquired CP.

b). Congenital Cerebral Palsy

In this group the damage occurs in the prenatal, perinatal or immediate postnatal periods. Historically the primary cause of CP was considered to be birth trauma. Nowadays with improved diagnostic methods, improved prenatal care and improved care for at-risk newborn infants, birth trauma is no longer the main cause. Low birth weight, survival of a premature birth and birth asphyxia are the risk factors most closely associated with a diagnosis of CP (Workinger, 2005).

Prevalence of Cerebral Palsy in South Africa

Levin (2006) asserts that tuberculosis meningitis, malaria, particularly cerebral malaria, and HIV/AIDS are primary causes of CP in South Africa. In addition the high rate of road accidents in South Africa also adds to the number of children suffering from acquired CP. Near drowning or accidental choking can also lead to a diagnosis of CP.

In South Africa the situation with regards to the resultant neurodevelopmental outcomes from premature birth or low birth weight are comparable to overseas. However, what makes South Africa unique is the fact that large sectors of the population are poor, cannot afford pre-natal care, live in unsanitary circumstances, have inadequate nutrition, simply do not have access to specialized care and intervention, and lack the necessary knowledge about basic social, health and educational services. This situation is mostly due to illiteracy and inadequate/non-existent education (Intergrated National Disability Strategy, White Paper on Disability, 1997).

The prevalence of CP in South Africa, according to governmental reports, is very high (Statistics South Africa, 2007). Accurate numbers are unavailable, but a study by Couper (2002) put the approximate number at 10/1000 children under the age of ten years in Kwa-Zulu-Natal. The World Health Organization 2005 report (WHO, 2005) indicated that 10% of the 18 million children in South Africa have some form of neurological impairment from a variety of etiologies.

2.2. Operculum Syndrome

Neurophysiology of the Operculum

In order to understand the resultant anarthria/dysarthria that occurs in operculum syndrome and the possible relationship found in this study between articulation, drooling and the use of Botox®, it is necessary to have an overview of the neurophysiology of the operculum. The operculum, short for the operculum insulae, is the area of the brain that covers the insula Reili. It is made up of frontal, parietal and temporal cortical convolutions (Bruyn & Gathier, 1969; Christen, Hanefeld, Kruse, Imhäuser, Ernst & Finkenstaedt, 2000). Figure 2.2.1 shows the position of the operculum within the brain. The extent of the operculum insulae has been indicated by the green area.

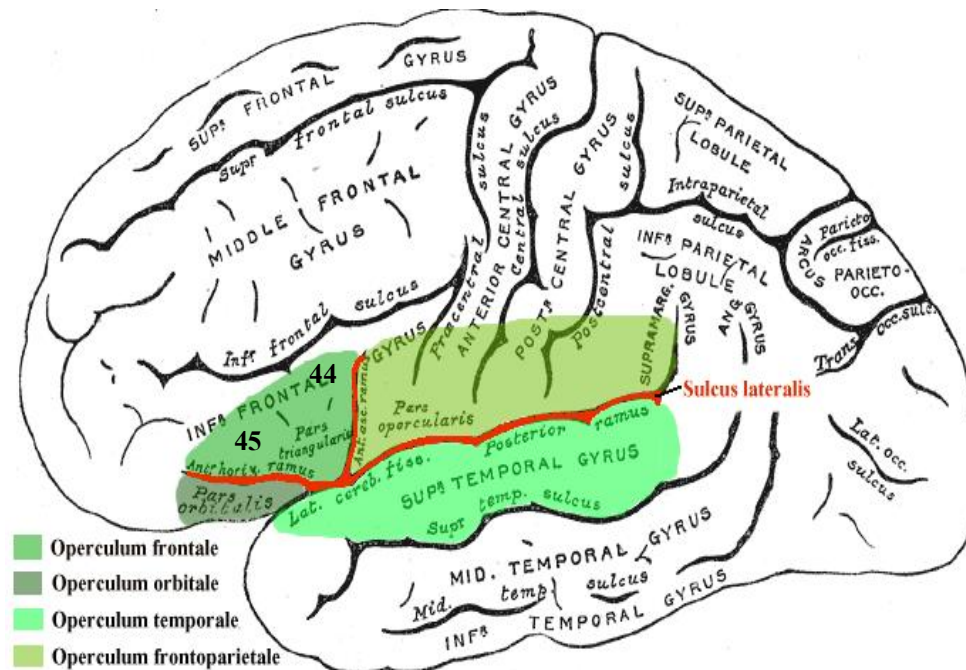


Figure 2.2.1: The Operculum Insulae of the Left Hemisphere with Areas 44 and 45 (Wikipedia, 2007)

In 1969 Bruyn and Gathier argued that the connections between the opercula and other parts of the brain had been established only in part, despite the fact that areas 44 and 45 approximately constituted Broca's motor speech area. Major input to Broca's region arrives through corticocortical fibers of the arcuate fascicle, which originates in Wernicke's area of the temporal lobe. Efferents from areas 44 and 45 terminate in the face region of the primary motor cortex. Broca's region controls the complex motor pattern of neuronal assemblies in the face region of the primary motor cortex, which in turn command the motor cranial nerve nuclei for the muscle activity during vocalization (Zilles, 2004).

In the 1940's studies were conducted that clearly showed connections between the different opercula regions, i.e. temporal, parietal and frontal, as well as connections to the insulae Reili (McCulloch, 1944, 1949, in Bruyn & Gathier, 1969). Connections with other parts of the brain have also been shown,

particularly the thalamus. Pritchard and Norgren (2004) gave a description of the likely pathways for the human gustatory system, from peripheral innervation, via the VII facial nerve, the IX glossopharyngeal nerve, and the X vagus nerve to the nucleus of the solitary tract (Sol) in the medulla, to the ventroposteromedial nucleus (VPMpc) of the thalamus. From the thalamus, the pathway seems to go to the insula. Most recent studies implicate this area as the taste cortex. As discussed in the following section on drooling, saliva is necessary to be able to taste. However, Bornstein (1940, in Pritchard & Norgren, 2004, p. 1181) placed the end destination firmly in the parietal operculum.

Electrophysiological studies, conducted on monkeys, have shown that stimulation of the chorda tympani and glossopharyngeal nerves produces evoked potentials from the insula and inner operculum (Pritchard & Norgren, 2004). The word 'likely' has been used deliberately, as at this stage, most information on the pathway of the gustatory system has come from experiments conducted on nonhuman primates, with a few published clinical human studies providing corroborating evidence.

Symptoms of Operculum Syndrome

The clinical symptoms of opercular lesions were first reported by Magnus in 1837, but it was not until 1926 that the clinical picture was described in the neurological literature by the French neurologists Foix, Chavany and Marie. A congenital type was described by the neurologist Worster-Drought in 1953, giving rise to the Worster-Drought syndrome (Christen et al, 2000).

The Foix-Chavany-Marie syndrome (FCMS) has a unique clinical picture of a supranuclear (pseudobulbar) palsy, an upper motor neuron disorder, caused by bilateral anterior opercular lesions. FCMS is therefore also known as bilateral anterior operculum syndrome. FCMS represents the cortical type of supranuclear/pseudobulbar palsy. A bilateral interruption of the connections, known as the corticobulbar fibers, between the cortical motor areas and the brain stem nuclei of the V trigeminal nerve, VII facial nerve, IX glossopharyngeal

nerve, and X vagus nerve, is needed to bring up the symptomatology of FCMS, as the connections are ipsilateral and contralateral. The XII hypoglossal nuclei are also affected, although most of their fibers are crossed (Bruyn & Gathier, 1969; Christen et al, 2000; Greenstein & Greenstein, 2000).

Presenting symptoms are as follows: facial paralysis and paralysis of the pharyngeal, laryngeal, and lingual muscles; severe spastic dysarthria or anarthria; impairment of chewing and swallowing; impassive open mouth and constant often excessive drooling; automatic- voluntary dissociation of the orofacial muscles, ie. automatic, involuntary, emotional movements are preserved, such as smiling at a joke, but voluntary movements are impaired, such as showing your teeth on command; exaggerated jaw reflex; preserved gag reflex; however, signs of tongue atrophy and fasciculation are missing (Bruyn & Gathier, 1969; Christen et al, 2000).

Causes of Operculum Syndrome

FCMS may be congenital or acquired as well as persistent or intermittent. In adults, the main cause of FCMS appears to be multiple subsequent strokes affecting the anterior operculum bilaterally. This area is predisposed to ischaemic lesions, as it is the final destination of the medial cerebral artery (Weller, 1993). In children, the causes of FCMS are different. Congenital bilateral dysgenesis of the perisylvian region, epileptic disorders, meningoencephalitis with the herpes simplex virus as the agent of infection, and perinatal difficulties have been proposed as causes (Christen et al, 2000; Koeda, Takeshita & Kisa, 1995; Nakajima, 2004; Van der Poel, Haenggeli & Overweg-Plandsoen, 1995).

Prevalence of Operculum Syndrome in South Africa

At present there are no statistics available to determine the prevalence of operculum syndrome within the South African population. What is possible is that children with operculum syndrome are misdiagnosed as having CP or developmental apraxia of speech. In the DTP two children presented with

operculum syndrome, one of whom had previously been diagnosed as a child with CP. Both children had severe and constant drooling, as rated on the Thomas-Stonell and Greenberg scale (1988) by qualified speech, language and hearing therapists. Clinically I have observed that their drooling has a negative impact on their participation within the classroom, relationships with other children and adults, and speech clarity.

2.3. Speech Characteristics of Cerebral Palsied Children and Operculum Syndrome Children

Normal speech production results from the combined functions of the respiratory system, the laryngeal system, the velopharyngeal system and the orofacial system. As CP has been described as a movement and posture disorder, it is not surprising that many CP children exhibit speech disorders. The most frequently occurring speech disorder is dysarthria. Darley, Aronson and Brown (1975, p. 2) state that dysarthria is ña collective name for a group of speech disorders that are due to disturbances in muscular control of the speech mechanism resulting from impairment of any the basic motor processes involved in the execution of speech.ò The speech characteristics of the CP child are dependent on the type and severity of the CP. Slow rate, dysrhythmia, reduced stress, inappropriate voice stoppage, breathy voice quality, a strained and strangled voice quality, monopitch, monoloudness, hypernasality, and a decreased number of words per breath, are all symptoms of CP speech. Some CP children are incapable of producing intelligible speech and the use of an alternative, augmentative communication device (AAC) is the only means of communication for them.

As Broca's motor speech area, areas 44 and 45, appear to be part of the operculum and the X vagus nerve, the V trigeminal nerve, the VII facial nerve and the XII hypoglossal nerve are all involved in the production of speech (Darley et al, 1975) it is understandable that severe dysarthria is a major presenting symptom of FCMS. The speech characteristics associated with developmental apraxia of speech are often used to describe the speech of individuals with operculum syndrome. The quality of voice is often nasal, as movement of the velopharynx is

limited. The production of sibilant/fricative sounds, eg. *sh* and *ch* is difficult and often impossible. Speech is therefore unintelligible in many cases and an AAC system is often warranted.

2.4. Feeding Problems in Cerebral Palsied Children and Operculum Syndrome Children

A feeding and swallowing dysfunction and a failure to thrive are common in CP children. Moreover, gastro-esophageal reflux, constipation and pneumonia due to aspiration can be complications. Poor oral-motor skills and oral sensitivity to different food textures can also make feeding the CP child difficult. These children often require help to develop safe feeding and swallowing. Correct body positioning, head positioning with a chin tuck, oral control, finger feeding, cut-out cups, and a graduated introduction to differing textures of food are just some examples of techniques that can be used to ensure safe eating and drinking in the CP population.

Clinically I have found that the automatic-voluntary dissociation causes a unique method for swallowing food/drink in children with operculum syndrome. In the oral stage, which requires voluntary movement of the tongue, lips and cheeks to chew food, the children display limited chewing ability and they are unable to propel the bolus towards the back of the mouth. Therefore they tip their heads back to allow gravity to propel the bolus backwards towards the pharynx where automatic, reflexive swallowing in the pharyngeal stage can occur. Due to paralysis of the muscles of the face, lips and tongue chewing is restricted to an up-down movement, with minimal lateral, rotary movement. These children often use their fingers to remove food from the buccal cavities, or to push food between their teeth for chewing.

2.5. The Role of The Speech, Language and Hearing Therapist

In South Africa the most common and popular approach, used by speech, language and hearing therapists, to treat neurological disabilities, particularly CP,

is NeuroDevelopmental Therapy, NDT (Bobath, 1980). NDT treatment emphasizes the whole body and focuses on developing functional abilities of the individual. Therapeutic handling is used to facilitate correct body positioning, alignment and movement. For the NDT trained speech, language and hearing therapist this means that to achieve better speech production or safe, correct eating and drinking patterns, the individual needs to be seated correctly, and the use of oral control may be necessary. A team approach, where physiotherapists, occupational therapists and speech, language and hearing therapists work together, is the ultimate approach advocated by NDT proponents. However, for many disabled individuals, especially in South Africa, this combined therapeutic approach is just a dream. NDT trained speech, language and hearing therapists are expected to be able to facilitate the correct body and head positioning of their clients, before they work on oral-motor skills, feeding and drinking patterns, or indeed language development.

Speech, language and hearing therapists also work on developing the language skills of their disabled children. This often means assessing the child and selecting the most appropriate AAC device for that child. Teaching the child and his/her parent/primary caregiver how best to facilitate communication is a most important part of a speech, language and hearing therapist's job. Knowing how to make a simple communication book using pictures from magazines or newspapers, as well as knowing how the latest computer aided AAC device works, is all part of the job. Watching the smile on a child's face when she can finally tell her mother, by pointing to a picture of a glass of water, that she wants a drink, is an experience I wouldn't have missed.

Finally, our job entails improving the quality of life for our children and their parents/primary caregivers and that may mean working on decreasing drooling.

2.6. The South African Perspective on Childhood Disability

Whilst knowledge of prevalence rates is important, it is more important to recognize and understand that within South Africa the majority of neurologically

impaired children have unmet health, welfare and educational needs (Saloojee, Phohole, Saloojee & IJsselmuiden, 2006, p. 230). It is often the case that parents/primary caregivers of a disabled child cannot afford the myriad of extras that caring for that child entails, even if the child is lucky enough to attend a specialized school. Overseas disabled children and their families have access to a variety of social and welfare grants, services and help, including access to respite care. This type of care enables a parent/primary caregiver to relinquish the responsibility of caring for a disabled child for a short while, knowing that the child will be well looked after. In South Africa respite care is unavailable, unless other family members, friends or neighbours are prepared to take over the burden of care for a period of time. In many cases this help is not forthcoming. Barratt (2007) found that in rural South Africa parents/primary caregivers often felt desperate and isolated from their communities.

Social grants are available to families of disabled children, but usually only cover the basic costs of living. In addition, to obtain a social grant, a parent of a disabled child needs that child's official birth certificate and/or identity document and numerous forms need to be completed. Many parents, especially in rural areas or informal settlements, do not have the relevant official birth documents. This necessitates an application to the Department of Home Affairs to obtain the relevant documents and the wheels of officialdom turn slowly. As found in Saloojee et al's study (2006) a main reason for parents not receiving a social grant was administrative and bureaucratic obstacles.

Funding for the extras which would allow a disabled child to participate more within his/her community or would facilitate a more independent lifestyle, has to be obtained from donations and private funding. Splinting, AAC devices, wheelchairs, not to mention electric wheelchairs, all cost a great deal of money. Certain wheelchairs are available on state tender and can be obtained via a state hospital, as can splinting. AAC devices are not available via a state hospital.

In recent years the Gauteng Department of Education has allocated a certain amount of money towards AAC devices for individual learners who are indigent. This has to be applied for by the individual's school. The vast majority of disabled children in South Africa do not benefit from educational funding or special services available in a school, as the vast majority of disabled children are not in school. The Department of Education in 2001 (White Paper 6, 2001) put the figure at approximately 76% of disabled children not in school. Saloojee et al (2006) found that 56% of disabled children, aged 7 to 15 years, from an informal settlement were not in school. The Education Department's 20 year plan for inclusion hopefully will allow more disabled learners to be educated, but one has to ask how are teachers supposed to cope with children whose needs are very specialized, unless they themselves receive additional specialized training? Just as important, what happens to the vast majority of disabled children not receiving education now? Do they become another lost generation?

As mentioned previously, QoL is a concept of considerable importance to the speech, language and hearing therapist. It is therefore appropriate to discuss QoL in relation to disability, drooling and with reference to the South African perspective.

2.7. Quality of Life

Definitions of Quality of Life

Quality of life (QoL) is an individual, subjective concept. What is important to one person may not be important to another. It depends on factors such as lifestyle, past experiences, hopes for the future, dreams and ambitions (Eisner & Morse, 2001). Further, what is important to an adult may not be important to a child.

The multifaceted nature of QoL has resulted in a variety of theories and definitions. Lindstrom and Eriksson (1993) associated QoL with success, wealth,

productivity and happiness in four spheres of life: the global sphere, (ecology, society and politics); the external sphere, (employment, education and independent living); the interpersonal sphere, (marriage and relationships); and the personal sphere, (self-esteem and self-concept). The discrepancy theory proposed that a poorer QoL results from the discrepancies between the child's actual self and the ideal self (Eisner, Vance & Seamark, 2000). In the utility theory, health states are given different values by experts or lay people. These values can be between zero, equivalent to death, and one, perfect health (Feeny, Furlong & Barr, 1998).

Davis, Waters, Mackinnon, Reddihough, Graham, Mehmet-Radji and Boyd (2006) in their review of pediatric quality of life instruments, clearly state why these three theories of QoL are not particularly appropriate. Lindstrom's model does not take into account the child's physical, social or emotional well-being, nor does it have a child self-report section. The discrepancy theory does not determine which factors contribute to a low or high quality of life and therefore does not provide guidelines for interventions to increase QoL. Finally the utility theory is best suited to measuring cost effectiveness of treatment, rather than QoL per se. As children often have difficulty distinguishing between quantity versus quality, this theory is rarely applied to children's QoL (Davis et al, 2006). Davis et al (2006) recommend that a pediatric theory of QoL be developed and evaluated across cultures and countries.

I agree that a child self-report section must be included, but suggest that it is vital to include countries in the evaluation, such as South Africa, that have a diverse population, with large semi-urban and rural groups of people, whose socio-economic development is poor. In 1993, the WHO defined quality of life, as "the perception by individuals of their position in life, in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns."

It has been shown that individuals in a rural setting may have different views on QoL (Walker, Winkelstein, Land, Lewis-Boyer, Quartey, Pham & Butz, 2008).

This is especially true in South Africa. Support, including medical, financial and social, is often lacking in the lives of our semi-urban and rural populations. Poor nutrition, inability to work, inaccessibility to medical resources, lack of education, different cultural beliefs and practices, and above all poverty, contribute to a differing QoL in the semi-urban and rural populations. As Levin (2006, p. 290) states "it is critical to address the specific needs of rural communities."

In relation to child disability, initial definitions of QoL focused on the health status of the child, with an emphasis on the physical functioning of the child. Several instruments measuring health-related quality of life (HRQoL) have been developed (King, Schweltnus, Russell, Shapiro & Aboelele, 2005). With the introduction of the WHO's definition of health (2001) as being more than the absence of disease, but also encompassing physical, social and psychological aspects of health, the concept of QoL widened to include these aspects.

QoL is most often described in terms of well-being across a variety of domains (Bjornson & McLaughlin, 2001). These domains consist of health domains and non-health domains. HRQoL can therefore be considered a sub-domain of QoL (Spilker & Revicki, 1996, in Waters, Maher, Salmon, Reddihough & Boyd, 2005). According to Davis et al's review (2006) the most common domains of QoL are those that refer to: emotions, social interactions, medical/treatment, cognition, activities, school, family, independence/autonomy, pain, behaviour, the future, leisure, and body image.

No general QoL or HRQoL measure seems to take into consideration the effect of drooling on the QoL in a pediatric population. Van der Burg et al (2006a) have developed a questionnaire designed specifically to investigate drooling severity and its consequences for a child and the family. They looked at the impact drooling has on specific life situations, daily care, economic consequences, social interactions, emotional development and self-esteem. The results of this study are discussed later in the chapter.

Measures of Quality of Life/Health-Related Quality of Life

From the literature it seems evident that there are two types of QoL/HRQoL measures, generic and condition-specific. Generic measures are designed to be relevant to all population groups and are useful for comparing QoL/HRQoL between population groups with different conditions. They provide a superficial evaluation of a person and tend not to identify the specific effects of a certain disease (Schneider, Gurucharri, Gutierrez & Gaebler-Spira, 2001). Disease or condition specific measures are designed for a specific disease and are useful for detecting changes in symptoms, problems or side-effects associated with a particular disease. They are also more sensitive in detecting treatment effects (Schneider et al, 2001; Waters, Maher et al, 2005). Both generic and condition-specific measures have been used with the cerebral palsied population.

Research on children's QoL used to rely on parental or proxy reports, but it is now realised that the child's view is just as important. Measures often include a child report section as well as the parent report section. Unfortunately these measures do not allow for the non-verbal child to communicate his/her opinions.

Several reviews of QoL/HRQoL measures have been published, citing their usefulness and relevance to the cerebral palsied population. Foremost of these is the review by Davis et al (2006) where 14 generic and 25 condition-specific measures are identified.

A detailed critique of QoL measures is not the aim of this research report; suffice it to say there are many such measures, for example, the Child Health Questionnaire, CHQ (Landgraf, Abetz & Ware, 1996 in Waters et al 2005); the Lifestyle Assessment Questionnaire, LAQ (Mackie, Jessen & Jarvis, 1998); and the Pediatric Quality of Life Questionnaire Cerebral Palsy Module, PedsQL (Varni, Burwinkle, Berrin, Sherman, Artavia, Malcarne & Chambers, 2006). However, Waters et al (2005) feel that these instruments measure the absence of health difficulties or limitations rather than well-being.

A recently developed QoL questionnaire, designed specifically for cerebral palsied children, CP QOL-Child, assesses the aspects of life that parents and children think are important, including friends, family, school and health (Waters, Davis, Boyd, Reddihough, Mackinnon, Graham, Lo, Wolfe, Stevenson, Bjornson, Blair & Ravens-Sieberer, 2006, p. 1). It is designed for children aged 4-12 years and has two versions; the parent proxy version, for parents of children aged 4-12 years, and the child self-report version, for children aged 9-12 years. As parents and children may report different levels of QoL, both versions should be used (Waters, Davis et al, 2006).

The development of the questionnaire was based on 13 themes of quality of life, extracted from discussions with parents and children (Waters, Maher et al, 2005). Table 2.7.1 lists the 13 themes and gives a definition for each theme. All the domains of health as identified by the WHO (2001), including physical well-being, i.e. physical health, mental well-being, i.e. emotional well-being and self-esteem, and social well-being, emerged as themes. In addition, themes specific to children, i.e. family health and themes specific to cerebral palsy, i.e. body pain/discomfort emerged. Some themes appeared to consider the practicalities of having a cerebral palsied child, i.e. access to services, supportive environments, family financial stability and acceptance in the community. The latter themes would appear to be particularly relevant to the semi-urban and rural South African population.

However, as can be seen from Table 2.7.1, the definition of financial stability does not take into account the severe effects of poverty, such as the ability to provide basic necessities, for example, food and clothing. Of interest to me is the fact that no reference to drooling is made and in the questionnaire there is no specific section or questions that deal with the effects of drooling on the quality of life.

Table 2.7.1: Quality of Life Themes Important to Parents and Cerebral Palsied Children (Waters, Maher et al, 2005).

Physical health	Gross/fine motor skill, ability to use aides, overall physical health.
Body pain & discomfort	Stiffness & soreness in joints, pain associated with therapy.
Daily living tasks	Ability to carry out normal tasks including dressing, feeding, toileting and being independent.
Participation in physical & social activities	Participating in school, sporting and community activities.
Emotional well-being & self-esteem	Being happy, being able to achieve goals, being satisfied with one's body and emotions.
Interaction with the community	Being socially accepted, being a valued member of the community, being treated 'normally'.
Communication	Communication skills with family, peers and people in the community.
Family health	Parental emotional health, family relations, restrictions on the family to go out socially.
Supportive physical environment	Supportive school, family and community environments, having the necessary equipment and devices.
Future Quality of Life	Opportunities to do everything they desire, being able to do things as well as their peers, being able to make choices in their lives.
Provision of and access to services	Access to therapy, respite and having the support required.
Financial stability	Earning capacity of parents, ability to cover the expenses of equipment and treatment.
Social well-being	Ability to interact with family members, peers and people in the community.

2.8. Quality of Life in South Africa

The diverse nature of the people of South Africa means that quality of life for one group is very different from that of another group. The population differs in terms of cultures, languages and religions. More importantly there is a wide divide between the socio-economic status of our people. South Africa's population can be split into a section that resembles the population of well developed countries and a much larger section that resembles the population of poor, under developed countries.

This division usually follows racial lines (Makiwane & Kwizera, 2006). The policy of apartheid, defined as the separate development of people based on their colour, under which South Africa operated until 1994, meant that the majority of South African people experienced restricted access to education, health care, residence and employment opportunities (Westaway, Olorunju & Rai, 2007). Due to this legacy, despite being one of the richest countries on the African continent, South Africa is still struggling to provide its entire people with a better quality of life. According to The South African Quality of Life Project (Møller & Dickow, 2002, p. 267) "In most democratic countries around the globe, the average citizen says he or she is satisfied with life in general. In South Africa this is *not* the case."

Westaway et al (2007) suggest that happiness and life satisfaction, elements of quality of life, are related to race in South Africa. From 1983 to 1999 white South Africans were happier and more satisfied with their lives than black South Africans. The quality of life and perceived happiness for older, black South Africans has been made bleaker by the fact that they are often the principle caregiver for their families. They become the principle caregiver as a result of the death of the parents, which is often due to AIDS/HIV, or because both parents have to work leaving "granny" to look after the children. A disabled child is often sent to live with the grandmother in a rural area. Makiwane and Kwizera (2006) found the quality of life of older, black people in Mpumalanga to be poor and attributed this poor quality of life to low income, few household amenities, the

legacy of life long poverty and the heavy burden of caring for children, disabled children and sick adults.

Barratt (2007) found a number of themes emerged from black, rural caregivers' experiences of caring for a child with cerebral palsy. These themes included the impact of gender on care giving, the influence of traditional beliefs and practices, and the experience of western medicine. Within the theme of gender, Barratt (2007) found that most of the care giving was performed by the mothers or grandmothers, although some fathers were involved with their disabled child. She comments further that 'a distinct absence of men' was noticed in the homes and community (Barratt, 2007, p. 113). More importantly, the effects of poverty influenced every aspect of care giving. Caregivers felt a sense of isolation from their communities, experienced fear for the future and depression. A sense of desperation at the heavy burden they carried was experienced by some caregivers. These factors would seem to indicate a poor quality of life for the caregivers and their children. Jelsma and Ferguson (2004) contend that the disabled are still in the lowest socio-economic group, despite South Africa's National Disability Strategy (1997). This strategy aims at the full integration of people with disabilities into society.

As already stated, there appears to be a difference in the quality of life between urban and rural populations (Hammal, Jarvis, & Colver, 2004; Walker et al, 2008). The factors that affect the semi-urban and rural populations certainly make for a bleaker QoL in South Africa.

2.9. Quality of Life for Neurologically Impaired Children

There appears to be some dissent in the literature as to whether there is a difference in the quality of life or well-being between a CP child and a 'normal' child. Some authors feel there is a difference (Vargus-Adams, 2006; Varni, Burwinkle, Sherman, Hanna, Berrin, Malcarne & Chambers, 2005). Livingston, Rosenbaum, Russell and Palisano (2007) reviewed assessments of well-being in CP individuals, conducted over a period of ten years. In their opinion, several

themes emerged. First, the well-being of CP individuals can be considered to be lower than the 'normal' population. Second, gross motor functioning has an effect on physical well-being. Third, there is very little literature on the factors that affect well-being for adolescents. At this stage there is little research on the well-being of South African children with neurological disabilities. Several models for assessing South African children's well-being have been discussed (Bray & Dawes, 2007). A South African Rights-Based Approach to Monitoring Child Well-Being (Dawes, Bray & Van der Merwe, 2007) has been proposed, while Schneider and Saloojee (2007) considered aspects of monitoring childhood disability. As yet, no study using this approach seems to have been published.

The issue of pain and its effect on quality of life in the CP population have been investigated (Houlihan, O'Donnell, Conaway & Stevenson, 2004). It seems obvious that quality of life would be decreased if there is constant pain. Some authors have found that individuals classified with moderate to severe CP have lowered scores on a quality of life measure (Liptak, O'Donnell, Conaway, Chumlea, Worley, Henderson, Fung, Stallings, Samson-Fang, Calvert, Rosenbaum & Stevenson, 2001).

Conversely, certain literature seems to suggest that the quality of life for CP children is not necessarily poorer than for children in the general population (Dickinson, Parkinson, Ravens-Sieberer, Schirripa, Thyen, Arnaud, Beckung, Fauconnier, McManus, Michelsen, Parkes & Colver, 2007). The Study of Participation of Children with Cerebral Palsy Living in Europe (SPARCLE) investigated the self-reported quality of life of CP children. They looked at parental employment and educational qualifications, area of domicile, the child's gross motor function, fine motor function, seizures, feeding, communication, intellect, schooling, family dynamics and CP type. The findings from this study indicated that 'children with cerebral palsy had similar QoL to children in the general population in all domains except schooling, in which evidence was equivocal, and physical well-being, in which comparison was not possible' (Dickinson et al, 2007, p. 2171).

A systematic review of the self-concept in children with CP compared with children without disability was unable to establish whether self-concept was lower in the disabled children compared to the non-disabled children (Shields, Murdock, Loy, Dodd & Taylor, 2006).

Levels of functioning and their effects on quality of life have been researched (Shelly, Davis, Waters, Mackinnon, Reddihough, Boyd, Reid & Graham, 2008). This study differentiated between physical well-being domains of QoL and psychosocial well-being domains and found that a child with poor functioning, although he/she may report poor physical well-being, may have good social and emotional well-being. The study by Majnemer, Shevell, Rosenbaum, Law and Poulin (2007, p. 470) found that quality of life is "highly variable" with about half experiencing a life quality similar to typically developing children.

It would appear that whether the quality of life of a CP child is found to be good or poor, the same or different to the general population, depends on the type of instrument used to measure quality of life and the domains of quality of life being studied.

Studies of children with a variety of disorders such as:

- physical impairments (Grue, 2003);
- behaviour and learning difficulties (Watson & Keith, 2002);
- speech and language difficulties (Markham & Dean, 2006);
- traumatic brain injury (Hameed, Miller, Curran, Pauldhas, Mccarter, Hunt & Sharples, 2008);
- and asthma (Walker et al, 2008)

also provide conflicting evidence about how the quality of life of these children compares with that of the general population. What is clear is that health care workers, speech, language and hearing therapists included, need to take cognizance of the quality of life of the children with whom they work, so that their treatments are appropriate and worthwhile.

2.10. The ‘Disability Paradox’

The idea that individuals with disabilities can have a good quality of life has been called the ‘disability paradox’ (Albrecht & Devlieger, 1999). In their article ‘The disability paradox: high quality of life against all odds’ Albrecht and Devlieger (1999) argue that quality of life must be viewed as a holistic notion of well-being, not just health related. Quality of life encompasses more than just activity limitations, health and disease categories. It must include the social, psychological and spiritual domains for a true reflection of the quality of life of disabled individuals to be gained.

Their explanation for the ‘disability paradox’ lies in the disabled individual’s ability to establish and maintain a sense of balance between the body, mind and spirit and with the individual’s social context and environment. For example, individuals who: understand their condition; take control and introduce order and predictability in their lives; are able to set realistic goals; have a positive and supportive social context; can have a good quality of life. However, those who are unable to maintain a balance due to their health condition, limited resources, lack of knowledge or environmental constraints are likely to have a poor quality of life.

This explanation of what is involved in a good or poor quality of life has implications for disabled individuals in South Africa. As most disabled South African individuals are in the lower socio-economic group, live in semi-urban or rural areas, have limited resources, generally lack knowledge about their disability, the implication is that their QoL is poor.

At this stage it is impossible to comment accurately on the quality of life for disabled or CP children in South Africa. We have no central data base giving accurate numbers of disabled/CP children in this country to start with. Secondly, although studies have looked at QoL for specific South African communities (Barratt, 2007; Hinks & Gruen, 2007; Jelsma & Ferguson, 2004; Makiwane & Kwizera, 2006; Møller & Dickow, 2002; Westaway, 2006), and the ‘unmet needs of disabled children in a poor township’ (Saloojee et al, 2006, p. 230) there does

not appear to be any specific research into the quality of life for South African disabled/CP children.

2.11. The Relationship between Drooling and Quality of Life

According to Hockstein, Samadi, Gendron & Handler (2004) the impact of drooling on an individual's QoL is the most important factor in determining the necessity for treatment. Blasco (2002, p. 780) states "the ultimate test of whether treatment (for drooling) will be continued or not is whether it makes the caregiver's life easier and the child's life is improved." Van der Burg et al (2006b) investigated parental perceptions of drooling on daily life, and the social interaction and self-esteem of 45 cerebral palsied children following treatment for severe drooling. Table 2.11.1 indicates the results from their study. As can be seen, drooling clearly has an effect on QoL.

Reid, Johnstone, Westbury, Rawicki and Reddihough (2008) in their randomized trial of botulinum injections to reduce drooling in children, measured the impact of drooling at baseline and after treatment via questions to the primary caregivers. Besides the severity and frequency of drooling, and the number of bib/clothing change questions, the researchers wanted to know the following:

- How offensive was the smell of saliva on your child?
- How much skin irritation has your child had?
- How embarrassed did your child seem to be about his/her drooling?
- To what extent did the drooling affect your child's life?
- To what extent did the drooling affect you and your family's life?

The inclusion of these types of questions leads me to believe that drooling is being acknowledged as having a major detrimental effect on the quality of life of neurologically impaired children.

Table 2.11.1: The Effects of Drooling on Quality of Life, based on Van der Burg et al (2006b).

Care Given to a Child/Economic Consequences	Social Interaction	Self-esteem
Child told to swallow often. Mouth and chin wiped regularly. Bibs, shawls, terry cloth wristbands replaced regularly. Complete change of clothing needed. Multiple laundry loads in a week. Damage to clothes, toys, books, furniture, communication aids, electronic communication devices, computers and audio equipment. Curtailing of child's play to prevent damage to objects.	Limited play and social interaction with children and adults. Child often avoided by other children. Child often avoided by familiar and unfamiliar adults. Child assessed by outsiders as being mentally incapable due to unsightly look of drooling.	Unhappiness with physical appearance. Feelings of incompetence. Lack of peer acceptance.

Clinically, I have witnessed the detrimental effect of drooling in schools, hospitals and in homes, over a period of more than 20 years. As such, questions regarding the effect any drooling has on a disabled/CP child's life should be included in pediatric quality of life questionnaires for the neurologically impaired. **Further, I believe that drooling has an effect on the QoL of South African neurologically impaired children and their parents/primary caregivers.** For this reason parents/primary caregivers in the DTP were interviewed and given a QoL questionnaire (Appendices L & M).

This chapter has dealt with the neurological impairments of the participants in the DTP, QoL in South Africa and the effects of disability on QoL. In the present study drooling is considered to have an influence on QoL. Saliva, drooling and treatments for drooling, including Botox® injections, therefore are discussed in the next chapter.

CHAPTER 3

SALIVA, DROOLING AND BOTOX®

In this chapter I consider saliva and its important functions, what constitutes drooling, the problems that drooling can cause, the variety of techniques to measure drooling and treatment strategies, including the use of Botox®. An overview of the history and pharmacology of Botox® is given, followed by the clinical uses of Botox®, with specific reference to the fields of Speech Pathology and Audiology. The chapter concludes with a critical review of previous studies that have used Botox® to reduce drooling in neurologically impaired children.

3.1. Saliva

Saliva is secreted by six major salivary glands: two parotid glands, two submandibular glands and two sublingual glands. In addition there are hundreds of minor glands located throughout the surface of the palate, tongue and oral mucosa (Hockstein et al, 2004).

In adults, approximately 1 to 1,5 litres of saliva are produced by the major glands per day (Lal & Hotaling, 2006; Hockstein et al, 2004). In healthy children aged between 6 and 11 years, approximately 677 millilitres of saliva are produced in a day (Rotteveel, Jongerius, van Limbeek & van den Hoogen, 2004). In an unstimulated state, the submandibular gland produces 70% of the saliva, with the parotid glands producing 20%, as a result of stimulations such as food or even just the smell of food. The remaining 10% is produced by the sublingual glands and the minor glands. When stimulated, salivary flow increases five times. (Stuchell & Mandell, 1988).

As can be seen from Figure 3.1.1 the parotid glands are located deep in the soft tissue of the cheek and they produce a watery secretion. The submandibular and the sublingual glands drain into the floor of the mouth and the secretions are more

viscous. Generally, it is this thicker saliva that is troublesome in drooling (Brotsky, 2002).

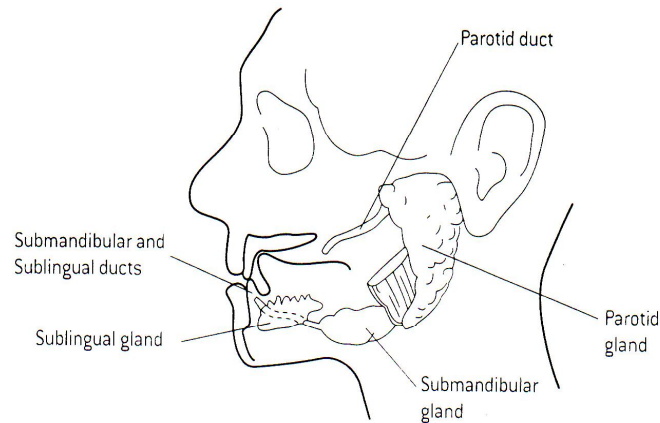


Figure 3.1.1: The Positions of the Salivary Glands (Johnson & Scott, 1993)

A clear understanding of the neural pathways and control of salivation is needed to understand drooling. Therefore a brief description follows.

Neurophysiology of Salivation

The majority of secretory control lies with the parasympathetic nervous system, but the sympathetic nervous system does play a part. Stimulation of the parasympathetic nerves causes production of saliva, whereas sympathetic stimulation causes secretion of protein and glycoprotein (Ferguson, 1988). In addition, the flow of saliva is enhanced by sympathetic innervation, which promotes contraction of muscle fibers around the salivary glands (Hockstein et al, 2004).

The autonomic nervous system (ANS) supplies the involuntary muscles, the heart and the secreting glands. The parasympathetic and sympathetic nervous systems together form the peripheral ANS. As the name implies, most activities of the ANS are not under voluntary control, but are usually regulated by the reflex arc. The peripheral ANS is efferent, that is a motor system, but most of the nerves

containing ANS fibers also have afferent neurons. The efferent fibers convey the reflex response to afferent information. The ANS is a two neuron system. The place where the first neuron ends in a synapse with the second neuron is termed a ganglion. The nerve fiber before the synapse is the preganglionic fiber and after the synapse is the postganglionic fiber. The chemical transmitter in the parasympathetic system, at both the synapse and the postganglionic termination is acetylcholine.

As can be seen from Figure 3.1.2, the sympathetic nerves leave the central nervous system between the first thoracic and the second lumbar segments of the spinal cord. The route of the sympathetic fibres from the superior cervical ganglion to the salivary glands is also shown. Figure 3.1.3 shows that the parasympathetic nerves leave the central nervous system in the spinal region only at the second, third and fourth sacral segments, but in addition there is an important outflow in some of the cranial nerves which arise from the brain itself (Green, 1976; Despopoulos, 2003). The parasympathetic fibers from the otic and submandibular ganglions to the salivary glands are also illustrated.

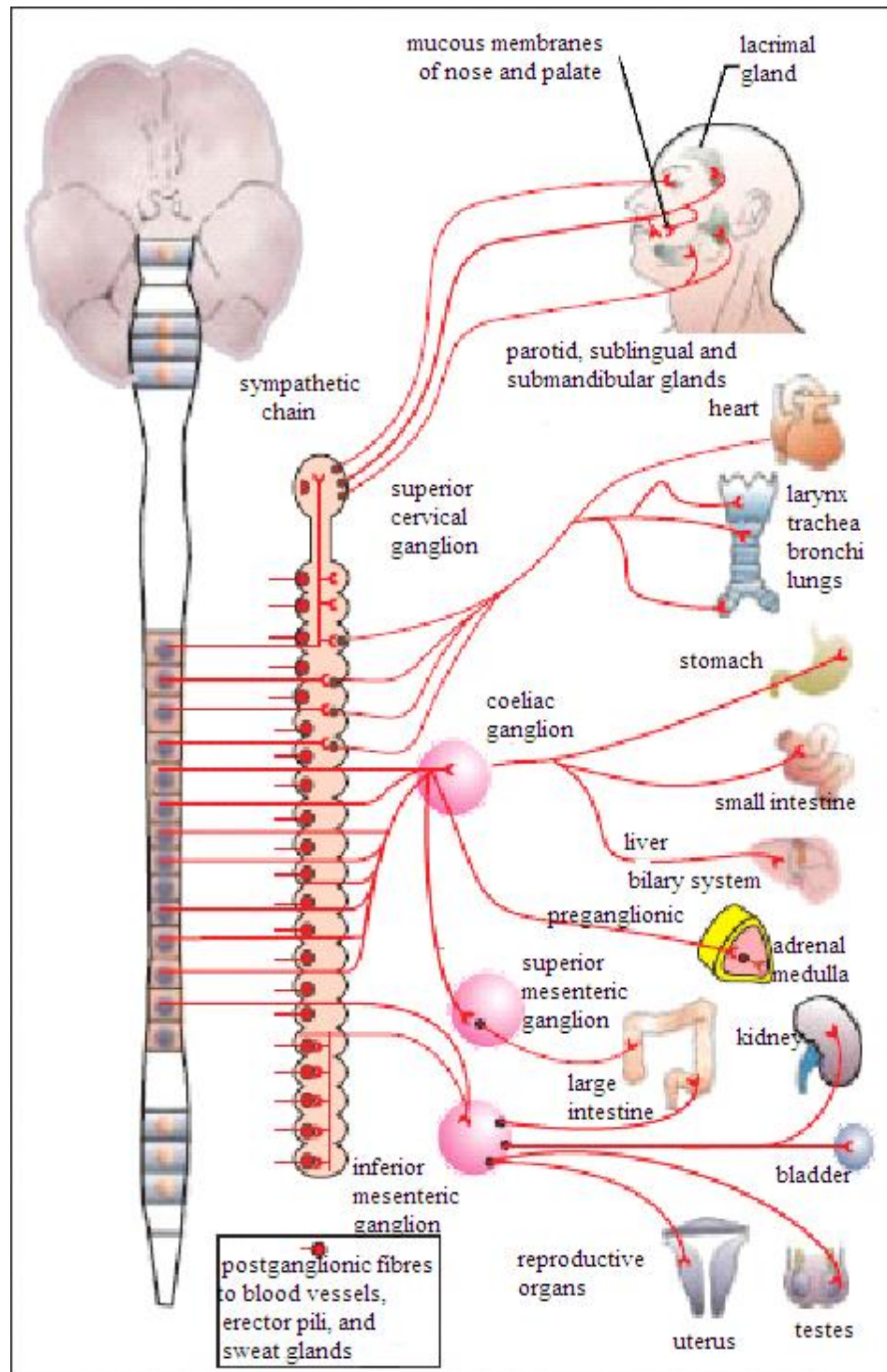


Figure 3.1.2: Fibers of the Sympathetic Nervous System (Greenstein, 2000)

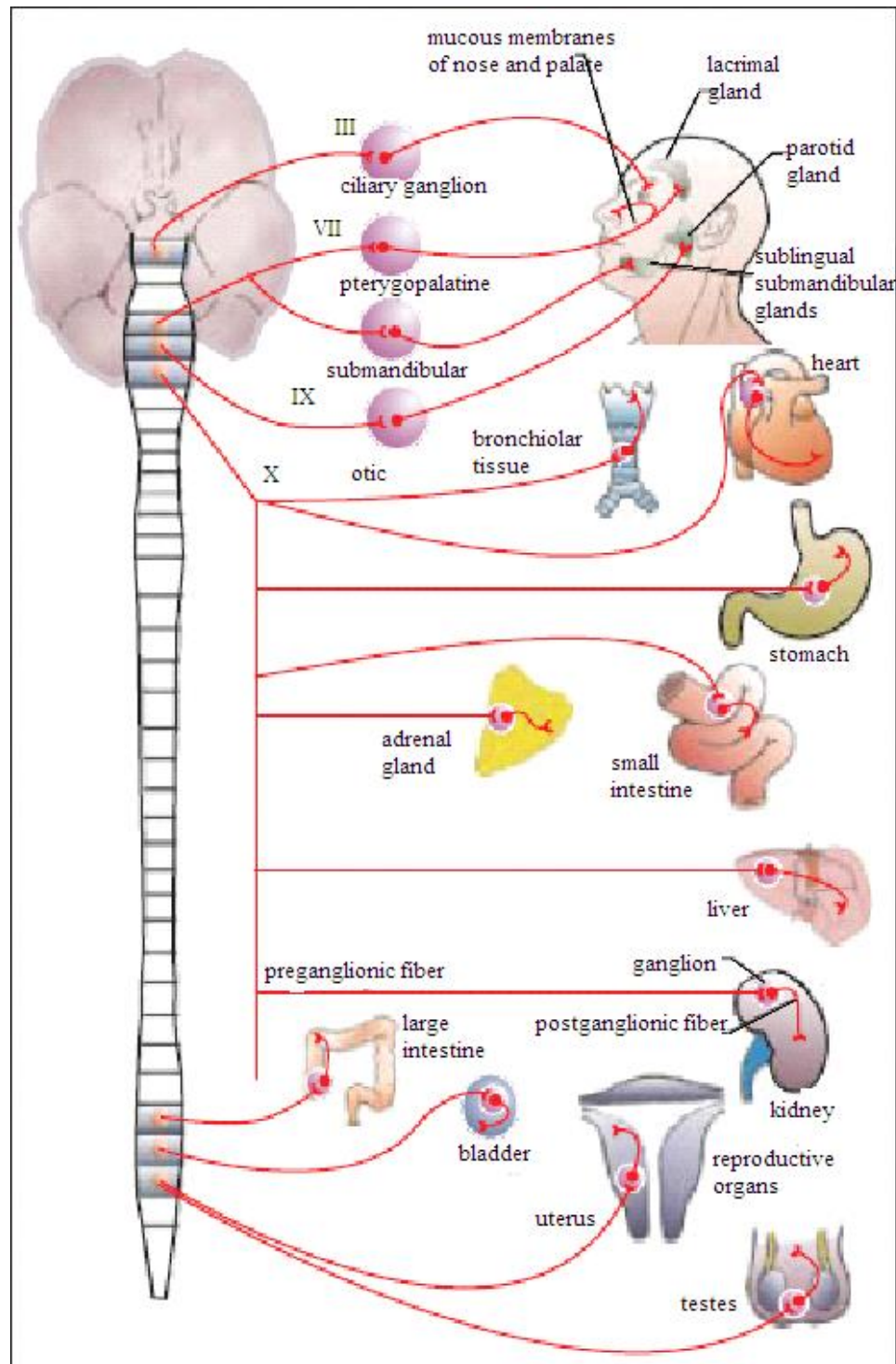


Figure 3.1.3: Fibers of the Parasympathetic Nervous System
(Greenstein, 2000)

Parasympathetic fibers are found in the cranial nerves III, VII, IX and X. The parasympathetic fibers in the VII, facial nerve, reach the submandibular and sublingual salivary glands by a complex pathway. These fibers arise in the superior salivary nucleus which lies in the reticular formation in the lower pons, in the brain stem. The fibers travel in the VII, facial nerve, until they leave in the chorda tympani nerve just above the stylomastoid foramen. The chorda tympani run across the ear drum to reach the lingual nerve. A branch from this nerve runs to the submandibular ganglion. Postganglionic fibers supply secretory function to the submandibular and sublingual glands (Green, 1976).

The parasympathetic fibers in the IX, glossopharyngeal nerve, supply the parotid gland. They arise in the inferior salivary nucleus which lies just below the superior salivary nucleus. The fibers travel in the tympanic branch of the glossopharyngeal nerve to the lesser superficial petrosal nerve to reach the otic ganglion. The postganglionic fibers run in the auriculotemporal nerve to the parotid gland (Green, 1976).

Sympathetic fibres pass from the superior cervical ganglion with blood vessels to the salivary glands (Ferguson, 1988).

As already mentioned, activities of the ANS are regulated by a reflex arc. The salivary taste reflex is a prime example of the reflex arc. When gustatory stimulus is placed on the anterior two thirds of the tongue, the salivary glands increase their saliva output. The afferent stimulus is carried by taste fibers in the facial nerve to the nucleus of the solitary tract. Connecting fibers from this nucleus go to parasympathetic neurons in the superior and inferior salivary nuclei. The efferent stimulus is carried back to the salivary glands via the previously described routes. The reflex pathway for gustatory stimuli on the posterior one third of the tongue is similar to that of the anterior two thirds of the tongue, except the afferent stimulus is carried by the glossopharyngeal nerve (Gillman & Newman, 1992). Conditioned reflexes also have a role to play in the stimulation of saliva secretion. For example, the clattering of plates when preparing a meal can elicit a saliva response (Despopoulos, 2003).

Functions of Saliva

Saliva has several functions: it keeps the vocal cords damp; it aids articulation by keeping the tongue, lips and palate lubricated; it protects the teeth and gums from bacteria, which can cause gingivitis and tooth decay; it helps to decrease bad smelling breath by cleaning the mouth; it is an essential component in swallowing, as it lubricates the oral mucosa and mixes with food in the mouth to form a bolus; it facilitates tasting, as food can only be tasted in solution; and it promotes digestion by breaking down proteins and carbohydrates with amylase (Brodsky, 2002; Hockstein et al, 2004; Lal & Hotaling, 2006; Mathur, Vaughn & Brown, 2006; Winstock, 2005).

As saliva has many important functions, when considering the treatment of drooling, it is essential to preserve an adequate amount of saliva production. If the majority of saliva production is eliminated, which is often the case with radical surgical procedures, swallowing becomes difficult, tooth decay can occur, the lips and mouth can become encrusted with bits of dry food, and the smooth movement of the oral musculature, needed for the co-articulation of sounds, can be hampered. These were some of the reasons it was decided to inject only the submandibular glands with Botox® in the DTP, thus leaving the other major and minor salivary glands to continue producing saliva.

Factors Affecting the Production of Saliva

There are several factors which can affect the production of saliva. As can be seen from Table 3.1.1 different factors influence the amount of saliva produced, either causing an increase or a decrease in the amount of saliva produced. Although the participants in the DTP were a convenience sample, it is interesting to note that the majority were males.

Table 3.1.1: Factors that Influence the Production of Saliva
(Based on Winstock, 2005)

Factors that ↑ Saliva Production	Factors that ↓ Saliva Production
<u>Age</u>: saliva production ↑ up to the age of 15 years. <u>Gender</u>: males produce more saliva. <u>Fluid intake</u>: a ↑ in the amount of fluid drunk can ↑ the amount of saliva produced. <u>Chewing</u>: ↑ in frequency and amount of chewing can ↑ the amount of saliva produced. <u>Taste</u>: citric acid ↑ saliva production. <u>Time</u>: saliva production peaks during the afternoon. <u>Visual imagination</u>: good visual imagination ↑ saliva production. <u>Illness</u>: saliva production ↑ with nausea and vomiting.	<u>Age</u>: saliva production decreases after 15 years of age. <u>Gender</u>: females produce less saliva. <u>Fluid intake</u>: a ↓ in the amount of fluid drunk can ↓ the amount of saliva produced. <u>Time</u>: saliva production ↓ during sleep. <u>Season</u>: saliva production ↓ in summer. <u>Emotions</u>: fear and depression ↓ saliva production. <u>Darkness/blindfold</u>: saliva production ↓ in the dark or if blindfolded. <u>Medication</u>: certain medications ↓ saliva production.

Key: ↑ - Increase; ↓ - Decrease.

3.2. Drooling

Definition of Drooling

ñDrooling is the unintentional, involuntary loss of saliva from the mouth due to a lack of control over oral secretions (Lal & Hotaling, 2006, p. 381). The medical term for drooling is sialorrhea and the literature is full of authors who basically all give the same definition of drooling. (Bax, 1992; Blasco & Allaire, 1992;

Crysdale, 1989; Meningaud, Pitak-Arnop, Chikhani & Bertrand, 2006; Nunn, 2000; Suskind & Tilton, 2002; Wilkie, 1967).

Development of Drooling

Drooling is a physiological phenomenon, considered to be normal in children under the age of two years. Table 3.2.1 illustrates that the development of drooling occurs in stages.

Table 3.2.1: Developmental Stages of Drooling (Alexander, Boehme & Cupps, 1993; Boner & Perlin, 1994)

Age	Development
1-2 months	Little drooling in supine, but drooling $\hat{y}$ in prone or supported sitting, as the jaw and tongue move in wider excursions.
3-5 months	Drooling $\hat{z}$ in positions with greater stability, but does $\hat{y}$ with teething.
6 months	Drooling is controlled in supine, prone and sitting. It does occur with babbling, reaching and teething, but is less during feeding.
7-9 months	Drooling rarely occurs, even with new gross motor activities. With new upper extremity activities drooling may occur, also when teething.
10 to 12 months	Drooling rarely occurs, except when teething.
15 months	No drooling with new gross motor activities, but it does occur with new fine motor activities.
18 months	No drooling with early fine motor activities, but it does occur with feeding, random play and undressing.
24 months	No drooling with more advanced fine motor activities, drawing, self-feeding, random play, undressing, or during two-word utterances.

Key: $\hat{y}$ - Increase; $\hat{z}$ - Decrease.

Occasionally children up to the ages of four to six may exhibit drooling, especially if they are teething. However, drooling resolves with the maturation of oro-facial movement and swallowing (Mathur et al, 2006).

Etiology of Drooling

Drooling is rarely caused by an increase in the production of saliva, commonly known as hypersecretion or primary sialorrhea (Mathur et al, 2006; Senner, Logemann, Zecker, Gaebler-Spira, 2004). In fact, it has been shown that patients who produce less saliva can drool (Proulx, de Courval, Wiseman, & Panisset, 2005). Primary sialorrhea is usually caused by: inflammation, such as during teething; dental caries; mouth infections; rabies; certain medications, as a side effect from the use of tranquilizers or anticonvulsants; toxin exposure (mercury vapour); and gastro esophageal reflux (Hockstein et al, 2004; Winstock, 2005). Before considering any treatment that reduces the amount of saliva produced, it is essential to consider and attend to any of the above mentioned causes.

More commonly, drooling is caused by impaired neuromuscular control and/or sensory dysfunction. This impaired neurological control results in poor coordination of the oral musculature and poor suction force, leading to an inadequate swallowing function. Swallowing studies of CP children point to three areas of difficulty: incomplete lip closure; low suction force; and a prolonged delay between suction and the backwards propelling of food stage (Lespargot, Langevin, Muller & Guillemont, 1993). Excessive pooling of saliva in the anterior portion of the mouth and the unintentional loss of saliva from the mouth are the results (Brodsky, 1999; Meningaud et al, 2006). This is known as secondary, anterior drooling.

The list of disorders/deformities that can cause secondary drooling is extensive, as can be seen from Table 3.2.2 on the following page.

Table 3.2.2: The Etiology of Drooling (Based on Meinigaud et al, 2006)

Neurological Deficits	Anatomical Deformities
<u>Predominantly Adult Deficits</u> Motor neuron disease (amyotrophic lateral sclerosis) Multiple sclerosis, Facial paralysis Parkinson's disease Cerebrovascular accidents	Macroglossia (enlarged tongue) Dental malocclusion Orthodontic problems Nasal obstruction Head and neck surgical defects (i.e. 'Andy Gump' deformity)
Seizures, Traumatic brain injury	
<u>Predominantly Childhood Deficits</u> Cerebral palsy Congenital suprabulbar palsy Severe mental retardation, Down's syndrome Worster Drought syndrome, Operculum syndrome Landau Kleffner syndrome, Angelman's syndrome Freeman-Sheldon syndrome, Moebius syndrome Encephalitis, Hydrocephalus, Hypoxic encephalopathy Early sign of Sjogren's syndrome	

It is important to distinguish between anterior and posterior drooling. Posterior drooling, in which saliva spills over the tongue through the faucial isthmus, can cause congested breathing, coughing, gagging, vomiting and occasionally aspiration into the trachea that results in recurrent pneumonia (Jongerus, van Hulst, van den Hoogen & Rotteveel, 2005). A diagnosis of posterior drooling warrants additional investigations, not just treatment for the drooling. Although Jongerus et al (2005) have treated children with posterior drooling with Botox® successfully, it was decided for reasons of safety that all participants in the DTP had to exhibit anterior drooling not posterior drooling.

Impaired sensory awareness, hyposensitivity, on or within the mouth may be a primary causative factor in the ability to control saliva (Rosenfeld-Johnson, 2002). In fact, according to Allaire (1999, p. 107) 'experts believe that the perception of sensation within and around the mouth of a child who drools is different from that

of other children. The relationship between oral sensations and drooling was examined by Weiss-Lambrou, Tetreault and Dudley (1989). Their results suggested that CP children who drool may have an oral sensory problem, possibly associated with a perceptual deficit, as those children scored lower on tests of oral sensation compared to CP children who did not drool. Normal oral sensation activates the movement of the jaw, tongue and throat and provides the cue to swallow (Allaire, 1999). If sensation is impaired, a wet chin may feel normal (Winstock, 2005, p. 172).

Although Morris and Klein (2000) acknowledge that some CP children may lack oral sensory awareness, they also argue that saliva accumulates in the mouth because of a reduced frequency of swallowing and this can cause drooling. Further, the constant drooling and wet face can reduce the sensory cues needed to trigger a proper swallow. The old saying "which comes first, the chicken or the egg" comes to mind. Suffice it to say, if there is an indication of reduced oral sensation, treatment should include increasing the child's awareness in and around the mouth.

When drooling persists after the age of six years, it is usually as a result of neurological deficits or anatomical problems. Mathur et al (2006) contend that within the CP population more than 85% of patients with drooling are younger than 21 years. They attribute this to the shortened life span of persons with CP.

3.3. Factors that Exacerbate Drooling

Poor postural and head control, poor oral-motor control, a constantly open mouth, enlarged tonsils and adenoids, increased concentration during a task, and certain medications, such as clozapine and lithium, can all exacerbate drooling. These factors should be taken into consideration when planning therapy for drooling. In the study by Senner et al (2004) a positive correlation was found between severity of drooling and severity of dysarthria. This finding highlights the importance of oral-motor control in controlling saliva and producing clear speech.

Complications of Drooling

Most authorities agree that the complications of drooling can range from mild and inconvenient to severe problems that negatively affect the quality of life.

Complications are usually divided into three areas:

a). The physical symptoms include: sore lips and chins; dehydration; the discomfort of a dry mouth; halitosis; gum and dental problems; wet clothes, which have to be changed frequently, leading to an increased work load for the parents/primary caregivers; wet furniture, toys, books and computer keyboards (Winstock, 2005). The severity of the drooling affects the severity of the physical symptoms.

b). The psychosocial complications include: social unacceptability and embarrassment, leading to isolation; increased dependency and level of care; caretakers, family and friends may find it difficult to demonstrate affection; strangers or the uninformed may assume the child is severely mentally retarded (Banerjee, Glasson & O'Flaherty, 2006; Hockstein et al, 2004; Mathur et al, 2006; Winstock, 2005).

c). The third area is barriers to participation: negative attitudes of teaching staff and other pupils often lead to exclusion from school activities (Mihaylov, Jarvis, Colver & Beresford, 2004; Hemmingson & Borell, 2002; Pivik, McComas & Laflamme, 2002). Castaneto and Willemsen (2007) found there was subtle prejudice against disabled children, while Nadeau and Tessier (2006) discovered that in a mainstream school, CP children particularly the females, suffered social isolation and victimization. These studies seem to imply that the education of the disabled child may not be as comprehensive as the non-disabled child. One study on higher education and employment of CP individuals indicated that only 29% of the participants, despite some of them having a main stream education, were employed in the open labour market (Michelsen, Uldall, Kejs & Madsen, 2005).

The authors postulate that one reason for the low employment rate is the fact that CP individuals have problems with social interaction.

It would appear, based on extensive clinical experience, that drooling, amongst other symptoms, has a negative effect on the social interaction of a CP individual.

3.4. Prevalence of Drooling

The prevalence rate for drooling in children with operculum syndrome is 100%. A diagnosis of operculum syndrome can only be made if significant drooling is present (Christen et al, 2000). The actual prevalence rate for drooling in the CP population is unknown. Ten to 37% of CP persons world wide are reported to have difficulty with drooling. Ten percent of Swedish children, 37% of Belgian children, and 13% of Indian children with CP have severe drooling. However, drooling is not related to any particular ethnic background (Mathur et al, 2006). The variation in percentages of drooling therefore is due to the use of different measurement tools. At present there is no universal measurement of drooling. Severe drooling is estimated to be present in 10-15% of children born with CP (Brodsky, 2002). Meningaud et al (2006) consider drooling to be a relatively common clinical sign and provide evidence for this statement by quoting the Oxford Feeding Study (Sullivan, Lambert, Rose, Ford-Adams, Johnson & Griffiths, 2000) which estimates that 28% of children with neurological impairments suffer from continuous drooling.

In 2003, Tahmassebi and Curzon investigated the prevalence of drooling in children with CP who attended special schools. Their results showed that 93 of the 160 children (58%) had a drooling condition and of these 53 (33%) had severe drooling. They also looked at the prevalence rates in relation to the maturation of the child's oral-musculature. In other words, they compared the prevalence of drooling in different dental age groups. They hypothesized there would be no difference in drooling prevalence between the CP children in different dental age groups. However, they found that drooling decreased as the child's dental age increased. They concluded that any invasive treatment to reduce drooling should

be postponed until the child's oral-musculature has matured. This conclusion has repercussions for the management of drooling in CP children. It must be mentioned, however, that the invasive treatment they were referring to was surgery. As the participants in the DTP were not going for surgery, but rather Botox® injections, it was decided to include some children whose oral-musculature was not fully matured.

Prevalence rates for drooling in South African CP children are unknown at this stage, but one would estimate them to be quite high, as large sections of the CP population live in rural areas or informal settlements, and do not have access to therapeutic or medical services. Based on clinical experience, in one LSEN school in Gauteng, 50% of the learners are diagnosed with CP and of those 20% drool.

3.5. Techniques to Measure Drooling

An accurate evaluation of drooling is difficult because of variations between individuals, but also because drooling fluctuates throughout the day and between activities. Several systems have been devised and used by authors, either in isolation or in combination. Measurement can be objective and quantitative or subjective and qualitative.

a). Objective, Quantitative Measures

Salivary duct cannulation is considered the gold standard for drool measurement (Suskind & Tilton, 2002). The drool quantification system developed by Sochaniwskyj (1982) consists of a head bonnet, a saliva collection cup, a collection chamber with calibrated test tubes and a vacuum pump. Technetium scanning has also been used to assess salivary flow (Lal & Hotaling, 2006). These methods are primarily used for research purposes and were considered unsuitable for use in the clinical setting of the DTP.

Roll saturation and weighing dental rolls which have been placed in the oral cavity have also been used. These methods are considered non-invasive for

measuring drool and have been used in a number of studies (Jongerius, van den Hoogen et al, 2004; Hassin-Baer, Scheuer, Buchman, Jacobson & Ben-Zeev, 2005). However, Suskind and Tilton (2002) found that their patients either continually gagged or tried to swallow the rolls. Some authors have used weighing the saliva collected on a dental bib (Banerjee et al, 2006). These methods were also considered impractical for use in the clinical setting of the DTP.

The Drooling Quotient (DQ) is a validated, semi-quantitative direct observational method developed by Rapp (1980). Drooling is scored during two periods of 10 minutes separated by a 60-minute break. Every 15 seconds (40 observations in 10 minutes) the presence or absence of drooling is assessed. Drooling is defined as new saliva on the lip margin or dropping from the chin. The DQ is expressed as a ratio of the observed drooling episodes divided by the total number of observations. Although this is a validated method it was felt that it would be too disruptive to the children's school day to use this method in the five different situations that were being investigated in the DTP.

Counting the number of bibs changed in a day, despite being an objective quantitative measure, relies on teacher or parent observation and their judgements as to when a bib is sufficiently soaked to require changing. As only 4 children wore bibs or scarves at the time of the DTP, this method was only used as part of the descriptive analysis applied to the parental perceptions on drooling.

b). Subjective, Qualitative Measures

A variety of subjective scales have been developed. One of the initial scales was developed by Wilkie and Brody (1977) to classify the results of surgical drooling procedures:

- Excellent – normal salivary control
- Good – slight loss of saliva with or without dried froth on the lips
- Fair – improved, but with significant residual saliva loss or with thickened, offensive, brown, gummy froth

- Poor i failure to control saliva or too dry

The Visual Analogue scale (VAS), a semi-quantitative scale, is usually given to parents/primary caregivers. Scales of exactly 10 cm without visible subdivisions, on which the average degree of drooling is marked, are given. Ten means severe drooling and 0 means no drooling. An independent person then scores the VAS with a ruler in millimetres, resulting in a number ranging from 0 to 100 (Jongerius, van den Hoogen et al, 2004).

Jongerius, van den Hoogen et al (2004) used The Teacher Drooling Score (TDS), which is a subjective expression on an ordinal scale. As can be seen from Figure 3.5.1 this scale does not separate severity and frequency of drooling and therefore was not considered sensitive enough for the purposes of the DTP.

1-----	No drooling
2-----	Infrequent drooling; small amount
3-----	Occasional drooling; intermittent all day
4-----	Frequent drooling but not profuse
5-----	Constant drooling; always wet

Figure 3.5.1: The Teacher Drooling Score (Jongerius, van den Hoogen et al, 2004)

The Drooling Severity and Frequency rating scales are a qualitative, questionnaire based scoring system, originally developed by Thomas-Stonell and Greenberg (1988). They are a validated method of assessing drooling severity and frequency and have been used by a number of authors (Banerjee et al, 2006; Wong, Sun & Wong, 2001). In addition, they are presently used by The Saliva Control Clinic at The Royal Children's Hospital, Melbourne, Australia (Saliva Control in Children, retrieved June 2007).

Although a subjective qualitative measure it allows one to separate severity and frequency scores, has descriptions as to what each score means, as can be seen from Figure 3.5.2, and is relatively quick to administer. This last factor was considered to be important in the clinical setting of the school, as each child in the DTP had to be assessed in five different situations at baseline, 8 weeks post treatment and 24-26 weeks post treatment. Parents/primary caregivers were also asked to assess their child's drooling in the five different situations and at the same time intervals. It was felt that the severity and frequency rating scales would be easy and appropriate for them to use.

Frequency Scale:	
1-----	Never drools
2-----	Occasionally (not every day)
3-----	Frequently (part of every day)
4-----	Constantly
Severity Scale:	
1-----	Dry (never drools)
2-----	Mild (only wet lips)
3-----	Moderate (wet on lips and chin)
4-----	Severe (drool extends to wet clothes)
5-----	Profuse (drool extends to wet hands, tray and objects)

Figure 3.5.2: Drooling Frequency and Severity Scales (Thomas-Stonell & Greenberg, 1988)

Perhaps the most important factor in the choice of this measure was the fact that it is a qualitative measure and the aims of the DTP were to establish whether there would be a **visible** decrease in drooling in representative daily situations, not just a reduction in saliva production rate. In addition, if there was a **visible** decrease in drooling, would the children's and the parents/primary caregivers' qualities of life have improved.

An additional subjective measure is the Drooling Impact Scale. Although used previously in the Saliva Control Clinic at The Royal Children's Hospital, Melbourne, Australia for parents/primary caregivers to assess their children's drooling, in 2008 it was used in a randomized controlled study of children's drooling. It consists of 10 questions that are rated between 1 and 10 on a semantic differential scale. The maximum possible total for the scale is 100 (Reid et al, 2008).

Reid et al (2008) comment that objective measures may be invasive, unsuitable and sometimes inaccurate and that the main aim of reducing drooling is to improve quality of life.

3.6. Management Options

In the last 20 years there have been many approaches to alleviate the problem of drooling in the neurologically impaired population. One aspect of treatment is agreed upon by everyone working in the field. A multi-disciplinary team approach must be used (Brodsky, 2002; Crysdale, McCann, Roske, Joseph, Semenuk & Chait, 2006; Faulconbridge, Tranter, Moffat & Green, 2001; Hockstein et al, 2004; Lal & Hotaling, 2006; Meningaud et al, 2006).

A team may comprise the following members: dentist/orthodontist who assesses and treats dental and oral diseases and malocclusion; otolaryngologist/ENT surgeon who medically evaluates the child, paying particular attention to the oral cavity and structural problems encountered in the upper aerodigestive tract and who may perform surgery; plastic surgeon who may also perform surgery; social worker who offers education and counselling; occupational therapist and/or speech, language and hearing therapist who assesses the oral-motor function and swallowing skills of the child.

The speech, language and hearing therapist may obtain information regarding previous management and assess the attitudes of the parents/primary caregivers, teachers and child. In addition she/he assesses the frequency and severity of

drooling, the presence of odour, skin changes, body posture and head position (Brodsky, 2002; Crysdale et al, 2006). In South Africa, it has been my experience that the speech, language and hearing therapist provides information to the parents/primary caregivers regarding the possible options of treatment for drooling and then refers to the relevant specialist.

Once all available information has been gathered, team recommendations should be made. Treatment should progress from least invasive to most invasive, and should be safe, cost-effective, side effects should be minimal and it should have no permanent adverse consequences, even if it is successful (Brodsky, 2002; Lal & Hotaling, 2006).

3.7. Treatment Strategies

a). The first strategy is no treatment. This is the treatment of choice if there is minimal drooling or parents/caregivers perceive drooling as a low priority, children are under the age of five to six years, or in adults with unstable neurological function, following an acquired neurological deficit, In addition, where aspiration is a significant concern or other airway problems exist, no treatment may be the wisest choice (Brodsky, 2002; Crysdale et al, 2006).

b). Control of certain situational factors may lead to a reduction in drooling: improving head control, seating and/or positioning; correction of dental problems; improving oral hygiene and promoting healthy dentition; orthodontic care to permit closure of the mouth; removal of adenoids and tonsils that are enlarged; and the replacement or removal, if possible, of medication that increases drooling, can all help to reduce drooling (Brodsky, 2002; Crysdale et al, 2006; Winstock, 2005).

c). Behaviour modification strategies include activities designed to increase the child's awareness of drooling. Verbal and/or gestured reminders to close the mouth and swallow, together with praise for the child's efforts are often used. Building an awareness of the language concepts "wet" and "dry", "open" and

closed can also be of help (Morris & Klein, 2000). Biofeedback and automatic cueing techniques use timed auditory stimuli to remind the client to swallow or wipe the saliva. Usually these techniques are applicable to a small number of clients, those who are highly motivated, have good cognition and only mild to moderate drooling (Brotsky, 2002; Lal & Hotaling, 2006; Meningaud et al, 2006; Winstock, 2005). Hockstein et al (2004) feel that patients eventually become used to the stimulus or forget to wear the cue-producing device.

For South Africans automatic cueing devices are expensive as they must be imported from overseas. Therefore their use is limited. The participants in the DTP had all received training in behavioural modification strategies, prior to their inclusion in the project. However, success was minimal. This was most probably due to limited motivation, limited cognition and poor carry-over into the home situation. This last fact is a reality in South Africa. Most of the parents/primary caregivers of the children were in the low socio-economic sector, had to work long hours and often had to travel large distances to get to work and home. As Saloojee et al comment (2006, p. 234) "the sense of despair and hopelessness felt by caregivers of more severely disabled children was unmistakable." In these circumstances it is not surprising that parents/primary caregivers do not consider it a priority to remind their child to swallow, to keep his/her mouth closed, or to wipe the chin.

Several orthodontic appliances have been used to treat drooling. Customized plates formed to fit the palate, used in conjunction with oral-motor treatment, can aid in better lip closure, developing jaw stability, increased oral awareness leading to increased oral-motor activity and increased frequency of swallowing. Palatal training appliances (PTA's) have been described in the literature by Limbrock, Hayer & Scheying (1990). The plate has the advantage of lowering the hard palate thereby improving tongue-palate contact (Hockstein et al, 2004; Meningaud et al, 2006; Winstock, 2005). PTA's should not be used with children under the age of six, as their dentition is not usually mature enough to be able to wear a PTA (Faulconbridge et al, 2001).

One child in the DTP had an orthodontic appliance fitted to correct the alignment of her teeth, thereby improving lip closure. At the time of the DTP she had worn the appliance for nearly two years and little improvement in her drooling had been noticed. It must be mentioned that the specialist involved had donated his time and the appliance was paid for by donations, illustrating once again that for the majority of South Africans treatments for drooling are not within their budgets.

A small prospective Chinese study, involving 10 children who drooled, found that the use of acupuncture subjectively improved drooling in seven of the children (Wong, Sun, & Wong, 2001). As far as I know acupuncture has not been used in South Africa to treat drooling.

d). Compensatory strategies help those in the child's environment cope better with the drooling, although they do not reduce the amount of saliva falling from the mouth. They may include providing information to the parent/primary caregiver on the use of bibs, scarves, specialized super-absorbent material from which clothes can be made, terrycloth wristbands for wiping, deodorant sprays to help reduce the odour from drooling, barrier creams applied to the chin to prevent the skin from chapping, specially designed pillows that prevent the child from sleeping in a pool of saliva, and the use of a slanted work surface to minimize the use of a head forward posture (Allaire, 1999; Crysdale et al, 2006). Most children who drool at the LSEN school in Gauteng now use bibs, scarves or wristbands to minimize the effects of their drooling, as well as using slanted work surfaces.

e). Oral i motor therapy is the realm of the speech, language and hearing therapist, occupational therapist and physiotherapist. They often work together, using a NDT approach, to normalize muscle tone, improve sensory awareness on the face and within the mouth, improve positioning of the patient, improve biomechanical alignment of the body, and improve head and trunk control. (Allaire, 1999; Morris & Klein, 2000).

Oral-motor therapy is intended to increase coordinated muscle function in the oral cavity and to improve swallowing and control of secretions. It is considered to be

the first line of action for persons who drool and is usually started at an early age (Brotsky, 2002). Lal and Hotaling (2006, p. 382) contend that ñoral motor training is the keystone of non-surgical intervention and a minimum of a six month trial is indicated before other therapeutic options.ò

According to Rosenfeld-Johnson (2002), four variables in the oral-motor function form the basis for the control of drooling.

- Body Posture: Stability in the body allows for mobility in the mouth.
- Sensory Awareness: Hyposensitivity in the oral area is a primary cause of drooling.
- Lip Closure: Lip closure is achieved when there is jaw stability and dissociation between lips and jaw. Nasal breathing is essential, as mouth breathing inhibits lip closure.
- Saliva Retraction: Saliva must be retracted back over the tongue to position it for effective swallowing. A tongue thrust or reverse suckle swallow make it difficult for saliva to be retracted.

Rosenfeld-Johnson (2002) advocates working on all four areas to improve drooling. Exercises using bite blocks, tongue depressors, horn blowing exercises, bubble blowing exercises, button-pull exercises, and straw drinking exercises all form part of her Drooling Remediation Programme (Rosenfeld-Johnson, 2002).

This programme has been used with some success at the LSEN School in Gauteng to improve the oral-motor functioning of the children. However, sustained significant improvement in the children's drooling has not been achieved. This finding corroborates with the following conclusions: Hockstein et al (2004) comment that a feeding programme, aimed at improving oral motor control, is rarely successful in treating drooling problems; Suskind and Tilton (2002) state that numerous therapies, including oral motor therapy, have been advocated to reduce drooling, but none has produced optimal results.

f). Pharmacologic treatment has been used by several researchers to decrease drooling in the neurologically impaired population. As salivation is under

parasympathetic control, anti-cholinergic medications have an inhibitory effect on salivary flow (Tuchman & Walter, 1994). Camp-Bruno, Winsburg, Green-Parsons and Abrams (1989) used benztropine and found a significant reduction in drooling. However, there was only a short follow up time to assess any possible side effects of the drug.

Transdermal scopolamine, applied as patches, has been shown to be of use in the short term (Siegel & Klingbeil, 1991; Jongerius, van den Hoogen et al, 2004). The side effects from the use of anti-cholinergic medications can be numerous and often cause non-compliance and cessation of treatment. Such side effects include: overly dry mouth; constipation; blurred vision; urinary retention; confusion; and even toxic psychosis (Brodsky, 2002; Lal & Hotaling, 2006).

The use of drugs is often contraindicated, for example, when there is a history of cardiac problems. Drug interactions with other medications must also be considered. Despite the negative aspects of oral medications, Blasco (2003, p.845) feels it is "the best option at this point." Several drugs are available in South Africa, but their use is limited by their expense.

g). Surgery is the most invasive approach to drooling and is usually deferred until after six years of age. It is recommended for patients with profuse and constant drooling and those with severe cognitive impairment. It is also recommended for those who continue to have severe drooling despite appropriate non-surgical therapy (Crysdale et al, 2006; Lal & Hotaling, 2006). Since the 1960s many procedures have been described as treatments for drooling. Table 3.7.1 describes the various surgical procedures but more importantly indicates the disadvantages of each procedure.

Several procedures have been used in South Africa, but their use is limited.

Table 3.7.1: Surgical Options for Drooling (Based on Brodsky, 2002; Meningaud et al, 2006)

Procedure	Reference	Rationale	Efficacy	Advantages	Disadvantages
Parotid duct transposition	Wilkie, 1967	Redirect saliva from parotid gland to posterior oral cavity	80%	Redirects flow in stimulated state	Duct stenosis, potential for aspiration
Tympanic neurectomy	Friedman & Kaplan, 1975	Disrupts parasympathetic innervation to parotid gland	47-100% short term	Technically easy	Possible caries, middle ear surgery, return of salivary function, possible hearing loss
Chorda tympani section	Parisier, Blitzler, Binder, Friedman & Marovitz, 1978	Disrupts parasympathetic innervation to sublingual & submandibular glands	47-100% short term	Technically easy	Loss of taste, possible caries, middle ear surgery
Parotid duct ligation	Dundas & Peterson, 1979	Eliminate salivary flow from parotid gland	80%	Simple procedure, successful	Loss of saliva with possible caries, risk of sialocele
Submandibular (Wharton's) duct relocation	Crysdale & White, 1989	Redirect saliva to posterior oral cavity for swallowing by reflex control	80-100%	Highly successful, technically easy, physiologically acceptable	Possible ranula, intra-oral dissection
Submandibular gland excision	Rosen, Komisar, Ophir & Marshak, 1990	Almost always done in conjunction with parotid duct ligation/transposition	86%	Eliminates 50% of total salivary secretion	External incisions, loss of saliva with possible caries

h). Meningaud et al (2006) reported on a study that used laser photocoagulation to partially destroy the parotid glands and occlude the parotid ducts. Significant improvement in drooling severity and frequency was measured in the majority of cases. However, transient facial swelling was noted in all patients (Chang & Wong, 2001, in Meningaud et al, 2006).

i). The use of botulinum toxin to reduce drooling has been the subject of numerous studies since 1999. Although still in the early stages of use, and studies to date have included relatively small groups of participants, the outcomes have been favourable, with rare reports of serious complications (Meningaud et al, 2006). The use of Botox® to control drooling appears to fit in the scale of treatment options between pharmacotherapy and surgery. This is especially true when used with children, as at this stage general anaesthetic seems warranted in the administration of Botox® with children. The history of Botox®, together with a description of the pharmacology of botulinum toxins follows. A detailed critique of the studies using Botox® to control drooling in children is also given.

3.8. Botulinum Toxin Type A: Botox®

Historical Perspective

Botulinum toxin, the most potent poison known, is a neurotoxin, which has often been feared as a possible biological weapon (Arnon, 2001, in Jankovic, 2004). In 1817 Justinus Kerner, a German poet and physician, provided the first account of food borne botulism. From this outbreak, he recognized the potential of the toxin as a therapeutic agent. He noticed that the toxin paralyzed skeletal muscles and parasympathetic function. Kerner hypothesized that the toxic substance causing botulism could be helpful in treating hypersalivation, as severe dry mouth was one of the first manifestations of botulism (Erbguth, 2004).

It was not until 1949 that Burgen, Dickens and Zatman (in Jankovic & Brin, 2002) discovered that botulinum toxin blocks neuromuscular transmission. This discovery laid the foundation for the development of the toxin into a therapeutic

tool. According to Jankovic and Brin (2002, p. 100) the use of botulinum toxin represents one of the most dramatic role reversals in modern medicine: a potential evil transformed into a health benefit.

In 1973 Dr Alan Scott used botulinum toxin type A to treat strabismus in non-human primates. By 1980 he reported on its use to treat strabismus in humans (Scott, 1980). Since then botulinum toxin has been used to treat a large number of neurological and non-neurological disorders.

In 1989, after extensive laboratory and clinical testing of botulinum toxin type A (Botox®, Allergan Inc, Irvine, California, USA) the Food and Drug Administration (FDA) approved it as a therapeutic agent in patients with strabismus, blepharospasm and other facial nerve disorders, including hemifacial spasm. In 2000 the FDA approved Botox® and botulinum type B (Myobloc, Elan Pharmaceuticals Inc, Morristown, New Jersey, USA) as treatments for cervical dystonia and Botox® cosmetic for the treatment of glabellar (frown) lines (Jankovic, 2004).

Pharmacology of Botulinum Toxins

The botulinum toxins work by inhibiting the release of the neurotransmitter, acetylcholine, at the neuromuscular junction thus causing muscle relaxation. Acetylcholine is also the neurotransmitter in postganglionic fibres of the parasympathetic division of the autonomic nervous system. These fibres innervate various glands, such as the salivary glands (Aoki & Guyer, 2001; Jankovic & Brin, 2002). By inhibiting the release of acetylcholine at the neuroglandular junction, a temporary salivary flow rate reduction can be achieved (Jongorius, Rotteveel, van Limbeek, Gabreëls, van Hulst, & van den Hoogen, 2004).

Strains of *Clostridium botulinum* produce seven immunologically distinct toxins designated A to G. All these neurotoxins are proteins of similar molecular structure and weight. Most types are bound by enzymes and form potent di-chain molecules

which consist of a heavy chain joined to a light chain by a disulphide bond. The action of botulinum toxin involves a four step process:

1. serotype specific binding by the heavy chains to acceptors on the presynaptic membrane of cholinergic nerve endings;
2. the toxin complex is internalised by endocytosis;
3. once internalised and within a vesicle, the light chain translocates across the vesicle membrane and is released into the neuronal cytoplasm;
4. the light chain cleaves various components of SNARE, including SNAP-25, and thus prevents the fusion of the acetylcholine synaptic vesicle with the plasma membrane. This blocks the release of the neurotransmitter, acetylcholine, into the synaptic cleft, causing local chemodenervation (Glickman and Deane, 2001; Jankovic, 2004).

SNARE, (soluble NSF, N-ethyl maleimide-sensitive factor, attachment receptors, and proteins essential for regulated exocytosis) is the complex of proteins that is involved in the regulated fusion of the synaptic vesicle with the plasma membrane. The complex consists of the following proteins; synaptobrevin, syntaxin and SNAP-25. The light chains of botulinum toxin A and E cleave SNAP-25, but at different sites; the light chains of botulinum toxin B, D and F cleave synaptobrevin and type C cleaves both SNAP-25 and syntaxin (Glickman and Deane, 2001; Jankovic, 2004; Lim, Mace, Reza Nouraei, & Sandhu, 2006). So far, types A and B have been studied and used the most.

Different commercial preparations have unique properties that account for different potencies and clinical effects. Potency of a product is determined through in vivo mouse essays. One unit (U) of botulinum toxin is defined as the amount of toxin, administered intraperitoneally, needed to kill 50% of a group of 18-20 gram female Swiss-Webster mice. This unit is referred to as a mouse unit or a Unit. As numerous factors influence the clinical potency of a preparation, units are neither clinically equivalent nor interchangeable between products. Different preparations require different doses to achieve similar clinical effects. Therefore it is of vital importance that the specific product used is noted (Jankovic, 2004; Jankovic & Brin, 2002).

In a small cohort of patients who received repeat botulinum toxin treatments for various movement disorders, there was a lack of response to subsequent treatments. This is thought to be as a result of the development of blocking antibodies. The presence of these antibodies means that the patient will no longer respond to the serotype that induced the antibodies (Jankovic, 2004). To minimize immunoresistance, preparations of botulinum toxin with the lowest antigenicity should be used, such as the current Botox®; the smallest possible effective dose should be used; the interval between treatments should be extended as long as possible; and the use of booster injections should be avoided (Jankovic, 2004; Jankovic & Brin, 2002). Barnes, Best, Kidd, Roberts, Stark, Weeks and Whitaker (2005) investigated using botulinum toxin type B on patients with cervical dystonia who had become unresponsive to botulinum toxin type A. The overall responses to botulinum toxin type B were disappointing. Jankovic's comment (2004, p. 955) that "because of epitope homology between various serotypes, the cross reactivity may result in immuno-resistance to the alternate serotype" may explain the disappointing results.

There has been only one case study reporting on the failed response to repeated botulinum toxin type B injections to control drooling (Berweck, Schroeder, Lee, Bigalke & Heinen, 2007). After three successful treatments, no clinical response was shown to subsequent treatments. It was postulated that this secondary non-response was associated with the formation of neutralizing antibodies against botulinum toxin type B.

Several authors have hypothesized that atrophy of the injected salivary glands may be induced due to long lasting denervation of the salivary glands, (Jongorius, van Hulst, van den Hoogen, & Rotteveel, 2005; Kim, Lee, Weiner, Kaye, Cahill & Yudkoff, 2006). Although atrophy of the prostate gland in rats has been shown to occur following Botox® injections (Doggweiler, Zermann, Ishigooka & Schmidt, 1998) this result has not been found with Botox® injections to the rat submandibular gland. Moreover it was observed that the Botox® injection did not have a direct effect on the cells in the submandibular gland, but it did cause a homogenic shrinking in gland size without atrophy and no change in

vascularization (Coskun, Savk, Cicek, Basak, Basak & Dadas, 2007). This finding is of interest in relation to the theory that locally injected Botox® has a central effect (Currà, Trompetto, Abbruzzese & Berardelli, 2004). Perhaps as there is no change in the blood supply to the submandibular gland, Botox® is transported to the brain via the blood supply.

3.9. Clinical Use of Botox® with Specific Reference to the Fields of Speech Pathology and Audiology

The use of Botox® as a therapeutic agent has dramatically increased over the last two decades. Few therapeutic agents have been better understood in terms of how they work or have had a greater beneficial impact on patients's functioning than Botox®. As can be seen from Table 3.9.1, Botox® has been most widely used in the treatment of disorders manifested by abnormal, excessive or inappropriate muscle contractions, but its use has rapidly expanded to include the treatment of a variety of ophthalmologic, gastrointestinal, urological, orthopaedic, dermatological, secretory, pain management and cosmetic disorders (Brin, Hallett & Jankovic, 2002). Expansion of the use of Botox® as a therapeutic agent within the speech pathology and audiology areas has also occurred. These areas have been highlighted in Table 3.9.1 by the use of a bold font.

Table 3.9.1: Clinical Applications of Botulinum Toxin (Brin et al, 2002).

Dystonia

Blepharospasm and lid apraxia

Oromandibular-facial-lingual dystonia

Cervical dystonia (torticollis)

Laryngeal dystonia (spasmodic dysphonia)

Limb dystonia

Task specific dystonia (eg. writer's or other occupational cramps)

Other focal/segmental dystonias (primary, secondary)

Other Involuntary Movements**Hemifacial spasm**Limb, head, **voice**, chin **tremor**

Palatal myoclonus

Motor and **phonic tics** (including coprolalia)

Nystagmus and oscillopsia

Myokymia

Inappropriate Muscle Contractions

Spasticity (stroke, cerebral palsy, head injury, multiple sclerosis)

Painful rigidity

Strabismus

Bruxism and **temporo-mandibular joint disorders (tinnitus)****Stuttering**

Chronic tension (muscle contraction) headaches

Lumbosacral strain and back spasm

Myofascial pain syndromes

Achalasia (lower oesophageal sphincter spasm)**Spasm of the inferior constrictor of the pharynx**

Spasm of the sphincter of Oddi

Spastic bladder, detrusor sphincter dyssynergia

Anismus

Vaginismus

Other Applications

Protective ptosis,

Hyperlachrymation

Drooling (sialorrhoea) anterior and posterior

Hyperhidrosis,

Gustatory sweating

Anal fissure,

Constipation,

Obesity (distal stomach)

Cosmetic (wrinkles, brow furrows, frown lines, "crow's feet", platysma lines, facial asymmetry).

Tennis elbow and other sports injuries.

Oromandibular dystonia is manifested by involuntary jaw closure, jaw opening or jaw deviation. It rarely improves with drug treatment and there are no surgical treatments. An injection of Botox® into the masseter and temporalis for jaw closure or into the submental muscle complex and lateral pterygoid muscles for jaw opening can often improve the symptoms. In addition, **temporomandibular joint disorders**, such as tinnitus, **dysarthria** and **chewing difficulties** can be helped (Jankovic, 2004).

Laryngeal dystonia or spasmodic dysphonia is a neurological voice disorder characterized by involuntary adductor or abductor vocal fold spasms during phonation, which result in phonatory breaks. The degree of difficulty in speaking can be variable, but if severe the disease can cause emotional, functional and social effects that significantly reduce the patient's quality of life. A local injection of Botox® into the laryngeal muscles is currently the gold standard of treatment and can produce clinical improvements in speech (Watts, Nye & Whurr, 2006) and measurable improvements in the quality of life (Jankovic, 2004).

Less consistent improvements have been reported with the laryngeal injections for the treatment of **stuttering and voice tremor** (Brin, Stewart & Blitzer, 1994). **Palatal tremor** is a rare hyperkinetic disorder, characterized by high frequency, rhythmic jerks of the soft palate and ear clicks. Botox® injected into the levator veli palatine muscle is an effective treatment for distressing ear clicks (Deuschl, Lohle, Heinen & Lucking, 1991).

Hemifacial spasm is characterized by chronic involuntary and unilateral contractions, involving lower and upper facial muscles. It is usually caused by compression or irritation of the facial nerve by vascular loops at the level of the brain stem. Treatment with Botox® is currently considered the treatment of choice (Jankovic, 2004; Ward, Molenaers, Colosimo & Berardelli, 2006).

Disorders such as **dysphagia** caused by spasm of the cricopharyngeal component of the inferior constrictor of the pharynx, and **achalasia** which is a rare idiopathic

motility disorder of the esophagus, have also been treated successfully with local injections of Botox® (Jankovic, 2004).

3.10. Botox® to Control Drooling

The idea to use botulinum toxin to treat drooling was first suggested by Justinus Kerner, as already discussed. In experimental animals botulinum toxin produced significant reductions in salivary secretion without direct toxicity to the acinar cells (Shaari , Bei-Lian, Biller, Chuang & Sanders, 1998). In the last six to seven years, botulinum toxin has been used to treat drooling in human subjects.

The first study on humans was published by Pal, Calne, Calne and Tsui in 2000. Nine adults with Parkinson's disease were injected with 15-22,5 units of botulinum toxin A (Botox®) into the parotid glands. Approximately 66% of the patients had subjective improvement in drooling. A second report using Botox® was published by Giess, Naumann, Werner, Riemann, Beck, Puls, Reiners and Toyka in 2000. They injected five patients who had amyotrophic lateral sclerosis (ALS) and drooling. 6-20 units of Botox® were injected into each parotid gland. If no clinical response was noted within two weeks, injections were repeated. Submandibular glands were only injected if parotid gland injections were not effective. After four weeks there was a pronounced reduction in the number of handkerchiefs used per day. Porta, Gamba, Bertacchi and Vaj (2001) demonstrated that the efficacy of Botox® was increased if the submandibular gland was also injected and the site of injection was guided by ultrasound.

In these early open-label studies, the amount of Botox® used varied and the exact site of injection was chosen by individual preference. Since 2001, there have been numerous published studies which provided corroborative evidence supporting observations in the early studies (Lal and Hotaling, 2006; Tan, 2006).

More robust evidence came from controlled studies. In a double-blind, placebo-controlled study, Mancini and colleagues (2003) injected into the submandibular and the parotid glands of 20 patients diagnosed with Parkinson's disease, either

with 450 units of Dysport® or 2ml of placebo. No anaesthetic was given, but ultrasound was used. The average secretion of saliva in the Dysport® group was significantly lower than in the placebo group.

In a double-blind, placebo-controlled dose-finding study, Lipp, Trottenberg, Schink, Kupsch and Arnold (2003) injected into the parotid glands of 32 patients, age unspecified, and diagnosed with a variety of neuromuscular disorders. No anaesthetic was given and ultrasound guidance was not used. Patients were randomized into 4 groups, placebo, 18.75 units, 37.5 units or 75 units of Dysport®. Although 12 out of 18 Dysport® treated patients reported less drooling, only patients treated with the highest dose showed statistically significant improvement over placebo treated patients.

Researchers also tested the efficacy of using Botox® in neurologically impaired children. Suskind and Tilton (2002) injected 22 subjects, diagnosed with cerebral palsy and significant drooling, aged between 8-21 years. Subjects were divided into two groups. Group 1 received injections of 10, 20 or 30 units in escalating doses into the submandibular glands. Group 2 received injections of 30 units into the submandibular glands and 20, 30 or 40 units into the parotid glands. Although this was a dose escalation study, there was no comment on the optimum dosage within the groups.

Jongerius, van den Hoogen et al (2004) conducted a controlled clinical trial with single injections of Botox® into the submandibular glands and compared it with scopolamine treatment in 45 school-aged children diagnosed with cerebral palsy. The injections were performed under general anaesthetic with ultrasound guidance and dosages were based on the child's weight. The mean decrease in salivary flow was 25% during scopolamine and 42% following the Botox® injection. In addition, fewer and less serious side effects were noted with the Botox® injection.

Some researchers feel that the use of botulinum toxin type A is a minimally invasive, effective and potentially safe treatment for drooling and has the potential to become the treatment of choice for sialorrhoea (Lim, Mace, Reza Nouraei, and

Sandhu, 2006, p. 272.). Tan (2006, p. 63.) feels that botulinum toxin holds ñgreat promise for the treatment of patients suffering from sialorrhea.ò Table 3.10.1, based on Lim et al (2006), Meningaud et al (2006) and Tan (2006), illustrates the studies that have used botulinum toxin type A to treat drooling in cerebral palsied children. As can be seen in this table, a variety of outcomes measures have been used. As discussed in the previous section on measurement techniques for drooling, there is no universally accepted measurement of drooling. Consequently we are unable to compare results between the different studies.

Table 3.10.1: Studies that have Used Botulinum Toxin Type A to Treat Drooling in Children.

Study	Design	No. of Subjects	Age Range (years)	BTX/A Dose (mouse unit -U) in each gland	Glands Injected	Outcomes Measures	Results of Outcome Measures	Side Effects
Jongerius, Rotteveel, van den Hoogen, Joosten, van Hulst & Gabreels (2001)	Case series	3	11,13,13	15,20 & 25	Submandibular	Salivary flow rate. Q of L questionnaire	↓ salivary flow rate at 2 to 16 weeks. All parents expressed satisfaction with ↓ in drooling.	Mild transient thickening of saliva in 1 subject
Suskind & Tilton (2002)	Open labelled study	22	8-21	20-40 10-30	Parotid Submandibular	DQ Q of L questionnaire	↓ drooling in 8 subjects at 2 weeks	None
Bothwell, Clarke, Dooley, Gordon, Anderson, Wood, Camfield, & Camfield, (2002)	Open labelled study	9	4-17	5	Parotid	Weight of saliva. Freq. of drooling	↓ in drooling freq. at week 4. 8 subjects had ↓ in saliva weight.	No serious side effects
Ellies, Rohrbach-Volland, Arglebe, Wilken, Laskawi & Hanefeld, (2002)	Case series	5	None given	50-65 U in total on both sides	Parotid and Submandibular	Clinical impression of drooling sev. Saliva flow rate	Distinct improvement in drooling. Reduced flow rate of saliva	None

Key: No.- Number; BTX/A- Botox®; QoL- Quality of Life; ↓- Decrease; DQ- Drooling Quotient; Freq.- Frequency; Sev.- Severity.

Table 3.10.1 continued: Studies that have Used Botulinum Toxin Type A to Treat Drooling in Children.

Study	Design	No. of Subjects	Age Range (years)	BTX/A Dose (mouse unit -U) in each gland	Glands Injected	Outcomes Measures	Results of Outcome Measures	Side Effects
Jongerius, van den Hoogen et al (2004)	Control led clinical trial	45	3-18	15,20 & 25	Submandibular	DQ,VAS,TDS	Statistical ↓ drooling at 2 to 24 weeks	Temp. difficulty in swallowing for 2 subjects
Savarese, Diamond, Elovic & Millis (2004)	Open labelled study	21	5-18	15	Parotid	VAS, bibs/scarves used, saliva production	Statistical ↓ drooling at 4 to 8 weeks	None
Hassin-Baer et al (2005)	Open labelled study	9	6-18	10-25	Parotid	Roll saturation Drooling sev. & freq. rating scales	Statistical ↓ in saliva prod. in 7 subjects. Subjective ↓ drooling in 3 subjects.	None
Jongerius, van Hulst et al (2005)	Case report	1	9	25	Submandibular	Roll saturation, DQ,VAS, TDS For posterior and anterior drooling	↓ saliva prod. ↓ posterior drooling, ↓ pneumonia, gagging, coughing. ↓ anterior drooling.	None

Key: No- Number; BTX/A- Botox®; ↓- Decrease; DQ.- Drooling Quotient; VAS- Visual Analogue Scale; TDS- Teacher Drooling Score.
Temp.- Temporary; Sev.- Severity; Freq.- Frequency.

Table 3.10.1 continued: Studies that have Used Botulinum Toxin Type A to Treat Drooling in Children.

Study	Design	No. of Subjects	Age Range (years)	BTX/A Dose (mouse unit -U) in each gland	Glands Injected	Outcomes Measures	Results of Outcome Measures	Side Effects
Banerjee et al (2006)	Open labelled study	20	6-16	1.4U/kg weight 0.6U/kg weight	Parotid and Submandibular	Drooling sev. & freq. DQ. Weight of saliva on dental bib. Bibs/scarves used. Qof L scores.	Statistical $\bar{Z}$ in no.of bibs. Statistical $\bar{Z}$ drooling sev. & freq. Statistical improvement in Q of L scores, 4-12 weeks.	None
Kim et al (2006)	Case series	2	3 6	1U/kg weight 1U/kg weight	Submandibular Submandibular	Suctioning of saliva Pneumonia episodes	$\bar{Z}$ in no. of times of suctioning. $\bar{Z}$ in no. of episodes of pneumonia	None
Reid et al (2008)	Randomized controlled trial	48	6-18	25 or 4U/kg if child weighed less than 25kg.	Parotid And Submandibular	Comparison of drooling impact scale, consisting of 10 questions, rated on a scale of 1-10 by parent/primary caregiver. Shortened version, 3 questions-frequency, severity of drooling and no. of bibs given to treatment group only.	Comparison between treatment and control group scores. $\hat{y}$ in the difference of scores between control and treatment groups. $\bar{Z}$ in drooling impact scale score of treatment group.	Thicker, more viscous saliva in 4 children. $\hat{y}$ difficulty with swallowing food, reluctance to eat dry or hard food, in some families.

Key: No- Number; kg- Kilogram; BTX/A- Botox®; $\bar{Z}$ - Decrease; $\hat{y}$ - Increase; DQ- Drooling Quotient; QoL- Quality of Life; Sev.- Severity; Freq.- Frequency.

As can be seen from Table 3.10.1, comparisons between studies are difficult. Some studies frequently involved small numbers of participants, and thus may have lacked statistical power for meaningful analysis (Bothwell, Clarke, Dooley, Gordon, Anderson, Wood, Camfield, & Camfield, 2002; Ellies, Rohrbach-Volland, Arglebe, Wilken, Laskawi & Hanefeld, 2002; Jongerius, Rotteveel, van den Hoogen, Joosten, van Hulst & Gabreels, 2001; Hassin-Baer et al, 2005).

The amount of Botox® used varied and the exact site of injection was often chosen by individual preference. The relative superiority of injecting the parotid glands and the submandibular glands over injecting just one pair of glands has not been clarified. Different outcomes measures, ranging from visual analogue scales to counting of dental rolls, bibs, to clinical rating scales, such as the one used in the DTP have all been used. As already stated, the use of different outcomes measures makes it difficult to compare the results of drooling reductions between different studies. Whether the use of ultra-sound is worthwhile is still unclear as well.

Some studies did not comment on the reliability of their subjective measures results (Banerjee et al, 2006; Ellies, Rohrbach-Volland, Arglebe, Wilken, Laskawi & Hanefeld, 2002; Hassin-Baer et al, 2005; Savarese, Diamond, Elovic & Millis, 2004). Suskind & Tilton (2002, p. 80) did not explain what they meant by their "best clinical results."

These studies looked at drooling as a whole and did not separate frequency and severity, even though frequency and severity rating scales were used (Banerjee et al, 2006; Hassin-Baer et al, 2005). In a study investigating the severity and frequency of drooling in patients with Parkinson's disease, 52% of patients did not present with an improvement in the frequency of drooling, despite an improvement in severity of drooling. The authors postulated that the lack of improvement in the frequency of drooling could be attributed to a swallowing dysfunction, whereas the improvement in severity of drooling could be attributed to a decrease in the production of saliva (Nobrega, Rodrigues, Torres, Enzo & Melo, 2007).

More importantly none of these studies looked at whether there was an improvement in drooling, following botulinum toxin injection, in different contexts. Banerjee et al (2006), despite injecting the parotid glands, as well as the submandibular glands, did not assess drooling during an eating or drinking activity. This omission seems to me to be a lost opportunity to assess any reduction in drooling that may have occurred during eating and drinking. The same can be said for the Suskind & Tilton (2002) study.

In the study by Jongerius, van den Hoogen et al (2004) drooling assessments were made while the child watched television and during one other activity chosen by the child, which required a higher level of concentration or physical effort. However, they did not separate these results nor compared them to establish if there was a difference in drooling rate during the two activities.

Despite being a randomized controlled trial, with a sufficient number of participants, and a pilot study having been conducted previously, using data on the Drooling Impact Scale from the Saliva Control Clinic, drooling was not assessed during different activities in the study by Reid et al (2008). In fact the scores from the Drooling Impact Scale, provided by the parents/caregivers, were totalled to give an overall numerical rating of the degree and impact of drooling over the course of a week.

3.11. Concluding Remarks

In the previous 3 chapters I have produced a review of the literature on the topic of Botox® to control drooling in neurologically impaired South African children. I have highlighted some methodological challenges in the published literature and have considered treatment options particularly within the South African context. At this stage little is known about the use of Botox® to control drooling in the South African pediatric population. The present study attempts to resolve some of the issues by analyzing the effects of Botox® on drooling within five different daily situations. In addition, the study examines whether Botox® has a different effect on drooling frequency as opposed to drooling severity. The study also

compares the effects of Botox® on drooling in the CP and operculum syndrome participants, as well as comparing the effects on drooling within different types of CP. As mentioned throughout chapter 3, there is no universal measure of drooling, which makes comparisons between studies difficult. I chose the severity and frequency of drooling scale (Thomas-Stonell & Greenberg, 1988) as it was appropriate for use in the clinical setting of the DTP. This study intends to illustrate that this scale is a reliable, quick and relevant scale for South African speech, language and hearing therapists to routinely use in their assessments of neurologically impaired children. I have also discussed in the introductory chapters that drooling has the potential to significantly affect QoL in the pediatric neurologically impaired population. Little is known about this phenomenon in South Africa. Some understanding of the QoL of the participants and their parents/primary caregivers and the effect drooling has on their QoL is obtained from the interview form and the parent/primary caregiver questionnaire. Finally it is hoped that this study provides speech, language and hearing therapists with information that will allow them to make informed decisions when considering the use of Botox® injections to control drooling. Chapter 4 explains the methodology of the present study.

CHAPTER 4

METHODOLOGY

This chapter outlines the aims of the study, provides background information as to where the DTP of 2006 took place and describes the DTP. The research design, data collection methods and data analyses are explained.

4.1. Aims of the Study

This study comprised of an analysis of the clinical data collected during a Drooling Treatment Project (DTP) conducted at a cerebral palsy school in Gauteng. The study's main aim was to determine if Botox®, injected bilaterally into the submandibular salivary glands, had an effect on drooling in nine neurologically impaired children in a number of situations.

Within this main aim, several sub-aims were developed. These sub-aims were to:

1. Ascertain if there was a reduction of drooling in participants in the following situations:
 - **General appearance of the child**
 - **Child participating in a table top activity**
 - **Child eating**
 - **Child drinking**
 - **Child communicating**
2. Compare the effects of Botox® on drooling in the participants with CP and operculum syndrome;
3. Compare the effects of Botox® on drooling within different types of cerebral palsy;
4. Explore relationships between severity of drooling and efficiency of the Botox® injection;
5. Explore the duration of effect of Botox®;

6. To ascertain parents' primary caregivers' perceptions and feelings towards their children's drooling, before and after the injection, and their perceptions towards the Botox® injection.

4.2. The Drooling Treatment Project (DTP)

Context of the DTP and the Present Study

The school where I work is 60 years old this year. It was started by a group of parents who wanted to provide education for their CP children. At present the school caters for 340 learners between the ages of 3 and 18 years. Types of disabilities range from CP, a variety of syndromes, children with Attention Deficit/Hyperactivity Disorder (ADD/ADHD) and severe learning difficulties, epilepsy, partially hearing and sighted children and children with low cognitive development. We even have a child with a cochlear implant. Learners come from a 60km radius around greater Johannesburg, Gauteng, using the school's own transport system, local taxis, and parental transport.

Services offered by the school, besides education by qualified teachers, include: speech, language and hearing therapy; occupational therapy; physiotherapy, - most of the therapists are NDT trained; social work and psychological intervention; skills training and a work experience programme. We also have a qualified nurse who dispenses medication and emergency care, if needed.

Specialized clinics are regularly run and we have the generous, donated services of a neurologist, pediatric neurologist, orthopaedic surgeon, plastic surgeon and an ENT specialist. The Wits dental school also provides dental care for our children.

The Physiotherapy Department runs a very successful Botox® clinic for the lower limb and the Occupational Therapy Department runs the Botox® clinic for the upper limb and hands. The Speech Therapy Department is in the process of establishing a Botox® clinic for drooling. We are exceedingly grateful to all specialists who donate their time and especially to Genop South Africa,

distributors of Botox® for Allergan Ltd, who donate the Botox®. As Botox® is unavailable at governmental hospitals, children who are indigent and not on a medical aid are given the chance to receive Botox®. This school is the only organization to offer this service in South Africa. In addition, the therapy departments provide wheelchairs, specialized seating inserts, low and high technology AAC devices, as well as regular therapy.

The Umsebe Welanga Sunbeam Caregiver training programme is also run at the school. Caregivers from historically disadvantaged centres in rural, semi-urban and urban areas throughout Gauteng come for training provided by the staff of the school.

The DTP of 2006

This project was carried out as a treatment regime, under the supervision of an Ear, Nose and Throat (ENT) Specialist, competent with the procedure of injecting Botox®. Botox® was injected bilaterally into the submandibular glands of the participants, under general anaesthetic, by the ENT Specialist. The submandibular salivary glands were chosen for the site of injection as they produce the majority of saliva, and the production of saliva is not stimulus related, as with the parotid glands (Faulconbridge et al, 2001). In addition, the submandibular secretions are more viscous and it is this thicker saliva that is usually troublesome in drooling (Brodsky, 2002). The ENT Specialist calculated the required dosage, 15 to 25 units per gland, dependent on each child's body weight and guidelines from the Pharmaceutical Company. Ultrasound guidance was not used. According to Lim et al (2006) no added advantage is demonstrated in using ultrasound guidance.

Individual speech, language and hearing therapists working at the above-mentioned school, were asked to provide a list of children who drooled. Parents/primary caregivers were initially contacted telephonically to briefly explain and outline the procedure and to discover if they were interested in their children taking part in the DTP. Any parent/primary caregiver who was interested was then invited to a meeting, held at the school. Present at this meeting were the

children's individual speech, language and hearing therapists, the school nurse, who provided translation into a home language when necessary, any interested parents/primary caregivers and myself. Each parent/primary caregiver was given: an information sheet; detailed verbal explanations, as to what would happen in the treatment procedure; the telephone number of the ENT Specialist who would perform the injections, in case they wanted more information; and an informed consent form, which invited them to be participants. An assent form, specifically for the children to sign, was also given to the parents. As a general anaesthetic was used during the procedure, a consent to anaesthetic form was also given to the parents/primary caregivers.

Parents/primary caregivers were encouraged to discuss the treatment project with their children, before giving their consent. Parents/primary caregivers and children who were willing to be participants returned all the relevant forms. From these parents/primary caregivers and children, the final selection of participants was made. Written consent was obtained for the children to be photographed at different stages of the treatment project, from the parents/primary caregivers and children. This consent also entailed allowing their child's drooling to be rated in a face to face setting by each parent/primary caregiver and three fully qualified neurodevelopmental speech, language and hearing therapists.

A description of what is entailed in neurodevelopmental therapy has been given in chapter 2.

Participants in the DTP were selected from the initial list of children who drooled, using the following criteria:

- Participants of the project were between the ages of 5-17 years, with a mean age of 9,3 years. Drooling has been defined as an abnormality in a child more than four years of age in the awake state (Crysdale, 1989). Crysdale et al (2006) in their report on 30 years of experience in team management of drooling state that treatment of children with cerebral palsy is frequently delayed until the ages of five to six years. The reason for this delay is that drooling can improve spontaneously due to maturation of oral-motor

function. In the operculum syndrome, dysarthria and excessive drooling are part of the distinct clinical picture of suprabulbar (pseudobulbar) palsy. In this condition, an improvement in drooling is not dependent upon oral-motor maturation (Christen et al, 2000). Therefore it was feasible to include the operculum syndrome participant who was five years old.

- Participants had all been diagnosed with neurological impairment by neurologists with special expertise in childhood neurological impairments. Seven participants were diagnosed with different types of cerebral palsy; two participants were diagnosed with operculum syndrome.
- All participants were diagnosed by the three fully qualified neurodevelopmental speech, language and hearing therapists with anterior drooling. The difference between anterior and posterior drooling and any relevance to the present study has been discussed in chapter 3.
- Drooling was present, varying in severity and frequency from mild and occasionally drools to profuse and constantly drools, in all participants (Thomas-Stonell & Greenberg, 1988).
- All participants had to have undergone at least six months of oral-motor therapy (Lal & Hotaling, 2006).
- Prior to the DTP, submandibular salivary glands had to be present in all participants, although one participant had undergone a tympanic neurectomy, five years previously. Drooling had returned to severe and constant in that child.
- Participants had not received Botox® for another indication in the previous six months.
- None of them had a known hypersensitivity to Botox®.
- None of them suffered from systemic diseases such as bronchial asthma or congenital heart failure, or diseases of the neuromuscular junction such as myasthenia gravis. Patients with these types of diseases are extremely sensitive to botulinum toxin and adverse reactions have been recorded (Gioltzoglou, Cordivari, Lee, Hanna & Lees, 2005).
- Participants had variable cognitive abilities, as determined by an educational psychologist.
- No participants were on drugs which control drooling.

4.3. Research Design

The research consisted of two phases.

Phase One

In this phase, a retrospective, explanatory, multiple case study design was used to review the findings of the DTP. According to Schiavetti and Metz (2006, p. 69), the danger in retrospective research can be the lack of validity and reliability of the data. Although not involved specifically with the ratings of the children's drooling, I did have administrative control over the collection of the data in the DTP. This control ensured uniformity of measurement and drooling rating by the three speech, language and hearing therapists (Schiavetti & Metz, 2006, p. 69).

The small number of participants in the DTP allowed each one to be treated as a case study. Case studies are an ideal methodology when a holistic, in-depth investigation is needed. They are designed to bring out the details from the viewpoint of the participants by using multiple sources of data (Tellis, 1997). Baker (1994) contends that effective case studies are used as classic examples of how social research can be performed. Yin (1993) has identified three specific types of case studies: exploratory, explanatory and descriptive. Explanatory case studies can be used in causal investigations, which the DTP could be considered.

Case study is also known as a triangulated research strategy. Denzin (1984, in Tellis, 1997) identified four types of triangulation: data source; theory; methodological triangulation; and investigator triangulation. Investigator triangulation is when several investigators examine the same phenomenon. In the DTP, observations and ratings of the same phenomena were made by parents/primary caregivers and three speech, language and hearing therapists. In the second phase of the study a 'blind' independent rater also examined the same phenomena.

Finally, support for the use of a case study design comes from Blasco (2003, p. 846). He contends that in the final analysis, the best comparison will be a study, probably single subject design, directly comparing these various treatments. The treatments he was referring to were intraglandular botulinum toxin injections and the intra-oral appliance to reduce drooling in the neurologically impaired population.

Phase Two

In phase two of the study, further management and expansion of the clinical data by a blind independent rater were conducted. Cohen's Kappa coefficients (Cohen, 1988) were calculated to assess the reliability/agreement of the data obtained from the three speech, language and hearing therapists in the DTP compared with the data obtained from the blind independent rater.

4.4. Participants

Demographic Information

The participants in the DTP were nine neurologically impaired children, their parents/primary caregivers and the three neurodevelopmentally trained speech, language and hearing therapists. These therapists had many years of experience working with neurologically impaired children. The blind independent rater was also a qualified neurodevelopmental speech, language and hearing therapist, who had previously worked with cerebral palsied children.

In this study the parents were predominantly single mothers. As can be seen from Table 4.4.1, only three participants had fathers actively involved. This aspect of gender in care giving has been referred to in chapter 2 with a discussion of Barratt's study (2007). The primary caregiver in the present study was the grandmother. Some of the single mothers did have support from their mothers, i.e. the child's grandmother. It was also mentioned in chapter 2, that older, black South Africans are often the primary caregivers for their families. This heavy

burden results in a decreased QoL for them and their dependents. It is therefore incumbent on South African health personnel to consider parental/primary caregiver demographics when planning treatment.

All children were classified according to the Gross Motor Functional Classification system, which has been described in chapter 2. The diagnoses, ages, case history and therapy notes are given. Parental/primary caregiver socio-economic statuses and race have been included in the demographics as this information provides support for the comments, discussed in chapter 2, that in South Africa the majority of disabled people are in the lower socio-economic sector and that most are African. Six of the participants were black and all of them were in the low or low to medium bracket. Six participants were males. This fact would appear to correlate with the finding that males produce more saliva than females (Winstock, 2005), implying that in the neurologically impaired population males drool more than females.

Table 4.4.1: Participant Demographics.

Child	Gen.	P/CG	Age (years)	Diagnosis	GMFC	Case History & Therapy Notes	S-E.Status	Race
1	M	Mom/Dad	11	Spastic quadriplegic CP	Level 5	Non-verbal. Oral hypersensitivity, open mouth posture, forward tongue placement, little lateral tongue movement, tongue thrust during swallowing, poor oral sensory awareness.	Medium	White
2	F	Mom	6	Spastic hemiplegic CP	Level 1	Severe dysarthria. Open mouth posture, forward tongue placement, no lateral tongue movements, high tone in lips, poor oral sensory awareness.	Low to medium	Black
3	M	Mom	17	Athetoid CP	Level 1	Mild dysarthria. Open mouth posture, some lateral tongue movement, adequate oral sensory awareness.	Low	Black
4	M	Mom/Dad	6	Athetoid CP	Level 4	Non-verbal. Gastro-esophageal reflux in 2002. Low oral tone, tone increases with activity, open mouth posture, forward tongue placement, little lateral tongue movement, poor oral sensory awareness.	Low to medium	Black
5	M	Mom/Dad	10	Athetoid CP	Level 5	Non-verbal. Mouth breather, enlarged adenoids, previous bout of pneumonia. Fluctuating oral tone, forward tongue placement, no lateral tongue movement, very poor sensory awareness. Poor head control. Low motivational levels.	Medium	Indian
6	M	Mom	5	Ataxic CP	Level 2	Severe dysarthria. Open mouth posture, forward tongue placement, tongue thrust during swallowing, little lateral tongue movement, poor oral sensory awareness. Choked on food when a baby. Low cognitive abilities.	Low	Black
7	F	Mom	16	Ataxic CP	Level 1	Moderate dysarthria. Open mouth posture, some lateral tongue movement, some oral sensory awareness. Tympanic neurectomy 5 years previously. Drooling returned to severe and constant.	Low	Black
8	F	Mom	5	Operculum syndrome	Walker	Severe drooling and dysarthria. Open mouth posture, forward tongue placement, no lateral tongue movement, poor oral sensory awareness.	Low	White
9	M	Granny	8	Operculum syndrome	Walker	Severe drooling and dysarthria. Open mouth posture, forward tongue placement, no lateral tongue movement, poor oral sensory awareness.	Low	Black

Key: Gen ĩ Gender; M ĩ Male; F ĩ Female; P ĩ Parent; CG ĩ Caregiver; CP ĩ Cerebral Palsy; S-E Status ĩ Socio-Economic status;
GMFC ĩ Gross Motor Functional Classification (Palisano et al. 1997).

Sampling Strategy

The children and the parents/primary caregivers could be considered to be a non-probability convenience sample. Dooley (1995) states that convenience sampling is a common non-probability method, which depends on the convenient availability of participants. Generalisations to the wider population cannot be made as information regarding how or if the chosen sample matches the wider population is unavailable. However, it was not possible to use random sampling, due to the nature of the DTP. A matched control group was not used, as selection of a matched control group in the CP population is difficult due to the wide variations in the degree of deficit. Rather each child acted as her/his own control by comparing the data from the pre- and post intervention states (Franklin, Allison and Gorman, 1996; Schiavetti and Metz, 2006, p. 93).

4.5. Ethical Considerations

Ethical clearance to undertake the study was granted by the University Committee for Research using Human Subjects (Appendix A). Permission from the Gauteng Department of Education (GDE) to conduct the study at a GDE school was given (Appendix B). Written permission from the ENT Specialist concerned was also given for me to use all data related to the DTP (Appendix C). Permissions from the Principal of the school (Appendix D), the parents/primary caregivers and the participants (Appendices E & F) were given to allow me to use any or all data from the DTP, including photographs, case history information and rating results. All participants were assured that they could withdraw from the study at any time if they wished to, and feedback was given to parents/primary caregivers by me when this was requested.

4.6. Data Collection

The following data from the DTP was used in the present study. It was collected from the Speech Therapy Department of the school, where it had been kept safely.

Case history information from the children's school files. Factors analyzed included the diagnosis, age and relevant medical histories of the participants. Speech therapy notes made by the three speech, language and hearing therapists at baseline, 8 weeks and 24-26 weeks post Botox® injection were obtained. This information allowed me to consider the causes of drooling in the study participants. It also allowed me to investigate any influence Botox® may have had on oral motor skills and oral sensory processing.

A saliva control assessment form, based on the form used at the Saliva Control Clinic at The Royal Children's Hospital, Melbourne (Saliva Control in Children, 2007), was completed by the parents/primary caregivers before the DTP began (Appendix G). This form required information pertaining to how the parents/primary caregivers viewed their children's communication skills, walking ability, head position, oral motor skills, dental health, general health, and whether there had been any bouts of pneumonia. I was able to compare the information obtained from this form with the information obtained from the speech therapy notes.

Drooling rating scales: The three neurodevelopmental speech, language and hearing therapists used a severity rating scale and a frequency rating scale to assess the participants' drooling (Thomas-Stonell & Greenberg, 1988). The therapists completed the ratings independently, but at the same time. Any discrepancies in ratings were discussed by the therapists and a consensus was reached. I was not involved in the rating of the participants' drooling, thus minimising the problem of experimenter bias or the Rosenthal Effect (Schiaivetti & Metz, 2006, p. 151). Table 4.6.1 explains the different rating scores for drooling severity and drooling frequency used in the DTP.

Table 4.6.1: Rating Scores for Severity and Frequency of Drooling (Thomas-Stonell & Greenberg, 1988)

Severity Rating Scale		Frequency Rating Scale	
Dry ĩ Never drools	1	Never drools	1
Mild ĩ Wet lips only	2	Occasionally drools ĩ not every day	2
Moderate ĩ Wet lips and chin	3	Frequently drools ĩ part of every day	3
Severe ĩ Clothing becomes damp	4	Constantly drools	4
Profuse ĩ Clothing, hands, tray, Table, objects are wet	5		

These drooling rating scales are a subjective outcome measure and have been used by researchers in random controlled trials (Ondo, Hunter & Moore, 2004; Senner et al, 2004; Banerjee et al, 2006) and currently are in use by The Saliva Control Clinic at The Royal Children's Hospital, Melbourne (Saliva Control in Children, 2007). As discussed in chapter 3, these ratings scales were chosen as they provided an unobtrusive means of measuring the participants's drooling. Objective, quantitative measures, such as the weighing of dental rolls soaked in a child's saliva, calculating the drooling quotient, or the cannulation of the salivary ducts, were deemed to be inappropriate for the DTP and impractical in a time-constrained clinical setting. Van der Burg, Jongerius, van Limbeek, van Hulst and Rotteveel (2006a, p. 179) contend that 'a statistically significant change in salivary flow rate does not always necessarily imply a change in drooling severity.' As the aim of the DTP was to establish if any changes in drooling severity or frequency occurred and not changes in salivary flow rates, the drooling rating scales were thought to be appropriate.

The speech, language and hearing therapists made notes as to the body/head posture, tongue placement, jaw stability, lip position and sensory awareness of each child in each situation (Appendix H). The parents/primary caregivers used the same severity and frequency rating scales, but without making any notes (Appendix I).

The rating scales were completed at baseline, 8 weeks and 24-26 weeks post Botox® injection, in the following five different situations and in a face to face setting:

1. **General appearance of the child**
2. **Child participating in a table top activity**
3. **Child eating**
4. **Child drinking**
5. **Child communicating**

The intervals of 8 and 24-26 weeks were chosen as according to Tan (2006) in his review of different studies, the maximum effect for botulinum toxin injections is between 2 to 8 weeks. By 24-26 weeks the effects of the Botox® should be wearing off. As discussed in chapter 3, previous studies have not looked at the effect Botox® may have on drooling in different contexts. In the DTP we wanted to establish if Botox® would have an effect on drooling in different situations. The five different situations were chosen as they represented a cross section of activities that occur throughout a normal day.

Drooling is known to increase during concentrated activity, therefore the **table top activity** was included (Brodsky, 2002). In a stimulated state, such as during eating and drinking, drooling increases because the parotid glands and other salivary glands produce saliva, therefore the **eating and drinking activities** were included (Mathur et al, 2006). The DTP aimed to establish if injecting only the submandibular glands with Botox® would decrease drooling noticeably during eating and drinking, despite the production of saliva by the parotid and other glands. Although saliva is needed when we speak, all the children in the DTP drooled significantly when they spoke, therefore the **communicating activity** was included. Moreover, as speech, language and hearing therapists we are concerned with improving all aspects of communication.

Procedures for Rating Severity and Frequency of Drooling

The procedures for rating the severity and frequency of drooling in the DTP were standardized for each participant. The time of day each participant was assessed and the positioning of each participant in each different situation, across all three time periods were the same. The same routine was used to eliminate extraneous variables. Assessments were completed in the morning, just before and during the tea break, 10am. to 10.30am. In situations 2 to 5, the children were seated at a desk or in their wheelchairs with a lap tray attached. In situation 1, the children were quietly standing or sitting, but not engaged in any activity or talking. Activities in situation 2 included colouring or drawing a picture, for those who had sufficient hand control, and fitting shapes into a post box, using hand over hand manipulation, for those who did not have adequate fine motor control. Oral motor control was used for cup drinking for two participants across the three time periods, as they were unable to drink from a cup independently. Communication was elicited by asking the participants what they had done over the weekend. As accuracy of speech/articulation was not being investigated in the DTP, any vocalization was accepted as communication. Three participants could be considered predominantly non-verbal communicators. They used gestures and picture communication symbols on their communication boards to communicate.

Interview form: Parents/primary caregivers were interviewed, in a face to face setting, at the end of the DTP. The interview aimed to establish parents/primary caregivers' perceptions and feelings towards their children's drooling and the Botox® injection. The social consequences of drooling were also discussed with the parents/primary caregivers. Parents/primary caregivers entered their responses on the interview form (Appendix J).

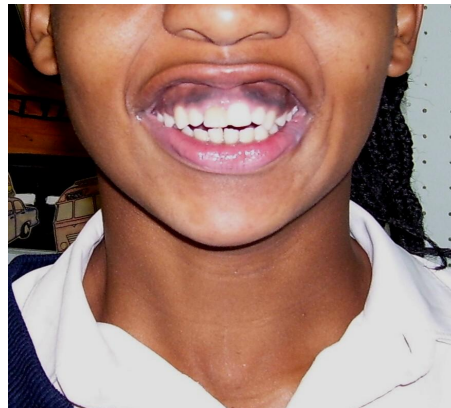
Questionnaire: A quality of life questionnaire, based on the questionnaire used by Van der Burg et al (2006a) was given to parents/primary caregivers at the beginning and again at the end of the DTP. These questionnaires aimed to establish during which time of day parents/primary caregivers thought their children drooled the most and during which activities drooling occurred the most.

Parents/primary caregivers were asked to rate the severity of drooling on the five point severity rating scale. In addition bib use, the number of laundry loads completed in a week, and overall quality of life were investigated (Appendix K).

Digital photographs were taken at every stage of the DTP and during every situation. Photographs were taken of the participants's mouths and were taken in such a way as to prevent identification and were numbered for identification purposes. The amount of drool present was not altered in any way. In other words, participants did not have their mouths wiped, nor were they told to swallow, before a photograph was taken. In many instances the participants were unaware of the exact moment a photograph was taken. These photographs provided a record of treatment effects. In addition they allowed a 'blind' independent rater to rate the treatment effects and thus the reliability of the rating scales could be investigated. Figure 4.6.1 illustrates the edited photographs and the different situations used in the DTP.



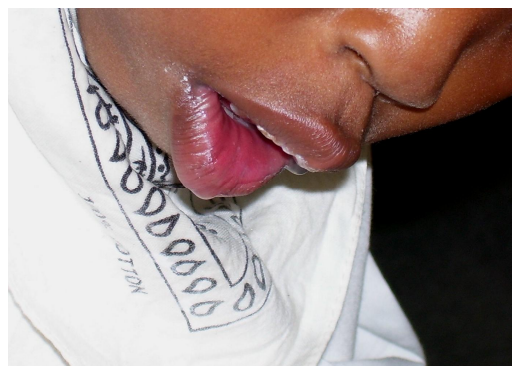
Before: General



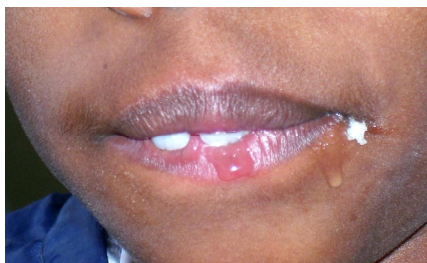
After: General



Before: Table Top Activity



After: Table Top Activity



Before: Eating



After: Eating



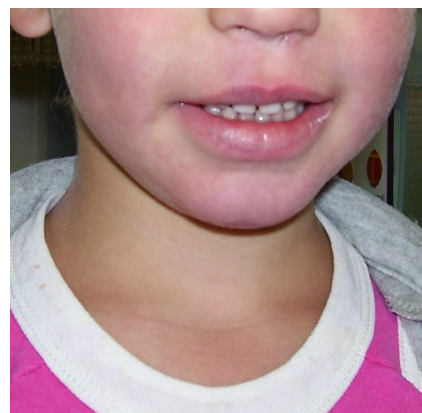
Before: Drinking



After: Drinking



Before: Talking



After: Talking

Figure 4.6.1: Edited Photographs of Participants During Different Activities
Before and 8 Weeks After the Botox® Injection

Pilot study: A pilot study was conducted, where nine different photographs of one child's mouth and any drooling were rated by two independent raters. These raters were qualified speech, language and hearing therapists, employed by the University of the Witwatersrand as senior lecturers. Three photographs from each

time point, baseline, 8 weeks and 24-26 weeks and in the different situations were used. Results indicated the following:

- The independent raters could rate using only the severity scale and not the frequency scale. As frequency of drooling is measured over time, they were unable to gauge the frequency of drooling from one instant in time, as captured by a photograph.
- Explanations of what exactly was included in each point rating were needed to avoid confusion. For example, if a droplet of saliva was on the outer edge of the lip and clearly was about to fall onto the table, then a severity rating of five was indicated.
- Participant confidentiality was maintained by the editing of the photographs and the assignment of a number to the photographs for identification purposes.
- Cohen's kappa coefficients were calculated and showed fair agreement of measurement, 0.5432, between the independent raters' scores and the three speech, language and hearing therapists' scores for each time point and each situation.
- Use of digital photography provided clear pictures, but did not allow for sequences of events to be recorded.

Data Collection in Phases One and Two of the Study

Phase One: When all consents had been obtained, all relevant records from the DTP were collected from the speech therapy department of the participants' school, where they had been safely kept. The review and analyses of the DTP records were then conducted by me. At the time the parents/primary caregivers gave their consent, approximately ten months after the Botox® injection, they were asked two additional open-ended questions: "how long do you think the treatment effect of Botox® lasted?" and "would you consider Botox® treatment again?" These questions aimed to find out if parents/primary caregivers thought the Botox® was still having an effect on their children's drooling and their feelings towards a further injection of Botox®.

Phase Two: The blind independent rater was given access to 296 digital photographs, presented in random order and asked to rate the severity of drooling for each photograph (Appendix L). The presentation of photographs in random order prevented the blind independent rater from knowing whether the photograph she was rating came from the baseline, 8 weeks post injection or 24-26 weeks post injection time frame. In this way, treatment, halo and expectancy biases had little effect on her ratings (Schiavetti & Metz, 2006, p. 191). She rated the photographs on the severity drooling scale only. As frequency of drooling is measured over time, she was unable to gauge the frequency of drooling from one instance in time, as captured by a photograph. Her rating scores for each photograph were also collected by me. Table 4.6.2 indicates the records that were analysed in the study and who completed each record.

Table 4.6.2: Records of Data Analysed.

	PARENTS	THERAPISTS	BLIND RATER
CASE HISTORY/ THERAPISTS'S NOTES	X	X	
SALIVA CONTROL ASSESSMENT FORM	X		
RATING-FREQUENCY	X	X	
RATING-SEVERITY	X	X	X
QUESTIONNAIRES	X		
INTERVIEW	X		
DIGITAL PHOTOS OF PARTICIPANTS'S MOUTHS			X

4.7. Data Analyses

The analyses of the results were handled in two ways. Some aspects, such as the demographic information, the information from the saliva control assessment form, and the results from the parental/primary caregiver interview and questionnaires, were handled using descriptive analyses. The small sample size

necessitated a case study design and the use of descriptive analyses in places. Other areas, such as the severity and frequency drooling rating scores, were handled using statistical analyses. It is important to acknowledge that although the rating scores are considered to be ordinal, I have used a parametric measure. This type of analysis is required when comparing 3 points in time, which the results from the baseline, 8 weeks and 24-26 weeks severity and frequency rating scores were. However, a small possibility exists that by using this method a false positive result may have been given.

Case history information and therapy notes were tabulated to provide expanded demographic information at baseline.

Information from the saliva control assessment form was tabulated to provide a qualitative, baseline assessment of the participants' communicative skills, walking ability, head position, oral motor skills, dental health and general health, as perceived by the parents.

Results from the severity and frequency rating scales from the three speech, language and hearing therapists were tabulated on spread sheets (Microsoft Excel) and mean scores and standard deviations were calculated. Parents/primary caregivers' ratings were also tabulated on spread sheets. The 'blind' independent rater's ratings were cross-referenced to the situation and the time frame which the photographs depicted and were also tabulated on spread sheets. Thereafter, grids were made to compare parents/primary caregivers' versus therapists' ratings for severity and frequency. Further grids were made to compare therapists' ratings and the 'blind' independent rater's ratings for severity only.

Reliability measures: Some form of inter-rater reliability was deemed necessary, as rating of the children's drooling relied on clinical or parental/primary caregiver judgement, as opposed to already validated test scores. Treatment, halo and expectancy biases can affect behavioural observations (Michelson, Mannarino, Marchione, Kazdin & Costello, 1985). In addition, therapeutic misestimations and unrealistic optimism can also affect the judgements made by parents/primary

caregivers and research participants (Appelbaum, Roth, Lidz, Benson & Windale, 1987; Horng & Grady, 2003; Jansen, 2006).

Inter-rater reliabilities/agreements were calculated, for parental/primary caregivers versus therapists ratings and therapists versus blind independent rater's ratings, using Cohen's Kappa (Cohen, 1988), which is defined as follows:

$$K = \frac{E_{fo} - E_{fe}}{N - E_{fe}}$$

Where E_{fo} = the sum of the observed values of the diagonals

E_{fe} = the sum of the expected values of the diagonals

N = the total number of ratings.

This measure of agreement is more stringent than a simple percentage agreement measure, as it corrects for chance agreements by subtracting the potential number of chance agreements from the numerator and the denominator of the kappa formula and then forming a ratio of the two chance-corrected values (Cohen, 1988; Howell, 1992).

Statistical analyses:

All statistical analyses were carried out using the speech, language and hearing therapists ratings. Bar graphs were made to illustrate the following:

- Any effect the Botox® injection had on drooling severity and frequency across all participants and all situations;
- Comparisons of drooling for severity and frequency between cerebral palsied participants and operculum syndrome participants in all situations and across the three time periods;
- Any effect the Botox® injection had on drooling severity and frequency in each situation, across all participants;
- Response to the Botox® injection by different types of cerebral palsied participants, to be used in a descriptive analysis.

Mean scores and standard deviations for severity ratings and frequency ratings for each time period were calculated. One-way analyses of variances (ANOVA) were computed, followed by Bonferroni post tests. The Bonferroni post test is a modified t test, which accounts for multiple comparisons, repeated measures, as well as for the fact that the comparisons are interrelated. It adjusts the t test analysis to account for the additional probability of rejecting a true null hypothesis, Type 1 error (Schiavetti & Metz, 2006, p. 351). The statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS Inc, Chicago, IL).

Cohen's d was calculated to estimate effect size between each time period. Cohen's d is generally defined as the difference between two group means, $M1 - M2$ divided by the standard deviation, s , of either group (Cohen, 1988).

$$d = \frac{M1 - M2}{s}$$

Cohen (1988) suggests that the interpretation of d is as follows:

- $0.20 < d < 0.50$, small effect size;
- $0.50 < d < 0.80$, medium effect size;
- $d > 0.80$, large effect size.

The American Psychological Association (2001, p. 25) advises for the reader to fully understand the importance of your findings, it is almost always necessary to include some index of effect size. Huck (2004) asserts that researchers are increasingly reporting the effect size of their results, as well as the statistical significance of their results. Effect sizes give some indication as to the practical significance of the data. A statistician was consulted to assist with the relevant data analyses.

Descriptive Analyses:

Demographic information together with drooling severity rating scores were used to investigate whether different types of cerebral palsy responded differently to the Botox® injection and whether severity of drooling at baseline, across all

situations, influenced any reduction of drooling post Botox® injection. A total severity rating score for each child was calculated by adding the severity rating scores from each situation together. For example, a score of 5 for each situation gives a total severity rating score of 25. The responses of individual participants to the Botox® injection were also analysed.

The results from the parental/primary caregiver interview and questionnaires were analyzed and tabulated to provide a qualitative review on the following: parental/primary caregiver perceptions of their children's drooling; social consequences of drooling; at what time of day and during which activities drooling occurred the most; any effects on drooling the Botox® may have had and how long that effect lasted; finally whether they would consider further treatment with Botox® injections for drooling.

This chapter has provided an overview of the DTP, the results from that project and how they were analyzed. The analyses and discussion of the results follows in chapter 5.

CHAPTER 5

RESULTS AND DISCUSSION

The results from the two phases of this study provide findings which are particularly relevant to the speech, language and hearing therapist working with neurologically impaired children who drool. Although results cannot be generalized to the wider population, they are consistent with other published studies. Unique aspects of the present study are that it has compared the drooling response to Botox® in the CP children and the operculum syndrome children, as well as the response to Botox® of different types of CP. More importantly it has compared the drooling response to Botox® in five different contexts.

The results are presented in line with the aims of the study and according to whether the information came from phase one or phase two of the study.

5.1. Phase One

Case history information and therapy notes were tabulated to form expanded demographic information which was presented in chapter 4, page 84.

The Saliva Control Assessment Form

The results obtained from the saliva control assessment, completed by the parents/primary caregivers at baseline, are summarized in Table 5.1.1 and are discussed under the following, separate headings:

- Communication
- Mobility
- Illness
- Head control
- Oral motor control
- Oral sensory awareness/sensitivity

It can be seen from Table 5.1.1 that most parents/primary caregivers felt that poor oral motor skills, as exemplified by mouth position, lip position, ability to pucker lips and presence of a tongue thrust, were a significant factor in their child's drooling. In addition, most parents/primary caregivers felt that their children had poor oral sensitivity, as shown by notices saliva on lips/chin.

Table 5.1.1: Number of Participants Rated by the Parents/Primary Caregivers on Different Components of the Saliva Control Assessment Form

Skill	No.	Skill Description
Communication	4 2 1 1 1	Some functional speech Uses speech but with difficulty Difficulty making some sounds in words No speech No problems
Walking	4 2 3	No difficulty Some difficulty, but walks independently Wheelchair most/all of the time
Head Position	8 1	Head held up with no difficulty Sits with head down mostly
Mouth Position	7 2	Mouth always open Mouth usually closed
Lip Position	4 3 1 1	Bring lips together only briefly Hold lips together with effort for limited time Unable to bring lips together Lips together easily and for long time
Pucker Lips	6 3	Unable to do Can do
Tongue Thrust	5 2 2	No Yes Sometimes
Straw Use	5 2 2	Difficulty using straw Cannot use straw Easily uses straw
Eating/Drinking	6 2 1 7	Food needs to be cut into small pieces Eats a wide range of food Eats foods that are difficult to chew Can use a cup independently
Messy Eater	9	Yes
Swallows Saliva when Asked	6 3	Yes Attempts to swallow saliva
Notices Saliva on Lips/Chin	7 2	No Yes
Frequently Blocked or Runny Nose	5 4	No Yes
Bouts of Pneumonia	8 1	No Yes
Recent Dental Check-up	5 4	Yes No

Key: No. i Number

a). Communication.

According to the parents/primary caregivers, only one participant was non-verbal. This result was not supported by the speech therapy notes, which indicated that three participants were non-verbal, four participants displayed severe dysarthria resulting in speech being mostly unintelligible, one participant displayed moderate dysarthria and only one participant could be classified with mild dysarthria. In the study by Van der Burg, Jongerius, van Limbeek, van Hulst and Rotteveel (2006b) 51% of the children could not speak. This percentage of non-verbal participants is consistent with the percentage of non-verbal participants indicated by the speech therapy notes.

In my clinical experience, parents/primary caregivers tend to over-estimate their children's ability to use speech and no doubt this accounts for the fact that only one child was considered to be non-verbal by the parents/primary caregivers. Lack of ability to speak does not appear to be a factor in the cause of drooling, nor in the reduction of drooling for the participants in this study.

b). Mobility.

Six participants (67%) could walk. This number of walkers was supported by the speech therapy notes. Four participants were classified as being at Level 1 or 2 on the Gross Motor Functional Classification system (Palisano et al, 1997) and both operculum syndrome participants could walk. In the study by Thomas-Stonell and Greenberg (1988), which investigated "Three Treatment Approaches and Clinical Factors in the Reduction of Drooling," mobility was one of the variables associated with successful treatment. It must be mentioned that Botox® injection was not one of the treatment strategies. However, in the study by Van der Burg et al (2006,b) only 19% of participants could walk. It is therefore doubtful that degree of mobility has an effect neither on drooling nor on the reduction of drooling with the use of Botox® injections.

c). Illness.

Four participants had a frequently runny/blocked nose and one participant had had a previous bout of pneumonia. Banerjee et al (2006) assert that illness, particularly oropharyngeal, increases drooling. This has certainly been the case in my experience. This view is supported by the fact that when one of the operculum syndrome participants, who had marked reduction of drooling following the Botox® injection, had a cold, drooling increased considerably whilst she had the cold.

d). Head Control.

Most participants (8) had good head control and displayed a good head position. This was confirmed by the speech therapy notes. This result was pleasing, as all of the participants had received neurodevelopmental therapy, which emphasizes the importance of body and head positioning and alignment (Bobath, 1980). In Thomas-Stonell and Greenberg's study (1988) good head control was found to be positively associated with decreased drooling. However, in the present study six participants were classified with severe drooling at baseline, despite having good head control. It would seem that other factors influenced the drooling experienced in the present study participants.

e). Oral Motor Control.

Poor oral motor control is a major factor negatively influencing drooling, as already discussed in chapter 3 (Morris and Klein, 2000; Brodsky, 2002; Winstock, 2005; Lal and Hotaling, 2006). Although all of the participants had received oral motor therapy previously, including being taught correct feeding patterns, the majority of the participants still had poor oral motor skills. This result was indicated by: difficulty bringing lips together, 8 participants; an inability to purse the lips, 6 participants; an open mouth posture, 7 participants; and a forward tongue position or tongue thrusting, 4 participants. Poor oral motor skills were confirmed by the speech therapy notes, but these indicated that the majority of

participants, 7 participants, had a forward tongue position, had poor stability of the jaw and poor grading of opening and 3 participants had minimal or no lateral tongue movements. Two of these participants were the children with operculum syndrome. Lack of lateral tongue movement and even very little tongue movement in any plane, is characteristic of the child with operculum syndrome. This lack of lingual movement is due to the paresis/paralysis of the tongue (Christen et al, 2000), as discussed in chapter 2.

Banerjee et al (2006) contend that drooling is exacerbated by constant tongue thrusting. Lespargot et al, (1993) felt that adequate suction of saliva from the front of the mouth to the pharynx during swallowing was hampered by poor lip closure, thus drooling is the result. With such poor oral motor skills, it is not surprising that all of the participants were considered messy eaters and exhibited drooling.

f). Oral Sensory Awareness

The majority of participants were unaware of saliva on their lips or chin, 7 participants. This was supported by the speech therapy notes. Banerjee et al (2006) state that drooling can be exacerbated by diminished intra-oral tactile sensitivity. Hyposensitivity is defined as an inability or reduced ability to respond to sensory input (Rosenfeld-Johnson, 2002). Rosenfeld-Johnson (2002) feels chronic drooling can be attributed to the inability or reduced ability to feel saliva build up on or within the mouth. The majority of the participants in this study would seem to support these statements.

Morris and Klein (2000) contend that drooling can also be caused by the accumulation of saliva in the mouth, as a result of reduced frequency of swallowing and/or inadequate oral movement and control during the swallow. As a result, a constantly wet face from drooling can reduce the sensory cues needed to trigger a proper swallow. One participant in the study exhibited oral hypersensitivity. It is unclear from the case history notes what caused the hypersensitivity or when it was first noticed. This child illustrates that drooling can occur with increased oral-tactile sensitivity. It is possible that the act of

swallowing causes this child unpleasant sensations. Thus he swallows during feeding and drinking, but not to rid his mouth of saliva. Only 2 participants had some oral sensory awareness, as observed by their efforts to occasionally remove saliva from their lips/chins.

The etiology of drooling in cerebral palsy and operculum syndrome has been discussed in detail in chapter 3, as has the relationship between oral sensation and drooling.

It would appear that poor oral motor skills, diminished oral sensory awareness and oral hypersensitivity were the main factors that influenced the participants' drooling. In most areas of the saliva control assessment, the parent/primary caregivers were in agreement with the speech therapy notes.

5.2. Reliability Measures in Phase One

The results of the reliability measures in phase one, between the parents/primary caregivers and the three speech, language and hearing therapists are shown in Table 5.2.1. As can be seen, there was poor agreement for severity and frequency ratings for all children across all situations (Cohen, 1988).

Table 5.2.1: Cohen's Kappa Coefficients for Parents and Therapists (Cohen, 1988)

Ratings	Cohen's Kappa	Agreement
Severity Ratings All Situations	0.2458	Poor
Frequency Ratings All Situations	0.1398	Poor

These results could be due to the fact that parents/primary caregivers do not have the clinical skill or experience to objectively rate the severity and frequency of

their children's drooling. Another reason may be that the parents/primary caregivers, some of whom were English second language speakers, did not fully understand the definitions of each level of the rating scales, despite the fact that home language interpreters were used.

An analysis of the parental/primary caregiver ratings indicated that they tended to rate their child's drooling, particularly after the Botox® injection, more favourably than the speech, language and hearing therapists. This could be due to the 'treatment bias' – I know my child's drooling has improved because he/she has received the treatment (Michelson et al, 1985). In fact, Michelson et al (1985) contend that treatment, halo and expectancy biases can affect behavioural observations, even among well-trained and reliable raters.

The concepts of the therapeutic misestimation and unrealistic optimism correspond to treatment and expectancy biases. In misestimations a person underestimates the risk of treatment and/or overestimates the benefits of treatment. Unrealistic optimism is a kind of bias where a person believes that the outcome of her/his treatment is more likely to be positive, as compared to others who are in a similar situation (Appelbaum et al, 1987; Horng & Grady, 2003; Jansen, 2006).

The results of the reliability measures in phase one confirmed the decision to use a 'blind' independent rater to ensure that ratings were not influenced by biased perceptions or therapeutic misestimations (Cicchetti, & Sparrow, 1981; Horng & Grady, 2003). The results of the reliability measures from phase two are discussed later in this chapter.

5.3. Quantitative Results

Reduction of Drooling in Neurologically Impaired Participants

The main research aim to determine if Botox® had an effect on the drooling of nine neurologically impaired children was positively answered. As can be seen

from Figures 5.3.1 and 5.3.2, drooling severity and frequency rating scores decreased at 8 weeks and increased at 24-26 weeks post Botox® injection. The increase was not, however, back to baseline levels.

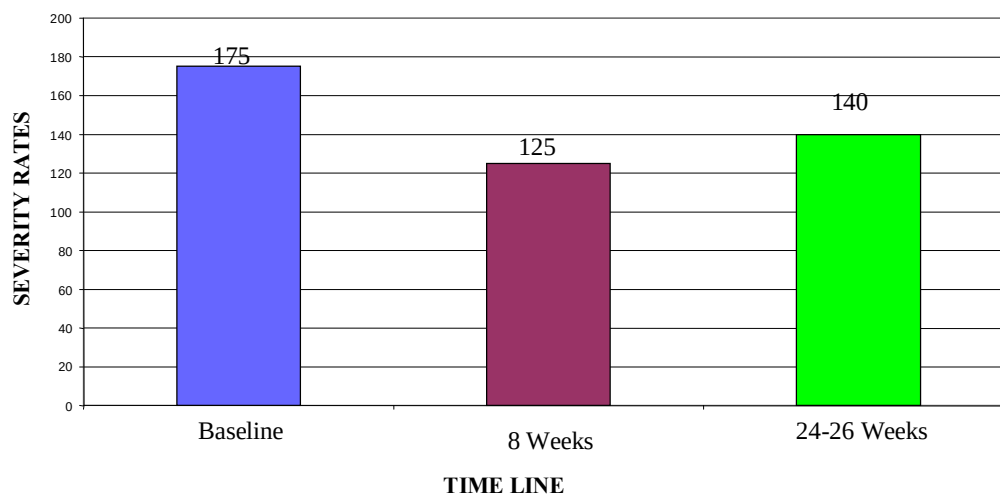


Figure 5.3.1: Severity Rating Totals of Drooling for All Children across All Five Situations in the Study

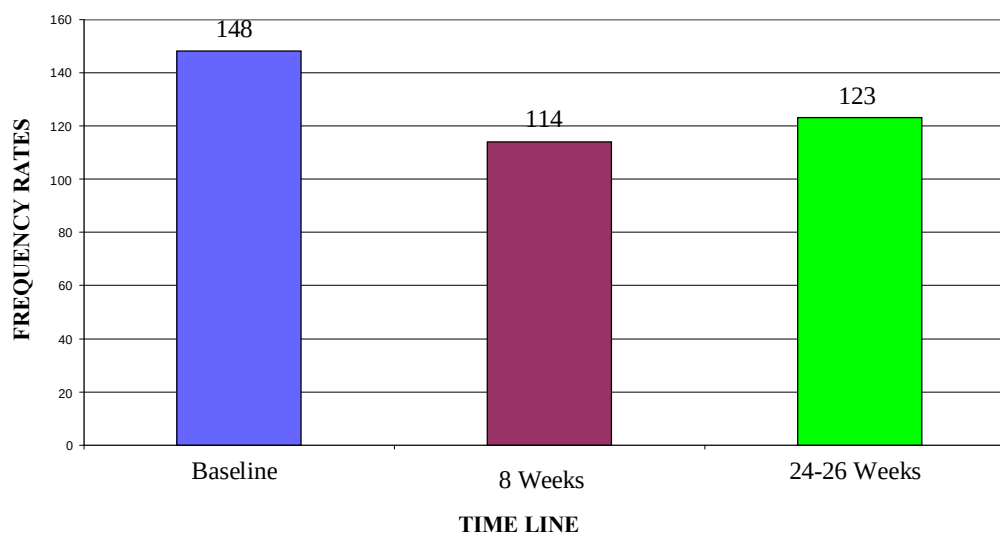


Figure 5.3.2: Frequency Rating Totals of Drooling for All Children across All Five Situations in the Study

From the raw totals, mean scores and standard deviations for severity and frequency ratings for each time period were calculated. Table 5.3.1 illustrates these values.

Table 5.3.1: Overall Mean Scores and Standard Deviations for Severity and Frequency Ratings of Drooling

Time	Mean	Std. Dev.	No. of Obs.
Severity			
Baseline	3.8888889	1.1720654	45
8 Wks	2.7777778	.90173794	45
24-26 Wks	3.1111111	1.1525115	45
Total	3.2592593	1.1715722	135
Frequency			
Baseline	3.2888889	.84267491	45
8 Wks	2.5333333	.69413124	45
24-26 Wks	2.7333333	.78044276	45
Total	2.8518519	.83325041	135

Key: Std. Dev. ĩ Standard Deviation; No. of Obs. ĩ Number of Observations;
Wks ĩ Weeks.

One-way ANOVAS were computed to assess whether there were statistically significant reductions of drooling severity and frequency rating scores. The Bonferroni *t* tests established between which time periods there were significant reductions of drooling severity and frequency rating scores. An alpha level of .05 was used for all statistical tests.

Cohen's *d*'s were calculated to estimate the effect sizes between each time period for severity and frequency ratings. Table 5.3.2 indicates the significant values and effect sizes for severity and frequency ratings at the three time periods, for all children across all five situations.

The interpretation of d was as follows (Cohen, 1988):

- $0.20 < d < 0.50$ ï small effect size
- $0.50 < d < 0.80$ ï medium effect size
- $d > 0.80$ ï large effect size

Table 5.3.2: Significant Values and Effect Sizes for Severity and Frequency
Ratings of Drooling

	Significance	Effect Size
Severity	F (2,132) = 12.49, $p < 0.0001$	
Baseline - 8 Weeks	$p < 0.001$	Large
Baseline ï 24-26 Weeks	$p = 0.003$	Moderate
8 Weeks ï 24-26 Weeks	No significance: $p = 0.439$	Small
Frequency	F (2,132) = 11.49, $p < 0.0001$	
Baseline - 8 Weeks	$p < 0.001$	Large
Baseline ï 24-26 Weeks	$p = 0.003$	Moderate
8 Weeks ï 24-26 Weeks	No significance: $p = 0.669$	Small

Key: Bold Font indicates Significant Results

As can be seen from Table 5.3.2, the statistical analyses indicated that Botox® injected bilaterally into the submandibular glands reduced the judged severity and frequency of drooling rating scores across all situations and for all children with a significant, large effect from baseline up to 8 weeks. In addition, the reduction in drooling severity and frequency rating scores was statistically significant, but with a moderate effect, from baseline to 24-26 weeks. This result suggests that at 24-26 weeks the effect of Botox® was on-going, although reduced. The small effect sizes and lack of statistically significant differences between 8 weeks and 24-26 weeks supports the idea that at 24-26 weeks the effect of the Botox® injection was still in place. The probability of these results occurring by chance is $p < 0.001$

at 8 weeks and $p = 0.003$ at 24-26 weeks and the results are significant at the 5% level.

The results from this study are consistent with results obtained in other published studies. Jongerius, van den Hoogen et al (2004) found the greatest reduction in drooling at 2 weeks post Botox® injection. At the end of their study, 24 weeks post Botox® injection, there was still a statistically significant reduction of drooling in some participants. It must be mentioned that in Jongerius, van den Hoogen et al's study (2004), the drooling quotient (DQ) and the visual analogue scales (VAS) were used to assess the amount of drooling. As mentioned in chapter 3, they did not differentiate between severity and frequency of drooling, as has been done in this study. Despite the different methods of quantifying drooling, a significant reduction in drooling was seen in their study and the present study.

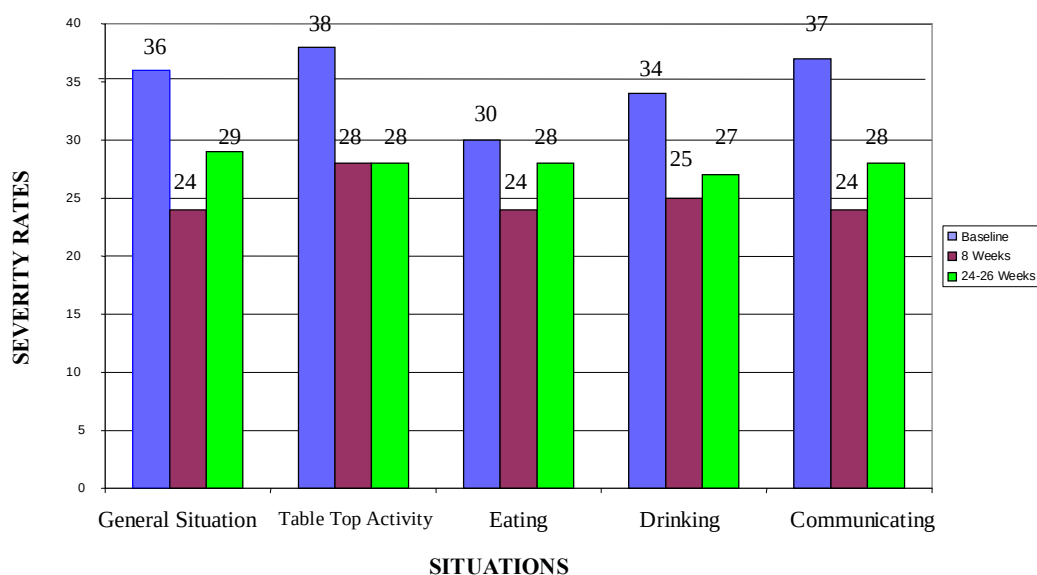
Bannerjee et al (2006) used the DQ, weighing the saliva collected on dental bibs, the number of bibs/scarves changed per day to assess drooling and they looked at the severity and frequency of drooling as assessed by the parent/primary caregiver, using the same scales as in this study. However, they injected the parotid glands as well as the submandibular glands and their study only lasted 12 weeks. Nevertheless, there were statistically significant reductions of severity and frequency drooling scores at 4 weeks and 12 weeks.

Reduction of Drooling in Different Situations

As discussed in chapter 3, very little research has been done in investigating the reduction of drooling in different contexts. The present study looked at whether there were any reductions of drooling severity and frequency rating scores across all participants in five different situations. The results indicated that the context in which drooling occurs is a significant factor. As such, the results suggest the value of considering the situational context when making drooling judgements. This viewpoint is supported by Banerjee et al (2006), even though they did not investigate drooling in different contexts.

As part of their study on the impact of drooling on daily life, social interaction and self-esteem, Van der Burg et al (2006,a & b) investigated parental perceptions of decreased drooling in different situations. The results from this particular study are discussed later in the chapter and comparisons are made between the perceptions of South African parents/primary caregivers in the present study and parental perceptions from Van der Burg's study.

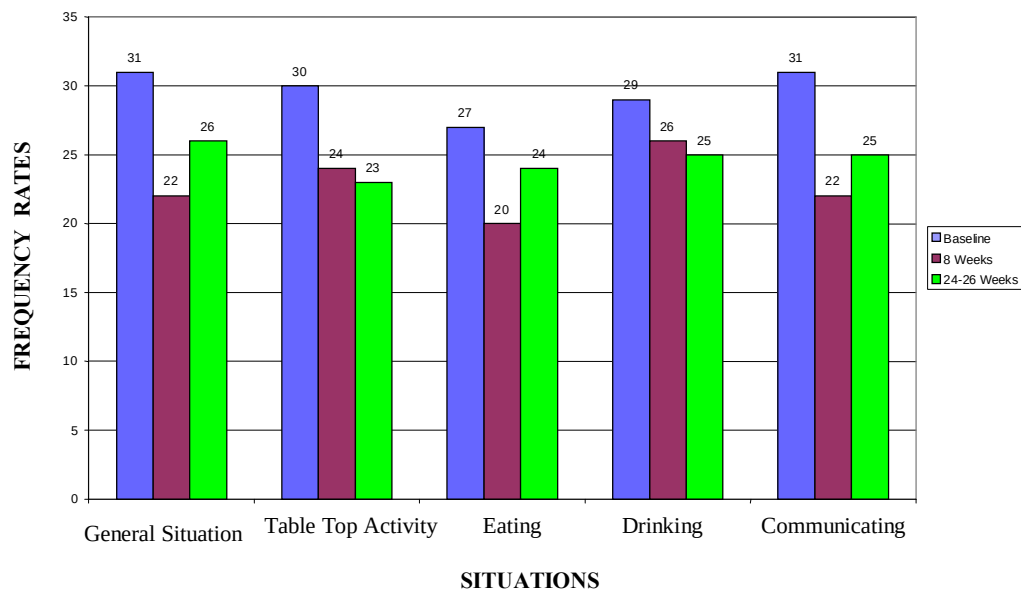
It can be seen from Figure 5.3.3 that the severity drooling rate at baseline was the highest in the **table top situation**. As all participants were considered to be messy eaters and saliva production is increased during stimulated states, one would have expected the **eating and drinking situations** to provide the highest severity drooling rates. However, it is known that drooling increases with concentration (Brotsky, 2002). This factor probably accounted for the high rate of drooling in the **table top activity**. The severity drooling rate in the **table top situation** did not increase at 24-26 weeks. In the other situations, severity drooling rates did increase, but not back to baseline levels.



Key: Baseline ■ ; 8 Weeks ■ ; 24-26 Weeks ■

Figure 5.3.3: Severity Drooling Rates of All Children in Different Situations

Figure 5.3.4 shows that the frequency of drooling rate was the highest in the **general appearance** and the **communicating situations**. Again, one would have expected the frequency of drooling rate to be the highest in the **eating and drinking situations**. In the **table top and drinking situations** the reductions of drooling frequency rates were continuing to decrease at 24-26 weeks. These reductions in frequency were not statistically significant. However, in the **table top** situation the effect size was large.



Key: Baseline ■ ; 8 Weeks ■ ; 24-26 Weeks ■

Figure 5.3.4: Frequency Drooling Rates of All Children in Different Situations

Statistical analyses were computed for each different situation for severity of drooling rates and frequency of drooling rates across all children. Effect sizes, Cohen's d , were also calculated (Cohen, 1988).

As can be seen from Table 5.3.3, statistically significant reductions were found in the ratings of drooling severity in the **general appearance** of the child: $F(2, 24) = 4.11, p = 0.0291$; and in the **communicating situation**: $F(2, 24) = 5.43, p = 0.0114$. In the **table top activity, eating and drinking situations**, reductions of

drooling severity ratings were not statistically significant. Bonferroni t tests established that for the **general appearance** of the child and the **communicating situation**, statistically significant reductions in drooling severity ratings occurred between the baseline and 8 week time periods only. Significant values are highlighted in bold font.

Table 5.3.3: Effect Sizes and Significant Reductions in Drooling Severity for Each Situation

Situation	Base - 8 Wks			Base - 24 to 26 Wks			8 Wks - 24 to 26 Wks		
	Effect Size d	Interpretation	Signif $\hat{Z}$	Effect Size d	Interpretation	Signif $\hat{Z}$	Effect Size d	Interpretation	Signif. $\hat{y}$
Gen. Appear.	1.333	Large	Yes	0.647	Mod.	No	-0.46	Small	No
Table Top	0.853	Large	No	0.853	Large	No	0	Small	No
Eating	0.503	Mod.	No	0.168	Small	No	-0.38	Small	No
Drinking	0.832	Large	No	0.588	Mod.	No	-0.16	Small	No
Comm.	1.37	Large	Yes	0.948	Large	No	-0.42	Small	No

Key: Base-Baseline; Wks-Weeks; Signif-Significance; Gen.Appear.-General Appearance; Comm.-Communication; $\hat{Z}$ - Decrease; $\hat{y}$ - Increase

Table 5.3.4 illustrates that as with the severity ratings, statistically significant reductions were found in the ratings of drooling frequency in the **general appearance** of the child: $F(2, 24) = 4.78, p = 0.0178$; and in the **communicating situation**: $F(2, 24) = 4.67, p = 0.0194$. In the **table top activity, eating and drinking situations**, reductions of drooling frequency ratings were not statistically significant. Bonferroni t tests established that for the **general appearance** of the child and the **communicating situations**, statistically significant reductions in drooling frequency ratings occurred between the baseline and 8 week time periods only.

The effect sizes were large for drooling severity and frequency ratings in the **general appearance** and the **communicating situations** at the baseline to 8 week time periods. Once again, significant results are highlighted in bold font.

Table 5.3.4: Effect Sizes and Significant Reductions in Drooling Frequency for Each Situation

Situation	Base - 8 Wks			Base - 24 to 26 Wks			8 Wks - 24 to 26 Wks		
	Effect Size d	Interpretation	Signif. $\hat{Z}$	Effect Size d	Interpretation	Signif. $\hat{Z}$	Effect Size d	Interpretation	Signif. $\hat{y}$
Gen. Appear.	1.376	Large	Yes	0.710	Mod.	No	-0.56	Small	No
Table Top	0.769	Mod.	No	0.898	Large	No	0.153	Small	No
Eating	0.777	Mod.	No	0.333	Small	No	-0.53	Small	No
Drinking	0.343	Small	No	0.406	Small	No	0.101	Small	No
Comm.	1.376	Large	Yes	0.917	Large	No	-0.45	Small	No

Key: Base-Baseline; Wks-Weeks; Signif-Significance; Gen.Appear.-General Appearance; Comm.-Communication; $\hat{Z}$ - Decrease; $\hat{y}$ - Increase.

In the **general and communicating situations**, from 8 weeks to 24-26 weeks, drooling severity and frequency rates started to increase. The effect sizes for drooling severity and frequency rate increases were small between 8 weeks and 24-26 weeks and were not statistically significant. Together these results provide support for the conclusion that at 24-26 weeks the Botox® was still exerting an effect on saliva production. In the **communicating situation**, the effect sizes for severity and frequency rates between baseline and 24-26 weeks were large. These large effect sizes are surprising, as the differences in drooling severity and frequency ratings in the **communicating situation** from baseline to 24-26 weeks were not statistically significant. However, the large effect sizes provide added support to the notion that at 24-26 weeks Botox® was still in effect.

The lack of statistically significant reductions in drooling severity and frequency ratings in the **table top activity** could be accounted for by the fact that the head was in a downward position, thus gravity would have exerted an effect, causing saliva to drop more often from the mouth or lips onto the table. In addition, the child's level of concentration would have been higher, thus increasing the amount of saliva produced (Brodsky, 2002).

The lack of statistically significant results during the **eating and drinking situations** could be as a result of increased saliva production, as the parotid glands produce saliva when stimulated by food or drink. Poor oral motor skills, causing an inability to deal effectively with food and drink mixed with increased amounts of saliva, could be another possibility (Brodsky, 2002; Winstock, 2005).

Contrary to the results in the present study, Suskind & Tilton (2002) felt there was a significant decrease in drooling during eating. This discrepancy can probably be accounted for by the fact that they injected the parotid glands as well as the submandibular glands.

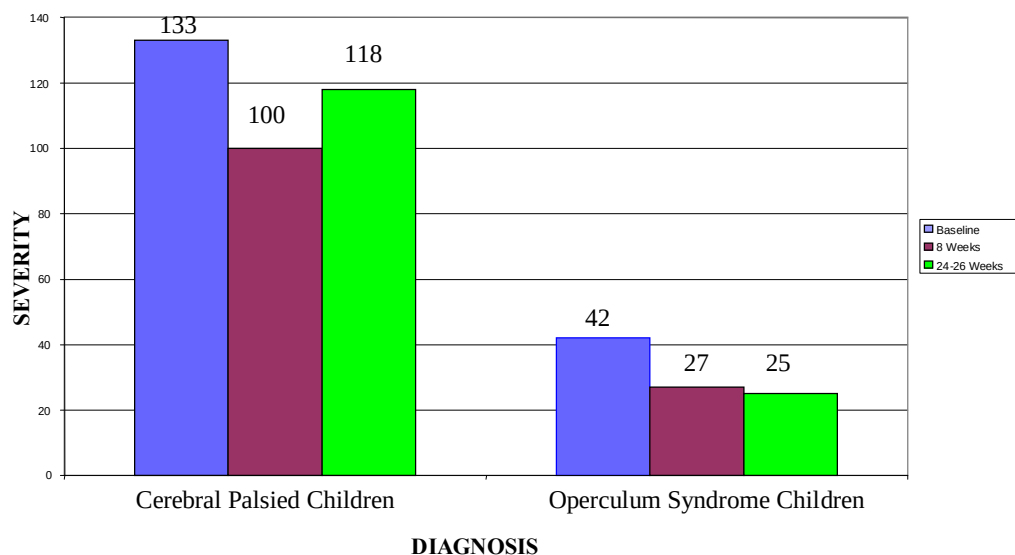
It is interesting to note, that despite the lack of statistically significant reductions in the drooling severity rating scores for the **table top and drinking activities**, the effect sizes of the treatment were large, from baseline to 8 weeks and baseline to 24-26 weeks for the **table top activity** and from baseline to 8 weeks for the **drinking activity**. These large effect sizes correlate with the positive parental/primary caregiver perceptions of improved drooling during their children's drinking activities and activities that required concentration.

5.4. Descriptive Analyses

Reductions in Drooling in the Cerebral Palsied Participants versus the Operculum Syndrome Participants

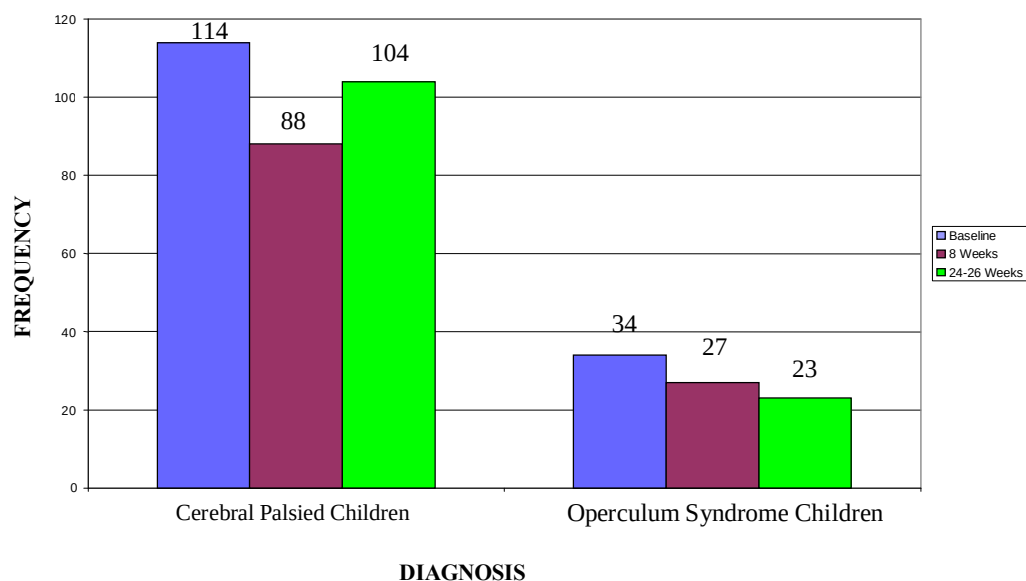
The results demonstrated that there was a reduction of drooling in the participants with cerebral palsy and the participants with operculum syndrome. Figures 5.4.1

and 5.4.2 respectively show the comparison of drooling reduction rates for severity and frequency between the cerebral palsied participants and the operculum syndrome participants in all situations and across the three time periods. It is clear that the patterns of reduction for severity and frequency rates are different between the two diagnostic groups.



Key: Baseline ■ ; 8 Weeks ■ ; 24-26 Weeks ■

Figure 5.4.1: Comparison of Drooling Reduction for Severity between the CP and the Operculum Syndrome Participants



Key: Baseline ■ ; 8 Weeks ■ ; 24-26 Weeks ■

Figure 5.4.2: Comparison of Drooling Reduction for Frequency between the CP and the Operculum Syndrome Participants

It was not possible to calculate statistical differences with such small groups, but percentage reductions were calculated from the raw rating scores.

A reduction in drooling of 25 to 50% seems to be considered a successful outcome to therapy (Hassin-Baer, Scheuer, Buchman, Jacobson & Ben-Zeev, 2005; Jongerius, Van den Hoogen, et al, 2004). As can be seen from Table 5.4.1, successful outcomes were evident for all participants. However, it is noteworthy that the reductions in drooling severity and frequency rates for the participants with operculum syndrome were continuing to decrease at 24-26 weeks, as opposed to most of the participants with cerebral palsy, whose drooling severity and frequency rates were increasing, although not back to baseline levels.

Table 5.4.1: Percentage Values of Drooling Reduction According to Diagnosis

Time Line	Cerebral Palsied Children	Operculum Syndrome Children
Severity		
Baseline ï 8 Wks	26% Ź	36% Ź
Baseline ï 24-26 Wks	14% Ź	40% Ź
Frequency		
Baseline ï 8 Wks	24% Ź	21% Ź
Baseline ï 24-26 Wks	12% Ź	32% Ź

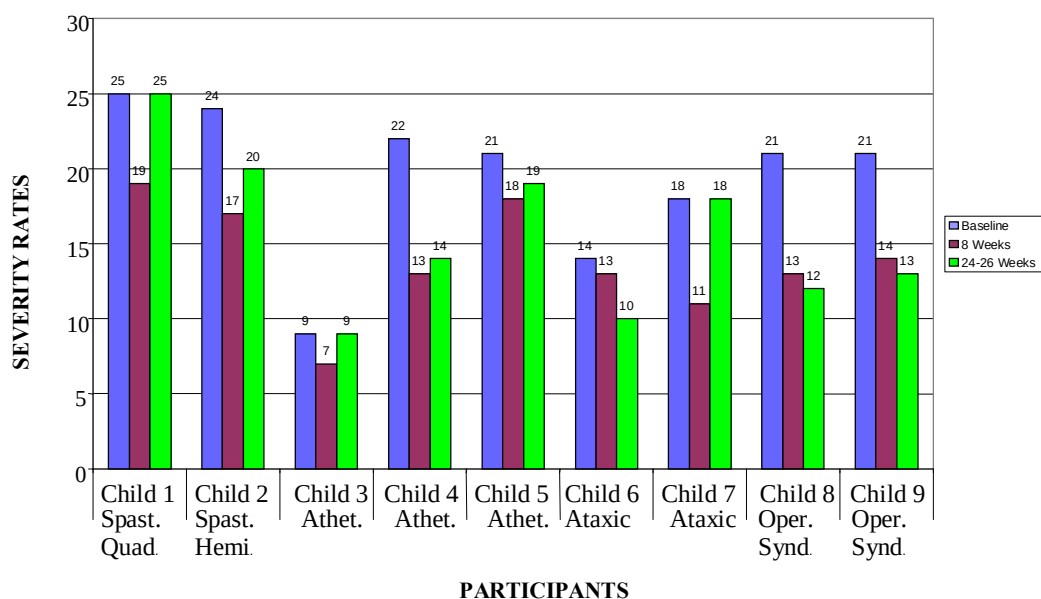
Key: Wks ï Weeks; Ź - Decrease; ŷ - Increase; % - Percentage

This finding implies that the effect of Botox® injections lasted longer with the operculum syndrome participants. According to Suskind & Tilton (2002) the basis for the difference in duration of action is uncertain at this stage. One explanation for this result could be provided by the fact that damage to the brain is restricted to the operculum area.

The neurophysiology of saliva production and swallowing involves pathways that eventually reach the cerebral cortex, as discussed in chapter 3. The possibility of Botox® affecting a central nervous system structure, for example the operculum, either directly or indirectly, is at this stage without proof. However, Currà, Trompetto, Abbruzzese and Berardelli (2004, p. S60) present various experimental and clinical studies that provide information on the theory that ñlocally injected BT-A could produce central effects directly, by being transported into central structures, or indirectly, by altering central sensorimotor integration through a peripheral mechanism.ò

Individual Severity and Frequency Scores of Drooling by Diagnosis

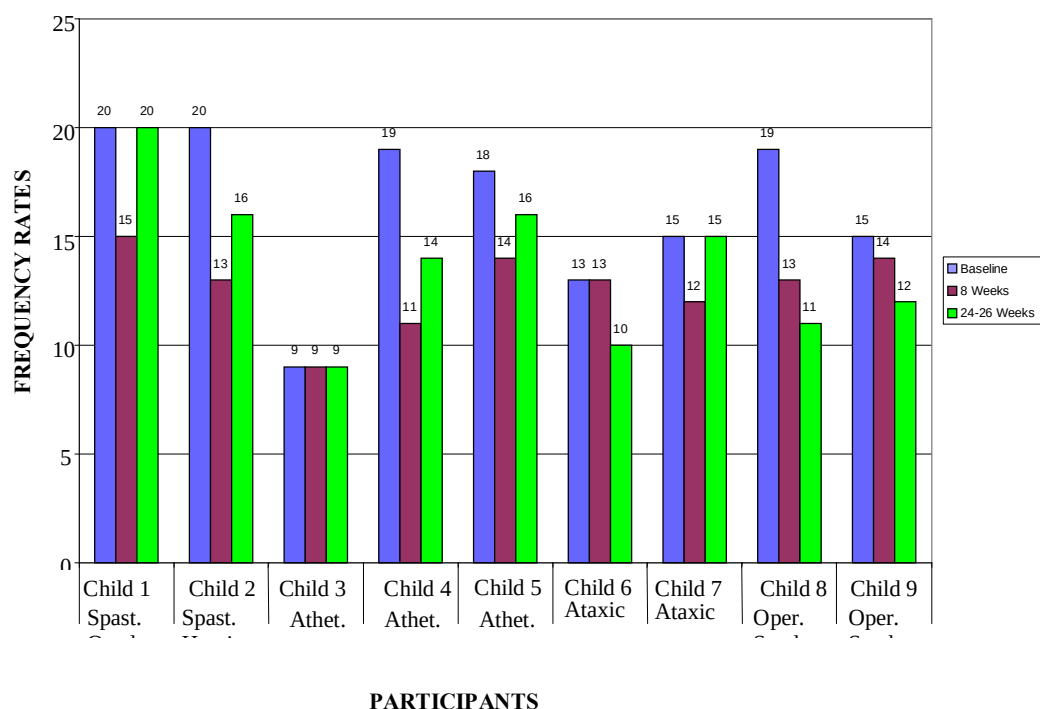
As can be seen from Figures 5.4.3 and 5.4.4, participants 1 to 7 are CP individuals and participants 8 and 9 are the operculum syndrome participants. The severity and frequency drooling scores for individual participants are for all five situations. Totals scores were arrived at by adding together each drooling severity or frequency score from each situation for each individual at each time point.



Key: Baseline ■ ; 8 Weeks ■ ; 24-26 Weeks ■

Spast. Quad. ï Spastic Quadriplegic; Spast. Hemi. ï Spastic Hemiplegic;
Athet. ï Athetoid; Oper. Synd. ï Operculum Syndrome

Figure 5.4.3: Total Individual Severity Drooling Responses to Botox® Organized by Diagnosis



Key: Baseline ■ ; 8 Weeks ■ ; 24-26 Weeks ■
 Spast. Quad. ï Spastic Quadriplegic; Spast. Hemi. ï Spastic Hemiplegic;
 Athet. ï Athetoid; Oper. Synd. ï Operculum Syndrome

Figure 5.4.4: Total Individual Frequency Drooling Responses to Botox®
 Organized by Diagnosis

As illustrated in Table 4.4.1: Participant Demographics in chapter 4, page 84, participant 3 was a 17 year old male. From the above figures, it can be seen that despite a reduction in drooling severity, he did not show a reduction in drooling frequency. This could be accounted for by the fact that his drooling was considered to be mild and occasional at baseline. Mild drooling (severity score 2) by definition states that only the lips are wet and occasional drooling (frequency score 2) is only on some days, not every day (Thomas-Stonell & Greenberg, 1988). For this participant, a reduction in drooling frequency would have meant that he would have been rated as never drooling (frequency score 1). A rating of never drooling (1) would have been false; therefore he had to remain rated as occasionally drooling (2).

Participant 6 was a 5 year old male. Although diagnosed with cerebral palsy, he showed a continuing decrease in drooling severity at 24-26 weeks. However, the initial reduction in drooling severity at 8 weeks was less than in the other cerebral palsied participants. The frequency of his drooling did not show any decrease at 8 weeks. However, by 24-26 weeks a reduction in drooling frequency was noted. This participant was considered to have an overall developmental delay and it is possible that this contributed to a delayed reaction of reduced drooling severity and frequency. In addition, it is possible that the continuing decreases in drooling severity and frequency rates can be attributed to the fact that drooling improves with the maturation of oro-facial movement and swallowing (Mathur et al, 2006).

As already discussed, the 2 participants with operculum syndrome showed a continuing decrease in drooling severity and frequency rates at 24-26 weeks post Botox® injection.

From the present study, it seems clear that the response to Botox® is variable between individuals. It is also possible that Botox® has a different effect on drooling severity as opposed to drooling frequency in some individuals. This possibility has been referred to in chapter 3 with a description of the study by Nobrega et al, (2007).

These factors should be taken into account when deciding to use Botox® as a treatment in the neurologically impaired population. A 'one size fits all' approach cannot be advocated. Previous studies on the use of Botox® to reduce drooling in neurologically impaired children have not differentiated between the responses of different diagnostic categories. Nor has there been a separation between severity and frequency of drooling. The results described in this section have provided further areas for research.

Response of Different Types of Cerebral Palsy to Botox®

Although the demographic information of the participants has been given in the methodology section, Table 5.4.2 illustrates the baseline drooling severity ratings

and the 8 weeks post Botox® injection drooling severity ratings across all five situations for each participant. These ratings were conducted by the three speech, language and hearing therapists in the DTP. From these ratings a simple percentage analysis was conducted to answer the question of whether different types of cerebral palsy responded differently to the Botox® injection.

Table 5.4.2: Participant Demographics, Baseline and 8 Weeks Severity Ratings for Each Participant, Across All Situations

Child	Diagnosis	Baseline Severity Ratings	8 Weeks Post Botox® Severity Ratings		Percentage Ż
1	Spastic quadriplegic CP	25	19		26,5%
2	Spastic hemiplegic CP	24	17		
3	Athetoid CP	9	7		26,9%
4	Athetoid CP	22	13		
5	Athetoid CP	21	18		
6	Ataxic CP	14	13		25%
7	Ataxic CP	18	11		
			8 Weeks	24-26 Weeks	
8	Operculum syndrome	21	13	12	35,7%
9	Operculum syndrome	21	14	13	40%

Key: CP ĩ Cerebral Palsy; Ż - Decrease; % - Percentage

As can be seen from Table 5.4.2, the spastic cerebral palsied participants had a 26,5% decrease in drooling rates, the athetoid participants had a 26,9% decrease in drooling rates and the ataxic participants had a 25% decrease in drooling rates. These results seem to imply that different types of cerebral palsy did not respond very differently to the Botox® injection. Again, it is interesting to note that the operculum syndrome participants had a 35,7% decrease in drooling severity rates at eight weeks. This had improved to a 40% decrease in drooling severity rates by 24-26 weeks. Individual variations in response to the Botox® injections were

found, however the results seem to imply that there is very little difference in response between participants with different types of CP. Tahmassebi and Curzon (2003) in their study on the prevalence of drooling in children with CP found that the children diagnosed with spastic quadriplegia displayed the most drooling. While this result was confirmed in the present study, the participant with spastic quadriplegia did not show the most reduction in drooling following the Botox® injection.

Previous studies to determine the effect of Botox® injections on drooling have not looked at different responses to Botox® according to different types of CP or neurological impairment in children (Banerjee et al, 2006; Jongerius, van den Hoogen et al, 2004; Hassin-Baer et al, 2004; Suskind & Tilton, 2002.) Banerjee et al (2006) listed the number of children in each diagnostic CP category, but did not correlate their results to the different types of CP participants. Hassin-Baer et al (2004) also listed only the different diagnostic categories of the participants, including one participant with operculum syndrome, but with no correlation to the results of their study.

Interestingly, the study by Lipp et al (2003) compared the response of drooling to Botox® injections of various participants with a wide range of neurological disorders. It must be mentioned, however, that the participants were adults and not CP. In addition, the study did not include participants with operculum syndrome. Nevertheless, they found that the response to Botox® was similar between participants with Parkinson's disease, amyotrophic lateral sclerosis, multiple system atrophy and corticobasal degeneration. These results correspond to the overall lack of difference in response found in the present study, between different types of CP participants. Certainly within each CP diagnostic group, there were slight variations in individual responses to the Botox® injection. Furthermore, there appeared to be a very different response to the Botox® injection by the participants with operculum syndrome. Banerjee et al (2006) feel that variations in responses are at present unexplained.

Influence of Baseline Severity of Drooling

According to the severity rating scales (Thomas-Stonell & Greenberg, 1988), A total drooling severity score, S , across all situations can be interpreted thus:

- $5 < S < 15$ indicates mild drooling
- $15 < S < 20$ indicates moderate drooling
- $S > 20$ indicates severe to profuse drooling

Using the information in Table 5.4.2, the relationship between severity of drooling and efficiency of the Botox® injection was investigated.

The participants with severe to profuse drooling, participants 1, 2, 4, and 5, had a 27% decrease in drooling severity rate at 8 weeks. If the operculum syndrome participants, 8 and 9, are included in the calculation, there was a 29,9% decrease in drooling severity rate at 8 weeks; the participant with moderate drooling, 7, had a 38,8% decrease in drooling severity rate; and the participants with mild drooling, 3 and 6, had a 13% decrease in drooling severity rate at 8 weeks.

From these results it would seem that severity of drooling at baseline had some influence on the amount of drooling reduction post injection. In other words, the participant with moderate drooling showed a greater reduction in drooling than those with severe or mild drooling at baseline. As most other studies included participants with severe drooling only, it is difficult to assess the validity of these results. Suskind and Tilton (2002, p. 81) observed "the best clinical results" in those with the least drooling. However, they did not quantify the level of "least drooling" nor did they explain what their "best clinical results" were.

Duration of Effect.

The question of how long the effect of the Botox® injection lasted appears to be related to the participants' diagnoses. At 24-26 weeks post injection, the severity and frequency ratings for the CP participants had increased, implying that although the effect of Botox® was still apparent, it was wearing off. However, the

ratings for the operculum syndrome participants were still decreasing at 24 to 26 weeks. This seems to imply that the effect of Botox® would have lasted longer in the participants with operculum syndrome. Site and extent of brain damage may be a factor in determining how long Botox® lasts.

Previous studies indicate that the duration of effect of Botox® on drooling is variable, anywhere between 3 and 24 weeks (Banerjee et al, 2006; Bothwell et al, 2002; Ellies et al, 2002; Jongerius, van den Hoogen et al, 2004; Hassin-Baer et al, 2004; Kim et al, 2006; Lipp et al, 2003; Ondo et al, 2004; Savarese et al, 2004; Suskind & Tilton, 2002).

Ellies et al (2002) feel that the individual duration of effect with Botox® is more variable with intra-glandular injections as opposed to intra-muscular injections. Suskind and Tilton (2002) postulate that the effect lasts longer at the glandular level.

At ten months post injection, when parents/primary caregivers gave their permission for the DTP data to be used in this study, most felt that the effect of the Botox® injection had worn off. However, the parent/primary caregiver of participant 4, a 6 year old male athetoid CP child, felt that the drooling had not returned to baseline levels. From the speech therapy notes it was clear that he had received oral motor therapy on a regular basis following the Botox® injections.

There is emerging evidence that functional outcomes last beyond the pharmacologically effective period of Botox® when combined with therapy. This evidence comes from studies involving the use of Botox® to improve upper limb function (Lowe, Novak & Cusick, 2006). Theodoros, Scudamore, Baldock, Coman and Hancock (2007) present a case study where improvements in voice production were maintained longer following Botox® injection and additional voice therapy. There is reason to believe, therefore, that reductions in drooling can last longer when Botox® injections are combined with oral motor therapy. This combination of treatments would have the positive aspect of decreasing the

number of injections needed in the long term and reducing the likelihood of antibody formation.

Parental/primary Caregivers' Perceptions.

Parental/primary caregivers' perceptions and feelings towards their children's drooling, before and after the Botox® injections and their perceptions towards the Botox® injection itself were analyzed using the following areas:

a). Time of Day Drooling Peaked

Parents/primary caregivers were asked to indicate during which time of day drooling occurred the most, before and after the Botox® injections. As can be seen from Figure 5.4.5, 7 parents/primary caregivers agreed that drooling occurred the most during the afternoon, before and after treatment. This result corresponds with the literature that states saliva production peaks during the afternoon (Winstock, 2005). Although the same percentage of parents/primary caregivers thought that drooling still occurred more often in the afternoon, they thought the severity of drooling was less after the treatment.

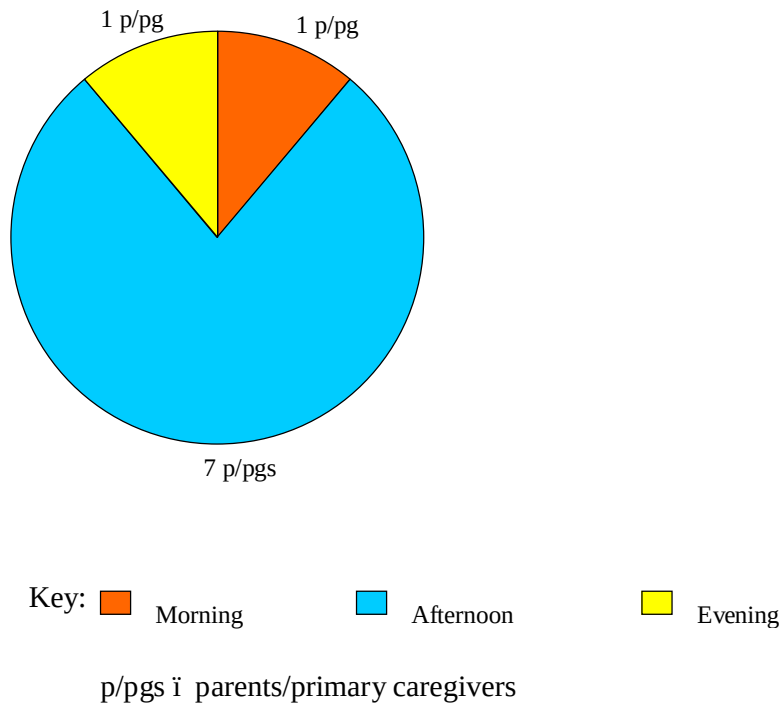


Figure 5.4.5: Parental/primary caregivers' Perceptions of the Time of Day Drooling Peaked, Before and After Botox® Treatment

b). Severity during Activities/Feelings

Parents/primary caregivers rated the severity of their children's drooling during certain activities and feelings, before and after treatment, using the five point severity rating scale (Thomas-Stonell & Greenberg, 1988). Table 5.4.3 indicates the activities rated from 'severe' to 'mild'. As can be seen, activities that required concentration were placed on the 'severe' end of the scale, whereas sleeping and walking were on the 'mild' end of the scale. These results correspond with the literature, which states that drooling increases with concentration and is usually less during sleep (Winstock, 2005).

Table 5.4.3: Parental/Primary Caregiver Severity Ratings of Drooling during Activities/Feelings from the Quality of Life Questionnaire (based on Van der Burg et al, 2006, a)

	Before Botox® Treatment	After Botox® Treatment
Severe ↓ Mild	Brushing Teeth	Concentrating
	Concentrating; sick; anxious; Upset/crying	Brushing teeth; upset/crying
	Drinking	Sick
	Eating	Anxious
	Watching TV; happy	Happy; drinking
	Tired	Watching TV; eating
	Communicating	Tired
	Smelling food	Communicating; smelling food
	Sitting unsupported	Sitting unsupported
	Sitting supported	Sitting supported
	Walking	Walking
	Sleeping	Sleeping

The parental/primary caregivers' ratings of drooling severity before the Botox® correspond to the results of the three speech, language and hearing therapists. As mentioned previously, the **table top situation**, involving an activity requiring concentration, was the situation with the worst drooling. After treatment the parents/primary caregivers felt the mildest drooling was when the child was **communicating**, excluding sitting, walking and sleeping. This result also corresponds to the speech, language and hearing therapists' evaluations, where the reductions in drooling during the **communicating situation** were found to be statistically significant. In this instance it seems reasonable to assume that statistical significance corresponds to clinical significance (Goldstein, 1990).

c). Reduction/Improvement in Drooling during Activities

Parents/primary caregivers were then asked to indicate, again using the five point severity rating scale (Thomas-Stonell & Greenberg, 1988), during which activities or feelings they thought the most reduction in drooling had occurred. As can be

seen from Table 5.4.4, parents/primary caregivers thought the most improvement in drooling occurred during the **eating and drinking activities**. The least amount of improvement was thought to occur during **sleeping**.

Table 5.4.4: Parental/Primary Caregivers' Perceptions of Drooling Improvement in Activities/Feelings following Botox® Treatment (based on Van der Burg et al, 2006, a)

Improvement	Activities/Feelings
Most  Least	Eating
	Drinking; anxious
	Brushing teeth; tired; sick; watching TV; communicating
	Concentrating.
	Upset/crying; supported sitting
	Walking
	Unsupported sitting; smelling food; happy
	Sleeping

These results do not coincide with the therapists' ratings. From their results, there was a significant reduction in drooling severity and frequency in the **general and communicating situations**. The parents/primary caregivers perceived the most reduction or improvement in drooling to have occurred during **eating and drinking**. In this instance, there is very little/no correlation between statistical significance and clinical significance (Goldstein, 1990). Does this mean we should ignore the perceptions of parents/primary caregivers? In my view if treatment results do not make a difference in the lives of those we treat and the lives of their families, we have not done our job. To improve the quality of life of our clients we need to listen to them and understand what will make a difference to them. Watson, Abbott and Townsley (2006) argue convincingly for the voices of children with complex health care needs to be heard, not only in decisions about treatments, but also in research.

In chapter 2, I discussed the aspects of quality of life, with particular reference to the South African context. As a speech, language and hearing therapist, in other words a communication therapist, it was pleasing that the reduction in drooling ratings was significant for the **communicating situation**. However, in the South African context that the parents/primary caregivers of this study live, the improvement in drooling during **eating and drinking** was the most important.

d). Bib Use

In the present study, only 4 children used a bib. Before the Botox® injection 17 bibs were used in a day, giving an average of 4.25 bibs per day. After the treatment, only 10 bibs were used in a day, giving an average of 2.5 bibs a day, thus giving a 41% reduction in bibs used. This result correlates with results found in other studies. Banerjee et al (2006) found the reduction in the number of bibs worn in a day to be statistically significant, $p < 0.001$. As discussed in chapter 3, counting the number of bibs used in a day, before and after treatment, has been used to quantify the reduction in drooling.

Van der Burg et al (2006 a) used the wearing of bibs to investigate the impact drooling has on daily care and the economic consequences thereof. In their study, 84% of the participants wore bibs, almost twice the number of participants wearing bibs in the present study. This difference could be accounted for by the fact that 74% of the participants in Van der Burg et al's study (2006 a) had a developmental level of below six years and therefore could be expected to wear bibs. The bibs had to be replaced on average six to seven times a day. Participants also had to have several changes of clothing in a day because of their drooling.

e). Laundry Loads in a Week

In the study of Van der Burg et al (2006 a) on average 9 laundry loads per family were done in a week. In the present study, 3 parents/primary caregivers indicated that they ran three to four laundry loads a week before the treatment and the same parents/primary caregivers ran two to three loads after the treatment, giving a 30-

50% reduction in laundry loads. Three parents/primary caregivers indicated there was no difference in the number of laundry loads run, before and after the treatment. These results would seem to indicate that the parents/primary caregivers ran less laundry loads overall as compared to overseas studies.

This factor could be due to the participants requiring fewer bib/clothing changes in a day. In addition, some of the parents/primary caregivers were not in a position to run laundry loads every day, due to economic circumstances. It is highly likely that the majority of parents/primary caregivers in the present study do not run laundry loads. As indicated in the participant demographics, most of the parents/primary caregivers fall in the low socio-economic bracket, and probably do their washing by hand. The measure of laundry loads run has little relevance in the context of poverty and hand-washing. A more appropriate question would be to ask how the treatment had affected the amount of washing done. In a hand washing scenario, a 30-50% reduction in the amount of washing would provide considerable relief to parents/primary caregivers.

f). The Impact of Drooling on Social Interaction

Parents/primary caregivers were asked to indicate whether they thought drooling influenced:

- The amount of contact the children had with other children or adults;
- The amount of hugs and kisses given to the children;
- The estimation of mental ability by strangers.

As can be seen from Table 5.4.5, parents/primary caregivers felt their children's social interaction improved following the treatment. Comparisons are made to the results obtained in the Van der Burg et al study (2006 b).

Table 5.4.5: Parental/Primary Caregivers' Perceptions of their Children's Social Interaction

Social Interaction	No. & (%) of P/PCGs Who Felt Drooling Influenced Social Interaction			
	Present Study		Van der Burg et al's Study (2006b)	
	Before Trt.	Aft. Trt. Improvement	Before Trt.	Aft. Trt. Improvement
Avoided by other Children	3 (33%)- child was avoided 1 (11%)- child teased	6 (67%)- contact increased	35% - child was avoided	75% - contact increased
Avoided by Adults	4(44%) - child was avoided	4(44%) - contact increased	30% - child was avoided	No sign. change
Hugs and Kisses Received from Parents/primary caregivers	8 (89%) - gave hugs & kisses	4(44%) - no. of hugs & kisses increased	85% gave hugs & kisses. 15% of parents avoided child	No sign. change
Underestimation of Mental Ability by Strangers	6 (67%) - strangers underestimated ability	4 (44%) - underestimation by strangers was less	17% felt strangers underestimated ability	No sign. change

Key: No. = Number; % - Percentage; P/PCG - Parents/primary caregivers;
Trt - Treatment; Aft.- After; Sign. = Significant.

It is interesting to note that only 17% of parents in Van der Burg et al's study (2006 b) felt their children's mental ability was underestimated. This was probably due to the fact that 74% of the participants had a developmental level below six years. Van der Burg et al (2006 b) considered the effect of drooling on social interaction to be considerable. In support, they cite the fact that eight parents in their study avoided their own children. Although results from the present study did not include avoidance by parents, it was clear that the

parents/primary caregivers felt that drooling has a considerable effect on their children's social interaction.

g). General Quality of Life

Parents/primary caregivers were asked how they felt about their children's drooling. Five parents/primary caregivers felt it was a big problem and would do anything to reduce the drooling. Two parents/primary caregivers felt it was a problem, but would like non-invasive help. One parent/primary caregiver felt it was somewhat of a problem and might like non-invasive help. Only one parent/primary caregiver felt the drooling was not a problem.

The impression created from these results contradicts the clinical impression I have formed from talking to parents/primary caregivers. Most are not interested in the invasive procedure of surgery. I have no doubt that drooling is a big problem for the parents/primary caregivers of the present study, but it is possible that they felt they had to indicate that they would do anything to improve the drooling, to be considered for inclusion in another round of Botox® injections.

Eight parents/primary caregivers felt their children's quality of life had improved after the Botox® injections. They also felt the injection was worthwhile and would repeat the treatment. One parent/primary caregiver felt there had been little change in his child's quality of life, but the child's awareness of drooling had improved. One parent/primary caregiver did not respond to the general quality of life questions. This was the same parent/primary caregiver who indicated that drooling was not a problem and would not repeat the treatment.

Parental/primary caregiver comments included:

- Child is better behaved generally
- Child is more confident
- There is less teasing
- People in the African community are more willing to take an interest in the child

- Child is more aware of the drooling and makes an effort to wipe or swallow the drool.

The comment that people in the African community were more willing to interact with the child is particularly significant. As mentioned in chapter 2, Barratt (2007) found that parents/primary caregivers of disabled children often felt a sense of abandonment and isolation from their communities. It is possible that a reduction in drooling would foster better integration into the community for disabled children and their parents/primary caregivers.

h). Speech Therapy Notes Post Treatment

According to the therapy notes, there were no adverse reactions by any of the participants, following the Botox® injection. This result is consistent with published studies (Banerjee et al, 2006; Hassin-Baer et al, 2005; Jongerius, van den Hoogen et al, 2004; Kim et al, 2006).

It was felt that oral sensory awareness improved in 7 children post treatment. The grading of jaw opening appeared to have improved in all participants. Tongue placement appeared to have improved, as slightly less tongue thrusting was observed. However, 3 participants, including the 2 with operculum syndrome, still had little or no lateral tongue movement. Lip closure appeared to have improved, particularly in the operculum syndrome participants. An interesting observation commented on by not only the therapists but also by the parents/primary caregivers of the operculum syndrome participants, was that articulation in this group appeared to be clearer.

These findings seem to imply that with a decrease in the amount of saliva produced, oral motor skills and oral sensory processing improve. By extension, one could argue that Botox® injections into the salivary glands improve oral motor skills and oral sensory processing.

5.5. Phase Two

Reliability Measures in Phase Two

The results of the reliability measure in phase two, between the three speech, language and hearing therapists and the 'blind' independent rater are shown in Table 5.5.1. Reliability measures were calculated, using severity ratings only, not only for all children across all situations, but also for all children in each different situation. As can be seen from Table 5.5.1, they showed a fair to good agreement, except in the **drinking situation** (Cohen, 1988).

Table 5.5.1: Cohen's Kappa Coefficients for Therapists and 'Blind' Independent Rater (Cohen, 1988)

	Cohen's Kappa	Agreement
Severity - All Situations	0.50648	Fair
Severity - General Situation	0.4540	Fair
Severity- Table Top Activity	0.608699	Good
Severity - Drinking	0.2931	Poor
Severity - Eating	0.5027	Fair
Severity - Communicating	0.73937	Good

These values suggest that different speech, language and hearing therapists can rate drooling on the severity rating scale with some degree of reliability, particularly in the areas of **table top activities and communication situation**.

The severity of drooling rating scale itself (Thomas-Stonell & Greenberg, 1988) has good inter-rater reliability, as this scale, together with the frequency scale, has been used in other studies of drooling and shown good reliability (Ondo, Hunter & Moore, 2004; Senner, Logemann, Zecker & Gaebler-Spira, 2004). In addition, they are currently used in The Saliva Control Clinic at The Royal Children's Hospital, Melbourne with good reliability (Saliva Control in Children, 2007). It seems reasonable to assume therefore that the **drinking situation**, rather than the

scale, produced the poor reliability result. The independent rater was rating drooling from photographs, which show one instance in time, and not in a face to face setting. The three speech, language and hearing therapists were rating in a face to face setting. In addition, in some photographs it may have been difficult to distinguish between juice and drool, unless the colour of the juice could be seen. The use of a digital video camera, capturing the whole sequence of drinking and resultant drooling may have produced better inter-rater reliability/agreement.

In summary, the drooling severity rating scale (Thomas-Stonell & Greenberg, 1988) appeared to provide a reliable measure of drooling. It was an appropriate measure for use with the South African neurologically impaired children, in the clinical setting of the DTP. It was unfortunate, however, that the blind independent rater could not use the frequency rating scale.

5.6. An Additional Consequence from the Use of Botox®?

The children in the DTP, who were diagnosed with anterior operculum syndrome, following the Botox® injection, displayed not only decreased drooling but also improved articulation. This was noticed by their mothers and the speech therapist working with them. What could account for this seemingly improved articulation?

In their article "The motor theory of speech perception reviewed" Galantucci, Fowler and Turvey (2006) discuss the concept of "mirror neurons" found in the premotor cortex of primates and humans. "Individuals recognize actions made by others because the neural pattern elicited in their premotor areas during action observation is similar to that internally generated to produce that action" (Rizzolatti & Arbib, 1998, in Galantucci, Fowler & Turvey, 2006, p. 190). There is now evidence that perceiving speech involves neural activity of the motor system.

Galantucci et al (2006) cite two recent studies involving the use of transcranial magnetic stimulation of the motor cortex, which demonstrate activation of speech related muscles during the perception of speech. In addition, Wilson, Saygin,

Sereno and Iacoboni (2004, in Galantucci, Fowler & Turvey, 2006) demonstrated that there is an overlap between the cortical areas active during speech production and those active during passive listening to speech. Does this mean that because there was less saliva produced in the child's mouth following the Botox® injection, she perceived her own speech as being clearer, which in turn affected her articulation of the speech sounds?

Another possible explanation is that there was diffusion of the Botox® from the salivary glands to the tongue (D.Giampaulo, Neurologist, Personal Communication, 9 September, 2007). Studies of Botox® have shown its ability to disseminate beyond fascial planes (Suskind & Tilton, 2002). Botox® exerts its effect at the neuromusculature junction by inhibiting the release of acetylcholine, thus producing muscle relaxation (Brin & Aoki, 2002). Acetylcholine is the neurotransmitter in the nerves of the tongue. If, as according to Gordon (2002), operculum syndrome presents with weakness and spasticity of the oral musculature, a reduction in spasticity, following diffusion of Botox®, should facilitate easier articulation.

As mentioned previously in this chapter, it is possible that Botox® affects a central nervous system structure either directly, by being transported into central structures, or indirectly by altering central sensorimotor integration through a peripheral mechanism (Currà et al, 2004, p. 60). Articulation would be improved in both scenarios.

At this stage it is unclear what the reason for the improvement in articulation was or even if other children with anterior operculum syndrome treated with Botox® injections to the salivary glands would show improved, clearer articulation. If this is so, however, the use of Botox® would provide a potent therapeutic tool to improve articulation in a disorder that has a poor prognosis for improved clarity of speech. Further research into this area is warranted.

The results presented in this chapter have shown that Botox® injected into the submandibular salivary glands, is a safe option to reduce drooling in South

African neurologically impaired children. This result is consistent with previously published studies. Significant reductions in drooling rating scores were achieved in two contexts, the **general appearance** of the child and **the communicating situation**. These results are unique to this study, as drooling reductions in different daily situations following Botox® injections, as assessed by qualified, healthcare professionals, have not been considered before. The present study also showed that there was a difference in the pattern of response to the Botox® injection between the CP participants and the operculum syndrome participants. This result seems to imply that etiology is a factor in the response to Botox®. The South African parents/primary caregivers in the present study felt that the Botox® injections reduced their children's drooling and consequently improved the QoL of the children and themselves. Moreover, they felt it was a worthwhile procedure and would repeat it. As stated previously, the apparent improvement in the articulation of the operculum syndrome participants warrants further investigation.

In conclusion, there are many factors that need to be taken into account when deciding to use Botox® as a treatment for drooling. Although Lim et al (2006, p. 272) contend that Botox® "has the potential to become the treatment of choice for sialorrhea," the results from this study indicate that each neurologically impaired child's drooling needs to be assessed on an individual basis and the most appropriate treatment offered based on those needs. Therefore I believe that Botox® at the moment is not automatically the treatment of choice for drooling for every child.

Chapter 6 discusses the clinical implications of this study. The reliability of the measure of drooling used in the present study is discussed and suggestions are made regarding its use. As I feel that Botox® is not the automatic treatment of choice at the moment, an assessment model to determine eligibility for Botox® injections to reduce drooling is presented. The improved QoL of the participants and their parents/primary caregivers is considered in relation to theories of QoL. Limitations of the present study are discussed and improvements for future studies are suggested. The results from the present study have indicated several areas

where further research is needed. Thus implications for research are presented.

Finally, the relevance of using Botox® in the South African context is considered.

CHAPTER 6

CONCLUSIONS

The results of the present study indicate that severity and frequency of drooling can be reduced in South African neurologically impaired children with the use of Botox® injections into the submandibular glands. While these results are consistent with previously published studies, a difference in the pattern of drooling reductions between the CP group and the operculum syndrome group was shown in this study. The reductions in drooling severity and frequency for the participants with operculum syndrome were continuing to decrease at 24-26 weeks post Botox® injection, as opposed to most of the participants with CP, whose drooling severity and frequency rates were reverting back to baseline levels.

I also considered drooling in different contexts and a significant reduction in drooling rating scores and large effect sizes were obtained, following the Botox® injection in 2 situations – the **general appearance** of the child and the **communicating situation**. These results have implications for the speech, language and hearing therapist who works with neurologically impaired children who drool.

6.1: Clinical Implications

As most speech, language and hearing therapists know who work with severely drooling children, a significant reduction in drooling using non-invasive means is hard to achieve. Although Botox® cannot be considered non-invasive, it is less invasive than surgery and has none to few side effects, which most pharmacologic treatments have. As mentioned above, significant reductions in drooling severity and frequency rating scores, particularly during communication, can be achieved safely with Botox®. Thus speech, language and hearing therapists should consider using Botox® as a treatment option. However, a word of caution is needed.

A recent article in the Saturday Star (February 16 2008) reported on information that the US Food and Drug Administration (FDA) had received concerning systemic adverse reactions, including respiratory compromise and death, following the use of botulinum toxins (botox). The article goes on to explain that the use of botox has increased tremendously in South Africa, not only for use in neurological conditions but predominantly for a variety of cosmetic uses. Concern was expressed as to who was injecting botox, citing dentists, GPs, and physiotherapists.

One of the recommendations arising from the present study is that Botox® should only be administered by qualified medical personnel. I believe that while it is essential for speech, language and hearing therapists to be knowledgeable regarding Botox® and its uses, allowing us to be able to offer sound advice to parents/primary caregivers, we are not qualified to administer the toxin.

It is hoped that the results contained in this study provide South African speech, language and hearing therapists with information and guidelines regarding the use of Botox® to reduce drooling in pediatric clients.

My results have indicated in which situations a significant reduction in drooling rates can be expected to occur. Further, they inform speech, language and hearing therapists that individual variations in response to Botox® injections can be expected. The different pattern of response to the Botox® injection between the CP participants and the operculum syndrome participants seems to imply that the duration of effect of Botox® may be related to etiology. However, within the CP participants, there was little variation in response to Botox® between the different types of CP.

What does seem to influence the efficiency of Botox® is the severity of drooling at baseline. The CP participant with moderate drooling at baseline showed a greater reduction in drooling at 8 weeks, 38,8% than those with severe or mild drooling at baseline. It must be noted that even though the participants with operculum syndrome were rated with severe drooling at baseline, they responded

optimally with a 40% reduction in drooling at 24-26 weeks post injection. It is possible that severity of drooling at baseline may also affect the efficiency of Botox® in the CP population.

In chapter 3, I reviewed the various measures used to quantify drooling and justified the choice of the severity and frequency drooling rating scales (Thomas-Stonell & Greenberg, 1988) in the DTP. This study has shown that in the clinical setting of the DTP, these rating scales proved to be a reliable and appropriate measure of drooling for South African neurologically impaired children. It is suggested therefore that they should be used by speech, language and hearing therapists when assessing the drooling of neurologically impaired individuals. With the emphasis on evidence based treatment, initial ratings of drooling using these scales could be compared to ratings after treatment, thus providing evidence as to the efficacy of treatment.

Ideally drooling should be assessed at different times of the day, as drooling fluctuates throughout the day. In a clinical setting, assessments at different times of the day are often impossible to perform. It is then essential to rely on the parental/primary caregiver judgements of their child's drooling. In this study good reliability between the speech, language and hearing therapists' ratings and the parental/primary caregiver ratings was not shown. A possible method to improve this reliability is suggested later in this chapter.

What can and should be achieved in a clinical setting is the assessment of drooling in different contexts. The present study has shown that not only does drooling differ during different situations before treatment, but that the response to a treatment such as Botox®, is variable in different situations. As mentioned at the beginning of this chapter, there was a significant reduction in drooling severity and frequency rates in the general and communicating situations, while there was a moderate reduction of drooling severity and frequency rates in the table top activity, and the eating and drinking situations.

Perhaps a more important conclusion from the present study is that the use of Botox® for drooling must be based on individual needs and detailed assessments. For example, individuals with neuromuscular disorders such as myasthenia gravis, or significant pulmonary problems, should not use Botox®, as discussed in chapters 3 and 4 (Banerjee et al, 2006; Gioltzoglou et al, 2005; Tan, 2006).

The etiology of drooling needs to be carefully considered by the speech, language and hearing therapist before a recommendation to treat drooling with Botox® is made. Primary drooling is caused by an increase in saliva production, usually associated with inflammation, enlarged adenoids and tonsils, dental caries, mouth infections, certain medications, and esophageal reflux. Often drooling of this nature can be ameliorated by attending to the cause of the drooling.

Secondary drooling is due to impaired neuromuscular control and/or sensory dysfunction. Whether drooling is anterior or posterior also warrants close examination, as posterior drooling can lead to congested breathing, coughing, gagging, vomiting and occasionally aspiration into the trachea leading to pneumonia. Additional investigations, therefore, must be carried out if posterior drooling is suspected, not just treatment for drooling.

Factors that can exacerbate drooling, such as poor body and head positioning, poor oral-motor control, and a constantly open mouth need to be considered. Treatment should focus on these areas first before Botox® is recommended. In addition, the age of the child should be looked at as drooling can improve with oro-facial maturation. These issues have been explained in detail in chapter 3. It seems important to formalize an assessment model to determine eligibility for Botox® injections to reduce drooling. Figure 6.1.1 is an example of a possible model.

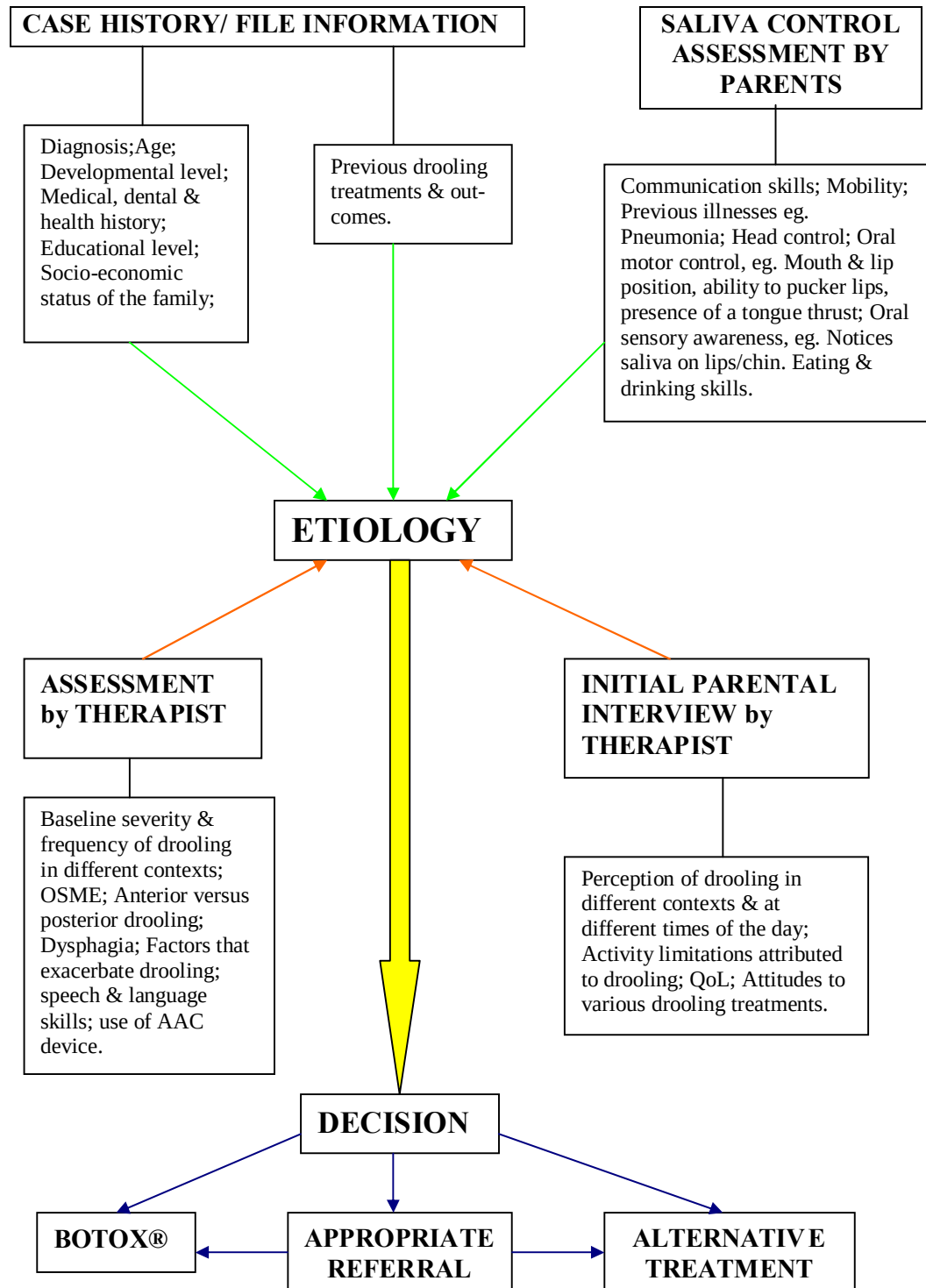


Figure 6.1.1: Proposed Assessment Model to Determine Eligibility for the Use of Botox® to Reduce Drooling in Neurologically Impaired Children

As can be seen from Figure 6.1.1, information from the case history, provided by numerous professional personnel, as well as the parents/primary caregivers, is needed. Assessments of factors that contribute to drooling and the situations in which drooling occurs are essential and should be obtained not only from the parents/primary caregivers but also from a speech, language and hearing therapist. An assessment of baseline drooling in the various contexts needs to be considered. Most importantly the effect of drooling on the child's and the parents/primary caregivers's lives must be considered. These factors point to the etiology and the impact of drooling. I suggest the use of this model is considered by healthcare professionals before making a recommendation as to the treatment of drooling, particularly when deciding to use Botox® to reduce drooling.

Returning to the article in The Star newspaper, the FDA also suggested that adverse reactions to Botox® could be related to overdosing and not from any defect in the product. This suggestion has major implications for the long term use of Botox®. It is imperative that the minimum dose necessary to produce a satisfactory response is used. As repeat injections of Botox® are needed, it is also essential to extend the duration of effect. In chapter 5, I discussed that it appears by combining intensive oral motor therapy with Botox®, the duration of effect can be prolonged and the functional outcome enhanced. Prolonging the duration of effect would also have a positive impact on the cost effectiveness of using Botox® to reduce drooling.

At present the use of Botox® is not covered by medical aid schemes in South Africa and it is certainly not used at government hospitals (K. Hofmeyr, 2007. Genop SA. Distributors of Botox® for Allergan Ltd. Personal Communication. 22 April 2007). Several studies have investigated the cost effectiveness of using Botox® for dystonia or spasticity. The conclusions are that the financial expense involved with Botox® is more than justified when compared to the cost of drugs, physiotherapy or surgery (Esquenazi, 2006; Jankovic, 2004). Cost effectiveness studies related to the use of Botox® for drooling need to be performed. As can be seen from figure 6.1.2 the use of Botox® to reduce drooling can possibly provide numerous benefits, one of which could be reduced overall costs.

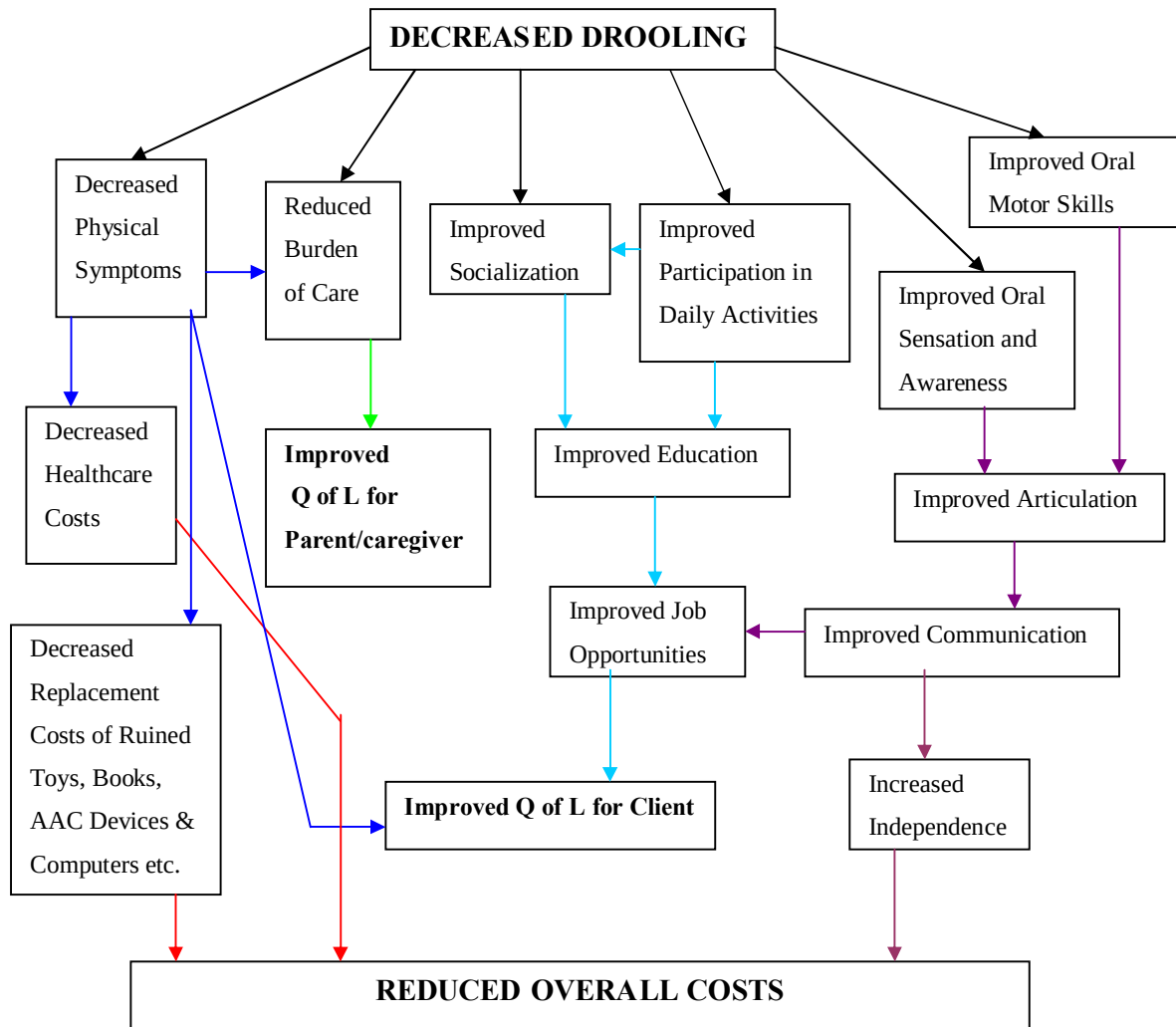


Figure 6.1.2: Possible Benefits from the Use of Botox® to Decrease Drooling

The possible benefits and reduced costs from the use of Botox® accrue not only to the parents/primary caregivers but also to the individuals who drool, as can be seen from the above figure. In addition, by increasing the independence and improving the job opportunities of the individuals who drool, the costs to the government could conceivably be reduced as well. As mentioned later in this chapter, costs analyses involved in the treatment of drooling by a variety of methods and comparisons between treatments, including Botox® need to be performed.

6.2: Quality of Life Revisited

One of the aims of reducing drooling is to improve the quality of life of the child and the parent/primary caregiver. Although at this stage very little is known about the relationship between drooling and the quality of life for South Africans, as discussed in chapter 2, I believe that drooling has a negative impact on the lives of South African neurologically impaired children and their parents/primary caregivers. The results from the present study seem to support my belief.

In chapter 2, I also discussed three theories of QoL – The Lindstrom and Eriksson model (1993), the discrepancy model (Eisner et al, 2000) and the utility model (Feeny et al, 1998). Although Davis et al (2006) argue that none of the models are appropriate for pediatric QoL, the descriptive analysis of the parents/primary caregivers' answers and views in the present study, as well as the views of caregivers expressed in Barratt's study (2007) and Saloojee et al's study (2006) seem to me to lend support for Lindstrom and Eriksson's model (1993).

In the global sphere, if the politics of a country do not allow for equal opportunities for disabled individuals and the community wherein the disabled individual and the parent/primary caregiver live isolates them (Barratt, 2007), then their quality of life is likely to be poor. The comments from the parents/primary caregivers in the present study indicate that they and their children had experienced isolation, but following the reduction in drooling, the isolation had lessened – people in the African community are more willing to take an interest in the child. Although South Africa supports the philosophy of equal opportunity for disabled individuals, and has an Integrated National Disability Strategy (1997) the practical implementation has yet to filter through to all people (Saloojee et al, 2006).

In the external sphere, the lack of educational and employment opportunities can impact negatively on QoL. Saloojee et al (2006) reported that 13% of the parents/primary caregivers interviewed had experienced difficulty in finding a school to accept their disabled children.

In the interpersonal sphere, disabled individuals often have difficulties with forming relationships (Nadeau & Tessier, 2006). Lack of friends can lead to feelings of isolation and consequently a negative QoL. Comments from the parents/primary caregivers following the reduction in drooling, such as "there is less teasing, more children will play with him, my child is better behaved" support the notion that the children had experienced difficulty in making friends with other children.

In the personal sphere, self-esteem and self-concept may be negatively affected in the disabled individual, particularly if the individual drools (Van der Burg et al, 2006 a). The comment "my child is more confident" supports the view that following a drooling reduction, the child's self esteem had improved and thus her QoL.

It is interesting to note that the parents/primary caregivers perceived the most improvement in drooling following the Botox® treatment, to have occurred during eating and drinking, whereas the speech, language and hearing therapists involved in the DTP judged the most improvement to be in the general and communicating situations. Reliability of the parental/primary caregivers' judgments may have been lacking, as determined by Cohen's Kappa coefficients (1988), but parents/primary caregivers are vital members of the team involved with the treatment of their disabled children and their views and the views of the disabled children should be paramount.

Parental/primary caregiver perceptions and the social consequences of drooling in the present study were found to be similar to views expressed by parents/primary caregivers in other studies (Van der Burg et al, 2006 b). It was clear that the South African parents/primary caregivers felt that their children's drooling had a considerable effect on their social interaction and quality of life and that these both improved after treatment with Botox®. These results support the belief of Tuna, Ünalán, Tuna and Kokina (2004, p. 648):

It is a well known fact that quality of life is subjective, and it should be considered that it may show important differences between countries or cultures. However, we believe that having a child with CP may well be deemed a universal problem which has profound shared characteristics experienced by all mothersé ..ô

An important footnote to this statement must be added. The parents/primary caregivers in the present study came from urban and semi-urban areas. If the statement by Tuna et al (2004) is true, then rural parents/primary caregivers should experience/perceive drooling in the same way. At this stage the accuracy of this statement is unknown. It is essential that the rural disabled population be consulted. A quality of life instrument that: includes considering the effects of drooling; is relevant to the unique South African rural disabled population, many of whom are illiterate; and considers the opinions of disabled children, needs to be formulated. Equally important, speech, language and hearing therapists must consider the QoL of the children they assess/treat and their parents/primary caregivers.

6.3: Research Implications

The results of this study have highlighted several areas for further research.

A replication of this study with larger numbers of participants in each category of CP would help to confirm the result that there is very little difference in response to Botox® within the different types of CP.

Likewise a replication of the study with larger numbers of participants categorized according to baseline ratings of drooling would confirm the hypothesis that there is a relationship between efficiency of response to Botox® and severity of drooling.

The difference in the pattern of response to Botox® between the CP participants and the operculum syndrome participants seems to imply that the duration of

Botox® effect is related to site or sites of lesions. Further research to validate this hypothesis is warranted.

As poor reliability was shown between the therapists' ratings and the parents/primary caregivers' ratings, it is suggested that further research is carried out to establish if providing the parents/primary caregivers with visual examples of drooling at each level of rating, would improve inter-rater reliability in this area. A universal clinical measure of drooling would then be available.

Previous studies on the use of Botox® to reduce drooling in neurologically impaired children have not differentiated between the response of the severity and the frequency of drooling to Botox®. The results of this study seem to indicate that there is a difference. Further research would confirm or refute this.

As mentioned in chapter 2, Rosenbaum et al (2007) feel there is a high priority to develop a scale for speech and laryngeal activity limitation in CP. Such a scale could include how much influence oral-motor functioning, oral sensitivity and awareness, and drooling have on activity limitations.

Senner et al (2004) found a positive relationship between severity of drooling and severity of dysarthria. They were, however, unable to explain the relationship. The results from the present study seem to indicate that articulation improves with a decrease in saliva production in the operculum syndrome participants.

The possibility that Botox® has an effect on oral motor skills, particularly articulation, provides another opportunity for research. The next step would be to investigate the effects of Botox® on drooling and oral motor skills, with an emphasis on articulation, within the operculum syndrome population versus a cerebral palsied population that is matched for age, gender, developmental level and severity and frequency of drooling. These criteria for sampling would necessitate a much larger sample size than the one in this study. Generalizations to the operculum syndrome population would then be possible.

Cost effectiveness studies in relation to the use of Botox® to improve drooling are needed.

The influence of drooling on quality of life, particularly in the rural population, should be considered together with the compilation of a pediatric quality of life instrument for the neurologically impaired. This measure should be relevant to the diverse population in South Africa and include a child self-report section. With such an instrument we would be able to compare the judged quality of life of South African neurologically impaired children and their parents/primary caregivers between an urban population and a rural population.

6.4: Limitations of the Study

Retrospective studies, as outlined in chapter 4, can lack validity and reliability of data. The fact that I had administrative control over the collection of the data in the DTP and the use of a 'blind' independent rater did control for validity and reliability to a certain extent.

The use of a convenience, small sample precludes generalization to the wider population. However, as already stated, the use of Botox® to control drooling should be based on individual assessments and needs.

The use of a still digital camera did not allow the 'blind' independent rater to assess drooling on the frequency rating scale. This could have been overcome by the use of a video digital camera. Unfortunately at the time of the DTP, one was not available.

Although drooling measurements were made during five different contexts, only one measurement was made for each context at each time period. As drooling is known to be variable, in the interests of scientific research it would have been appropriate to have taken several drooling measurements for each situation and each time period. An average could then have been calculated.

When comparing the repeated measurements over time, parametric analysis was used. However, as the drooling measurements can be considered ordinal, there is a slight possibility that a false positive result was given.

6.5: Concluding Remarks

There is every indication to suggest that the treatment of Botox® injections into the submandibular glands to reduce drooling in neurologically impaired South African children has worked. Further, the treatment worked for a period of time and across a number of dimensions. The treatment also provided an improved quality of life, not only for the participants, but also for their parents/primary caregivers. In addition, there is a compelling emerging suggestion that etiology may be important and that children diagnosed with operculum syndrome may be demonstrating a different overall response to this treatment, as opposed to the children with CP. This suggestion has potential implications in relation to proposed models of explanation with regard to neural pathways and their physiological structures.

If the judicious use of Botox® is to be extended, all stakeholders, from pharmaceutical companies, provincial hospitals, medical aids and government, need to be on board. We cannot allow only the wealthy to have access to the possible benefits. Botox® to reduce drooling must be available to all who would benefit. While I am cognizant of the expense and the tremendous hurdles needed to make this happen, and of other pressing issues, such as HIV/AIDS, alleviation of poverty, houses, electricity and sanitation for all, to name but a few, I am reminded of Martin Luther King's famous words:

‘I have a dream.....’

I, too, have a dream and this research has provided me with the impetus to continue to work towards that dream. As a clinician I have come a long way. Perhaps now I can call myself a clinician-researcher.

APPENDIX A**UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG**Division of the Deputy Registrar (Research)**HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)**

R14/49 Hay

CLEARANCE CERTIFICATE**PROTOCOL NUMBER M070540****PROJECT**

Botox to control drooling in South African neurologically impaired children: a retrospective study

INVESTIGATORS

Mrs N Hay

DEPARTMENT

Speech Pathology

DATE CONSIDERED

07.05.25

DECISION OF THE COMMITTEE*

APPROVED UNCONDITIONALLY

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.**DATE**

07.06.11

CHAIRPERSON

(Professors PE Cleaton-Jones, A Dhali, M Vorster, C Feldman, A Woodiwiss)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Prof C Penn

DECLARATION OF INVESTIGATOR(S)To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10005, 10th Floor, Senate House, University.I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES



UMnyango WezeMfundo
Department of Education

Lefapha Is
Thuto Departement van

Enquiries Shadrack PheJe

(011)3550265

12 June 2007

Mrs Nicola Mitchel Hay

12 Manor Close

Sandton 2055

Dear Mrs Nicola Hay

APPROVAL TO CONDUCT ACADEMIC RESEARCH

The Gauteng Department of Education hereby grants permission to conduct research in its institutions as per application.

Topic of research: "Botox® To Control Drooling In South African Neurologically Impaired Children; A Retrospective Study".

Degree: Master of Arts in Speech Pathology.

Name of university; University of the Witwatersrand.

Upon completion of the research project the researcher is obliged to furnish the Department with a copy of the research report (electronic or hard copy),

Wishing you success in your academic pursuit.

Sincerely,

pp Shadrack Phele

Albert Chanee
Divisional Manager
Education Financing, Planning and Monitoring.

Office of the Divisional Manager Education Financing, Planning and Monitoring
Room 1501, 111 Commissioner Street, Johannesburg, 2001.
P.O.Box 7710, Johannesburg, 2000 Tel:(011 365-0728) Fax:(011) 355-0670
E-mail: albertc@gpg.gov.za
Reference:2005efpm

APPENDIX C

Christopher A Joseph
M.B., B.Ch. (Wits), F.R.C.S. (Eng), F.C.S. (SA), M.Med. (Wits)
EAR NOSE & THROAT – HEAD & NECK SURGEON
MORNINGSIDE CLINIC
Honorary Associate Professor,
Dept. Otorhinolaryngology, Head and Neck Surgery
Medical University of South Africa

Tel: 884-5643/44
Fax: 884-5647
Residence: 011 883-2841
✉ 553 River Club 2149

29 January 2007

To whom it may concern

I have no objection to Ms. N. Hay using data from results of treating my patients with intraglandular Botox for excessive drooling.

Note that this is recognised treatment for excessive drooling.

Yours sincerely

A handwritten signature in black ink, appearing to read 'Chris Joseph'. The signature is written in a cursive style and is positioned above the printed name.

PROF. CHRIS JOSEPH

APPENDIX D

PRINCIPAL CONSENT FORM

I hereby consent to the use of all data, relating to the children in my school, obtained from the drooling treatment procedure last year. Furthermore, I give the researcher, Nicola Hay, permission to use the responses and all data relating to the children, in the write up of the study and in future publications or presentations.

I understand that participation in the study is voluntary and that I am free to refuse to participate or to give my consent to the use of any data relating to the children at my school at any time. I understand that nothing will be held against me or my school, should I refuse permission.

I understand that my and my school's privacy will be maintained, should I choose not to have the school's name included in the study report. I am aware that if I, the parents and the children have any questions at any time, they will be answered. It has been explained to me that the study procedures will not in any way interfere or disrupt the school day.

Please circle your response: I give Nicola Hay permission to use data from:

Initial, pre-injection assessment, completed by the parent and three qualified speech therapists. **YES** **NO**

Post injection assessments, completed at 7 weeks and 24 weeks, completed by the parent and three qualified speech therapists. **YES** **NO**

Assessments by an independent rater, who would be a qualified speech therapist, who was not involved with the initial project. **YES** **NO**

All photographs of the children drooling, taken in such a way that identification of a child is impossible. **YES** **NO**

Medical data obtained from the Ear, Nose and Throat specialist, Professor Joseph, concerning the amount of Botox used with a child. **YES** **NO**

A child's school file, such as case history details, diagnoses of neurological impairment, cognitive abilities and any previous treatment for drooling a child may have had, with consent from the child's parent. **YES** **NO**

Inclusion of the school's name in the study report. **YES** **NO**

I **AGREE** **DISAGREE** to the consent forms being given to the mothers and children.

Date:_____

Signature:_____

APPENDIX E

PARENT/CAREGIVER CONSENT FORM

I hereby consent to the use of all information, relating to my child, obtained from the drooling treatment procedure last year. Furthermore, I give the researcher, Nicola Hay, permission to use my responses and all information relating to my child, in the write up of the study and in future publications or presentations.

I understand that participation in the study is voluntary and that I am free to refuse to participate or to give my consent to the use of any information relating to my child at any time. I understand that this will not affect the way my child will be treated at school, should I refuse permission. I also understand that this also applies to my child. In other words he/she may refuse to give consent to use the information pertaining to him/her at any time.

I understand that my and my child's privacy will be maintained and that any information my child and I choose to divulge will remain strictly confidential. I am aware that if I and my child have any questions at any time, they will be answered and that appropriate referrals and recommendations will be made available to me should I and/or my child require them.

Please circle your response: I give Nicola Hay permission to use information from:

Initial, pre-injection assessment, completed by myself and three qualified speech therapists. **YES** **NO**

Post injection assessments, completed at 7 weeks and 24 weeks, completed by myself and three qualified speech therapists. **YES** **NO**

Assessments by an independent rater, who would be a qualified speech therapist, who was not involved with the initial procedure. **YES** **NO**

All photographs of my child drooling, taken in such a way that identification of my child is impossible. **YES** **NO**

Post injection questionnaires filled in by me and the interview information. **YES**
NO

Medical data obtained from the Ear, Nose and Throat specialist, Professor Joseph, concerning the amount of Botox used with my child. **YES** **NO**

My child's school file, such as case history details, diagnosis of neurological impairment, cognitive ability and any previous treatment for drooling my child may have had. **YES** **NO**

I do / do not wish to attend the second interview, scheduled for late June at Forest Town School.

Date: _____

Signature: _____

APPENDIX F**CHILD ASSENT FORM**

My name is Nicola Hay and I am doing a study based on the treatment drooling project that we did last year. I want to know if you want to be in the study. You do not have to say yes and you will not get into trouble if you say no.

You will not have to do anything in the study, but I do need your permission to use the results from the drooling treatment project and the photographs that were taken. Nobody will know that it is you in the results or the photographs, as your name will not be used and the photographs will just be of your mouth. I will not show the results or photographs to anyone if you do not want me to. You may tell me at any time that you do not give me permission to use your results and photographs.

Please circle if you want to be in my study and you give me your permission.

YES

NO

My name is _____

Today is the _____

APPENDIX G**SALIVA CONTROL ASSESSMENT FORM**

Date: _____

Name: _____

1. Communication Skills:

- ☐ No problems
- ☐ Some speech which is functional
- ☐ Uses speech to get message across but with difficulty
- ☐ Has difficulty making sounds in words
- ☐ Has no speech

2. Walking:

- ☐ No difficulty
- ☐ Has some difficulty but walks independently without an aid
- ☐ Needs a walking aid
- ☐ Uses a wheelchair all or most of the time

3. Head Position:

- ☐ Can hold head up without difficulty
- ☐ Tends to sit with head down mostly

4. Is mouth always open ?

- ☐ Yes ☐ No ☐ Unsure

5. Lips:

- ☐ Can hold lips together easily and for a long time
- ☐ Can hold lips together with ease for a limited time
- ☐ Can hold lips with effort for a limited time
- ☐ Can bring lips together only briefly
- ☐ Unable to bring lips together

6. Can he/she pucker lips (as in a kiss) ?

- ☐ Yes ☐ No ☐ Unsure

7. Does he/she push the tongue out when swallows ?

- ☐ Yes ☐ No ☐ Unsure

8. Straw:

- ☐ Can use straw easily
- ☐ Has difficulty using a straw
- ☐ Cannot use a straw

9. Eating/drinking:

- ☐ Can eat whole hard foods that are difficult to chew
- ☐ Eats a wide range of foods
- ☐ Needs to have food cut into small pieces
- ☐ Food needs to be mashed/pureed
- ☐ Drinks need to be thickened
- ☐ Has food through a tube (nasogastric/gastrstomy)

10. Is he/she a messy eater ?

- ☐ Yes ☐ No ☐ Unsure

11. Can he/she swallow saliva when asked to ?

- ☐ Yes ☐ No ☐ Attempts ☐ Unsure

12. Does he/she notice saliva on lips/chin (perhaps tries to wipe chin) ?

- ☐ Yes ☐ No ☐ Unsure

13. General Health

Does he/she have asthma ?

- ☐ Yes ☐ No ☐ Unsure

Does he/she have frequently blocked or runny nose ?

- ☐ Yes ☐ No ☐ Unsure

Does he/she have bouts of pneumonia ?

- ☐ Yes ☐ No ☐ Unsure

14. Are there any difficulties with teeth cleaning ?

- ☐ Yes ☐ No ☐ Unsure

15. Has there been a recent dental check ?

- ☐ Yes ☐ No ☐ Unsure

If Yes, who with ?

16. Are there any problems with bleeding gums or decayed teeth ?

- ☐ Yes ☐ No ☐ Unsure

Thank you for completing this questionnaire

THERAPISTS' ASSESSMENT FORM

NAME: _____

DATE: _____

FORM COMPLETED BY: _____

1. GENERAL APPEARANCE OF CHILD - when not doing an activity

	RATING
FREQUENCY OF DROOLING	
SEVERITY OF DROOLING	

	COMMENT
BODY POSTURE / POSITION	
HEAD POSITION / CONTROL	
TONGUE PLACEMENT	
JAW POSITION / STABILITY	
LIP POSITION	
SENSORY AWARENESS	

2. CHILD PARTICIPATING IN TABLE TOP ACTIVITY

	RATING
FREQUENCY OF DROOLING	
SEVERITY OF DROOLING	

	COMMENT
BODY POSTURE / POSITION	
HEAD POSITION / CONTROL	
TONGUE PLACEMENT	
JAW POSITION / STABILITY	
LIP POSITION	
SENSORY AWARENESS	

FREQUENCY OF DROOLING

NEVER DROOLS 1
 OCCASIONALLY DROOLS 2
 FREQUENTLY DROOLS 3
 CONSTANTLY DROOLS 4

SEVERITY OF DROOLING

DRY - NEVER DROOLS 1
 MILD - WET LIPS ONLY 2
 MODERATE - WET LIPS AND CHIN 3
 SEVERE - CLOTHING BECOMES DAMP 4
 PROFUSE - CLOTHING, HANDS, TRAY, 5
 TABLE, OBJECTS ARE WET

3. CHILD EATING - self feeding / assisted feeding

	RATING - self	RATING - with help
FREQUENCY OF DROOLING		
SEVERITY OF DROOLING		

	COMMENT
BODY POSTURE / POSITION	
HEAD POSITION / CONTROL	
TONGUE PLACEMENT	
JAW POSITION / STABILITY	
LIP POSITION	
SENSORY AWARENESS	

4. CHILD DRINKING - cup / straw

	RATING - cup	RATING - straw
FREQUENCY OF DROOLING		
SEVERITY OF DROOLING		

	COMMENT
BODY POSTURE / POSITION	
HEAD POSITION / CONTROL	
TONGUE PLACEMENT	
JAW POSITION / STABILITY	
LIP POSITION	
SENSORY AWARENESS	

FREQUENCY OF DROOLING

NEVER DROOLS	1
OCCASIONALLY DROOLS	2
FREQUENTLY DROOLS	3
CONSTANTLY DROOLS	4

SEVERITY OF DROOLING

DRY - NEVER DROOLS	1
MILD - WET LIPS ONLY	2
MODERATE - WET LIPS AND CHIN	3
SEVERE - CLOTHING BECOMES DAMP	4
PROFUSE - CLOTHING, HANDS, TRAY, TABLE, OBJECTS ARE WET	5

5. COMMENT ON CHILD WHEN COMMUNIATING

	RATING
FREQUENCY OF DROOLING	
SEVERITY OF DROOLING	

	COMMENT
BODY POSTURE / POSITION	
HEAD POSITION / CONTROL	
TONGUE PLACEMENT	
JAW POSITION / STABILITY	
LIP POSITION	
SENSORY AWARENESS	

GENERAL COMMENTS:

FREQUENCY OF DROOLING

NEVER DROOLS	1
OCCASIONALLY DROOLS	2
FREQUENTLY DROOLS	3
CONSTANTLY DROOLS	4

SEVERITY OF DROOLING

DRY - NEVER DROOLS	1
MILD - WET LIPS ONLY	2
MODERATE - WET LIPS AND CHIN	3
SEVERE - CLOTHING BECOMES DAMP	4
PROFUSE - CLOTHING, HANDS, TRAY, TABLE, OBJECTS ARE WET	5

GLOSSARY:

JAW POSITION FOR CONSONANT AND VOWEL PRODUCTIONS

HIGH	m b p f v n s z sh tch r	closed
MEDIUM	th 1 t d	
LOW	g k h	

SENSORY AWARENESS

Is the child able to feel the saliva pooling in the mouth or running down the lips and chin?

Hyposensitivity - inability or reduced ability to react to sensory input

Hypersensitivity - increased / abnormally heightened reaction to sensory input

Tactile Defensiveness - a learned tendency to respond negatively to sensory input

BODY POSTURE

Optimal body positioning will allow for better control of saliva

DROOLING

The inability or reduced ability to organise and swallow saliva

PARENTS' ASSESSMENT FORM

Name: _____

Date: _____

1. GENERAL APPEARANCE OF CHILD - when not doing an activity

	RATING
FREQUENCY OF DROOLING	
SEVERITY OF DROOLING	

2. CHILD PARTICIPATING IN TABLE TOP ACTIVITY

	RATING
FREQUENCY OF DROOLING	
SEVERITY OF DROOLING	

3. CHILD EATING - independent feeding / assisted feeding (with help)

	RATING - indep	RATING - with help
FREQUENCY OF DROOLING		
SEVERITY OF DROOLING		

4. CHILD DRINKING - cup / straw

	RATING - cup	RATING - straw
FREQUENCY OF DROOLING		
SEVERITY OF DROOLING		

5. COMMENT ON CHILD WHEN COMMUNICATING

	RATING
FREQUENCY OF DROOLING	
SEVERITY OF DROOLING	

SEVERITY OF DROOLING

DRY - NEVER DROOLS	1
MILD-WET LIPS ONLY	2
MODERATE - WET LIPS AND CHIN	3
SEVERE - CLOTHING BECOMES DAMP	4
PROFUSE - CLOTHING, HANDS, TRAY, TABLE, OBJECTS ARE WET	5

FREQUENCY OF DROOLING

NEVER DROOLS	1
OCCASIONALLY DROOLS	2
FREQUENTLY DROOLS	3
CONSTANTLY DROOLS	4

APPENDIX J

INTERVIEW QUESTIONS FOR PARENTS

1. Do you think the drooling injection was worthwhile? Yes No
2. Would you allow your child to have another injection? Yes No
3. How many bibs/scarves did your child use in a day before the injection?
4. How many bibs/scarves did your child use in a day after the injection?
5. Before the injection, how many loads of laundry did you do in a week?
6. Did the number decrease after the injection? Yes No If yes, how many?

Social Consequences of Drooling

1. Before the injection, did your child play with other children at home? Yes No
2. Did the amount of time other children played with your child increase after the injection? Yes No
3. Before the injection, was your child avoided by other children? Yes No
4. After the injection, did this improve? Yes No
5. Before the injection, did adults avoid contact with your child? Yes No
6. After the injection, did this improve? Yes No
7. Before the injection, how many hugs or kisses in a day, did you or another family member give your child?
8. After the injection, did the number increase? Yes No If yes, how many?
9. Before the injection, did strangers underestimate your child's mental ability? Yes No
10. Did this improve after the injection? Yes No If yes, how?
11. Do you think your child's quality of life improved after the injection? Yes No If yes, how?
12. How do you rate the problem of drooling, as part of your child's disability?

1-----Not really a problem

2-----Some problem, but not enough to warrant intervention

3-----A problem, would like non-invasive, conservative help

4-----A big problem, interferes with all aspects of life, would try anything to help.

13. How do you think your child rates his/her drooling? Use the above rating scale.

APPENDIX K**QUESTIONNAIRE TO PARENTS**

1a. Before the injection, at what time during the day did your child drool?

☐ Morning ☐ Afternoon ☐ Night

1b. After the injection, at what time during the day did your child drool the most?

☐ Morning ☐ Afternoon ☐ Night

2a. Before the injection, during what activities did he/she drool?

Concentrated activity ☐ Relaxed, watching TV ☐ Walking ☐ Doing sports ☐

Sitting ☐ Sleeping ☐ Drinking ☐ Eating ☐ Talking ☐ Brushing teeth ☐
with support

Sitting ☐ Smell or taste of ☐ When tired ☐ When ill ☐ Crying ☐
without support certain foods

When happy ☐ When anxious ☐ Lying on back ☐ Lying on tummy ☐
or laughing

2b. After the injection, during what activities did he/she drool?

Concentrated activity ☐ Relaxed, watching TV ☐ Walking ☐ Doing sports ☐

Sitting ☐ Sleeping ☐ Drinking ☐ Eating ☐ Talking ☐ Brushing teeth ☐
with support

Sitting ☐ Smell or taste of ☐ When tired ☐ When ill ☐ Crying ☐
without support certain foods

When happy ☐ When anxious ☐ Lying on back ☐ Lying on tummy ☐
or laughing

Severity of drooling: 1----no drooling

2----mild, wet lips only

3----moderate, wet lips and chin

4----severe, clothing becomes damp

5----profuse, clothing, hands, tray, table, objects are wet

APPENDIX L**INDEPENDENT RATER'S ASSESSMENT FORM**

NAME OF RATER: _____

DATE: _____

PHOTOGRAPH _____

	RATING
SEVERITY OF DROOLING	

PHOTOGRAPH _____

	RATING
SEVERITY OF DROOLING	

PHOTOGRAPH _____

	RATING
SEVERITY OF DROOLING	

PHOTOGRAPH _____

	RATING
SEVERITY OF DROOLING	

PHOTOGRAPH _____

	RATING
SEVERITY OF DROOLING	

REFERENCES

- African National Congress (1994). A National Health Plan for South Africa. The African National Congress: Johannesburg.
- Albrecht, G.L. & Devlieger, P.J. (1999). The disability paradox: high quality of life against all odds. Social Science and Medicine, 48, 977-988.
- Alexander, R., Boehme, R. & Cupps, B. (1993). Normal Development of Functional Motor Skills: The First Year of Life. Tucson: Therapy Skill Builders.
- Allaire, J.H. (1999). Parent Articles About NDT. Drooling: Ways to Manage a Difficult Problem. Tucson: Therapy Skill Builders.
- American Psychological Association. (2001). Publication Manual of the American Psychological Association. (5th ed.). Washington, DC: American Psychological Association.
- Aoki, K.R. & Guyer, B. (2001). Botulinum toxin type A and other botulinum toxin serotypes: a comparative review of biochemical and pharmacological actions. European Journal of Neurology, 8 (5), 21-29.
- Appelbaum, P.S., Roth, L.H., Lidz, C.W., Benson, P., and Windale, W. (1987). False hopes and best data: Consent to research and the therapeutic misconception. Hastings Centre Report, 12 (2), 20-24.
- Baker, T.L. (1994). Doing Social Research. (2nd ed.) New York: McGraw-Hill.
- Banerjee, K.J., Glasson, C., & O'Flaherty, S.J. (2006). Parotid and submandibular botulinum toxin A injections for sialorrhea in children with cerebral palsy. Developmental Medicine and Child Neurology, 48, 883-887.

Barnes, M.P., Best, D., Kidd, K., Roberts, B., Stark, S., Weeks, P. & Whitaker, J. (2005). The use of botulinum toxin type B in the treatment of patients who have become unresponsive to botulinum toxin type A – initial experiences. European Journal of Neurology, 12, 947-955.

Barratt, J.F. (2007). The experience of caring for a child with cerebral palsy in Tonga, Mpumalanga: caregivers's stories. Unpublished Master's Dissertation. Speech Pathology and Audiology, University of the Witwatersrand, Johannesburg.

Bax, M. (1964). Terminology and classification of cerebral palsy. Developmental Medicine and Child Neurology, 6, 295-307.

Bax, M. (1992). Drooling. Developmental Medicine and Child Neurology, 34 (10), 847-848.

Bax, M., Flomark, O. & Tydeman, C. (2007). Future directions. From syndrome toward disease. In A report: the definition and classification of cerebral palsy April 2006. Developmental Medicine and Child Neurology, 49, 1- 43.

Berweck, S., Schroeder, A.S., Lee, S-H., Bigalke, H. & Heinen, F. (2007). Secondary non-response due to antibody formation in a child after three injections of botulinum toxin B into the salivary glands. Developmental Medicine and Child Neurology, 49, 62-64.

Bjornson, K.F. & McLaughlin, J. (2001). The measurement of health-related quality of life (HRQL) in children with cerebral palsy. European Journal of Neurology, 8 (5), 183-193.

Blasco, P. (2003). "Blasco replies." Developmental Medicine and Child Neurology, 45 (12), 845-846.

- Blasco, P.A. & Allaire, J.H. (1992). Drooling in the developmentally disabled: management practice recommendations. Consortium on Drooling. Developmental Medicine and Child Neurology, 34 (10), 849-862.
- Bobath, K. (1980). A Neurophysiological Basis for the Treatment of Cerebral Palsy. (2nd edition). London: William Heinemann Medical Books.
- Boner, M.M. & Perlin, W.S. (1994). Oral-Motor and Swallowing Skills in the Infant and Child: An Overview. Ch.2. In Cherney, L.R. Clinical Management of Dysphagia in Adults and Children. (2nd ed). Maryland: Aspen.
- Bothwell, J.E., Clarke, K., Dooley, J.M., Gordon, K.E., Anderson, R., Wood, E.P., Camfield, C.S. & Camfield, P.R. (2002). Botulinum toxin A as a treatment for excessive drooling in children. Pediatric Neurology, 27 (1), 18-22.
- Bray, R. & Dawes, A. (2007). Monitoring the well-being of children: historical and conceptual foundations. In A. Dawes, R. Bray, & A. Van Der Merwe (Eds). Monitoring Child Well-Being: A South African Rights-Based Approach (pp. 5-52). Cape Town: HSRC Press.
- Brin, M.F. & Aoki, K.R. (2002). Botulinum Toxin Type A: Pharmacology. In Mayer, N.H. & Simpson, D.M., editors. Spasticity: Etiology, Evaluation, Management and the Role of Botulinum Toxin. WE MOVE_{TM}.
- Brin, M.F., Hallett, M. & Jankovic, J. (2002). Scientific and Therapeutic Aspects of Botulinum Toxin. Philadelphia: Lippincott Williams & Wilkins.
- Brin, M.F., Stewart, C. & Blitzer, A. (1994). Laryngeal botulinum toxin injections for disabling stuttering in adults. Neurology, 44, 2262-2266.

- Brodsky, L. (2002). Drooling in Children. Ch.11. In Arvedson, J.C. & Brodsky, L. Pediatric Swallowing and Feeding: Assessment and Management. (2nd ed). San Diego: Singular.
- Bruyn, G.W. & Gathier, J.C. (1969). The operculum syndrome. In: Vinken, P.J. & Bruyn, G.W., editors. Handbook of Clinical Neurology, Vol.2. Localization in Clinical Neurology. Amsterdam: North-Holland.
- Camp-Bruno, J.A., Winsberg, B.G., Green-Parsons A.R., & Abrams, J.P. (1989). Efficacy of benztropine therapy for drooling. Developmental Medicine and Child Neurology, 31, 309-319.
- Castaneto, M.V. & Willemsen, E.W. (2007). Social perception of the development of disabled children. Child: Care, Health and Development, 33, 308-318.
- Christen, H.J., Hanefeld, F., Kruse, E., Imhäuser, S., Ernst, J.P. & Finkenstaedt, M. (2000). Foix-Chavany-Marie (anterior operculum) syndrome in childhood: a reappraisal of Worster-Drought syndrome. Developmental Medicine and Child Neurology, 42, 122-132.
- Cicchetti, D.V., & Sparrow, S.A. (1981). Developing criteria for establishing inter-rater reliability of specific items: Applications to assessment of adaptive behaviour. American Journal of Mental Deficiency, 86, 127-137.
- Cohen, J. (1988). Statistical Power Analysis for the Behavioral Sciences. (2nd ed.). Mahwah, NJ: Lawrence Erlbaum Associates.
- Coskun, B.U., Savk, H., Cicek, E.D., Basak, T., Basak, M. & Dadas, B. (2007). Histopathological and radiological investigations of the influence of botulinum toxin on the submandibular gland of the rat. European Archives of Otorhinolaryngology, 264, 783-787.

- Couper, J. (2002). Prevalence of childhood disability in rural Kwa-Zulul Natal. South African Medical Journal, 92, 549-552.
- Crysdale, W.S. (1989). Management options for the drooling patient. Ear Nose Throat Journal, 68, 825-830.
- Crysdale, W.S., McCann, C., Roske, L., Joseph, M., Semenuk, D. & Chait, P. (2006). Saliva control issues in the neurologically challenged: a 30 year experience in team management. International Journal of Pediatric Otorhinolaryngology, 70, 519-527.
- Curà, A., Trompetto, C., Abbruzzese, G. and Berardelli, A. (2004). Central effects of Botulinum toxin Type A: Evidence and supposition. Movement Disorders, 19 (8), S60-S64.
- Darley, F.L., Aronson, A.E. & Brown, J.R. (1975). Motor Speech Disorders. Philadelphia: W. B. Saunders Company.
- Davis, E., Waters, E., Mackinnon, A., Reddihough, D., Graham, H.K., Mehmet-Radji, O. & Boyd, R. (2006). Paediatric quality of life instruments: a review of the impact of the conceptual framework on outcomes. Developmental Medicine and Child Neurology, 48, 311-318.
- Dawes, A., Bray, R. & Van Der Merwe, A. (Eds). (2007). Monitoring Child Well-Being: A South African Rights-Based Approach. Cape Town: HSRC Press.
- Despopoulos, A. & Silbernagl, S. (2003). Color Atlas of Physiology. 5thEd. Thieme ElectronicBook Library. Retrieved from <http://www.wits.ac/library/elecrec/ebook.htm> on 23/08/2007.
- Deuschl, G., Lohle, E., Heinen, F. & Lucking, C. (1991). Ear click in palatal tremor: its origin and treatment with botulinum toxin. Neurology, 41, 1677-1679.

- Dickinson, H.O., Parkinson, K.N., Ravens-Sieberer, U., Schirripa, G., Thyen, U., Arnaud, C., Beckung, E., Fauconnier, J., McManus, V., Michelsen, S.I., Parkes, J. & Colver, A.F. (2007). Self-reported quality of life of 8-12-year-old children with cerebral palsy: a cross-sectional European study. Lancet, 369, 2171-2178.
- Doggweiler, R., Zermann, D-H., Ishigooka, M. & Schmidt, R.A. (1998). Botox-induced prostatic involution. The Prostate, 37 (1), 44-50.
- Dooley, D. (1995). Social Research Methods. (3rd ed.) New Jersey: Prentice Hall.
- Eisner, C. & Morse, R. (2001). A review of measures of quality of life for children with chronic illness. Archives of Disease in Childhood, 84, 205-211.
- Eisner, C., Vance, Y.H. & Seamark, D. (2000). The development of a theoretically driven generic measure of quality of life for children aged 6-12 years: a preliminary report. Child Care and Health Development, 26, 445-456.
- Ellies, M., Rohrbach-Volland, S., Arglebe, C., Wilken, B., Laskawi, R., & Hanefeld, F. (2002). Successful management of drooling with botulinum toxin A in neurologically disabled children. Neuropediatrics, 33, 327-330.
- Erbguth, F.J. (2004). Historical notes on botulism, Clostridium botulinum, botulinum toxin, and the idea of the therapeutic use of the toxin. Movement Disorder, 19 (8), 2-6.
- Esquenazi, A. (2006). Improvements in healthcare and cost benefits associated with botulinum toxin treatment of spasticity and muscle overactivity. European Journal of Neurology, 13, 27-34.

- Faulconbridge, R.V., Tranter, R.M., Moffat, V. & Green, E. (2001). Review of management of drooling problems in neurologically impaired children: a review of methods and results over 6 years at Chailey Heritage Clinical Services. Clinical Otolaryngology, 26, 76-81.
- Feeny, D., Furlong, W. & Barr, R.D. (1998). Quality of life assessment: Health Utilities Index. Medical Pediatric Oncology, 1, 54-59.
- Ferguson, D.B. (1988). Physiology for Dental Students. UK: Butterworth & Co. Ltd.
- Franklin, R.D., Allison, D.B. & Gorman, B.S. (editors). (1996). Design and Analysis of Single-case Research. New Jersey: Lawrence Erlbaum Associates.
- Galantucci, B., Fowler, C. A., & Turvey, M.T. (2006). The motor theory of speech perception reviewed. Psychonomic Bulletin and Review, 13 (3), 361-377.
- Giess, R., Naumann, M., Werner, E., Riemann, R., Beck, M., Puls, I., Reiners, C. & Toyka, K.V. (2000). Injections of botulinum toxin A into the salivary glands improve sialorrhoea in amyotrophic lateral sclerosis. Journal of Neurology, Neurosurgery, and Psychiatry, 69, 121-123.
- Gillman, S. & Newman, S.W. (1992). Manter and Gatz's Essentials of Clinical Neuroanatomy and Neurophysiology. 8th Ed. USA: F.A. Davis Company.
- Gioltozoglou, T., Cordivari, C., Lee, P.J., Hanna, M.G. & Lees, A.J. (2005). Problems with botulinum toxin treatment in mitochondrial cytopathy: case report and review of the literature. Journal of Neurology, Neurosurgery, and Psychiatry, 76, 1594-1596.

- Glickman, S. & Deaney, C.N. (2001). Treatment of relative sialorrhoea with botulinum toxin type A: description and rationale for an injection procedure with case report. European Journal of Neurology, 8, 567-571.
- Goldstein, H. (1990). Assessing clinical significance. In L.B. Olswang, C.K. Thompson, S.F. Warren & N.J. Minghetti (Eds.). Treatment Efficacy Research in Communication Disorders. 91-98. Rockville: ASHA.
- Gordon, N. (2002). Worsteri Drought and congenital bilateral perisylvian syndromes. Developmental Medicine and Child Neurology, 44 (3), 201-204.
- Green, J.H. (1976). An Introduction to Human Physiology. 4th Ed. UK: Oxford University Press.
- Greenstein, B. & Greenstein, A. (2000). Color Atlas of Neuroscience. Thieme ElectronicBook Library. Retrieved from <http://www.wits.ac/library/elecres/ebook.htm> on 24/08/2007.
- Grue, I. (2003). Do adolescents with disabilities view themselves different from other young people? Developmental Medicine and Child Neurology, 45 (8), (Abstract).
- Hameed, B.A., Miller, H., Curran, A.L., Pauldhas, D., Mccarter, R.J., Hunt, L. & Sharples, P.M. (2008). Health-related quality of life and its determinants at 1, 6, and 12 months in children with traumatic brain injury and non-injured controls. BPNA Abstracts, p. 34.
- Hammal, D., Jarvis, S.N. & Colver, A.F. (2004). Participation of children with cerebral palsy is influenced by where they live. Developmental Medicine and Child Neurology, 46, 292-298.

- Hassin-Baer, S., Scheuer, E., Buchman, A.S., Jacobson, I. & Ben-Zeev, B. (2005). Botulinum toxin injections for children with excessive drooling. Journal of Child Neurology, 20 (2), 120-123.
- Hemmingson, A. & Borell, H. (2002). Environmental barriers in mainstream schools. Child: Care, Health and Development, 28, 57-63.
- Hinks, T. & Gruen, C. (2007). What is the structure of South African happiness equations? Evidence from quality of life surveys. Social Indicators Research, 82, 311-336.
- Hockstein, N.G., Samadi, D.S., Gendron, K. & Handler, S.D. (2004). Sialorrhea: a management challenge. American Family Physician, 69 (11), 2628-2634.
- Hornig, S., and Grady, C. (2003). Misunderstandings in Clinical Research: Distinguishing Therapeutic Misconception, Therapeutic Misestimation, & Therapeutic Optimism. IRB: Ethics & Human Research, 25 (1), 11-16.
- Houlihan, C.M., O'Donnell, M., Conaway, M. & Stevenson, R.D. (2004). Bodily pain and health-related quality of life in children with cerebral palsy. Developmental Medicine and Child Neurology, 46, 305-310.
- Howell, D.C. (1992). Statistical Methods for Psychology. Belmont, California: Duxbury Press.
- Howle, J.M. (2002). Neuro-developmental Treatment Approach: Theoretical Foundations and Principles of Clinical Practice. Laguna Beach, California: Neurodevelopmental Treatment Association.
- Huck, S.W. (2004). Reading Statistics and Research. (4th ed.) New York: Harper & Row.

- Jankovic, J. & Brin, M.F. (2002). Botulinum Toxin: Historical Perspective and Potential New Indications. Ch. 8. In Simpson, D.M. & Mayer, N.H. (Eds.). Spasticity: Etiology, Evaluation, Management and the Role of Botulinum Toxin. WE MOVE. Worldwide Education and Awareness for Movement Disorders.
- Jankovic, J. (2004). Botulinum toxin in clinical practice. Journal of Neurology Neurosurgery and Psychiatry, 75, 951-957.
- Jansen, L.A. (2006). The Problem with Optimism in Clinical Trials. IRB: Ethics & Human Research, 28 (4), 13-19.
- Jelsma, J. & Ferguson, G. (2004). The determinants of self-reported health-related quality of life in a culturally and socially diverse South African community. Bulletin of the World Health Organization, 82 (3), 206-212.
- Johnson, H. & Scott, A. (1993). A Practical Approach to Saliva Control. Austin: Communication Skill Builders.
- Jongerius, P.H., Rotteveel, J.J., van den Hoogen, F.J.A., Joosten, F., van Hulst, K., & Gabreëls, F.J. (2001). Botulinum toxin A: a new option for treatment of drooling in children with cerebral palsy. Presentation of a case series. European Journal of Pediatrics, 160, 509-512.
- Jongerius, P.H., Rotteveel, J.J., van Limbeek, J., Gabreëls, F.J., van Hulst, K. & van den Hoogen, F.J.A., (2004). Botulinum toxin effect on salivary flow rate in children with cerebral palsy. Neurology, 63, 1371-1375.
- Jongerius, P.H., van den Hoogen, F.J.A., van Limbeek, J., Gabreëls, F.J., van Hulst, K. & Rotteveel, J.J. (2004). Effect of Botulinum toxin in the treatment of drooling: A controlled clinical trial. Pediatrics, 114 (3), 620-627.

- Jongerius, P.H., van Hulst, K., van den Hoogen, F.J.A. & Rotteveel, J.J. (2005). The treatment of posterior drooling by botulinum toxin in a child with cerebral palsy. Journal of Pediatric Gastroenterology and Nutrition, *41*, 351-353.
- Kathard, H., Naude, E., Pillay, M. & Ross, E. (2007). Improving the relevance of speech-language pathology & audiology research and practice. The South African Journal of Communication Disorders, *54*, 5-7.
- Kim, H., Lee, Y., Weiner, D., Kaye, R., Cahill, M. & Yudkoff, M. (2006). Botulinum toxin type A injections to salivary glands: combination with single event multilevel chemoneurolysis in 2 children with severe spastic quadriplegic cerebral palsy. Archives of Physical Medical Rehabilitation, *87*, 141-144.
- King, M.L. (1963). I have a dream speech. Delivered 28 August 1963 at the Lincoln Memorial, Washington D.C. USA.
- King, S., Schwellnus, H., Russell, D., Shapiro, L. & Aboelele, O. (2005). Assessing quality of life of children and youth with disabilities: a review of available measures. Keeping Current. 01-2006. *CanChild* Centre for Childhood Disability Research. Retrieved 28 March 2007 from <http://www.canchild.ca/Default.aspx?tabid=1139>
- Koeda, T., Takeshita, K. & Kisa, T. (1995). Bilateral opercular syndrome: an unusual complication of perinatal difficulties. Brain & Development, *17*, 193-195.
- Lal, D. & Hotelling, A.J. (2006). Drooling. Current Opinion in Otolaryngology & Head and Neck Surgery, *14*, 381-386.

- Lespargot, A., Langevin, M.F., Muller, S. & Guillemont, S. (1993). Swallowing disturbances associated with drooling in cerebral palsied children. Developmental Medicine and Child Neurology, 35, 298-304.
- Levin, K. (2006). 'I am what I am because of who we all are': International perspectives on rehabilitation: South Africa. Pediatric Rehabilitation, 9 (3), 285-292.
- Lim, M., Mace, A., Reza Nouraei, S.A., & Sandhu, G. (2006). Botulinum toxin in the management of sialorrhoea: a systematic review. Clinical otolaryngology, 31, 267-272.
- Limbrock, G.J., Hayer, H. & Scheying, H. (1990). Drooling, chewing and swallowing dysfunctions in children with cerebral palsy: treatment according to Castillo-Morales. Journal of Dentition in Childhood, 57, 445-451.
- Lindstrom, B. & Eriksson, B. (1993). Quality of life among children in the Nordic countries. Quality of Life Research, 2, 23-32.
- Lipp, A., Trottenberg, T., Schink, T., Kupsch, A. & Arnold, G. (2003). A randomized trial of botulinum toxin A for treatment of drooling. Neurology, 61(9), 1279-1281.
- Liptak, G.S., O'Donnell, M., Conaway, M., Chumlea, W.C., Worley, G., Henderson, R.C., Fung, E., Stallings, V.A., Samson-Fang, L., Calvert, R., Rosenbaum, P. & Stevenson, R.D. (2001). Health status of children with moderate to severe cerebral palsy. Developmental Medicine and Child Neurology, 43, 364-370.
- Livingston, M.H., Rosenbaum, P., Russell, D.J. and Palisano, R.J. (2007). Quality of life among adolescents with cerebral palsy: what does the literature tell us? Developmental Medicine and Child Neurology, 49, 225-231.

- Llewellyn, G. (1996). Qualitative research. In Stein, F & Cutler, S.K. (Eds.) Clinical Research in Allied Health and Special Education. (3rd ed). San Diego: Singular.
- Lowe, K., Novak, I., & Cusick, A. (2007). Repeat injection of botulinum toxin A is safe and effective for upper limb movement in children with cerebral palsy. Developmental Medicine and Child Neurology, 49, 823-829.
- Mackie, P.C., Jessen, E.C. & Jarvis, S.N. (1998). The lifestyle assessment questionnaire: an instrument to measure the impact of disability on the lives of children with cerebral palsy and their families. Child: Care, Health and Development, 24 (6), 473-486.
- Majnemer, A., Shevell, M., Rosenbaum, P., Law, M. & Poulin, C. (2007). Determinants of life quality in school-age children with cerebral palsy. The Journal of Pediatrics, 151, 470-475.
- Makiwane, M. & Kwizera, S.A. (2006). An investigation of quality of life of the elderly in South Africa, with specific reference to Mpumalanga Province. Applied Research in Quality of Life, 1, 297-313.
- Mancini, F., Zangaglia, R., Cristina, S., Sommaruga, M.G., Martignoni, E., Nappi, G. & Pacchetti, C. (2003). Double-blind, placebo-controlled study to evaluate the efficacy and safety of botulinum toxin type A in the treatment of drooling in Parkinsonism. Movement Disorders, 18, 685-688.
- Markham, C. & Dean, T. (2006). Parents' and professionals' perceptions of quality of life in children with speech and language difficulty. International Journal of Language and Communication Disorders, 41, 189-212.

- Mathur, N.N., Vaughn, T.L. & Brown, K.R. (2006). Drooling. Retrieved from <http://www.emedicine.com/ent/topic629.htm> on 03/01/2007.
- Meningaud, J.P., Pitak-Arnnop, P., Chikhani, L. & Bertrand, J.C. (2006). Drooling of saliva: a review of the etiology and management options. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology, 101, 48-57.
- Michelsen, S.I., Uldall, P., Kejs, A.M.T., & Madsen, M. (2005). Education and employment prospects in cerebral palsy. Developmental Medicine and Child Neurology, 47, 511-517.
- Michelson, L., Mannarino, A., Marchione, K., Kazdin, A.E., & Costello, A. (1985). Expectancy bias in behavioral observations of therapeutic outcome: an experimental analysis of treatment and halo effects. Behaviour, Research and Therapy, 23 (4), 407-414.
- Mihaylov, S.I., Jarvis, S.N., Colver, A.F. & Beresford, B. (2004). Identification and description of environmental factors that influence participation of children with cerebral palsy. Developmental Medicine and Child Neurology, 46, 299-304.
- Møller, V. & Dickow, H. (2002). The role of quality of life surveys in managing change in democratic transitions: the South African case. Social Indicators Research, 58, 267-292.
- Morris, S.E. & Klein, M.D. (2000). Pre-Feeding Skills. A Comprehensive Resource for Mealtime Development. 2nd Ed. USA: Therapy Skill Builders.
- Mutch, L.W., Alberman, E., Hagberg, B., Kodama, K., & Perat, M.V. (1992). Cerebral palsy epidemiology: where are we now and where are we going? Developmental Medicine and Child Neurology, 34, 547-555.

- Nadeau, L. & Tessier, R. (2006). Social adjustment of children with cerebral palsy in mainstream classes: peer perception. Developmental Medicine and Child Neurology, 48, 331-336.
- Nakajima, M. (2004). Progressive anterior operculum syndrome i correlation to apraxia of speech with respect to semiology and etiology. Japanese Journal of Logopedics and Phoniatics, (Abstract), 45, 309-314.
- Nobrega, A.C., Rodrigues, B., Torres, A.C., Enzo, A. & Melo, A. (2007). Does botulinum toxin decrease frequency and severity of sialorrhea in Parkinson's disease? Journal of Neurological Sciences, 253 (1-2), 85-87.
- Nunn, J.H. (2000). Drooling: review of the literature and proposals for management. Journal of Rehabilitation, 27, 735-743.
- Ondo, W.G., Hunter, C. & Moore, W. (2004). A double-blind placebo-controlled trial of botulinum toxin B for sialorrhea in Parkinson's disease. Neurology, 62, 37- 40.
- Operculum of the Brain: Retrieved from:
[http://en.wikipedia.org/wiki/Operculum_\(brain\)](http://en.wikipedia.org/wiki/Operculum_(brain)) on 23 June 2007.
- Pal, P.K., Calne, D.B., Calne, S. & Tsui, J.K.C. (2000). Botulinum toxin A as treatment for drooling saliva in PD. Neurology, 54, 244-247.
- Palisano, R., Rosenbaum, P., Walter, S., Russell, D., Wood, E. & Galuppi, B. (1997). Development and reliability of a system to classify gross motor function in children with cerebral palsy. Developmental Medicine and Child Neurology, 39, 214-223.
- Penn, C. (2007). "Don't give me the theory, just tell me what to do in therapy!" The slippery slope challenge for the South African professions of Speech-

Language Pathology and Audiology. The South African Journal of Communication Disorders, 54, 13-17.

Pivik, J., McComas, J. & Laflamme, M. (2002). Barriers and facilitators to inclusive education. Exceptional Children, 69, 97-109.

Porta, M., Gamba, M., Bertacchi, G. & Vaj, P. (2001). Treatment of sialorrhoea with ultrasound guided botulinum toxin type A injection in patients with neurological disorders. Journal of Neurology Neurosurgery and Psychiatry, 70, 538-540.

Pritchard, T.C. & Norgren, R. (2004). The Gustatory System. In: Paxinos, G. & Mai, J.K., editors. The Human Nervous System. 2nd Ed. San Diego: Elsevier Academic Press.

Proulx, M., de Courval, F.P., Wiseman, M.A. & Panisset, M. (2005). Salivary production in Parkinson's disease. Movement Disorder, 20, 204-207.

Rapp, D. (1980). Drool control: Long-term follow-up. Developmental Medicine and Child Neurology, 22, 448-453.

Reid, S.M., Johnstone, B.R., Westbury, C., Rawicki, B. & Reddiough, D.S. (2008). Randomized trial of botulinum toxin injections into the salivary glands to reduce drooling in children with neurological disorders. Developmental Medicine and Child Neurology, 50, 123-128.

Rosenbaum, P., Paneth, P., Leviton, A., Goldstein, M. & Bax, M. (2007). A report: the definition and classification of cerebral palsy April 2006. Developmental Medicine and Child Neurology, 49, 1- 43.

Rosenfeld-Johnson, S. (2002). Drooling Remediation Program For Children and Adults. Tucson: Talk Tools Innovative Therapists International.

- Rotteveel, L.J.C., Jongerius, P.H., van Limbeek, J. & van den Hoogen, F.J.A. (2004). Salivation in healthy school children. International Journal of Pediatric Otorhinolaryngology, 68 (6), 767.
- Saliva Control in Children. The Royal Children's Hospital, Melbourne, Australia. Retrieved from http://www.rch.org.au/plastic/units.cfm?doc_id=4833 on 24 June 2007.
- Saloojee, G., Phohole, M., Saloojee, H. & IJsselmuiden, C. (2006). Unmet health, welfare and educational needs of disabled children in an impoverished South African peri-urban township. Child: Care, Health and Development, 33, 230-235.
- Savarese, R., Diamond, M., Elovic E. & Millis, S.R. (2004). Intraparotid injection of botulinum toxin A as a treatment to control sialorrhoea in children with cerebral palsy. American Journal of Physical Medicine and Rehabilitation, 83 (4), 304-311.
- Schiavetti, N. & Metz, D.E. (2006). Evaluating Research in Communicative Disorders. Boston: Pearson Education, Inc.
- Schneider, J.W., Gurucharri, L.M., Gutierrez, A.L. & Gaebler-Spira, D.J. (2001). Health-related quality of life and functional outcome measures for children with cerebral palsy. Developmental Medicine and Child Neurology, 43, 601-608.
- Schneider, M. & Hartley, S. (2006). International Classification of Functioning, Disability and Health (ICF), and CBR. In S. Hartley (Ed). CBR As Part of Community Development. A Poverty Reduction Strategy (pp. 96-115). London: University College London.
- Schneider, M. & Saloojee, G. (2007). Monitoring childhood disability. In A. Dawes, R. Bray & A. Van Der Merwe (Eds). Monitoring Child Well-Being:

A South African Rights-Based Approach (pp. 191-212). Cape Town: HSRC Press.

- Scott, A.B. (1980). Botulinum toxin injection into extraocular muscles as an alternative to strabismus surgery. Journal of Pediatric Ophthalmologic Strabismus, 17, 21-25.
- Senner, J.E., Logemann, J., Zecker, S. & Gaebler-Spira, D. (2004). Drooling, saliva production, and swallowing in cerebral palsy. Developmental Medicine and Child Neurology, 46, 801-806.
- Shaari, C.M., Bei-Lian, W.U., Biller, H.F., Chuang, S-K, & Sanders, I. (1998). Botulinum toxin decreases the salivation from canine submandibular glands. Otolaryngology Head Neck Surgery, 118, 452-457.
- Shelly, A., Davis, E., Waters, E., Mackinnon, A., Reddiough, D., Boyd, R., Reid, S. & Graham, H.K. (2008). The relationship between quality of life and functioning for children with cerebral palsy. Developmental Medicine and Child Neurology, 50, 199-203.
- Shields, N., Murdock, A., Loy, Y., Dodd, K.J. & Taylor, N.F. (2006). A systematic review of the self-concept of children with cerebral palsy compared with children without disability. Developmental Medicine and Child Neurology, 48, 151-157.
- Siegel, L.K. & Klingbeil, M.A. (1991). Control of drooling with transdermal scopolamine in a child with cerebral palsy. Developmental Medicine and Child Neurology, 33, 1013-1014.
- Sochaniwskyj, A.E. (1982). Drool quantification: Non-invasive technique. Archives of Physical Medicine and Rehabilitation, 63, 605-607.
- Statistics South Africa. Retrived from: www.statssa.gov.za/, on 3 April 2007.

- Stuchell, R.N. & Mandel, I.D. (1988). Salivary gland dysfunction and swallowing disorders. Otolaryngology Clinic of North America, 21, 649-661.
- Sullivan, P.B., Lambert, B., Rose, M., Ford-Adams, M., Johnson, A. & Griffiths, P. (2000). Prevalence and severity of feeding and nutritional problems in children with neurological impairment: Oxford Feeding Study. Developmental Medicine and Child Neurology, 42, 674-680.
- Suskind, D.L. & Tilton, A. (2002). Clinical study of botulinum- A toxin in the treatment of sialorrhea in children with cerebral palsy. Laryngoscope, 112 (1), 73-81.
- Swanepoel, D. (2007). Research-driven: A scientific profession accountable within contextual realities. The South African Journal of Communication Disorders, 54, 10-11.
- Tahmassebi, J.F. & Curzon, M.E.J. (2003). Prevalence of drooling in children with cerebral palsy attending special schools. Developmental Medicine and Child Neurology, 45, 613-617.
- Tan, E.-K. (2006). Botulinum toxin treatment of sialorrhea: comparing different therapeutic preparations. European Journal of Neurology, 3 (1), 60-64.
- Tellis, W. (1997). Application of a case study methodology. The Qualitative Report, 3 (3), On-line serial. Retrieved from <http://www.nova.edu/ssss/QR/QR3-2/tellis1.html> on 17 June 2007.
- Theodoros, D., Scudamore, S., Baldock, P., Coman, S. & Hancock, K. (2007). The effects of Botox and voice therapy in the management of severe muscle tension dysphonia: a case study. Journal of Medical Speech & Language Pathology, 15, 293-305.

- Thomas-Stonell, N & Greenberg, J. (1988). Three treatment approaches and clinical factors in the reduction of drooling. Dysphagia, 3, 73-78.
- Tuchman, D.N. & Walter, R.S. (1994). Disorders of Feeding and Swallowing in Infants and Children: Pathophysiology, Diagnosis and Treatment. San Diego: Singular.
- Van der Burg, J., Jongerius, P., van Limbeek, J., van Hulst, K. & Rotteveel, J. (2006, a). Drooling in children with cerebral palsy: a qualitative method to evaluate parental perceptions of its impact on daily life, social interaction, and self-esteem. International Journal of Rehabilitation Research, 29, 179-182.
- Van der Burg, J., Jongerius, P., van Limbeek, J., van Hulst, K. & Rotteveel, J. (2006, b). Social interaction and self-esteem of children with cerebral palsy after treatment for severe drooling. European Journal of Pediatrics, 165, 37-41.
- Van der Poel, J.C., Haenggeli, C.A., & Overweg-Plandsoen, W.C.G. (1995). Operculum syndrome: unusual feature of herpes simplex encephalitis. Pediatric Neurology, 12 (3), 246-249.
- Vargus-Adams, J. (2006). Longitudinal use of the Child Health Questionnaire in childhood cerebral palsy. Developmental Medicine and Child Neurology, 48, 343-347.
- Varni, J.W., Burwinkle, T.M., Berrin, S.J., Sherman, S.A., Artavia, K., Malcarne, V.L. & Chambers, H.G. (2006). The PedsQL in pediatric cerebral palsy: reliability, validity, and sensitivity of the Generic Core Scales and Cerebral Palsy Module. Developmental Medicine and Child Neurology, 48, 442-449.
- Varni, J.W., Burwinkle, T.M., Sherman, S.A., Hanna, K., Berrin, S.J., Malcarne, V.L. & Chambers, H.G. (2005). Health-related quality of life of children

and adolescents with cerebral palsy: hearing the voices of the children.

Developmental Medicine and Child Neurology, 47, 592-597.

Walker, J., Winkelstein, M., Land, C., Lewis-Boyer, L., Quartey, R., Pham, L. & Butz, A. (2008). Factors that influence quality of life in rural children with asthma and their parents. Journal of Pediatric Health Care, Article in Press, 1-8.

Ward, A.B., Molenaers, G., Colosimo, C. & Berardelli, A. (2006). Clinical value of botulinum toxin in neurological indications. European Journal of Neurology, 13 (4), 20-26.

Waters, E., Davis, E., Boyd, R., Reddihough, D., Mackinnon, A., Graham, H.K., Lo, S.K., Wolfe, R., Stevenson, R., Bjornson, K., Blair, E. & Ravens-Sieberer, U. (2006). Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL-Child) Manual. Melbourne: Deakin University.

Waters, E., Maher, E., Salmon, L., Reddihough, D. & Boyd, R. (2005). Development of a condition-specific measure of quality of life for children with cerebral palsy: empirical thematic data reported by parents and children. Child: Care, Health and Development, 31, 127-135.

Watson, D., Abbott, D. & Townsley, R. (2006). Listen to me, too! Lessons from involving children with complex healthcare needs in research about multi-agency services. Child: Care, Health and Development, 33, 90-95.

Watson, S.M.R. & Keith, K.D. (2002). Comparing the quality of life of school-age children with and without disabilities. Mental Retardation, 40, 304-312.

Watts, C., Nye, C. & Whurr, R. (2006). Botulinum toxin for treating spasmodic dysphonia (laryngeal dystonia): a systematic Cochrane review. Clinical Rehabilitation, 20, 112-122.

- Weiss-Lambrou, R., Tetreault, S. & Dudley, J. (1989). The relationship between oral sensation and drooling in persons with cerebral palsy. American Journal of Occupational Therapy, 43, 155-161.
- Weller, M. (1993). Anterior opercular cortex lesions cause dissociated lower cranial nerve palsies and anarthria but no aphasia: Foix-Chavany-Marie syndrome and "automatic voluntary dissociation" revisited. Journal of Neurology, 240 (4), 199-208.
- Westaway, M.S. (2006). A longitudinal investigation of satisfaction with personal and environmental quality of life in an informal South African housing settlement, Doornkop, Soweto. Habitat International, 30, 175-189.
- Westaway, M.S., Olorunju, S.A.S & Rai, L-C. J. (2007). Which personal quality of life domains affect the happiness of older South Africans? Quality of Life Research, 16, 1425-1438.
- White Paper on an Integrated National Disability Strategy. (1997). Office of the Deputy President. November 1997.
- White Paper 6. (2001). Department of Education: Special education: Building an inclusive education and training system. Pretoria, South Africa: Government Printer.
- Wilkie, T.F. (1967). The problem of drooling in cerebral palsy: a surgical approach. Canadian Journal of Surgery, 10, 60-67.
- Wilkie, T.F. & Brody, G.S. (1977). The surgical treatment of drooling: a ten year review. Plastic, Reconstructive Surgery, 59, 791-798.
- Winstock, A. (2005). Eating and Drinking Difficulties in Children: A Guide for Practitioners. Oxon: Speechmark.

- Wong, V., Sun, J.G. & Wong, W. (2001). Traditional Chinese medicine (tongue acupuncture) in children with drooling problems. Pediatric Neurology, 25, 47-54.
- Workinger, M.S. (2005). Cerebral Palsy Resource Guide for Speech-Language Pathologists. New York: Thomson Delmar Learning.
- World Health Organization (1993). Measuring Quality of Life: the Development of the World Health Organization Quality of Life Instrument (WHOQOL). Division of Mental Health, World Health Organization, Geneva, Switzerland. Retrieved from <http://www.who.int/mediacentre/factsheets/fs220/en/print.html> on 1 August 2007
- World Health Organization (2001). International Classification of Functioning, Disability and Health. Geneva. World Health Organization. Retrieved from <http://www.who.int/classifications/icf/en/> 1 August 2007
- World Health Organization. World Health Report 2005. Make every mother and child count. Retrieved from: www.who.int.whr/2005/en/index.html, on 3 April 2007.
- Yin, R. (1993). Applications of Case Study Research. Newbury Park, California: Sage Publishing.
- Zilles, K. (2004). Architecture of the Human Cerebral Cortex. In: G. Paxinos & J.K. Maieditors, (Eds). The Human Nervous System. 2nd Ed. San Diego: Elsevier Academic Press.